Egyptian

Herbal Monograph

2023

Egyptian Herbal Monograph

Egyptian Drug Authority (EDA)

2023

Contents

Foreword

With the expansion in the use of traditional medicine worldwide, safety and efficacy as well as quality control of herbal medicines are receiving extra ordinary importance and popularity and have become important concerns for both health authorities and the public.

The challenge now is to ensure that herbal medicine is used properly and to determine how research and evaluation of herbal medicine should be carried out. Standards, technical guidance and information on these issues are increasingly requested by authority and manufacturers. Recently there is an emerging trend in research to support the biological activities of the traditional medicinal plants.

There is no doubt that establishing a document whose purpose is to provide a scientific summary of all data available on the safety and efficacy of the herbal substances/preparations intended for medicinal use is a must. The Egyptian Herbal Monograph will be considered as the first step to achieve the purpose of promotion of the use of herbal medicines, to serve as a model for the development of national formularies and to improve the quality and value of research in traditional herbal medicine.

Egyptian Drug Authority
(EDA)

2023

Acknowledgment

Under the patronage of **Prof. Dr. Tamer Mohamed Essam** - Chairman of Egyptian Drug Authority (EDA), **Prof. Dr. Ayman Saad Nasr El-Din El-Khatib -** *Vice* president of EDA and **Prof. Dr. Hanan Amin Rizk** - Head of Central Administration of Pharmaceutical Products, EDA is honored to launch Egyptian Herbal monograph. EDA expresses its sincere appreciation to the commitment of the Committee team:

Members of the Specialized Scientific Committee of Herbal Medicines:

Prof. Dr. Mervat Ahmed Fouad	*Consultant of Pharmacognosy, Medicinal Plants and Special Foods- National Nutrition Institute (NNI). Head of Codex Committee on Spices and Culinary Herbs- Egyptian Organization for Standardization and Quality. Member of the Technical Harmonization Committee (TCH 82) in African Organization for Standardization (ARSO). Former member of the Evaluation Committee of Egyptian Guidelines for Registration of Herbal Medicines.*
Prof. Dr. Meselhy Ragab Meselhy	*Member of the Board of Directors of the Egyptian Drug Authority. Member of the Committee in Charge of Revising the Egyptian Pharmacopeia. Professor of Pharmacognosy and Medicinal plants, Faculty of Pharmacy– Cairo University. Member of National Drug Committee. Former Cultural Counselor and Director of the Cultural Bureau, Embassy of Egypt in Tokyo. Former member of the Evaluation Committee of Egyptian Guidelines for Registration of Herbal Medicines.*
Prof. Dr. Mona Hafez Hetta	*Dean of Faculty of Pharmacy- Nahda University (Beni-Suef). Former Dean- Faculty of Pharmacy- Fayoum University. Director of Natural Product Research Lab.- Faculty of Pharmacy- Fayoum University. Former Dean, Head of Pharmacognosy Department and Clinical Program Coordinator- Faculty of Pharmacy- Beni-Suef University. Former Vice-Dean of Post-Graduates– Faculty of Pharmacy- Beni-Suef University.*
Prof. Dr. Nahla Sayed Abdel-Azim	*Chemistry of Medicinal Plants Department- National Research Centre (NRC)· Former Head of Department. Co-Principal Investigator of the Project "Egyptian Encyclopedia of wild Medicinal Plants" between the NRC, Academy of Scientific Research & Technology. Ex-member of "National Surveys of Wild Medicinal Plants" between NRC and the Egyptian Environmental Affairs Agency (EEAA), United Nations Development Programme (UNDP) and Global Environmental Facility (GEF).*

EDA members:

Prof. Dr. Hanan Amin Rizk	*Head of Central Administration of Pharmaceutical Products- EDA. Professor of Pharmacology and Toxicology. Former Head of General Directorate of Registration, Central Administration of Pharmaceutical Affairs (CAPA). Former Member of the Evaluation Committee of Egyptian Guidelines for Registration of Herbal Medicines.*
Dr. Nora El-Sayed Amin	*General Co-ordinator for Training Affairs- Central Administration of Pharmaceutical Products- EDA. Former Head of Dietary Supplements & Herbal Medicines Registration Department- EDA. Former member of the Evaluation Committee of Egyptian Guidelines for Registration of Herbal Medicines.*
Dr. Nessma El-Sayed Mohamed	*General Manager of General Administration for Registration of Herbal Medicines- EDA. Rapporteur of Specialized Scientific Committee of Herbal Medicines. Former Head of Herbal Medicines Receiving Section. Former Rapporteur of the Evaluation Committee of Egyptian Guidelines for Registration of Herbal Medicines.*

EDA also acknowledges its deep gratitude to the Late Professors Loutfy Boulos and Kamal El Batanoni, remarkable Egyptian botanists by all measures of excellence, for their contributions and leading role in the field of Biodiversity and Flora of Egypt.

In recognition of the beneficial effects of these projects on enabling the completion of this monograph, EDA extends its sincere thanks to the contributors from NRC, EEAA, UNDP, and GEF at the project "National Surveys of Wild Medicinal Plants" as well as the experts from NRC and Academy of Scientific Research and Technology (ASRT) for establishing "Egyptian Encyclopedia of Wild Medicinal Plants".

EDA also use this opportunity to thank each and every member of the "General Committee of the Egyptian Pharmacopiea", the scientists and specialists in all different relevant fields who contributed in preparing and editing the different editions of the Egyptian Pharmacopiea.

Introduction

The habitat diversity in Egypt, as a result of geographical, physiographic, edaphic and climatic conditions, is reflected on the plant life. The remedies used by ancient Egyptian physicians came mostly from nature, more especially medicinal herbs. Most of medicinal modalities originated from ancient Egyptian; one of them was herbal medicine. The famous Ebers Papyrus, written in 1550 B.C., gives 842 prescriptions that are made of 328 different ingredients. Among them are plant species growing in Egypt or other North African countries, e.g. *Artemisia absinthium*, *Acacia spp. and Balanites aegyptiaca.* Nowadays; Medicinal plants are considered as an important health and economic component of the flora in developed as well as developing countries. Increasing world-wide interest in herbal remedies, expanding reliance of local health care of traditional remedies and a renewed interest in the development of pharmaceuticals from plant sources have greatly increased trade in medicinal plant materials but it is hindered by lack of technical and economic data. Important populations of medicinal plants are found not only in the regions and ecosystems with high biological diversity, but also in less diverse flora and in floristic communities that are not a common focus of conservation efforts. For instance, in the arid and semi-arid zones of the Middle East, the flora may comprise very important genetic resources of crop and medicinal plants. Conservation of threatened and endangered medicinal plant species in the wild is indispensable. Egyptian Herbal Monograph is crucial because it represents our nation's best chance at conserving our medicinal plants through the wise use of our unique biodiversity resources in the pharmaceutical industry. In addition to the conservation of such natural resources, the wild medicinal plants that grow in Egyptian phytogeographical regions can be cultivated in new reclaimed lands with the least harmful ecological impacts. Since 2020, EDA has developed three volumes of the Egyptian Herbal Monograph based on the format of the European, Canadian and WHO monographs. The moment has come to compile these volumes into a single monograph that can serve as a reference for the necessary scientific files needed for the registration process.

Purpose and content of the monograph

The purpose of the monograph is to:

- Provides updated scientific information on the safety, efficacy and quality of the Egyptian medicinal plants.
- Facilitates their appropriate use.
- Facilitates information exchange and registration procedures.

This monograph was put together by a working group comprised of members of the Specialized Scientific Committee of Herbal Medicines and the Egyptian Drug Authority (EDA). The Egyptian Monograph is a compilation of the medicinal plants used in Egypt that offers comprehensive data including botanical, chemical and pharmacological information that is properly organized.

The Egyptian Monograph aims to encourage the appropriate use of herbal remedies with the highest level of safety and efficacy based on previous and current research. Each monograph follows a standard format with information and followed by a reference list. Each monograph contains all the available information and scientific results on the selected species include the following: names, synonyms, parts used for medicinal purposes, major chemical constituents, medicinal uses (indications), herbal preparations correlated to the medicinal use, posology and method of administration correlated to medicinal use, contraindications, special warnings and precautions for use, interactions with other medicinal products, other forms of interaction, effects on fertility, pregnancy, lactation, ability to drive, using machines, undesirable effects, overdose, relevant biological activities and if any additional information. This monograph is expected to go through another revision soon in response to advances in the field of herbal medicine research.

Egyptian Herbal Monograph

Volume 1

Traditional wild medicinal plants

Egyptian Drug Authority (EDA)

2023

Preface

Drugs made from wild plants are widely traded everywhere. However, its socioeconomic implications are not given the proper consideration. From the conservation point of view, many of our traditional medicinal plants are now extinct. Some are endangered and some are totally threatened. Consequently, there is a great need for cultivation of these plants.

Benefits of the cultivation of wild medicinal plants include:

1- **Economic improvement**
   - Filling a gap in the domestic needs of folk medicine and pharmaceutical industries.
   - Potential products for exports, especially Pharmacopieal drug plants.
   - Creation of small industries in cutting, drying, extraction, packing, *etc.*
   - Providing cash income for settlers in newly reclaimed land and desert areas.

2- **Improvement of the wasteland economy**

3- **Environmental protection**

Dune stabilization, wildlife habitat and biodiversity conservation.

4- **Sustainable development**
   - Cultivation of wild plants doesn't introduce new weeds or pests to the ecosystem.
   - Wild plants do not need pesticides use under their natural habitat conditions.
   - Minimal ecological consequences for the agro-ecosystem
   - Minimal degradation, salinization, soil erosion, water logging, *etc.*

5- **Conservation of water**
   - Desert plants have low water consumption.
   - Use of seepage water along the margins of the farms and irrigation canals.
   - The unavailability tolerance of exogenous water supply for reasonable periods.

The safety and quality of Phytopharmaceuticals must be guaranteed, even if efficacy is already recognized and traditionally accepted.

This volume includes 15 traditionally used Egyptian wild medicinal plants, and it serves as one of the first stages in making use of these plants in the pharmaceutical sector.

Egyptian Herbal Monograph

Traditional wild medicinal plants

Acacia nilotica L. Delile السنط / القرض

1. Names & Synonyms (1-3)

***Acacia nilotica* L. Delile.**
Family: Fabaceae (Leguminosae).
Syn. *Mimosa nilotica* L.
Arabic: *Sant* سنط - *Aschawkah Al misriyah* الشوكة المصرية - Fruit: Qarad الثمرة: قرض
English: Egyptian Acacia, Egyptian Thorn.

Two subspecies occur in Egypt (2):
a. subsp. ***nilotica***
Pod glabrous.
b. subsp. ***tomentosa*** (Benth.)
Syns. *Mimosa arabica* Lam.
Acacia arabica (Lam.) Willd.
Pod whitish-grey tomentose.

2. Geographical distribution

Confined to the Nile region (south of Aswan) (3), The Nile Delta, Nile Valley, Oases, Sinai and Western Desert (2).

3. Parts used for medicinal purposes

The fruits (pods), the bark, the leaves (2) and the gum which *A. nilotica* tree exudes (3).

4. Major chemical constituents

The fruit: High percentage of phenolics; m-digallic acid, gallic acid, its methyl and ethyl esters, protocatechuic and ellagic acids, leucocyanidin, m-digallic dimer 3,4,5,7-tetrahydroxy flavan-3-ol, oligomer 3,4,7-trihydroxy flavan 3,4-diol and 3,4,5,7-tetrahydroxy flavan-3-ol and (-) epicatechol. Others: alkaloids, mucilage and saponins (4, 5).

The bark: Phenolics; gallic acid, protocatechuic acid, condensed tannins and phlobatannin, (+) - catechin, (-) epigallocatechin-7-gallate, and (-) epigallocatechin-5, 7-digallate (2).

The leaves: Phenolics; tannins (6), apigenin, 6-8-bis-D-glucoside, rutin, Quercetin 3-glucoside, quercetin 3-sophoroside (7), catechin, catechin 7-*O*-gallate, catechin 3'-*O*-gallate, catechin 4'-gallate, catechin 7,3'-di-*O*-gallate and catechin 7,4'-di-*O*-gallate (8).

Gum: Galactoaraban; on hydrolysis gives L-arabinose, D-galactose, L-rhamnose, D-glucuronic acid and 4-O-methyl- D-glucuronic acid (9).

5. Traditional medicinal uses (3)

Fruits: For diarrhea, dysentery, diabetes. It is also given for hemorrhage and as sedative in labour, for sore gum and loose teeth.

Bark: For cough, bronchitis, diarrhea, dysentery, burning sensation, piles. Decoction used as a nerve stimulant and aid for digestion.

Leaves: For bronchitis, piles, urethral discharges and as liver tonic. Antipyretic, cures leucoderma, gonorrhea and chewed for nausea.

Gum: For diarrhea, urinary/vaginal and uterine discharges, sore throat, diabetes mellitus, healing of fractures and as a liver tonic.

***Acacia nilotica* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (10)

a) Orally:

1. Infusion:

Pour freshly boiled water on 2 teaspoonful of the herbal substance in a cup, cover the cup with the lid and infuse for 5 minutes. Drink it sweetened if desired.

2. Decoction:

Pour cold water on 2 teaspoonful of the herbal substance and boil, Simmer for 10 minutes. Pour into a cup and drink it sweetened if desired.

b) Externally:

Place some herbal substance in a warm water bath.

7. Posology and method of administration correlated to medicinal use

a) Oral use:

1. Infusion: Average daily dose: 3 cups/day.
2. Decoction: Average daily dose: 3 cups/day (10).

b) External use:
Sit and relax in the water basin for half an hour, as often as required. Average daily dose: 1-2 times/day (10).

Duration of use:
Up to 30 grams daily has been used safely for 6 weeks (11).

If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or pharmacist should be consulted.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

10. Interactions with other medicinal products and other forms of interaction

Acacia gum can prevent the body from absorbing the antibiotic amoxicillin. To prevent this interaction, take *Acacia* gum at least four hours before or after taking amoxicillin (11).

11. Fertility, pregnancy and lactation

-Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

-No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- It may cause minor adverse effects, including gas, bloating, nausea, and loose stools (11).

14. Overdose

No case of overdose has been reported.

15. Relevant biological activities

- Chloroform extract of *Acacia* bark significantly decreased blood glucose of alloxan-diabetic rats and reversed values of TC, LDL-C, HDL-C and TGs (12).

- The aqueous extracts of *A. nilotica* leaves reduced pain, inflammation and fever mostly at dose of 150 mg/kg body weight in Albino mice (13).

16. Additional information:

-

17. Date of compilation/last revision

28/07/2022

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Omer, E. A., Shams, K. A. and Abd El-Azim, N. S. (2017). *Acacia nilotica* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **1**, 9-31. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Kamalpreet, S., Avninder, M., Bharpur, S. and Gagan, S. (2014). Studies on mucilage from *Acacia nilotica* fruits as suspending agent and binding agent. *Int. J. Pharm. Tech. Res.*, **6**(6), 1762-1767.
5	Rana, D. (2018). A review of ethnomedicine, phytochemical and pharmacological properties of *Acacia nilotica* (Babool/Kikkar). *IJBPAS*, **7**(5), 856-863. DOI: https://doi.org/10.31032/IJBPAS/2018/7.5.4443.
6	Abdulrazak, S. A., Ichinohe, T., Fujihara, T. and Hveplund, T. (2000). Nutritive evaluation of browse species from Kenya: *In sacco* degradability and intestinal digestibility. *Asian-Aus. J. Anim. Sci.,* **13**(Suppl. A), 477.
7	Thieme, H. and Khogali, A. (1975). The occurrence of flavonoids and tannins in the leaves of some African *Acacia* species. *Pharmazie*, **30**(11), 736-743.
8	El-Toumy, S. A., Farag, A. R. H., Ellithey, M. E. M. and Korien, K. M. (2011). Effect of plant derived–phenolic extracts on antioxidant enzyme activity and mycosal damage caused by indomethacin in rats. *J. Pharm. Res.*, **4**(1), 189-192.
9	Malviya, S., Rawat, S., Kharia, A. and Verma, M. (2011). Medicinal attributes of *Acacia nilotica* Linn. - A comprehensive review on ethnopharmacological claims. *Int. J. of Pharm. and Life Sci. (IJPLS)*, **2**(6), 830-837.
10	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
11	https://www.rxlist.com/acacia/supplements.htm
12	Wadood, A., Wadood, N. and Shah, S. A. (1989). Effects of *Acacia arabica* and *Caralluma edulis* on blood glucose levels of normal and alloxan diabetic rabbits. *J. Pak. Med. Assoc.*, **9**, 208–212.
13	Safari, V. Z., Kamau, J. K., Nthiga, P. M., Ngugi, M. P. and Orinda, G. (2016). Antipyretic, antiinflammatory and antinociceptive activities of aqueous bark extract of *Acacia nilotica* (L.) Delile in albino mice. *J. Pain Manage. Med.*, **2**, 113. doi:10.4172/jpmme.1000113.

Egyptian Herbal Monograph

Traditional wild medicinal plants

Achillea fragrantissima (Forssk.) القيصوم

1. Names & Synonyms (1-3)

***Achillea fragrantissima* (Forssk.)**
Family: Compositae (Asteraceae)
Syn.: *Santolina fragrantissima* Forssk.
Arabic: Gesoom جصوم (name used by the local community of Sinai Peninsula), Alegiaan الجيانَ و Baboonig بابونجَ
English: Lavender cotton

2. Geographical distribution

Oases of the Western Desert (Kharga), Mediterranean region, all the deserts of the country including that of Sinai, as well as the Red Sea coastal strip (3).

3. Parts used for medicinal purposes

The herbs and flower heads (3).

4. Major chemical constituents (3)

-Essential Oil: Caryophyllene oxide, camphor, bisabolene epoxide, sesquisabinene hydrate, 1-terpinen-4-ol viridiflorol, guaienol, limonene, menthol, azulene, thujone (4-9).

-Monoterpenes and Triterpenes: Two highly oxygenated santoline derivatives (irregular oxygenated monoterpenes) (10), chondrillasterol (11), traxasterol acetate and pseudo-taraxasterol acetate (12).

-Sesquiterpene Lactones: More than 10 compounds were isolated e.g. achillolide A, achillolide B, 1-oxoafraglaucolide and others (12, 13, 14).

-Flavonoids: Apigenin, apigenin 7-*O*-glucoside, luteolin 7-*O*-rhamnoside, 3'-methyl luteolin 7-*O*-glucoside, 7-*O*-rhamno-4'hydroxyflavone, and others (11, 12, 15).

Fatty Acids: Lauric, myristic, palmitic, stearic, linoleic, linolenic oleic and arachidic acids (12, 16).

Others: Bitter substance (keissosid) which yielded galactose and aglycone, tannins of the catechol type, 2-acetylmethyl-4-hydroxy-6-methyltetrahydropyran (12).

5. Traditional medicinal uses (17)

A. Gastrointestinal disturbances (anti-spasmodic, astringent, carminative, stomachic).
B. Respiratory diseases (expectorant, cough).
C. Anthelmintic.
D. For scorpion and snake bites.
E. Skin diseases (skin inflammations, wound healing, abscess, purulent sore and as insect repellent).
F. Antipyretic and in case of fever.

***A. fragrantissima* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal Preparations correlated to medicinal use

1. **Infusion** (17)

Pour freshly boiled water on 2 teaspoonful of the flowering herb in a cup; cover the cup with the lid, infuse for 5 minutes and drink it sweetened if desired.

2. **Decoction**

2.1. Add 2 teaspoonful of the flowering herb in a pot, pour cold water, boil and simmer for 10 minutes then pour into a cup and drink it sweetened if desired (17).

2.2. Prepared by boiling the ground leaves with water (17, 18).

3. **Oil** (17, 18).

7. Posology and method of administration correlated to medicinal use (17)

Preparation 1, 2.1
Indication A-D
Dosage: 3 cups/day.
Method of administration: Oral use (17).

Preparation 2.2, 3
Indication E, F
Apply the extract of the boiled leaves in water after cooling the extract.
Wash the body with the decoction.
Method of administration: Topical use (17,18).

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

- If the symptoms worsen during the use of medicinal product, a doctor or pharmacist should be consulted.

- Monitoring of blood glucose level should be done regularly when used for diabetics as *A. fragrantissima* has been used in traditional medicine for diabetes.

10. Interactions with other medicinal products and other forms of interactions

None reported.

11. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- Studies in animals have shown that the plant extract did not affect fertility (19) <<see section 15. Relevant biological activities >>.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- None known.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

14. Overdose

No case of overdose has been reported.

15. Relevant biological activities

- The safety and side effects of the different extracts (water, ethanolic and methanolic) of *A. fragrantissima* given acutely or on repeated doses (125 and 250 mg/kg) in rats, were studied. Acute and subchronic toxicity, as well as reproductive (fertility, embryotoxicity and teratogenecity, peri-and postnatal study) effects were recorded on treated and control rats. Daily administration of the plant extract revealed no significant changes on the body weight, heart rate,

and other physiological parameters. The plant extract induced a significant increase in total proteins and globulins in rats. It did not induce any abnormal liver and kidney functional changes as demonstrated by serum biochemical analysis in rats. Interestingly, the plant extract induced a significant decrease in alkaline phosphatase (ALP), urea and creatinine. Significant decrease in blood glucose level was detected in animals receiving 250 mg/kg of the extract. The plant extract did not affect fertility. Dosed males showed comparable data with the controls when dosed at 250 mg/kg b.wt. It did not cause any embryotoxic, teratogenic or any deleterious effects on the dosed females and their offspring. Litter size, survival rate and weight gain were comparable between groups. *A. fragrantissima* extract is a well-tolerated substance and had a wide safety margin. The tested plant extracts did not induce any toxic effects even on repeated administration in rats for 2 months. Additionally, no evidence of impaired fertility, or teratogenic potentials at higher doses up to several times the recommended maximum human doses were detected (19).

- The anti-inflammatory activity of *A. fragrantissima* extracts tested using the animal model of carrageenan-induced paw edema, was comparable to that of diclofenac (20, 21). The substance responsible for the anti-inflammatory effects of the plant could be a sesquiterpene lactone achillolid A. This lactone reduces levels of pro-inflammatory and toxic mediators and levels of intracellular reactive oxygen species in lipopolysaccharide-activated microglial cells (22, 23). Moreover, both non-polar and polar fractions revealed protective effects against rat ulcerative colitis and gastric ulcers (20).

- *A. fragrantissima* essential oil shows antimicrobial activity against gram-positive and gram-negative bacteria. It is also effective against *Listeria monocytogenes*, *Pseudomonas aeruginosa*, *Klebsiella* sp. and *Salmonella enteritidis* (24, 25). *A. fragrantissima* also acts against poliovirus, rotavirus Wa, human adenovirus 7 and coxsackievirus B4 (26, 27) and two fungal species *Candida albicans* and *Aspergillus niger* (28).

- Ethanolic extract of *A. fragrantissima* and its compounds significantly inhibited α-glucosidase activity *in vitro*, more potent than the positive control acarbose, used as an oral anti-diabetic drug (29). In streptozotocine and high-fat diet induced diabetic rats, elevated blood glucose levels, serum lipid profile, liver functions, and kidney functions were improved after *A. fragrantissima* extract treatment, as well as oxidative-stress and pro-inflammatory markers (30).

- The myorelaxant effect of *A. fragrantissima* is linked to the presence of the flavonoid cirsilol (31), which has been shown to effect relaxation of isolated rat ileum, bladder and uterus, and inhibits acetylcholine-induced contractions. Cirsilol is a low affinity competitive ligand of central benzodiazepine receptors and has sedative effects (32).

16. Additional Information

The effects of *A. fragrantissima* on humoral and cellular immunity in the rat model was tested. The oil extract appears to possess immunoprotected effects (both humoral and cellular immunity) in mice model (33).

17. Date of compilation/last revision

28/07/2022.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Hammouda, F. M. and Elsayed, A. O. (2017). *Achillea fragrantissima*. In: Egyptian Encyclopedia of Wild Medicinal Plants, **1**, 65-79. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Choucry, M. A. (2017). Chemical composition and anticancer activity of *Achillea fragrantissima* (Forssk.) Sch. Bip. (Asteraceae) essential oil from Egypt. *J. Pharmacognosy Phytother.*, **9**(1), 1- 5.
5	Elsharkawy, E. (2016). Anti-inflammatory activity and chemical compositions of essential oil of *Achillea fragrantissima*. *Nat. J. Physiol., Pharm. and Pharmacol.*, **6**(3), 258-262.
6	Shalaby, A. F. and Richter, G. (1964). Chromatographic investigation of the essential oil of *Achillea fragrantissima*. *J. Pharm. Sci.*, **53**, 1502–1505.
7	Aboutabl, E. A., Soliman, F. M., El-Zalabani, S. M., Brunke, E. J. and El-Kersh, T. A. (1986). Essential oil of *Achillea fragrantissima* (Forsk.) (Sch.) Bip. Egypt. *J. Pharm. Sci.*, **27**(1-4), 215-219.
8	Fleisher, Z. and Fleisher, A. (1993). Volatiles of *Achillea fragrantissima* (Forssk.) Sch. Bip. *J. Essent. Oil Res.*, **5**(2), 211-214.
9	Al–Gaby A. M. and Allam R. F. (2000). Chemical analysis, antimicrobial activity, and the essential oils from some wild herbs in Egypt. *J. Herbs Spices and Medicinal Plants*, **7**(1), 15-23.
10	Ahmed, A., A., Jakupovic, J., Seif El-Din, A. A. and Melek, F. R. (1990). Irregular oxygenated monoterpenes from *Achillea fragrantissima*. *Phytochemistry*, **29**(4), 1322-1324.
11	Ezzat, S. M. and Salama, M. M. (2014). A new α-glucosidase inhibitor from *Achillea fragrantissima* (Forssk.) Sch. Bip. growing in Egypt. *Nat. Prod. Res.*, **28**(11), 812-818.
12	Rizk, A. M., Elgendy, H. A. H., Ahmed, F. A. and Farag, S. H. (2017). Compositae, In: Phytochemistry of the Flora of Egypt – Chemical Constituents, Pharmacological and Biological Activities, Misr University for Science & Technology, 6th of October City, Egypt.
13	Segal, R., Dor, A., Duddeck, H., Snatzke, G., Rosenbaum, D. and Kajtár, M. (1987). The sesquiterpene lactones from *Achillea fragrantissima*, I. Achillolide A and B, two novel germacranolides. *Tetrahedron Lett.*, **43**(18), 4125-4132.
14	Abdel-Mogib, M., Jakupovic, J., Dawidar, A. M., Metwally, M. A. and Abou-Elzahab, M. (1989). Glaucolides from *Achillea fragrantissima*. *Phytochemistry*, **28**(12), 3528-3530.

15	Bakr, R. O., Arafa, R. K., Al-Abd, A. M. and Elshishtawy H. M. (2014). Phenolics of *Achillea fragrantissima* growing in Egypt and its cytotoxic activity. *J. Med. Plant Res.*, **8**(21), 763- 771.
16	Shalaby, A. F. and Steinegger, E. (1964). The phytochemical study of *Achillea fragrantissima* (Forssk.) Sch. Bip. *Pharm. Acta Helv.*, **39**(12), 756-761.
17	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
18	Hammouda, F. M., Ismail, S. I., Abdel-Azim, N. S. and Shams, K. A. (2005). A Guide to Medicinal Plants in North Africa (Batanouny K. H., editor). IUCN Centre for Mediterranean Cooperation. Malaga.
19	Mandour, M. A., Al-Shami, S. A., Al-Eknah, M. M., Hussein, Y.A., El-Ashmawy, I. M. (2013). The acute and long-term safety evaluation of aqueous, methanolic and ethanolic extracts of *Achillea fragrantissima*. *Afr. J. Pharm. Pharmacol.,* **7**(32), 2282-2290.
20	Maswadeh, H. M., Semreen, M. H. and Naddaf, A. R. (2006). Anti-inflammatory activity of *Achillea and Ruscus* topical gel on carrageenan-induced paw edema in rats. *Acta Pol. Pharm.*, **63**(4), 277-280.
21	Abdel-Rahman, R. F., Alqasoumi, S, I., El-Desoky, A. H., Soliman, G. A., Paré, P. W. and Hegazy, M. E. (2015). Evaluation of the anti-inflammatory, analgesic and anti-ulcerogenic potentials of *Achillea fragrantissima* (Forssk). *South African J. Botan.*, **98**, 122-127.
22	Elmann, A., Mordechay, S., Erlank, H., Telerman, A., Rindner, M. and Ofir, R. (2011). Anti-neuroinflammatory effects of the extract of *Achillea fragrantissima*. *BMC Complement Altern. Med.*, **11**, 98. doi: 10.1186/1472-6882-11-98.
23	Elmann, A., Telerman, A., Mordechay, S., Erlank, H., Rindner, M., Kashman, Y. and Ofir, R. (2015). Downregulation of microglial activation by achillolide A. *Planta Med.*, **81**(3), 215-221.
24	Kharma, A. and Hassawi, D. (2006). The antimicrobial activity and the genetic relationship of *Achillea* species. *Biotechnology,* **5**(4), 501-507.
25	Almadiy, A. A., Nenaah, G. E., Al Assiuty, B. A., Moussa, E. A. and Mira, N. M. (2016). Chemical composition and antibacterial activity of essential oils and major fractions of four *Achillea* species and their nanoemulsions against foodborne bacteria. *LWT-Food Sci. Techno.*, **69**, 529-537.
26	Soltan, M. M. and Zaki, A. K. (2009). Antiviral screening of forty-two Egyptian medicinal plants. *J. Ethnopharmacol.*, **126**(1), 102-107.
27	Mohamed, A. A., Ali, S. I., El-Baz, F. K. and El-Senousy, W. M. (2015). New insights into antioxidant and antiviral activities of two wild medicinal plants: *Achillea fragrantissima* and *Nitraria retusa*. *Int. J Pharma. Bio. Sci.*, **6**(1), 708-722.

28	Alsohaili, S. (2018). Seasonal variation in the chemical composition and antimicrobial activity of essential oil extracted from *Achillea fragrantissima* grown in Northern-Eastern Jordanian desert. *JEOP*, **21**(1), 139-145.
29	Ezzat, S. M. and Salama, M. M. (2014). A new a-glucosidase inhibitor from *Achillea fragrantissima* (Forssk) Sch. Bip. growing in Egypt. *Nat. Prod. Res*., **28**(11), 812-818.
30	El-Fattah, A. B. I., Ali, S. A., Aly, H. F., Abd-Alla, H. I., Shalaby, N. M. and Saleh, M. H. (2018). Therapeutic potential of *Achillea fragrantissima* extracts in amelioration of high-fat diet and low dose streptozotocin diabetic rats. *J. Complement. Med. Res*., **7**(2), 115-130.
31	Mustafa, E. H., Abu Zarga, M. and Abdalla, S. (1992). Effects of cirsiliol, a flavone isolated from *Achillea fragrantissima*, on rat isolated ileum. *General Pharmacology: The Vascular System*, **23**(3), 555-560.
32	Marder, M., Viola, H., Wasowski, C., Wolfman, C., Waterman, P. G., Medina, H. and Paladini, A. C. (1996). Cirsiliol and caffeic acid ethyl ester, isolated from *Salvia guaranitica* are competitive ligands for the central benzodiazepine receptors. *Phytomedicine,* **3**(1), 29-31.
33	Al-Sarraf, A. M., Hussien, Y. A., Yahiya, Y. I. and Al-Aubaidy, H. A. (2020). The protective effects of *Achillea fragrantissima* on immune response in mice model: A pilot study. *Sys. Rev. Pharm.,* **11**(4), 243-246.

Egyptian Herbal Monograph

Traditional wild medicinal plants

***Adiantum capillus-veneris* L.** كزبرة البئر، شعر البنات

1. Names & Synonyms (1-3)

***Adiantum capillus-veneris* L.**
Family: Adiantaceae.
Arabic: Kuzbarat el-bir كزبرة البئر
شعر الأرض ، شعر البنات و شعر الخنزير (2)
Eshbet gerri عشبة قرى (4).
English: Maidenhair, Venus's hair, Capillaire.

2. Geographical distribution (1-3)

Distributed in all the phytogeographical regions of the country.

3. Parts used for medicinal purpose

The whole plant above the ground which is represented by fronds (2).
Dried herb that collected at late summer (3).

4. Major chemical constituents

-Triterpenes: Adiantone, isoadiantone, adiantoxide, 21-hydroxy adiantone, adiantoxide, isoglaucanone, isoadiantol, hydroxyadiantone,4-α-hydroxyfilican-3-one, fernadiene,7-fernene (diploptene), hydroxyhopane (hopanol), neohop-12-ene (neohopene), trisnorhopane isoglaucanone (5-10).

-Flavonoids: Quercetin, quercetin 3-glucoside, rutin, isoquercitrin, quercetin 3-O-(6″-malonyl)-D-galactoside, quercituron, astragalin, nicotiflorin, naringin, populin, procyanidin, prodelphinidin, kaempferol 3,7-diglucoside, kaempferol 3-glucuronide, kaempferol 3-*O*-rutinoside sulphate, kaempferol 3-sulphate; Kaempferol-3-sophorotrioside, and daphnoretin.

-Phenolic acids and derivatives: 4-Hydroxybenzoic, chlorogenic, caftaric, rosmarinic, 5-*O*-caffeoylquinic, *p*-coumaric acids, and their derivatives; 1-caffeoylglucose, 1- caffeoylgalactose 3-sulphate, 1- caffeoylgalactose 6- sulphate, 1-*p*-coumaroyl glucose, 1-*p*-coumaroylglucose 2-sulphate, 1-*p*-coumaroylglucose 6-sulphate, and 1-*p*-coumaroyl galactose 6-sulphate (11, 12).

-Carotenoids and chlorophylls pigments: Lutein, chlorophyll b′, chlorophyll a, 9′-*Z*-neoxanthin and all-*E*-violaxanthin (12).

-Essential Oil: Carvone, carvacrol hexadecanoic acid, thymol, hexahydrofarnesyl acetone and n-nonanal (13).

-Oxygenated hydrocarbons: Dodecanoic acid ethyl ester; 3,7,11,15-tetramethyl-2-hexadecen-1-ol; butyloctyl ester; hexadecanoic acid, 9-octadecenoic acid, octadecenoic acid ethyl ester (14).

-Others: Phlobatannins (10, 11, 15), *β*-sitosterol, stigmasterol, campesterol, (*E*)-2-decanal, a saponin (on hydrolysis yields hydroxyhopanone aglycone, galactose, xylose and rhamnose) (10, 15), alicyclic acids; quinic acid and shikimic acid, phthalic acid and di-n-octylphthalate, diacylglycerol-O-4'-(*N,N,N*-trimethyl)-homoserine (containing palmitic, linoleic, linolenic and arachidonic acids) (10), mucilage and betaine lipid, alkaloids and cardiac glycosides (16).

5. Traditional medicinal uses (4)

A. Respiratory disorders
- Asthma
- Chest problems
- Cough
- Catarrh
- Cold
- Diaphoretic

B. Gastrointestinal disorders
- Hepatitis
- Dropsy
- Gall stones
- Splenitis
- Sour stomach

C. Diuretic and urinary disorders

D. Others
- Menstrual problems and emmenagogue
- Hair loss
- Treatment of snake and spider bites

***A. capillus-veneris* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use

1. **Herbal tea**

Prepared from 1 tablespoonful of finely cut leaves to 1-2 cups of water or hot milk (2).

2. **Infusion** (17)

Pour freshly boiled water on 2 teaspoonful of the finely ground or powdered drug in a cup; cover the cup with the lid, infuse for 5 minutes and Drink it sweetened if desired (4).

3. **Decoction** (2)

Add 2 teaspoonful of the finely ground or powdered drug in a pot, pour cold water, boil and simmer for 10 minutes then pour into a cup and drink it sweetened if desired (4).

7. Posology and method of administration correlated to medicinal use

Preparation 1,2: A tea prepared from 1.5g of the drug to 1 cup of liquid (17).

Preparation 3: Concentrated decoction of the fronds is used as emmenagogue (2).

Dose: 3cups/day (4).

Method of administration: Oral use.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation (18,19)

- The use during pregnancy should be avoided.

- Safety during lactation has not been established. In the absence of sufficient data, the use during lactation is not recommended.

- No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- None known.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

14. Overdose (18,19)

Large amount of *A. capillus-veneris* may cause vomiting in some people.

15. Relevant biological activities

- Both the aqueous extract and hydroalcoholic extract of *A. capillus-veneris* had dose-related beneficial effects on acetic acid-induced colitis on acetic acid-induced colitis in a rat model. The results showed that both extracts and these effects could be attributed to the anti-inflammatory, ulcer healing and antioxidant activities of the extracts (20).
- The ethyl acetate fraction of the ethanolic extract displayed significant anti-inflammatory activity when assessed through lipopolysaccharide-induced prostaglandin E2 generation in RAW 264.7 macrophage and interleukin 6 and tumor necrosis factor generation in the human monocyte model. This effect is possibly mediated through inhibition of nitric oxide release and reduction of the TNF-α level (21, 22).
- The 80% aqueous methanolic extract of the dried leaves of *A. capillus-veneris* was found to produce antidiarrheal and antispasmodic activities in castor oil-induced diarrhea in mice model. These activities are mediated possibly through ATP-dependent K^+ channels activation (23).
- The anti-asthmatic activity of *A. capillus-veneris* ethanolic extracts was evaluated in histamine aerosol-induced asthma in guinea pig. Animals treated with the extract showed significantly prolonged latent period of convulsions (PCT) as compared to control animals following the exposure of histamine aerosol. The histamine produced bronchial construction in animal model in histamine chamber. The study concluded that ethanolic extract of *A. capillus-veneris* possess anti-asthmatic activity, thus justifying to some extent the traditional use of the plant in asthma (24).
- The effect of supplementation of *A. capillus-veneris* (ACV) extract on Bax/B-cell lymphoma 2 (Bcl-2) ratio apoptotic index and remodeling of pulmonary alveolar epithelial cells in lung tissue of healthy Wistar rats during stressful conditions (hypoxia) was evaluated.

Supplementation of the ethanolic extract of *A. capillus-veneris* (fresh plant) modulates alveolar apoptosis under hypoxia condition in Wistar rats exposed to exercise. Interestingly, consuming the extract may modulate this state by reducing the Bax/Bcl-2 ration and increasing the pneumocytes I in the population of rats (25).

- The potential nephroprotective activity of 250mg/kg and 500mg/kg ethanolic extract of *A. capillus-veneris* dried fronds against Cisplatin induced oxidative stress in male Wistar rats, was investigated. Acute nephrotoxicity was induced by *i.p.* injection of Cisplatin (7mg/kg of body weight (b.w.)). Administration of ethanol extract at dose level of 500 and 250mg/kg (b.w.) to Cisplatin intoxicated rats (toxic control) for 14 days attenuated the biochemical and histological signs of nephrotoxicity of Cisplatin in a dose-dependent fashion. The ethanol extract at 500mg/kg (b.w.) exhibited significant and comparable nephroprotective potential (26).
- The *in vitro* and *in vivo* antimicrobial and diuretic effects of *A. capillus-veneris* L. were investigated. Double-fold dilution method was employed to observe the bacteriostatic action of the drug *in vitro*. Systemic *Candida albicans* infection model were established in mice to evaluate the protective effects of *A. capillus-veneris* L. in terms of survival rate, splenic bacteriuria counts and renal pathological characteristics. The water extract had *in vitro* and *in vivo* antimicrobial and diuretic effects, which provided strong pharmacologic proofs for its further treatment of urinary tract infections (UTI) (27).
- The oral administration of hydroalcoholic extract of *A. capillus-veneris* was evaluated for anti-calcium oxalate urolithiasic property in male Sprague Dawley rats. The test groups were treated with 127.6 mg/kg and 255.2mg/kg of test drug and standard control with Cystone (750mg/kg) for 21 days. The results revealed significant decrease in the number of crystals and reduction in the serum level of calcium, phosphorous and blood urea. In addition, the histopathology of kidney showed almost normal kidney architecture in treated groups (28). They also confirmed this effect during an *in vitro* study. The plant restrained the crystallization, crystal aggregation and reduction in the number and the sizes of crystals (29).
- The healing potential of *A. capillus-veneris* against bisphenol-induced hepatic toxicity in rats was evaluated. It was found that simultaneous exposure of *A. capillus-veneris* and bisphenol led to decline in serum biomarker levels and normal histopathological structures. It was concluded that the *A. capillus-veneris*, as antioxidant, can reduce the bisphenol-induced toxicity (30).
- The analgesic effect of the ethyl acetate fraction of the ethanolic extract from *A. capillus-veneris* L. (whole plant) has been confirmed through tail-flick and writhing methods (31). Similar investigation confirmed powerful analgesic effect

of the fraction through hot plate and tail immersion tests in mice (32). In addition, 4-α- hydroxyfilican-3-on, isolated from ethanolic extract of the plant, showed significant anti nociceptive activity in writhing test (22).

- The methanolic extract of *A. capillus–veneris* (whole plant) was tested for its antimicrobial effect against five gram positive, six gram negative (including multi-resistant bacteria *Staphylococcus aureus)* and eight fungal strains using standard microdilution assay. It exhibited good activity and very low MIC value (0.48 g/ml) against *Escherichia coli* (33).
- The hair growth-promoting effect of ethanolic extract of *A. capillus–veneris* (aerial parts) was evaluated through testosterone-induced alopecia model in mice. The results revealed considerable increase in follicular density and anagen/ telogen ratio (34).
- Different extracts of *A. capillus–veneris* were screened on different groups of female albino rats by intraperitonial route. The petroleum ether extract of *A. capillus–veneris* showed significant anti-implantation activity (83%) at a dose level of 100mg/kg dry extract. the alcoholic extract showed a slight activity, but was found to be toxic (35).

16. Additional information

Solid contents: 74.48%; ash values (total ash: 7.81%, acid insoluble ash: 4.42%, and water soluble ash: 0.42%); and successive extractive values (petroleum ether: 60-80º: 4.49%, chloroform: 3.03%, acetone: 4.60%, ethanol: 9.27% and distilled water: 14.07%) (36).

Mineral content: Ten elements; Mg, Ca, K, Mn, Fe, Co, Na, Ni, Cu, and Zn were detected in Adiantum leaves. Among which Ca, Mg and K were found to be at significantly high concentration (37).

17. Date of compilation/last revision

28/07/2022.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Abdel Rehim, F. A., Shams, K. A., and El Garf, I. A. (2017). *Adiantum capillus* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **1**, 112-125. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
5	Berti, G., Bottari, F. and Marsili, A. (1964). The structure of a diantoxide, a triterpenoid epoxide with a new type of carbon skeleton. *Tetrahedron Lett.*, **5**(1), 1-5.
6	Nakane, T., Arai, Y., Masuda, K., Ishizaki, Y., Ageta, H. and Shiojima, K. (1999). Fern constituents: Six new triterpenoid alcohols from *Adiantum capillus-veneris*. *Chem. Pharm. Bull.*, **47**(4), 543-547.
7	Nakane, T., Maeda, Y., Ebihara, H., Arai, Y., Masuda, K., Takano, A., Ageta, H., Shiojima, K., Cai, S.-Q. and Abdel-Halim, O. M. (2002). Fern constituents: triterpenoids from *Adiantum capillus-veneris*. *Chem. Pharm. Bull.*, **50**, 1273-1275.
8	Jankowski, C. K., Aumelas, A., Thuery, P., Reyes-Chilpa, R., Jimenz-Estrada, M., Barrios, H. and Diaz, E. (2004). X-ray, $^{1}H/^{13}C$, 2-D and 3-D NMR studies of the structures of davallene and adipedatol, two triterpenes isolated from American *Adiantum capillus-veneris*. *Polish J. Chem.*, **78**, 389-408.
9	Ibraheim, Z. Z., Ahmed, A. S. and Gouda, Y. G. (2011). Phytochemical and biological studies of *Adiantum capillus-veneris* L. *Saudi Pharm. J.*, **19**, 65-74.
10	Rizk, A. M., Elgendy, H. A. H. and El-Garf, I. A. (2013). Adiantaceae, in Phytochemistry of the Flora of Egypt. Chemical Constituents, Folk Medicine, Pharmacological and Biological Activities, Misr University for Science & Technology, 6th of October City, Egypt.
11	Imperato, F. (1982). Sulphate esters of hydroxycinnamic acid-sugar derivatives from *Adiantum capillus-veneris*. *Phytochemistry*, **21**(11), 2717-2718.
12	Zeb, A. and Ullah, F. (2017). Reversed phase HPLC-DAD profiling of carotenoids, chlorophylls and phenolic compounds in *Adiantum capillus-veneris* leaves. *Front. Chem.*, **5**, 29. doi: 10.3389/fchem.2017.00029.
13	Khodaie, L., Esnaashari, S., and Moghaddam, S. B. (2015). Essential oil of aerial parts of *Adiantum capillus-veneris*: Chemical composition and antioxidant activity. *J. Nat. Pharm. Prod.*, **10**(4), 3.

14	Kale, M.V. (2015). GC-MS analysis of phytocomponents on whole plant extract of *Adiantum capillus-veneris* L. A potential folklore medicinal plant. *Res. J. Life Sci., Bioinform., Pharm. Chem. Sci.*, **2**(1), 116-121.
15	Mahran, G. H., El-Alfy, T. S., El-Tantawy, M. and El-Sakhawy, F. (1994). Chemical constituents of *Adiantum capillus-veneris*, growing in Egypt. *Al-Azhar J. Pharm. Sci*., **13**, 1-14.
16	Shakir, U., Gul, J., Farzana, G., Siraj, K., Maria, K., Hameeda, B. and Jan, S. (2018). Phytochemistry, anti-inflammatory and antipyretic activities of *Adiantum capillus-veneris* in Swiss albino mice. *International Journal of Fauna and Biological Studies,* **5**(3), 19-25.
17	https://www.webmd.com/vitamins/ai/ingredientmono-559/maidenhair-fern
18	https://www.rxlist.com/maidenhair_fern/supplements.htm
19	PDR for Herbal Medicines (1998). Medical Economic Co. Montvale, New Jersey, 639. ISBN 1563633612, 9781563633614.
20	Ladan, K., Seyed, E. S. and Mohsen, M. (2020). Anti-inflammatory effect of *Adiantum capillus-veneris* hydroalcoholic and aqueous extracts on acetic acid-induced colitis in rats. *Avicenna J. Phytomed.,* **10**(5), 492-503.
21	Yuan, Q., Zhang, X., Liu, Z., Song, S., Xue, P., Wang, J. and Ruan, J. (2013). Ethanol extract of *Adiantum capillus-veneris* L. suppresses the production of inflammatory mediators by inhibiting NF-κB activation. *J. Ethnopharmacol.*, **147**(3), 603-611 .
22	Haider, S., Kharbanda, C., Alam, M. S., Hamid, H., Ali, M., Alam, M., Nazreen, S. and Ali, Y. (2013). Anti-inflammatory and anti-nociceptive activities of two new triterpenoids from *Adiantum capillus-veneris* Linn. *Nat. Prod. Res.*, **27**(24), 2304-2310.
23	Janbaz, K. H., Hassan, W., Mehmood, M. H., Gilani, A. H. (2015). Antidiarrheal and antispasmodic activities of *Adiantum capillus-veneris* L. *Bangladesh J. Pharmacol.*, **10**(1), 222-229.
24	Kumar, K. S. S. L. V. V. S. N, Anbu, J., Anjana, A., Sumithra, M., Sathish, R. (2012). Influence of ethanolic leaf extract of *Sargassum wightii* and *Adiantum capillus* on histamine induced asthma in animal model. *Int. J. Pharm. Pharm. Sci.*, **4**(4), 121-123.
25	Mehdi, Y., Maha, S., Simin, R., Shadmehr, M., Gholamreza, H., Ayoub, S., Abderraouf, B. A., Anthony, C., Hackney and Hassane Z. (2019). Supplementation of *Adiantum capillus-veneris* modulates alveolar apoptosis under hypoxia condition in wistar rats exposed to exercise. *Medicina (Kaunas)*, **55**(7), 401. doi: 10.3390/medicina55070401.
26	Kanchan, G., Swati, D., Joshi, Y. M. and Vilasrao, K. (2013). Protective effect of *Adiantum Capillus* against chemically induced oxidative stress by Cisplatin. *Journal of Applied Pharmaceutical Science,* **3**(02), 065-068.
27	Yuan, Q. Y., Ruan, J. L. and Cai, Y. L. (2010). Effect of water extracts of *Adiantum capillus-veneris* L. on urinary tract infections. *Chin. Pharm. J.,* **45**(18), 1389-1392.

28	Ahmed, A., Wadud, A., Jahan, N., Bilal, A. and Hajera S. (2013). Efficacy of *Adiantum capillus veneris* Linn in chemically induced urolithiasis in rats. *J. Ethnopharmacol.*, **146**(1), 411-416.
29	Ahmed, A., Bilal, A., Hajera, S., Jahan, N., Wadud, A. (2013b). *In vitro* effect of hydro alcoholic extract of *Adiantum capillus-veneris* Linn. on calcium oxalate crystallization. *International Journal of Green Pharmacy,* **7**(2), 106-110.
30	Kanwal, Q., Abdul Qadir., Fahad, A., Asmatullah, Hafiza, H. and Bushra, M. (2018). Healing potential of *Adiantum capillus-veneris* L. plant extract on bisphenol A-induced hepatic toxicity in male albino rats. *Environmental Science and Pollution Research*, **25**, 11884–11892.
31	Haider, S., Nazreen, S., Alam, M. M. (2011). Anti-inflammatory and anti-nociceptive activities of ethanolic extract and its various fractions from *Adiantum capillus veneris* Linn. *J. Ethnopharmacol.*, **138**(3), 741-747.
32	Jain, S. K., Singh, T., Pande, M. and Nema, N. (2014). Neuropharmacological screening of fronds of *Adiantum capillus veneris* Linn. *Pharm. Lett.*, **6**(3), 167-175.
33	Meenakshi, S., Neha, S., Khare P. B. and Rawat A. K. S. (2008). Antimicrobial activity of some important *Adiantum* species used traditionally in indigenous systems of medicine. *Journal of Ethnopharmacology*, **115**, 327–329.
34	Noubarani, M., Rostamkhani, H., Erfan, M., Kamalinejad, M,, Eskandari, M. R., Babaeian, M. and Salamzadeh, J. (2014). Effect of *Adiantum capillus veneris* Linn on an animal model of testosterone-induced hair loss. *Iran J. Pharm. Res.*, **13**, 113-118.
35	Murthy, R. S. R., B. D. M. V. (1984). Anti-implantation activity of isoadiantone. *Indian Drugs*, **2**1(4), 141-144.
36	Ahmed, A., Jahan, N., Wadud, A., Imam, H., Hajera, S. and Bilal, A. (2012). Physicochemical and biological properties of *Adiantum capillus –veneris* Linn: An important drug of Unani system of medicine. *Int. J. Cur. Res. Rev.*, **4**(21), 71-75.
37	Rajurkar, N. S. and Gaikwad, K. (2012). Evaluation of phytochemicals, antioxidant activity and elemental content of *Adiantum capillus veneris* leaves. *J. Chem. Pharm. Res.*, **4**(1), 365-374.

Egyptian Herbal Monograph

Traditional wild medicinal plants

Ambrosia maritima L. دمسيسة/ غبيرة

1. Names & Synonyms

***Ambrosia maritima* L.** (1,2)
Family: Compositae (Asteraceae).
Arabic: Demsisa دمسيسة , Ghobbeira غبيرة.
English: Sea ambrosia, Oak of Cappadocia (3).

2. Geographical distribution

The Nile valley and the Nile Delta, Oases, and the Mediterranean region (1).

3. Parts used for medicinal purposes

- The above ground flowering and fruiting herb (2).
- The whole plant, leaves and stems (3).

4. Major chemical constituents (3)

-Sesquiterpene Lactones: Ambrosin, neoambrosin, damsin, farnserin, hymenin, parthenin, and neombrasin.

-Sesquiterpenes: Damsinic acid.

-Polyphenols and Flavonoids: 6-Methoxy luteolin-4'-*O*-lactate, apigenin-4'-*O*-*α*-L-rhamnopyranoside (4).

-Volatile Oil: Carvone, camphor, caryophyllene and cineole (5, 6).

-Others: Sterols, coumarins, tannins.

5. Traditional medicinal uses

A. Gastrointestinal disturbance and abdominal pain, and as anti-spasmodic (7, 8).
B. Kidney problems (kidney inflammation, kidney stones, renal colic, spasms and frequent urination) and as diuretic (7, 8).
C. Externally for rheumatic pains (9, 10, 11).

***A. maritima* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (1, 3)

1. Decoction of the aerial parts for oral use (One teaspoonful of aerial parts is boiled and left till cold, then sweeten with honey).
2. Decoction or infusion of aerial parts for oral use.
3. The dried powdered plant mixed with small amount of oil and used externally.

7. Posology and method of administration correlated to medicinal use (12)

Preparations 1-3

Indication A & B: 3 cups/day.

Method of administration: Oral use.

Indication C: dosage: 4 times/ day.

Method of administration: External use.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- May exert estrogen like effect (3).

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation

-Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

-No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

-None known.

-If adverse reactions occur, a doctor or a pharmacist should be consulted.

14. Overdose

- High doses of the drug may be toxic (3).

15. Relevant biological activities

- Nephroprotective effect of methanolic extract of *Ambrosia maritima* leaves was studied in healthy albino rats (1.25-1.75 kg) of either sex. The renal toxicity was produced by administration of rifampin at dose rate of 70 mg/kg I/p for 28 days. The plant extract was given by simultaneous oral administration of the methanolic extract of *Ambrosia maritima* leaves at a dose rate of 300 and 600mg/kg for 28 days. The methanolic extract showed a marked nephroprotective effect depending on the concentration (13).
- No toxic signs could be detected on rats neither after oral administration of 5g/kg of dried leaves as a powder or as a methanolic extract, nor after the incorporation of 50,000 ppm powdered leaves in the feeding after 4 weeks. Toxicological effects of *Ambrosia maritima* in Nubian goats were investigated. The results revealed that goats drenched the plant for 126 days, showed chronic toxicity evident by clinical symptoms, pathological and biochemical changes (14).
- In rabbits, Demsisa (400mg/ kg body weight) produced significant estrogen-like activities (p<0.05) in the form of increased both uterine and ovarian weights as compared with the control group (15).

16. Additional information:

Each 100g of Demsisa leaf powder contains carbohydrate (29.40g), protein (26.20g), fat (5.30g) ash (20.67g), crude fiber (10.07g) and moisture (8.37g) (4).

17. Date of compilation/last revision

28/07/2022.

References

1	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
2	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
3	Abd El-Azim, N. S., Tawfik, W. A. and Shams, K. A. (2017). *Ambrosia maritima* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **2**, 93-106. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Said, T. M. A., Elgasim, E. A., Eltilib, H. H. A. B., Bekhit, A. A., Al-Juhaimi, F. Y and Ahmed, I. A. M. (2018). Antioxidant and antimicrobial potentials of Demsisa (*Ambrosia maritima*) leaf powder extract added to minced beef during cold storage, CyTA. *Journal of Food*, **16**, 1, 642-649, DOI: 10.1080/19476337.2018.1448456.
5	Mahran, G., El-Hosary, G., Seida, A. and Amin, W. (1990). A study of the volatile oil content of *Ambrosia maritima* L. cultivated in Egypt. *Bull. Fac. Pharm.,* **28**, 53-55.
6	Dominguez, X., Gomez E., Gomez, P., Villareal, A. and Rombold, C. (1970). Physical data on the essential oils of five Compositae plants. *Planta Med*., **19**, 52-54.
7	El-Sawy, M., Duacun, J. and Marshall, T. (1984). The mulluscicidal properties of *Ambrosia maritima* L. (Compositae). 2. Results from a field trial using dry plant material. *Tropenmed Parasitol.*, **35**(2), 100-104.
8	Ghazanfar, S. (1994). CRC Handbook of Arabian Medicinal Plants. CRC Press, Boca Raton, 265.
9	Abdelgaleil, S., Badawy, M., Suganuma, T. and Kitahara, K. (2011). Anti-fungal and biochemical effects of pseudoguaianolide sesquiterpenes isolated from *Ambrosia maritima* L. *Afri. J. Microbiol. Res.*, **5**(21), 3385-3392.
10	Khalid, H., Abdalla, W., Abdelgadir, H., Opatz, T. and Efferth, T. (2012). Gems from traditional North-African medicine: Medicinal and aromatic plants from Sudan. *Nat. Prod. Bioprospect*., **2**, 92-103.
11	Dirar, A. I., Mohamed, M. A., Ahmed, W. J., Mohammed, M. S., Khalid, H. S. and Garelnabi, E. A. (2014). Isolation and characterization of potential cytotoxic leads from *Ambrosia maritima* L. (Asteraceae). *J. Pharmacog. Phytochem.*, **3**(4), 38-41.
12	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
13	Bilal, T. H. A., Ramadan, E., Idris O. F., Mohamed, S. A. and Abdelrahman, S. H. (2019). The use of *Ambrosia maritima* methanolic extract as nephroprotective against rifampin induced nephrotoxicity in rats. Am. *J. Biomed. Sci. and Res.,* **5**(3). AJBSR.MS.ID.000919. DOI: 10.34297/AJBSR.2019.05.000919

14	Ahmed, I. M. O., Mohammed, A. S., Halima, M. O. and Ahmed, M. A. I. (2016). Toxicological effects of *Ambrosia maritima* in Nubian goats. *J. Plant Environ. Res*., **1**(1), 1-10.
15	Amer, H. A., Hammam, A. M., Shalaby, M. A., Hafez, S. M. M. and Hsssein, M. A. (2014). Phytoestrogen effect of *Ambrosia maritima* (Demsisa) on the ovarian activity of immature rabbits. *Glob. Vet*., **13**(4), 590-600.

Egyptian Herbal Monograph

Traditional Wild Medicinal Plants

Anastatica hierochuntica L. كف مريم

1. Names & Synonyms (1-3)

***Anastatica hierochuntica* L.**

Family: Cruciferae (Brassicaceae).

Arabic: Kaff Mariam كف مريم .

English: St. Mary's flower, Rose of Jericho, Jericho resurrection plant, Genggam Fatimah (4), Rumput Fatimah (5).

2. Geographical distribution (1- 3)

Uweinat Oasis, all the deserts of the country including that of Sinai, Red Sea coastal strip as well as Gebel Elba and the surrounding mountainous region.

3. Parts used for medicinal purposes (2)

Dry whole plant.

4. Major chemical constituents (3)

-Simple Flavonoids:

Luteolin, luteolin 7-O-glucoside, luteolin 6-C-hexosyl-8-C-pentoside, luteolin6-C-pentosyl-8-C-hexoside, luteolin 8-C-glucoside (orientin), luteolin 6-C-glucoside (isoorientin), luteolin-O-glucuronide, luteolin 6-C-glucosyl-2"-O-glucoside (isoorientin 2"-O-glucoside. Quercetin, rutin, aromadendrin, eriodictyol, diosmetin 8-C-glucoside.

Kaempferol 7-O-glucoside, kaempferol 3-O-glucoside, kaempferol 7-O-rhamnoglucoside, naringenin, Taxifolin, 3-O-methyltaxifolin, epitaxifolin, taxifolin O-hexoside. Apigenin 6-C-glucoside (isovitexin), apigenin 6-C-7-O-diglucoside (isovitexin 7-O-glucoside), apigenin 6-C-arabinosyl-8-C-hexoside (6-11).

-Benzofurano-Flavanones: Anastatin A and anastatin B (12).

-Flavonolignans: Silybin A, silybin B, isosilybin A, isosilybin B, (+)-silychristin and (-) - silychristin (9).

-Lignans: Evofolin B (9).

-Neolignans: Hierochin A, hierochin B and hierochin C, (+)-balanophonin, (+)-dehydrodiconiferyl alcohol and (+)-lariciresinol (12).

-Other Phenolic Compounds: *p*-Hydroxybenzoic acid, *p*-methoxy benzoic acid, 3,4-dihydroxy benzoic acid, 3-methoxy-4-hydroxy benzoic acid, *p*-hydroxy-benzaldehyde, 3,4-dihydroxy benzaldehyde, vanillin, aceto vanillone, 2,4'-dihydroxy-3'-methoxy acetophenone, ω-hydroxy propioguaiacone, (+)-2,3-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)-1-propanone, trans-cinnamic acid, trans-ferulic acid, conifer aldehyde (9), 5-O-caffeoylquinic acid, 3,4-O- dicaffeoylquinic acid and 4,5-O-dicaffeoylquinic acid (11).

Essential oil: The major constituents were cuminic aldehyde, *trans*-β-caryophyllene, linalool, caryophyllene oxide and α-copaen-11-ol and limonene (13).

5. Traditional medicinal uses (14)

*** Oral:**

A. Gynecology:

1. Reduces the pain and facilitates childbirth.
2. Abortifacient.
3. Emmenagogue.

B. GIT disorders

Violent purge for cases of Jaundice.

C. General

1. Fatigue.
2. Epilepsy.
3. Cold.

***External:**

Gynecology: To increase the probability of pregnancy, the dried leaves and flowers are mixed with *Anastatica hierochuntica* L. whole plant, boiled in water and used as pelvic bath**.**

***A hierochuntica* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (14)

1. The crushed dried plant.
2. Infusion of dried whole plant.

***Infusion:** Pour freshly boiled water on 2teaspoonful of *Anastatica hierochuntica* L in a cup, cover the cup with the lid and infuse for 5 minutes. Drink it sweetened if desired.

3. Decoction of the whole plant

7. Posology and method of administration correlated to medicinal use (14)

Preparation 1
Indication B
The dried plant crushed with sugar is taken as violent purge, followed by milk as diet.

Method of administration: Oral use.

Preparation 2
Indication A
The dried plant is soaked in water and the solution drunk by women at childbirth (2).

Indication C
The dried plant is soaked in water and the solution drunk by women at childbirth (2).

Method of administration: Oral use.

Preparation 3
Indication A
Boiled in water and used as pelvic bath**.**

Method of administration: External use.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

- Monitoring of blood pressure and blood glucose level should be done regularly.

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation

- Avoided during pregnancy.
- Safety during lactation has not been established. In the absence of sufficient data, the use during lactation is not recommended.
- No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- None reported.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

14. Overdose

No case of overdose has been reported.

15. Relevant biological activities (3)

- The effect of *A. hierochuntica* L. extract on the histology of myometrial cells and prostaglandin levels (PGE2 and PGF2α) of pregnant mice was investigated. It was found that a daily dose of 100 mg/kg b.wt./day of the 96% ethanolic extract of *A. hierochuntica* L. had a greater effect on the histology of myometrial cells in pregnant mice and prostaglandin levels in both PGE2 and PGF2α compared to that of 150 mg/kg/day dose. These results provide new scientific evidence for the activity of *A. hierochuntica* L. as a facilitator of labor during childbirth (15).
- In silico study of *A. hierochuntica* L. estrogenic activities and its potential as phytoestrogens was conducted using computer simulation methods (16). The prediction of estrogenic active compounds and its potential as a phytoestrogen with target agonists to the estrogen receptor were determined. It was found that active compounds in *A. hierochuntica* L. had low activity against estrogen receptor agonists because the average value of activity obtained was low (<0.3). In addition, Isopimaric acid was found to be one of the estrogen receptor ligands which provided the greatest affinity and good potential as phytoestrogens.
- Both aqueous extract of *A. hierochuntica* (whole plant) and the chloroform fraction of the ethanolic extract possessed potential central and peripheral antinociceptive and antiinflammatory activities in Swiss albino mice and Wistar rats (17).

- The potential toxicity effects of *A. hierochuntica* (whole plant aqueous extract) in pregnant Sprague-Dawley (SD) rats and their developing fetuses was investigated. Animals received daily 250, 500, and 1000 mg/kg *A. hierochuntica* aqueous extracts, respectively. The results suggested that exposure to the plant aqueous extract during implantation and period of organogenesis is potentially toxic to the pregnant rats as well as the developing fetuses (18).
- The aqueous extract of *A. hierochuntica* L. aerial parts; when used as an alternative of conjugated estrogen (Premarin) in rabbit females, increased the level of estrogen hormone (19).
- One month administration of the aqueous extract of *A. hierochuntica* (at a dose of 1g/day) significantly increased the levels of LH, FSH, PRL, and PRO hormones in female micromys minutus, compared to control group (20).
- A lyophilized extract of the plant was administered to pregnant mice (plug=day 0) for 3 consecutive but separate gestation days (GD) 8-9, 10-12, and 12-14, at oral doses of 0.25, 1, and 4g/kg; and controls received saline only. Results showed that resorption and exencephaly were the main developmental defects resulting from treatment with the extract. The incidence of exencephaly depended on both the dose and the developmental stage. In addition, the doses also induced incidence of fetal resorption. The resorption rates were stage dependent. Therefore, the plant, at the doses used may be considered teratogenic and embryolethal (21).
- The hepatoprotective activity of methanolic extract of *A. hierochuntica* whole plant using carbon tetra chloride (CCl_4)-induced hepatotoxicity in rats, was investigated. The levels of liver enzymes, protein, bilirubin, in addition to total antioxidant status levels were evaluated in experimental rats (with or without CCl_4- induced hepatotoxicity) following intake of 100 mg/kg p.o plant extract compared with standard silymarin at a dose of 100 mg/kg p.o. Histopathology of a liver tissue of the animals treated with the extract was also studied to monitor the liver status. Results showed that methanolic extract at a dose level of 100 mg/kg offered protective effect against CCl_4-induced hepatotoxicity in experimental rats. The liver biopsy of all experimental rat groups treated with the methanolic *A. hierochuntica* extract showed significant restoration of the normal histomorphologic pattern of liver cells (22).
- The gastro protective activity of “Kaff-e-Maryam” extract was evaluated in rats while toxicity studies were done in Brine shrimp and mice. Ethanol extract of the whole plant was prepared and animals were treated with the standard necrotizing agents. Different doses of the extract were used for pharmacological and toxicity evaluation. Pretreatment with *A. hierochuntica* extract offered protection against toxic damage to stomach wall. The extract was found to exert its defensive role through its free radical scavenging and prostaglandin inducing activities. The

toxicity studies revealed that the plant extract in the given dose range, was not toxic (23).

- The histological effects of *A. hierochuntica* in mice female liver tissues was evaluated. The administration of daily oral doses of (0.1g/ml)of the plant aqueous extract for more than one month produced significant changes (P≤0.05) on mice females liver tissues that included lymphocyte infiltration, necrosis, liver tissue fatty degeneration and congestion and dilatation of the hepatic vein. The prolonged use of the aqueous extract of the plant for more than one month is associated with significant side effects on mice liver (24).
- The antibacterial activity of the plant extracts was evaluated using agar well-diffusion method, The results indicated that plant extracts were more active against Gram-negative bacteria than Gram-positive bacteria, and that alcoholic extract has antibacterial activity stronger than hexane and aqueous extracts (25).
- The antiproliferative activities of *A. hierochuntica* whole plant extracts (ethanol, methanol, ethyl acetate, chloroform and water) were determined against a panel of cancer cells and normal primary dermal fibroblasts. The genotoxic effect of *A. hierochuntica* ethyl acetate on mice bone marrow cells was also evaluated. *A. hierochuntica* exhibited antiproliferative activity against leukemia (K-562) and melanoma (A-375) cells. *A. hierochuntica* ethyl acetate extract found to be the most cytotoxic of all extracts. Furthermore, the chloroform extract showed notable anti-proliferative effects against most cancer cell lines tested. The extracts proved to be highly safe on human normal skin fibroblasts. Furthermore, *A. hierochuntica* ethyl acetate extract was also found to have limited genotoxic effects, with these changes seen at very high doses only. The results indicate that *A. hierochuntica* extracts have significant selective anticancer activity and that genotoxicity is only observed at very high concentrations (26).
- The effect of ethanolic (KEE), and aqueous (KAE) extracts of Kaffe-Maryam (*Anastatica hierochuntica*) on CCl4 -induced oxidative stress and nephrotoxicity in rats was evaluated using the biochemical markers for renal functions and antioxidant status as well as histopathological examinations of kidney tissue *A. hierochuntica* presented superior antioxidant activity by inhibiting linoleic acid radicals and chelating oxidation metals. The HPLC analysis resulted in 9 and 21 phenolic acids and 6 and 2 flavonoids in KEE and KAE. *A. hierochuntica*, especially KAE, has the potential capability to restore oxidative stability and improve kidney function after CCl4 acute kidney injury better than KEE. Therefore, *A. hierochuntica* has the potential to be a useful therapeutic agent in the treatment of drug-induced nephrotoxicity (27).
- The dose-related relationship and selectivity of the toxic effects of *A. hierchuntica* extracts (AHE) on melanoma cells were investigated as well as providing a new option that can be used in the future treatment of melanoma. B16F10 Mus

musculus malign melanoma cells and L929 Mus musculus healthy fibroblast cells were treated with root and leaf AHEs in a dose-dependent manner. The results showed that when looking at melanoma-specific, AHE could be a source of inspiration as an active ingredient in future treatment protocols and can be recommended as potential nutraceuticals in the prevention of human melanoma cancer (28).

- The anticancer potential of the methanolic and aqueous extracts of different parts of *Anastatica hierochuntica* (seeds, stems and leaves) were assessed and explored their mechanisms of action using the human breast cancer cell line, MCF-7. The results indicate that the methanolic and aqueous extracts decreased MCF-7 cell viability in a dose-dependent manner. The aqueous and methanolic extracts of *A. hierochuntica* plant parts exerting antiproliferative effects through the induction of apoptosis in breast cancer MCF-7 cells. The aqueous seed and the methanolic leaves extracts were the most promising natural-based drugs for the treatment of breast cancer (29).
- The aqueous extracts of *Anastatica hierochuntica* L. (AHAE) were evaluated for mutagenic potential via in vitro and in vivo assays. The in vitro bacterial reverse mutation assay demonstrates that AHAE is mutagenic at 0.04 and 0.2 mg/ml., either through base-pair substitution or frameshift mutation in the bacteria. However, further evaluation of the mutagenic potential through in vivo mammalian erythrocyte micronucleus testing demonstrated that up to 2000 mg/kg of AHAE did not induce significant mutagenicity in rats. Although the in vivo results were negative, it does not represent a definite absence of mutagenic potential of AHAE in vivo at higher doses. Chronic in vivo toxicity studies may be required to draw pertinent conclusion on the safety aspect of *A. hierochuntica* aqueous extracts consumption (30).
- The aqueous extract of *Anastatica hierochuntica* L. was investigate for its effect on the cancer cell lines AMN-3. Twelve concentrations (0.04, 0.09, 0.195, 0.39, 0.78, 1.56, 3.125, 6.25, 12.5, 25, 50, 100) mg/mL were investigated for the anticancer activity against AMN-3 cell line in comparison with negative control. The aqueous extract of the plant *Anastatica hierochuntica* is effective in inhibiting the growth of cancer cells as well as its importance in the treatment of other diseases (31).
- The present research highlights the chemical composition and properties of A. hierochuntica L. that may be related to its beneficial effect. The plant was found to be a rich source of Mg, Ca, Mn, and phenolic compounds, and had potential antioxidant and free radical scavenging activities. The findings of the study indicated that the chemical properties of the plant may rationalize its use for the treatment of menstrual cramps, asthma, depression, headache, fatigue, depression, high blood pressure, and infertility problems, and to ease childbirth, as it is used in traditional medicine (32).

16. Additional Information

-

17. Date of compilation/last revision

13/10/2022.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Fahem, A. A., Ibrahim A. E. and Abdel-Fattah M. R. (2017). *Anastatica hierochuntica* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **2**, 193-208. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Saleh, J. and Machado, L. (2012). Rose of Jericho: a word of caution. *Oman Med. J.*, **27**, 338.
5	Heny, A., Budi, S. and Mangestuti, A. b. (2019). In silico study of Rumput Fatimah (*Anastatica hierochuntica* L.) estrogenic activities and its potential as phytoestrogens. *Drug Invention Today*, **11**(8).
6	Khalifa, T. I. and Ahmed, M. A. (1980). A pharmacognostic study of certain species of *Anastatica*. Ph. D. Thesis, Fac. Pharm., Cairo Univ.
7	Rizk, A. M. (1986). The Phytochemistry of the Flora of Qatar. Kingprint of Richmond, U. K., on behalf of the Scientific and Applied Research Centre, Qatar Univ., Doha, Qatar.
8	Rizk, A. M., Hammouda, F. M., Ismail, S. I., Hassan, N. M. and Ahmed, F. A. (1993). Constituents of plants growing in Qatar XX. Phytochemical investigation of *Anastatica hierochuntica*. *Int. J. Pharmacog.*, **31**(4), 327-329.
9	Nakashima, S., Matsuda, H., Oda, Y., Nakamura, S., Xu, F. and Yoshikawa, M. (2010). Melanogenesis inhibitors from the desert plant *Anastatica hierochuntica* in B16 melanoma cells. *Bioorg. Med. Chem.*, **18**(6), 2337-2345.
10	Marzouk, M. M., Al-Nowaihi, A. S. M., Kawashty, S. A. and Saleh, N. A. M. (2010). Chemosystematic studies on certain species of the family Brassicaceae (Cruciferae) in Egypt. *Biochem. Syst. Ecol.*, **38**(4), 680-685.
11	Al-Gamdi, N., Mullen, W. and Crozier, A. (2011). Tea prepared from *Anastatica hirerochuntica* seeds contains a diversity of antioxidant flavonoids, chlorogenic acids and phenolic compounds. *Phytochemistry*, **72**(2-3), 248-254.
12	Yoshikawa, M., Xu, F., Morikawa, T., Ninomiya, K. and Matsuda, H. (2003). Anastatins A and B, new skeletal flavonoids with hepato-protective activities from the desert plant *Anastatica hierochuntica. Bioorg. Med. Chem. Lett.*, **13**(6), 1045-1049.
13	Abd El-Gaber, A. S., El Gendy, A. G., Elkhateeb, A., Saleh, I. A. and El-Seedi, H. E. (2018). Microwave extraction of essential oil from *Anastatica hierochuntica* (L): Comparison with conventional hydro-distillation and steam distillation. *TEOP,* **21**(4), 1003–1010.
14	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.

15	Heny, A., Budi, S. and Mangestuti, A. (2019). The effect of *Anastatica hierochuntica* L. extract on the histology of myometrial cells and prostaglandin levels (PGE2, PGF2α) in pregnant mice. *Advances in Health Sciences Research*, **22**, 4th International Symposium on Health Research (ISHR), 81-86.
16	Heny, A., Budi, S. and Mangestuti, A. b. (2019). In silico study of Rumput Fatimah (*Anastatica hierochuntica* L.) estrogenic activities and its potential as phytoestrogens. *Drug Invention Today*, **11**(8), 1964-1970.
17	Alatshan, E. Q., Wedyan, M., Bseiso, Y., Elham, A., Rihan, B. and Alkhateeb, H (2018). Antinociceptive and antiinflammatory activities of *Anastatica hierochuntica* and possible mechanism of action. *Indian J. Pharm. Sci.*, **80**(4), 637-646.
18	Siti, R. M. Z., Normadiah, M., Kassim, Zahurin, M., Abdulmannan H. F., Mohammed A. A. (2019). Potential toxicity effects of *Anastatica hierochuntica* aqueous extract on prenatal development of Sprague-Dawley rats. *Journal of Ethnopharmacology*, **245**, 112180, doi.org/10.1016/j.jep.2019.112180.
19	Bushra, H. A., Rajaa, K. B., Taghreed U. M. and Huda A. H. (2014). *Anastatica hierochuntica* L. used as an alternative of conjugated estrogen (Premarin) in rabbit females. *Journal of Advances in Chemistry*, **9**(1), 1783-1786.
20	Baker, R. K., Mohammd, U. T., Ali, H. B., Jameel, M. N. (2013). The effect of aqueous extract of *Anastatica hierochuntica* on some hormones in mouse females. *Ibn Al-Haitham Jour. for Pure & Appl. Sci.*, **26** (2), 198-205.
21	Rasheed, R. A., Bashir, A. K., and Ali, B. H. (1997). Fetal toxicity of *Anastatica hierochuntica* L. in mice. *FASEB Journal*, **11**(3), A417.
22	Hasan, F. A. (2011). Anti-hepatotoxic effect of the methanolic *Anstatica hierochuntica* extract in CCl 4- treated rats. *Eng. & Tech. Journal*, **29**(2), 413-423.
23	Arif, H. S., Bhandari, M. P., Naif, O. A. and Riyadh, M. A. (2014). Kaff-E-Maryam (*Anastatica hierochuntica* L.): Evaluation of gastro-protective activity and toxicity in different eExperimental models. *Biology and Medicine*, **6**(1), 197. doi: 10.4172/0974-8369.1000197.
24	Asal, A. T. (2016). Histological effects of *Anastatica hierochuntica* aqueous extract in female mice livers. *The Pharmaceutical and Chemical Journal*, **3**(3), 31-37.
25	Arwa, H. M., AL-Saeed and Newres, N. J. (2013). Chemical content and antibacterial activity of some extracts of *Anastatica hierochuntica* leaves. *J. Thi-Qar Sci.*, **4**(1), 84-90.
26	Zaynab, E., Salim, M. A., Yasmin, A. M. S., Reem, A. and Yasser, B. K. (2022). *Anastatica hierochuntica* extracts: Promising, safe and selective anticancer agents. *The Natural Products Journal,* **12**(1), 78-87.
27	Tariq, I. A.,Yousef, M. A., Hassan, A. A. and Hassan, B. (2021). Antioxidant activity, phenolic profile, and nephroprotective potential of *Anastatica hierochuntica* ethanolic and aqueous extracts against CCl_4-induced nephrotoxicity in rats. *Nutrients*, **13**(9), 2973.
28	Mustafa, G. M. and Gulerbc, E. A. (2021). *Anastatica hierochuntica* extract exacerbates genotoxic, cytotoxic, apoptotic and oxidant effects in B16F10 melanoma cells. *Toxicon*, **198**, 73-79.

29	Rameshbabu, S., Messaoudi, S. A., Alehaideb, Z. I., Ali, M. S., Venktraman, A., Alajmi, H., Al-Eidi, H. and Matou-Nasri, S. (2020). *Anastatica hierochuntica* L. methanolic and aqueous extracts exert antiproliferative effects through the induction of apoptosis in MCF-7 breast cancer cells. *Saudi Pharmaceutical Journal*, **28**, 985–993.
30	Siti, R. Zin, M. d., Mohamed, Z., Alshawsh, M. A., Wong, F. W. and Kassim, M. N. (2018). Mutagenicity evaluation of *Anastatica hierochuntica* L. aqueous extract *in vitro* and *in vivo*. *Experimental Biology and Medicine*, **243**(4), 375–385.
31	Mohammd, T. U., Baker, R. K., Al-Ameri, K. A. H. and Abd-Ulrazzaq, S. S. (2015). Cytotoxic effect of aqueous extract of *Anastatica hierochuntica* L. on AMN-3 cell line *in vitro*. *Advances in Life Science and Technology*, **31**, 59-64.
32	Ihsanullah, D. (2012). Chemical properties of the medicinal herb Kaff Maryam (*Anastatica hierochuntica* L.) and its relation to folk medicine use. *African Journal of Microbiology Research*, **6**(23), 5048-5051.

Egyptian Herbal Monograph

Traditional Wild Medicinal Plants

***Artemisia judaica* L.** شيح

1. Names & Synonyms

***Artemisia judaica* L.** (1, 2).

Family: Compositae (Asteraceae) (3).

Arabic: Sheeh شيح (3).

English: Judean wormwood, Wormwood (1).

2. Geographical distribution

Mediterranean region, all the deserts including Sinai, Red Sea coastal strip, Gebel Elba and the surrounding mountainous region (3).

3. Parts used for medicinal purposes

Leaves (3) and the aerial parts collected during the flowering stage (1).

4. Major chemical constituents (3)

-Volatile oil:

North Coast plant sample (1.4±0.05 g/100 g fresh leaves):

Piperitone (45.0%), *trans*-ethyl cinnamate (20.8%) and ethyl-3-phenyl propionate (11.0%) were the predominant components, followed by spathulenol (6.27%), *cis*-ethyl cinnamate (5.64%), 2,6-dimethyl phenole (1.39%) and methyl cinnamate (1.06%) (4).

Sinai Peninsula plant sample (0.7% (w/w)):

The major components of the essential oil were piperitone (32.4%), camphor (20.6%), *trans*-ethyl cinnamate (8.2%) and terpinene-4-ol (4.6%). The essential oil of *A. judaica* L. is rich in monoterpenoids and ester of cinnamic acid (5).

The difference in the volatile oil content of *A. judaica* were found to be due to several factors such as plant age, season, different parts of the plant and also differences found in the samples which were collected from different place (6,7).

- Sesquiterpene Lactones: The bitter principle judaicin, 1-epi-erivanin, 1-epi-isoerivanin, 13-O desacetyl eudesma afraglaucolide, 13-O-desacetyl-1α-

hydroxyafraglaucolide, 13-O-desacetyl-1β-hydroxyafraglaucolide, 13-O-desacetyl-1α-hydroxyisoafraglaucolide and seco-isoerivanin pseudo acid (8).

- Flavonoid glycosides: 7-glucoside, 7-glucuronide, 4′-glucoside, 7-gentiobioside, 7-diglucuronide, 7-rutinoside of apigenin and chrysoeriol; the 7,3′-diglucoside of chrysoeriol; the 3′-glucoside, 4′-glucoside; 7-gentiobioside; 7,3′- diglucoside of luteolin; as well as the C-glycosides vicenin-2, schaftoside, isoschaftoside, neoschaftoside and neoisoschaftoside **in addition to aglycones** such as casticin, apigenin, acacetin, hispidulin, pectolinarigenin, cirsimaritin, luteolin, chrysoeriol, jaceosidin, eupatilin, cirsilineol and 5,7,3′-trihydroxy-4′,5′-trimethoxyflavon (9,10).

The 70% ethanolic extract of *A. judiaca* has a total phenolic content of 83.5±7.1mg gallic acid equivalent/g and a total flavonoidal content of 63.1±8.6mg quercetin equivalent/g (11).

5. Traditional medicinal uses (3)

A. **Oral**: Anthelmintic, stomachic, expectorant, diaphoretic, analgesic, and antispasmodic in case of intestinal colic.

B. **Inhalation**: Relieve cold congestion.

A. ***judaica* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use

1. **Infusion** (1,3):

   Pour freshly boiled water on 2 teaspoonful of the herb in a cup, cover the cup with the lid and let infuse for 5 minutes. Drink it sweetened if desired (12).

2. **Inhaled leaves** (1, 3).

7. Posology and method of administration correlated to medicinal use

Preparation 1
Indication A
Average daily dose: 3 cups/ day (12).

Method of administration: Oral use.

Preparation 2
Indication B
Method of administration: Inhalation.

Duration of use:
If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

- None reported.
- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- None reported.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

14. Overdose

No case of overdose has been reported.

15. Relevant biological activities

- The protective effect of oral administration of *A. judaica* extract (70% alcoholic extract) (300mg/kg and treated daily for 28 days) against hepatorenal damage in a high-fat diet/streptozotocin (HFD/STZ) rat model of hyperlipidemia and hyperglycemia was investigated. The results illustrated the antihyperglycemic, antihyperlipidemic, antioxidant, anti-inflammatory, and antiapoptotic activities of the plant extract against hepatorenal injury in HFD/STZ-induced diabetes Histopathological screening confirmed the biochemical findings (11).

- Toxicological and pharmacological studies were carried out on the water and alcoholic extracts of *Artemisia judaica* (*A. judaica*) plant. Results obtained revealed that no mortalities in mice following oral administration of aqueous extract of *A. judaica* up 50 to 5g/kg, while in the alcoholic extract the LD was 9.17g/kg. Single and multiple doses (0.25 and 0.5 g/kg b.wt.) for the water extract, (0.5 and 1 g/kg b.wt.) for the alcoholic extract produced insignificant effect on serum cholesterol levels but there was significant decrease in serum triglycerides levels. The single and multiple doses of both water and alcoholic extracts significantly reduced the blood glucose level in experimentally diabetic rats while no significant effect was shown on normal rats (13).
- Volatile oil prepared from flowering branches has insecticidal, anthelmintic, anti - inflammatory, analgesic, anti-pyretic and stimulant effects (14, 15).
- The hydro-methanolic extract obtained from aerial parts of *A. judaica* (AJ-HA) was investigated for its potential to inhibit key blood sugar modulating enzymes in vitro and its antioxidant activity with phytochemical composition. AJ-HA was tested for in vitro hypoglycemic effect by its potential to inhibit pancreatic α-amylase, intestinal α-glucosidase and dipeptidyl peptidase IV (DPP IV). Antioxidant activity was determined by assessing the potential of the extract through scavenging of 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals.54. Quantitative phytochemical evaluation was performed by determining the total content of phenolics, saponins, flavonoids, tannins and alkaloids. Interestingly the extract showed inhibitory potential for all the three key enzymes that are involved in modulating the blood glucose levels namely: α-amylase, α-glucosidase and DPP IV with IC50s in the range of 758.96–2447.40 µg/mL. AJ-HA also showed significant scavenging activity for DPPH radicals with IC50 of 85.89 µg/mL. Quantitative estimations confirmed the abundance of various phytochemical classes particularly saponins and tannins (16).
- The ethanol extracts of *A. judaica* was evaluated for its efficacy against a protozoan parasite (*Blastocystis*). Two different molecular subtypes of *Blastocystis* were used. Significant growth inhibition of *Blastocystis* was observed when exposed to *A. judaica* (99.3%) with minimal inhibitory concentration (MIC_{90}) at 2000 µg/mL. Under the effect of the extract, changes in *Blastocystis* morphology were noted, with the complete destruction of *Blastocystis* forms after 72 h with the dose of 4000 µg/ml (17).
- The analgesic, hepatoprotective, antidiabetic and antioxidant activities of 80% aqueous methanol extract (AME) of Artemisia Judaica aerial parts were investigated. Analgesic activity was evaluated using acetic acid induced writhing in mice; antipyretic activity was assessed using yeast suspension- induced hyperthermia in rats; anti-inflammatory activity was evaluated using carrageenan-induced paw edema; antidiabetic activity was estimated in alloxan hyperglycemia while hepatoprotective effect was studied by measuring liver enzymes in CCI4-

induced hepatotoxicity rats and antioxidant activities. The results indicated that AME was nontoxic; it exhibits significant analgesic, antipyretic, anti-inflammatory, antidiabetic, hepatoprotective and antioxidant activities in a dose- dependent manner (18).

- The antimicrobial activity of methanolic extracts of *Artemisia Judaica* plant against Staphylococcus aureus Sp. and others pathogenic bacteria, was evaluated in vitro. These bacteria are commonly found in hospital-acquired infections. The methanolic extract of Artemisia Judaica effective against the isolates microorganisms, S. aureus, E. coli, P. aeruginosa, the diameter of zone of inhibition was found to be in the range of 14 – 30 mm against various bacterial strains tested, with maximum diameter against bacteria (S. aureus, 30 mm). The methanolic extract of Artemisia Judaica presented the highest anti-staphylococcus aureus activity and was effective against others bacterial strains tested (19).
- The *in vitro* cytotoxic activity of *A. judaica* ethanolic extract was screened against a panel of cancer cell lines. The results revealed its cytotoxic activity against a lung cancer (A549) cell line with a promising IC50 of 14.2 µg/mL compared to doxorubicin as a standard. This was confirmed through the downregulation of antiapoptotic genes, the upregulation of proapoptotic genes, and the cell cycle arrest at the G2/M phase. Further in vivo study showed that a solid tumor mass was significantly reduced, with a tumor inhibition ratio of 54% relative to doxorubicin therapy in a Xenograft model. *A. judaica* is a fruitful source of polyphenols that are well-known for their antioxidant and cytotoxic activities. Herein, *A. judaica* L. may serve as an adjuvant therapy or a promising source of leading structures in drug discovery for lung cancer treatment (20).
- *Artemisia judaica* (ArJ) essential oil constituents and their wound healing activity were studied. The *in vitro* antioxidant and antibiofilm activities of ArJ essential oil as well as the *in vivo* pro/anti-inflammatory and oxidative/antioxidant markers were investigated. The ArJ results demonstrated potent wound healing effects, comparable to silver sulfadiazine (SS), attributable to antioxidant and anti-inflammatory effects as well as a high proportion of oxygenated monoterpenes and cinnamate derivatives (21).

16. Additional information

-

17. Date of compilation/last revision

13/10/2022.

References

1	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
2	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
3	Hammouda, F. M. and Abou-Setta, L. M. (2017). *Artemisia judaica* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **2**, 313-328. Academy of Scientific Research and Technology, Cairo, Egypt.
4	EL-Massry, K. F. EL-Ghorab, A. H. and Farouk, A. (2002). Antioxidant activity and volatile components of Egyptian *Artemisia judica* L. *Food chem.*, **79**, 331-336.
5	Abd-Elhady, H. K. (2012). Insecticidal activity And chemical composition of essential oil from *Artemisia judaica* L. against *Callosobruchus maculatus* (F.) (Coleoptera: Bruchidae). *Journal Of Plant Protection Research*, **52**(3), 347-352.
6	Karawya, M. S., Hifnawy, M. S., El-Hawary, S. S. (1979): A contribution to the study of the volatile oil of *Artemisia judaica* L. growing in Egypt. *Egyptian Journal of Pharmaceutical Science*, **20**(1– 4), 147–152.
7	Ravid, U., Putievsky, E., Katzir, I., Carmeli, D., Eshel, A., Schenk, H. P. (1992). The essential oil of *Artemisia judaica* L. chemotypes. *Flavour and Fragrance Journal*, **7**(2), 69–72.
8	Khafagy, S. M., Seif El-din, A. A., Jakupovic, J. J. (1988). Glaucolide-like sesquiterpene lactones from *Artemisia Judaica*, *Phytochemistry*, **27**(4), 1125-1128.
9	Saleh, N. A., EL-Negoumy, S. A. and Abo-Zaid, M. M. (1987). Flavonoids of *Artemisia judaica*, *A. monosperma* and *A. herba alba*. *Phytochemistry*, **26**(11), 3059-3064.
10	Rizk, A. M., Ahmed, F. A., Elgendy, H. A. and Farag, S. H. (2017). Compositae, in "Phytochemistry of the Flora of Egypt (Chemical Constituents, Folk Medicine, Pharmacological and Biological Activities", Vol. **5**, (Rizk, A. M., editor), Misr University for Science & Technology, 6th of October City, Egypt.
11	Albasher, G., Alwahaibi, M., Abdel-Daim, M. M., Alkahtani, S. and Almeer, A. (2020). Protective effects of *Artemisia judaica* extract compared to metformin against hepatorenal injury in high-fat diet/streptozotocine-induced diabetic rats. *Environ. Sci. Pollut. Res. Int.*, **27**(32), 40525-40536. doi: 10.1007/s11356-020-09997-2.
12	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
13	Nofal S. M., Mahmoud S. S., Ramadan A., Soliman G. A. and Fawzy R. (2009). Anti-diabetic effect of *Artemisia judaica* extracts. *Res. J. Medicine and Medical Sci.*, **4**(1), 42-48.
14	Soliman, R. A. (1995). Some Pharmacological Studies of Certain Medicinal Plants. M.Sc. Thesis, Cairo University, Cairo.
15	Abad, M., Bedoya, L., Apaza, L. and Bermejo, P. (2012). The *Artemisia* L. genus: a review of bioactive essential oils. *Molecules*, 17(3), 2542-2566.

16	Bhat, S. H., Ullah, M. F. and Abu-Duhier, F. M. (2019). Bioactive extract of *Artemisia judaica* causes *in vitro* inhibition of dipeptidyl peptidase IV and pancreatic/intestinal enzymes of the carbohydrate absorption cascade: implication for antidiabetic new molecular entities (NMEs). *Oriental Pharmacy and Experimental Medicine*, **19**, 71–80.
17	Mokhtar, A. B., Ahmed, S. A., Eltamany, E. E. and Karanis, P. (2019). Anti-blastocystis activity *in Vitro* of Egyptian herbal extracts (Family: Asteraceae) with emphasis on *Artemisia judaica. Int. J. Environ. Res.,* **16**(9), 1555. doi: 10.3390/ijerph16091555.
18	Moharram, F. and El Hosari, D. G. (2021). Pharmacological activity and flavonoids constituents of *Artemisia judaica* L. aerial parts. *Journal of Ethnopharmacology,* **270**, 113777.
19	Marakhova, A. I. and Elmanakhly, M. E. (2022). A Study of active medicinal plant (*Artemisia Judaica*) against *Staphylococcus aureus J. Clinical Case Reports and Studies,* **5**(5)-092, 1-7.
20	Goda, M. S., Nafie, M. S., Awad, B. M., Abdel-Kader, M. S., Ibrahim, A. K., Badr, J. M. and Eltamany, E. E. (2021). Antioxidants Article *In Vitro* and *in Vivo* studies of anti-lung cancer activity of *Artemesia judaica* L. crude extract combined with LC-MS/MS metabolic profiling, docking simulation and HPLC-DAD quantification. *Antioxidants*, **11**(1), 17.
21	Mohammed, H. A., Qureshi, K. A., Ali, H. M., Al-Omar, M. S., Khan, O. and Salman, A. A. (2022). Bio-evaluation of the wound healing activity of *Artemisia judaica* L. as part of the plant's use in traditional medicine; phytochemical, antioxidant, anti-inflammatory and antibiofilm properties of the plant's essential oils. *Antioxidants*, **11**, 332. doi: 10.3390/antiox11020332.

Egyptian Herbal Monograph

Traditional Wild Medicinal Plants

Balanites aegyptiaca L. Delile هجليج

1. Names & Synonyms

***Balanites aegyptiaca* L. Delile**. (1).
Family: Zygophyllaceae (2).
Syn.: *Ximenia aegyptiaca* L. (1).
Arabic: Higleeg هجليج, Shaashoat & Balah Haraara (names used by the Halaib Triangle Community) شاشوت و بلح حرارة (الثمار) (2).
English: Thorn tree, Egyptian balsam, Zachum oil tree, Desert date, Soap berry bush (2, 3).

2. Geographical distribution

Distributed in most of the phytogeographical regions of Egypt except those of the Mediterranean and Red Sea coastal strips (2).

3. Parts used for medicinal purposes

- The fruit.

However, various parts of *B. aegyptiaca* have their own traditional medicinal properties worldwide (2).

4. Major chemical constituents

- **Fruits:** fruit pulp is a good source of sugars (33g/100g dry matter (DM), polyphenols (264mg GAE/100g DM) and flavonoids (34.2mg/100g DM). The fruit kernel is rich in lipids (46.2g/100g DM) and proteins (29.5g/ 100g DM) (4). However, saponins, referred to as balanitinis, remain by far the most reputed chemical constituents of the *B. aegyptiaca* fruit, representing 7.2% in the pulp and 6.7% in the kernel (5).
- **Other constituents in the fruits:** Alkaloids, flavonoids, tannins and vitamins (4).

The plant is reported to contain 5.6% diosgenin. Diosgenin is a type of sapogenin compound which have been isolated from seed, leaves and fruit of *B. aegyptiaca* (6).

5. Traditional medicinal uses

In Egyptian folk medicine, the fruits are used as oral antidiabetic drug (7, 4).
Worldwide, *B. aegyptica* has multiple applications with almost every part of the plant; It is traditionally used in treatment of various ailments *i.e.* jaundice, intestinal worm infection, wounds, malaria, syphilis, epilepsy, dysentery, constipation, diarrhea, hemorrhoid, stomach aches, asthma and fever (8).

***B. aegyptica* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use

1. Fleshy pulp of the fruit is eaten fresh or dried (9).
2. Lozenges, the fruits are sucked (10).
3. Decoction (10).

7. Posology and method of administration correlated to medicinal use

At this time there is not enough scientific information to determine an appropriate range of doses for *B. aegyptica*. The appropriate dose depends on several factors such as the user's age, weight, health and several other conditions.

Method of administration: Oral.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

- Monitoring of blood glucose level should be done regularly.
- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation

- Nothing was reported in Egyptian folk medicine about the effect of *B. aegyptiaca* in Fertility, pregnancy and lactation; while, in Sudanese folk medicine, macerated

fruit mixed with millet to make porridge given to women, after childbirth and during lactation, to give them energy, strength and to increase milk production (11).

- In the context of fertility and pregnancy; Studies have shown fertility effects of *B. aegyptiaca* and reported that the use should be avoided during pregnancy (8, 12).

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- None reported.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

14. Overdose

- No case of overdose has been reported.

15. Relevant biological activities

- Aqueous extract of fruits showed spermicidal activity without local vaginal irritation in human being, up to 4% sperms becoming sluggish on contact with the plant extract and then immobile within 30 s; the effect was concentration related. Protracted administration of the fruit pulp extract produced hyperglycemia induced testicular dysfunction in dogs (8).
- Oral administration of *B. aegyptiaca* mesocarp extract (259 mg/kg) and *B. aegyptiaca* crude saponin (90 mg/kg) to pregnant-rats for the first 10 days of pregnancy produced post-coital antifertility. In addition, *B. aegyptiaca* saponins produced regression effect on the size of the implants observed on day 11 of pregnancy upon laparotomy, as well as a delay of delivery for up to 23-26 days compared to control group (23days). Mortalities were observed within newborn (12).
- The aqueous extract of *B. aegypticea* has hypoglycemic properties. It can decrease the plasma glucose level and can improve weight in diabetic experimental animals. 800 mg/kg aqueous extract decreased significantly the plasma glucose level ($P \leq 0.05$) in diabetic rats, and there is a considerable gain in body weight ($P \leq 0.05$) compared to the diabetic control group. 400mg/kg aqueous extract has a mild effect on body weights and plasma glucose levels, while 200 mg/kg aqueous extract has no significant effect on plasma glucose level and a little effect on body weight (13).

- The whole and extracted pulp of *B. aegyptiaca* fruits were reported to exhibite a hypocholesterolemic effect when tested on adult albino rats (14).
- The methanol extract of the pulp was found to exhibit anti-dermatophytic activity on *Microsporum gypseum* and *Trichophyton rubrum* (15).
- Hard gelatin capsules (400 mg/day) were tested on 30 type 2 diabetes (T2D) Egyptian patients for 8 weeks. According to sex, age and body mass index participants were divided into two equivalent groups, placebo and treatment. At the end of the 8-week treatment, the treated group showed 26.88% decrease in 2 h postprandial plasma glucose relative to 2.6% increase in the placebo group, while fasting plasma glucose was reduced to 10.3%. Treatment with BE capsules for 8 weeks produced significant reduction in the plasma triglyceride, total cholesterol and low-density lipoprotein cholesterol by 9.0, 12.76 and 21.35%, respectively, with 29.8% increase in the high-density lipoprotein cholesterol. Plasma alanine transaminase and aspartate transaminase were reduced by 42.6 and 43.3%, respectively (16).
- The potential antidiabetic and antioxidant impact of *B. aegypticea* fruits water extract (1.5 g/kg BW daily for 45 days) on streptozotocin-induced diabetic and normal rats were evaluated. The influences of the extract on body weight, plasma glucose, insulin, total antioxidant capacity (TAC), malondialdehyde (MDA) levels, and liver-pyruvate kinase (L-PK) levels were assessed. Furthermore, the weight and histomorphological changes of the pancreas were studied in the different experimental groups. The herbal preparation significantly reduced the mean plasma glucose and MDA levels and significantly increased the mean plasma insulin, L-PK, and TAC levels in the treated diabetic groups compared to the diabetic control group. An obvious increase in the weight of the pancreas and the size of the islets of Langerhans and improvement in the histoarchitecture were evident in the treated groups compared to untreated ones. In conclusion, the study provides scientific evidence for the traditional use of the extracts as antidiabetic and antioxidant agents in type 1 diabetes mellitus (17).
- *B. aegyptiaca* fruits as herbal tea showed hypoglycemic, anti-hyperlipidemic, and antioxidant effect in streptozotocin-induced diabetes mellitus in rats. Moreover, ameliorated liver and kidney functions associated with diabetes mellitus. All the different concentrations of *B. aegyptiaca* fruits tea (0.25, 0.5, and 1.0%) improved biomarker parameters compared to diabetic control and some biochemical parameters return to normal value. The most efficient concentration of *B. aegyptiaca* fruits tea was 1.0 g/100 ml. This makes *B. aegyptiaca* fruits applicable health product for treatment of diabetes mellitus (18).
- The saponin rich fraction of the butanol extract of *B. aegyptiaca* fruits showed significant aldose reductase inhibitory activity. These findings are of significant importance, because furostanol saponins have rarely been previously reported to

display aldose reductase inhibitory activity. Five new furostanol saponin derivatives isolated from fraction showed substantially higher activities than the crude butanolic extract and were highly active compared to the reference compound, quercetin. These isolated compounds may represent promising lead structures for novel or alaldose reductase drug development, depending on their bioavailability and safety profiles, which will be tested in appropriate future *in-vivo* and clinical studies. The findings for *Trigonella foenumgraeceum*, however, indicate that the furostanol saponins isolated from *B.aegyptiaca* may have more than one potential mechanism of action contributing to the antidiabetic activity, and that further studies on the disaccharidase and glycogen enzymatic activity modulation would be useful (19).

- The effect of fruit fleshes crude extract (70% ethanol), butanol, and dichloromethane fractions from *B. aegypticea* (50 mg/kg BW for one month) on the stress-activated protein kinase/c-Jun N-terminal kinase (SAPK-JNK) pathway in experimental diabetic rats was evaluated. The results suggested a protective role of treatment of diabetic rats with *B. aegypticea* against oxidative stress-induced SAPK-JNK pathway. Moreover, *B. aegypticea* treatment produced a reduction in plasma glucose, HbA1c, lactic acid, lipid profile, malondialdehyde levels and produced an increase in insulin. Reduction in glutathione levels, catalase and superoxide dismutase activities were observed compared with untreated diabetic rats. Moreover, it decreased apoptosis signal-regulating kinase 1, c-Jun N-terminal kinase 1, protein 53 and increased insulin receptor substrate 1 in rat pancreas while it increased glucose transporter 4 in rat muscle. In conclusion, *B. aegypticea* exerted hypoglycemic, hypolipidemic, insulinotropic and antioxidant effects. Additionally, it reduced apoptosis in pancreatic β-cells and increased glucose uptake in muscle. These results suggest that the hypoglycemic effect of *B. aegypticea* is due to the inhibition of the SAPK-JNK pathway (20).
- Oral administration of *Balanites* extract (1.5 g/kg) to STZ diabetic rats significantly reduced blood glucose level by 24% after 21 days of treatment. However, *Balanites*, under the conditions of the experiment, did not significantly affect the reduced serum insulin level of diabetic rats (21).
- Alcoholic extracts of fruit of an endangered medicinal plant *Balanites aegyptiaca* and its in vitro raised calli were analyzed for antimicrobial potential against various Gram positive and Gram- negative bacteria including those harbouring blagenes by agar well diffusion method. The alcoholic extract of parent plant as well as its callus showed good antibacterial activity against both Gram- positive and Gram-negative bacteria. Minimum inhibitory concentrations (MIC) of the extracts were determined by broth microdilution method. MIC against Gram positive bacteria ranged from 3.05 to 24.0 µg/ml, while MIC against Gram negative bacteria ranged from 1.53 to 49.0 µg/ml and MIC against resistant bacteria. harbouring blagenes ranged from 12.0 to 49.0 µg/ml. The present study shows that

extracts of *B. aegyptiaca* contain good antibacterial activity which can be used in the treatment of various infectious diseases. As its calli also gave good results (22).

- The antibacterial activity of the *Balanites aegyptica* oil at different concentrations on *staphylococcus aureus* and *Escherichia coli* bacteria and different meters in diameter of the zones was observed. The results shows significant effect of Balanites oil on bacteria by observing the presence of clear spaces known as the zone of inhibitions in the experiments (23).
- The Balanites aegyptiaca fruits are eaten by humans and animals and have many benefits. The fruits of the desert date contain oil, protein, sugar, vitamins, mineral salts, soap, and diosgenin. The oil is used in the cosmetic industry and is also used in the treatment of rheumatism, as well as some diseases that affect the reproductive system, sex hormones, infertility, and fertility diseases. Many scientific reports *Balanites aegyptiaca* mention the biological activities antioxidant, anticancer, antimicrobial, insecticidal activities of balanite kernel oil (24).

16. Additional information

-

17. Date of compilation/last revision

13/10/2022.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Mohamed A, El-Shanawany (2017). *Balanites aegyptiaca* (L.) Del. In: Egyptian Encyclopedia of Wild Medicinal Plants, **3**, 212-234. Academy of Scientific Research and Technology, Cairo, Egypt.
3	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
4	Abdelaziz, S. M., Lemine, F. M. M., Tfeil, H. O., Filali-Maltouf, A. and Boukhary, A. O. M. S. (2020). Phytochemicals, antioxidant activity and ethnobotanical uses of *Balanites aegyptiaca* (L.) Del. fruits from the arid zone of Mauritania, Northwest Africa. *Plants*, **9**, 401.
5	Yadav, J. P. and Panghal, M. (2010). *Balanites aegyptiaca* (L.) Del. (Hingot): A review of its traditional uses, phytochemistry and pharmacological properties. *Int. J. Green Pharm.*, **4**, 140–146.
6	Hammouda, F. M., Ismail, S. I., Abdel-Azim, N. S. and Shams, K. A. (2005). A Guide to Medicinal Plants in North Africa (Batanouny K. H., editor). IUCN Centre for Mediterranean Cooperation. Malaga.
7	Kamel, M. S. (1998). A furostanol saponin from fruits of *Balanites aegyptiaca*. *Phytochemistry*, **48**(4), 755-757.
8	Chothani, D. L. and Vaghasiya, H. U. (2011). A review on *Balanites aegyptiaca* Del (desert date): phytochemical constituents, traditional uses, and pharmacological activity. *Pharmacog. Rev.*, **5**(9), 55-62.
9	Tesfaye, A. (2015). Balanites (*Balanites aegyptiaca*) Del., multipurpose tree a prospective review. *International Journal of Modern Chemistry and Applied Science*, **2**(3), 189-194.
10	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
11	Abdelmuti, O. M. S. (1991). Biochemical and nutritional evaluation of famine foods of the Sudan. Ph.D. Thesis, Faculty of Agriculture-Khartoum: University of Khartoum, Sudan.
12	Babiker, M. N. E. (1988). Pharmacological and Phytochemical Studies on *Balanites aegyptiaca* Fruits. M.Sc. Thesis. University of Khartoum, Sudan.
13	Baragob, A. E. A., AlMalki, W. H., Shahid, I., Bakhdhar, F. A., Bafhaid, H. S. and Eldeen, O. M. I. (2014). The hypoglycemic effect of the aqueous extract of the fruits of *Balanites aegypticea* in alloxan-induced diabetic rats. *Pharmacogn. Res.*, **6**(1), 1-5.
14	Abdel-Rahim, E. A.; El-Saadany, S. S. and Wasif, M. M. (1986). Biochemical dynamics of hypocholesterolemic action of *Balanites aegyptiaca* fruit. *Food Chem.*, **20**, 69–78.
15	Hussain, S. A. M.; Velusamy, S. and Muthusamy, J. (2019). *Balanites aegyptiaca* (L.) Del. for dermatophytoses: Ascertaining the efficacy and mode of action through experimental and computational approaches. *Inform. Med. Unlocked*, **15**, 100177.

16	Rashad, H., Metwally, F. M., Ezzat, S. M., Salama, M. M., Hasheesh, A. and Abdel-Motaal, A. (2017). Randomized double-blinded pilot clinical study of the antidiabetic activity of *Balanites aegyptiaca* and UPLC-ESI-MS/MS identification of its metabolites. *Pharmaceutical Biology*, **55**(1), 1954–1961.
17	Abou Khalil, N. S., Abou-Elhamd, A. S., Wasfy, S. I. A., ElMileegy, I. H., Hamed, M. Y. and Ageely, H. M. (2016). Antidiabetic and antioxidant impacts of desert date (*Balanites aegyptiaca*) and parsley (*Petroselinum sativum*) aqueous extracts: Lessons from experimental rats. *Journal of Diabetes Research*, **10**. doi: 10.1155/2016/8408326.
18	Ghanem, K. Z., Ghanem, H. Z., Ramadan, M. M. and Mabrok, H. B (2016). The effect of herbal tea from *Balanites aegyptiaca* fruits on streptozotocin-induced diabetes mellitus in rats. *International Journal of PharmTech Research CODEN (USA): IJPRIF*, **9**(10), 8–15.
19	Abdel Motaal, A., ElAskary, H., Crockett, S., Kunert, O., Sakr, B., Shaker, S., Grigore, A., Albulescu, R. and Bauer, R. (2015). Aldose reductase inhibition of a saponin- rich fraction and new furostanol saponin derivatives from *Balanites aegyptiaca. Phytomedicine*, **22**, 829–836.
20	Hassanina, K. M. A., Mahmoud, M. O., Hassan, H. M., Abdel-Razik, A. H., Aziz, L. N. and Rateb, M. E. (2018). *Balanites aegyptiaca* ameliorates insulin secretion and decreases pancreatic apoptosis in diabetic rats: Role of SAPK/JNK pathway. *Biomedicine & Pharmacotherapy*, **102**, 1084–1091.
21	Gad, M. Z., El-Sawalhi, M. M., Ismail M. F. and El-Tanbouly N. D. (2006). Biochemical study of the anti-diabetic action of the Egyptian plants Fenugreek and Balanites. *Molecular and Cellular Biochemistry,* **281**, 173–183.
22	Noor, J. N., Razia, K. R., Shahzad, A. and Mohammad, S. M. (2013). Antimicrobial activity of medicinal plant *Balanites aegyptiaca* Del. and its in vitro raised calli against resistant organisms especially those harbouring blagenes. *Journal of Medicinal Plants Research*, **7**(25), 1692-1698.
23	Khanam, S. and Galadima, Z. F. (2021). Antibacterial activity of *Balanites aegyptiaca* oil extract on *Staphylococcus aureus* and *Escherichia coli*. *Biorxiv Preprint,* doi: https://doi.org/10.1101/2021.03.23.436600.
24	Mariod, A. and Ismail, E. M. I. (2022). Biological activities of *Balanites aegyptiaca* (Heglig) kernel oil. In book. Multiple Biological Activities of Unconventional Seed Oils, **27**, 339-344.

Egyptian Herbal Monograph

Traditional wild medicinal plants

***Capparis spinosa* L.** كبار- لصف

1. Names & Synonyms (1-3)

***Capparis spinosa* L.**

Family: Capparaceae.

Arabic: Kabbar كبار, Lasaf لصف, Laisouf ليصوف.

English: Common caper-bush.

2. Geographical distribution (1-3)

Deserts, Oases, and Sinai (Saint Catherine).

Four varieties occur in Egypt (1,3):

1) Var. ***spinosa***
Syns. *Capparis aegyptia* Lam.

Capparis spinosa L. var. *aegyptia* Lam. Boiss.

The oases of the Western Desert, all the deserts of the country as well as the Sinai Peninsula.

2) Var. ***canescens*** Coss.
Syns. *Capparis ovata* Desf.

Capparis sicula Duh.

Capparis leucophylla DC.

The oases of the Western Desert as well as Desert east of the Nile including that of Sinai.

3) Var. ***inermis*** Turra.
Syns. *Capparis orientalis* Duh.

Capparis rupestris Sibth. & Sm.

Capparis spinosa L. var. rupestris (Sibth. & Sm).

Capparis spinosa L. subsp. orientalis (Duh.).

Confined to the maritime cliffs of the Mediterranean coastal strip.

4) Var*. **deserti*** Zohary*.*

Syn. *Capparis deserti* Zohary Tàckh. & Boulos, publ.

Desert west of the Nile (North of Siwa Oasis).

3. Parts used for medicinal purposes (3)

Capers (flower buds), Caper berries (fruits), roots, seeds and leaves.

4. Major chemical constituents (3)

- Alkaloids:

Capparisines A, B and C, and others (fruits) (4).

Tetrahydroquinoline acid (stems and fruits) (5).

Modified amino acid or alkaloid (fruits) (6).

Stachydrine and cadabicin (fruits, flowers and flower buds) (7).

Spermidine alkaloids; capparispine, capparispine 26-O-*β*-D-glucoside and cadabicine 26-O-*β*-D-glucoside hydrochloride (roots) (8).

- Flavonoids:

C. spinosa is considered as an economical source of quercetin and rutin.

Quercetin (buds) (9), and various derivatives of its glycosides (fruits and other parts of the plant) (10). The quercetin derivative aglycone, isorhamnetin and its rutinoside glycoside (Leaves and flower buds) (11).

kaempferol and its glycosides are minor constituents from the fruits and buds (12, 13).

Other flavonoids and various classes of flavonoid sub-groups are represented in *C. spinosa*: ginkgetin, isoginkgetin chrysoeriol, apigenin, flavanone derivative (Sakuranetin), flavones (twogonin and oroxylin A, thevetiaflavone) (12, 14-18).

-Glucosinolates:

Glucocapparin, glucoiperin, glucobrassicin, neoglucobrassicin and 4-methoxy-glucobrassicin (19, 20).

-Seeds Oil:

The major constituents are linoleic and oleic acids followed by palmitic and other fatty acids (21, 22).

Approximately 145 chemical substances have been identified. Among them are aldehydes, esters, sulfur containing compounds monoterpenes, capric acid and sesquiterpenes (23, 24).

- Essential Oil:

Essential oil extracted from leaves, fruits and roots; the major components are thymol, methyl isothiocyanate, isopropyl isothiocyanate, butyl isothiocyanate, 2-hexenal (25).

- Other chemical constituents: Saponin, phenolic acids along with butanedioic acid, uracil and uridine, pentosans, indols, *β*-sitosterol and its glycoside (fruits) (6, 7, 16, 26, 27), benzofuranone enantiomers (fruits and stem) (5), triterpene, (28), *β*-carotene, ascorbic acid, phytic acid and oxalic acid (fruits) (29, 30).

5. Traditional medicinal uses (31)

***Oral:**

A. Renal System Diseases: Renal disinfectant and Diuretic.

B. Gastrointestinal System Diseases

1. Cholera.
2. Diarrhea.
3. Astringent.
4. Carminative, appetizer, laxative, purgative and anthelmintic.
5. Scurvy.

C. Respiratory System Diseases

1. Cough.
2. Chest disorders.
3. Expectorant.

D. Improving the sexual power

E. Gynecological diseases:

1. Treat feminine sterility and dysmenorrhea.
2. Emmenagogue.

F. Sciatica& back pain

G. Others:

1. Snake bites.
2. Febrifuge.
3. Treatment of chills.
4. Stimulant and tonic.
5. Gout.

***External:**

H. Rheumatism.

I. Ulcers, ganglions and scrofula.

J. Spleen troubles.

***C. spinosa* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (31)

1) Oral decoction or infusion of different parts of the plant.

- **Infusion:**

Pour freshly boiled water on 2 teaspoonful of *C. spinosa* in a cup, cover the cup with the lid and infuse for 5 minutes. Drink it sweetened if desired.

- **Decoction:**

Pour cold water on 2 teaspoonful of *C. spinosa* and boil, simmer for 10 minutes. Pour into a cup and drink it sweetened if desired.

A. Flower buds and root.

B.

1. Decoction of leaves.
2. Infusion prepared from the stem and root bark.
3. Roots.
4. Leaves and fruits.
5. Root bark.
6. Fruits.

C.

1. Decoction of seeds.
2. - Decoction of leaves.
   - Bark.
3. Bark.

D.

1. Decoction of seeds.
2. Leaves and fruits.

E.

1. Seeds.
2. Root bark.

F.

- Infusion of fruits.
- Powdered fruits mixed with honey.

G.

1. Water extract of leaves.
2. Infusion prepared from the stem and root bark.
3. Flower buds and roots.
4. Flower buds.
5. Bark.

2) **Paste of root bark.**
3) **Crushed flower buds.**
4) **Cataplasm (poultice):**

Simmer the root bark for 2 minutes, squeeze out any excess liquid and apply it while hot. Bandage the herb securely in place using piece of cloth. Leave on for up to 3 hours, as required.

7. Posology and method of administration correlated to medicinal use (31)

Preparation 1
Indications A-G
- Drinking the decoction or infusion 3 cups/day.
- For snake bites: Leaves added to water and taken once.

***Method of administration:** Oral use.

Preparation 2

Indication H

Apply the paste of root bark on the area of the affected area 4 times/ day.

***Method of administration:** External use.

Preparation 3

Indication I

Flower buds are crushed and applied externally on the affected area.

***Method of administration:** External use.

Preparation 4

Indication J

Apply the cataplasm every 4 hours.

***Method of administration:** External use.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Monitoring of blood glucose level should be done regularly (32).

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation

- The use should be avoided during pregnancy (32).
- Safety during lactation has not been established. In the absence of sufficient data, the use during lactation is not recommended.
- It is traditionally used for improving the sexual power, as emmenagogue and to treat feminine sterility and dysmenorrhea (3, 31).

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

-If adverse reactions occur, a doctor or a pharmacist should be consulted.

-Topical use of *C. spinosa* may cause contact dermatitis (32).

14. Overdose

No case of overdose has been reported.

15. Relevant biological activities

- The aqueous extracts of the fresh leaves and flower buds of *Capparis spinosa* were assessed *in vitro* for their antioxidant potential effect and the anthelmintic efficacy. Both plant extracts (flower buds (IC50 = 2.76 mg/ml and leaves (IC50 = 8.54 mg/ml) showed ovicidal activity at all tested concentrations. The flower buds extract showed higher inhibitory effects than leaves extract in the egg hatching

assay as well as inhibition more worms. These results proved that *C. spinosa* possesses *in vitro* anthelmintic properties which may be related to its high content of phenolic compounds such as flavonoids and tannins (33).

- Different parts of caper were investigated for their antioxidant effects, potentially useful against some degenerative diseases (34).
- The effects of the hydroalcoholic extract of *Capparis spinosa* fruit, quercetin, and vitamin E on monosodium glutamate – induced toxicity in rats were compared. All chemicals were orally administered for 14 consecutive days. The histopathological and biochemical evaluations showed that *C. spinosa* fruit extract, quercetin and vitamin E can produce approximately similar protective effects on tissue function through oxidative stress alleviation and antioxidant mechanisms restoration (35).
- The anti-arthritic activity of *C. spinosa* L. (Capparidaceae) fruits different extracts was investigated on an arthritic rat model. The fraction eluted by ethanol/water (50:50, v/v) had the most significant anti-arthritic activity (36).
- The aqueous extract of the fruits of *C. spinosa* was evaluated for the anti-inflammatory activity in carrageenan induced paw edema in mice (37). Different fractions separated from the aqueous extract were orally administrated to male Chinese (KM) mice. The anti-inflammatory effects exhibited by these fractions were compared with those of indomethacin used as positive control. Some fractions at 50 and 250mg/kg at 6h after induction inhibited the edema in mice in a dose-dependent manner.
- Several flavonoids and bioflavonoids were isolated from the fruits of *C. spinosa* and evaluated for their effects on NF-kB activation through a secreted placental alkaline phosphatase reporter assay. The isolated biflavonoid ginkgetin showed strong inhibitory effects on NF-kB activation with an IC50 value of 7.5 μM (15).
- The ability of *C. spinosa* L. preparation to orientate, *in vivo*, the immune response mediated by CD4+ T-cells towards an anti-inflammatory response was assessed. The obtained data indicated that *C. spinosa* regulates inflammation induced in mice *in vivo* and thus could be a source of anti-inflammatory molecules, which could be used in some T lymphocyte-dependent inflammatory diseases (38).
- The methanolic extract obtained from the fruits of *C. spinosa* was assayed for antiquorum sensing activity in *Chromobacterium violaceum* and *P. aeruginosa,* and for antibiofilm formation in *E. coli*, *Proteus mirabilis*, *S. marcescens* and *P. aeruginosa* (39). The results conducted that the fruits of *C. spinosa* showed a promising potential to be exploited in the treatment of emerging infections of antibiotic resistant bacterial pathogens.
- Caper was studied as a possible enhancer of bone regeneration (40). Ethanolic extract of *Caper* buds was administered at 20mg/kg b.w. to male Wistar albino rats, with maxillary incisions from applied springs. Results showed that the

administration of Caper extract accelerated osteoblastic activity in the early period.

- The methanolic extract of *C. spinosa* buds, rich in flavonoids such as quercetin and kaempferol derivatives, was proven to exert *in vitro* immunomodulatory effects in human peripheral blood mononuclear cells (23). In particular, the administration of extract inhibited the herpes simplex virus type 2.
- *In vitro* and *in vivo* studies on the methanolic extracts of leaves and fruits of *C. spinosa* confirmed the immunomodulatory activity (41). The methanolic extracts at 400μg/mL showed significant increases in the proliferation of cells in the presence of the mitogen concanavalin A (10μg/mL). In cyclophosphamide-treated and myelosuppressed Wistar mice, the administration of 100 and 200mg/kg b.w. of both methanolic extracts increased significantly the level of the total white blood cells.
- The relaxant effects of the aqueous extract of *C. spinosa* fruits were demonstrated on rat trachea in a dose dependent manner (42). Wistar rat trachea was excised and contracted with acetylcholine. At 1 and 10mg/mL the *Caper* fruit aqueous extract had a relaxant effect on acetylcholine precontracted trachea. On the other hand, leaf and seed extracts gave contractile effects (42). These results may be helpful in supporting the use of Caper extract in the treatment of asthmatic patients.
- The effects of *C. spinosa* as antihepatotoxic on rats against paracetamol and carbontetrachloride induced toxicity *in vivo* was evaluated, in addition to its effect on galactosamine and thioacetamide induced toxicities *in vitro*. The methanol soluble fraction of the aqueous extract of aerial parts of *C. spinosa* was reported to exhibit significant anti-hepatotoxic activity (27).
- Protective action of *C. spinosa* ethanolic root bark extract was evaluated in this study in an animal model of hepatotoxicity, which was induced by carbon tetrachloride. The results revealed that ethanolic root bark extract of *C. spinosa* could afford significant dose-dependent protection against CCl4 induced hepatocellular injury (43).
- Examination of the acute and sub-chronic toxicity of hydro-alcoholic extract of the *C. spinosa* on the liver, kidney, and serum enzymes were done. The doses of 200, 400 and 800mg/kg of hydro-alcoholic extract of *C. spinosa* were administrated by oral gavages for 28 consecutive days in mice. The results have shown that *C. spinosa* can cause nephrotoxicity and hepatotoxicity especially during sub-chronic consumption, dose-dependently. The extracts of *C. spinosa* must be used with caution especially in renal and liver pathologic conditions (44).
- The protective effects of the hydroalcoholic extract of *C. spinosa* L. on Cyclophosphamide-induced nephrotoxicity were evaluated. Different plant parts

(fruit, leaves, and petals) were examined for antioxidant activity by DPPH assay. The results indicate that *C. spinosa* extract ameliorates biochemical indices and oxidative stress parameters against Cyclophosphamide – induced nephrotoxicity (45).

- The antioxidant, nephroprotective and hepatoprotective effects of methanolic extract of *C. spinosa* leaves were studied. The methanolic extract showed interesting antioxidant capacity. This study supports the traditionally use of *C. spinosa* to cure kidney and liver diseases (46).
- *C. spinosa* L. has the potential to down regulate inflammation – involved genes in Alzheimer's disease (AD) due to its high levels of flavonoids and could be beneficial as a dietary complement in AD patients (47)

16. Additional Information

-

17. Date of compilation/last revision

06/08/2022.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Shams, K. A., Abdel-Azim, N. S. and Hamed, A. R. (2017). *Capparis Spinosa* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **4**, 319-350. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Yang, T., Wang, C. H., Chou, G. X., Wu, T., Cheng, X. M. and Wang, Z. T. (2010). New alkaloids from *Capparis spinosa*: structure and X-ray crystallographic analysis. *Food Chem*., **123**, 705-710.
5	Zhang, S., Hu, D. B., He, J. B., Guan, K. Y. and Zhu, H. J. (2014). A novel tetrahydroquinoline acid and a new racemic benzofuranone from *Capparis spinosa* L., a case study of absolute configuration determination using quantum methods. *Tetrahedron*, **70**, 869–873.
6	Fu, X., Aisa, H., Abdurahim, M., Yili, A., Aripova, S. and Tashkhodzhaev, B. (2007). Chemical composition of *Capparis spinosa* fruit. *Chem. Nat. Compd*., **43**, 181–183.
7	Gull, T., Anwar, F., Sultana, B., Alcayde, M. A. C. and Nouman, W. (2015). *Capparis* species: A potential source of bioactives and high-value components: A review. *Industrial Crops and Products*, **67**, 81-96.
8	Fu, X. P., Wu, T., Abdurahim, M., Su, Z., Hou, X. L., Aisia, H. A., and Wu, H. (2008). New spermidine alkaloids *from Capparis spinosa* roots. *Phytochem. Lett*., **1**, 59–62.
9	Rodrigo, M., Lazaro, M., Alvarruiz, A. and, Giner, V. (1992). Composition of capers (*Capparis spinosa*): influence of cultivar, size and harvest date. *J. Food Sci*., **57**, 1152–1154.
10	Sharaf, M., El-Ansari, M. and Saleh, N. (2000). Quercetin triglycoside from *Capparis spinosa*. *Fitoterapia*, **71**, 46–49.
11	Siracusa, L., Kulisic-Bilusic, T., Politeo, O., Krause, I., Dejanovic, B. and Ruberto, G. (2011). Phenolic composition and antioxidant activity of aqueous infusions from *Capparis spinosa* L. and *Crithmum maritimum* L. before and after submission to a two-step *in vitro* digestion model. *J. Agric. Food Chem*., **59**, 12453-12459.
12	Inocencio, C., Rivera, D., Alcaraz, F. and Tomás-Barberán, F. A. (2000). Flavonoid content of commercial capers (*Capparis spinosa*, *C. sicula* and *C. orientalis*) produced in Mediterranean countries. *Eur. Food Res. Technol*., **212**(1), 70–74.
13	Argentieri, M., Macchia, F., Papadia, P., Fanizzi, F. P. and Avato, P. (2012). Bioactive compounds from *Capparis spinosa* subsp. *Rupestris*. *Ind. Crops Prod*., **36**, 65–69.
14	Li, Y., Feng, Y., Yang, S. and Xu, L. (2007). Research on chemical constituents of *Capparis spinosa* L. *Zhong Cao Yao*, **38**, 510–512.
15	Zhou, H. F., Xie, C. and Jian, R. (2011). Bioflavonoids from Caper (*Capparis spinosa* L.) fruits and their effects in inhibiting NF-kappa B activation. *J. Agric. Food Chem*., **59**, 3060–3065.
16	Çaliş, I., Kuruüzüm, A. and Rüedi, P. (1999). 1H-Indole-3 acetonitrile glycosides from *Capparis spinosa* fruits. *Phytochemistry*, **50**, 1205-1208.

17	Joseph, B. and Jini, D. (2011). A medicinal potency of *Capparis decidua*: A harsh terrain plant. *Res. J. Phytochem*., **5**, 1–13.
18	Sher, H. and Alyemeni, M. N. (2010). Ethnobotanical and pharmaceutical evaluation of *Capparis spinosa* L., validity of local folk and Unani system of medicine. *J. Med. Plants Res*., **4**, 1751-1756.
19	Ahmed Z. F., Rizk A. M., Hammouda F. M. and Seif El-Nasr M. M. (1972). Glucosinolates of Egyptian *Capparis species*. *Phytochemistry*, **11**, 251-256.
20	Schraudolf, H. (1989). Indole glucosinolates of *Capparis spinosa*. *Phytochemistry*, **28**, 259–260.
21	Matthäus, B. and Özcan, M. (2005). Glucosinolates and fatty acid, sterol, and tocopherol composition of seed oils from *Capparis spinosa* Var. *spinosa* and *Capparis ovate Desf*. Var. *canescens* (Coss.) Heywood. *J. Agric. Food Chem*., **53**, 7136–7141.
22	Zhang, H. and Ma, Y. F. (2018). Phytochemical and pharmacological properties of *Capparis spinosa* as a medicinal plant. *Nutrients,* **10**(2), 116.
23	Arena, A., Bisignano, G., Pavone, B., Tomaino, A., Bonina, F., Saija, A., Cristani, M., D'Arrigo, M. and Trombetta, D. (2008). Antiviral and immunomodulatory effect of a lyophilized extract of *Capparis spinosa* L. buds*. Phytother. Res*., **22**, 313–317.
24	Romeo, V., Ziino, M., Giuffrida, D., Condurso, C., and Verzera, A. (2007). Flavor profile of Capers (*Capparis spinosa* L.) from the Eolian Archipelago by HS-SPME/GC-MS. *Food Chem*., **101**, 1272–1278.
25	Chedraoui, S., Abi-Rizk, A., Marc El-Beyrouthy, M., Chalak, L., Ouaini, N. and Rajjou, L. (2017). *Capparis spinosa* L. in a systematic review: A xerophilous species of multi values and promising potentialities for agrosystems under the threat of global warming. *Front. Plant Sci.*, **8**, 1845. doi: 10.3389/fpls.2017.01845.
26	Çalış, I. H., Kuruüzüm-Uz, A., Lorenzetto, P. A. and Rüedi, P. (2002). (6S)-Hy-droxy-3-oxo-α-ionol glucosides from *Capparis spinosa* fruits. *Phytochemistry*, **59**, 451-457.
27	Gadgoli, C. and Mishra, S. (1999). Antihepatotoxic activity of *p*-methoxy benzoic acid from *Capparis spinosa*. *J. Ethnopharmacol*., **66**, 187–192.
28	Yu, Y., Gao, H., Tang, Z., Song, X. and Wu, L. (2006). Several phenolic acids from the fruit of *Capparis spinosa*. *Asian J. Trad. Med*., **1**, 1-4.
29	Afsharypuor, S., Jeiran, K. and Jazy, A. A. (1998). First investigation of the flavour profiles of the leaf, ripe fruit and root of *Capparis spinosa* var. *mucronifolia* from Iran. *Pharm. Acta Helv.,* **72**, 307–309.
30	Juan, P. P. and Martinez, M. D. P. (1998). Flavonoid aglycones from Argentinian *Capparis* species (Capparaceae). *J. Biochem. Syst. Ecol*., **26**, 577–580.
31	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
32	https://www.drugs.com/npp/capers.html.
33	Akkari, H., B'chir, F., Hajaji, S., Rekik, M., Sebai, E., Hamza, H., Darghouth, M. A. and Gharbi, M. (2016). Potential anthelmintic effect of *Capparis spinosa* (Capparidaceae) as related to its polyphenolic content and antioxidant activity. *Veterinarni Medicina*, **61**(6), 308–316.

34	Nabavi, S. F., Maggi, F., Daglia, M., Habtemariam, S., Rastrelli, L. and Nabavi, S. M. (2016). Pharmacological effects of *Capparis spinosa* L. *Phytother. Res.*, **30**(11), 1733-1744.
35	Mirzakhani, N., Farshid, A. A., Tamaddonfard, E., Tehrani, A. and Imani, M. (2020). Comparison of the effects of hydroalcoholic extract of *Capparis spinosa* fruit, quercetin and vitamin E on monosodium glutamate-induced toxicity in rats. *Veterinary Research Forum*, **11**(2), 127–134.
36	Feng, X., Lu, J., Xin, H., Zhang, L., Wang, Y. and Tang, K. (2011). Anti-arthritic active fraction of *Capparis spinosa* L. fruits and its chemical constituents. *Yakugaku Zasshi*, **131**, 423–429.
37	Zhou, H., Jian, R., Kang, J., Huang, X., Li, Y., Zhuang, C., Yang, F., Zhang, L., Fan, X., Wu, T. and Wu, X. (2010). Anti-inflammatory effects of caper (*Capparis spinosa* L.) fruit aqueous extract and the isolation of main phytochemicals. *J. Agric. Food Chem.*, **58**, 12717–12721.
38	El Azhary, K., Jouti, N. T., El Khachibi, M., Moutia, M., Tabyaoui, I., El Hou, A., Achtak, H., Nadifi S., Habti, N. and Badou A. (2017). Anti-inflammatory potential of *Capparis spinosa* L. *in vivo* in mice through inhibition of cell infiltration and cytokine gene expression. *BMC Complementary and Alternative Medicine*, **17**, 81.
39	Abraham, S. V. P. I., Palani. A., Ramaswamy, B. R., Shunmugiah, K. P. and Arumugam, V. R. (2011). Antiquorum sensing and antibiofilm potential of *Capparis spinosa*. *Arch. Med. Res.*, **42**, 658–668.
40	Erdogan, M. S., Babacan, H., Kara, M. I., Gurler, B., Akgul, H. and Soyler, D. A. (2015). Effect of *Capparis spinosa* extract on sutural ossification: A stereological study. *Arch. Oral Biol.*, **60**, 1146–1152.
41	Aichour, R., Charef, N., Baghiani, A. and Arrar L. (2016). Immonumodulatory effects of Algerian Caper. *Int. J. Pharm. Pharm. Sci.*, **8**, 51–54.
42	Benzidane, N., Charef, N., Krache, I., Baghiani, A. and Arrar, L. (2013). *In vitro* bronchorelaxant effects of *Capparis spinosa* aqueous extracts on rat trachea. *J. Appl. Pharm. Sci.*, **3**, 85–88.
43	Aghel, N., Rashidi, I. and Mombeini, A. (2007). Hepatoprotective activity of *Capparis spinosa* root bark against CCl_4 induced hepatic damage in mice. *Iranian Journal of Pharmaceutical Research*, **6**(4), 285-290.
44	Fanoudi, S., Rakhshandeh, H., Afshari, A. R., Mollazadeh, H. and Boroushaki, M. T. (2017). Nephrotoxicity and hepatotoxicity of *Capparis spinosa* hydro-alcoholic extract in Mice. *JOJ Urology & Nephrology*, **4**(3), ID: 5555640.
45	Kalantar, M., Goudarzi, M., Khodayar, M. J., Babaei, J., Foruozandeh, H., Bakhtiari, N. and Alidadi, H. (2016). Protective effects of the hydro alcoholic extract of *Capparis spinosa* L. against cyclophosphamide-induced nephrotoxicity in mice. *Jundishapur Journal of Natural Pharmaceutical Products*, **11**(4), e37240.
46	Tlili, N., Feriani, A., Saadoui, E., Nasri, N. and Khaldi, A. (2017). *Capparis spinosa* leaves extract: Source of bioantioxidants with nephroprotective and hepatoprotective effects. *Biomedicine and Pharmacotherapy*, **87**, 171–179.
47	Shahrajabian, M. H., Sun, W. and Cheng, Q. (2021). Plant of the Millennium, Caper (*Capparis spinosa* L.), chemical composition and medicinal uses. *Bulletin of the National Research Centre*, **45**, 131. https://doi.org/10.1186/s42269-021-00592-0.

Egyptian Herbal Monograph

Traditional wild medicinal plants

Cleome droserifolia (Forssk.) Delile سموة

1. Names & Synonyms

***Cleome droserifolia* (Forssk.) Delile** (1, 2).

Family: Capparaceae (3).

Synonym: *Roridula droserifolia* Forssk. (1-3).

Arabic: Samwa سموة (3).

English: Cleome (1)

2. Geographical distribution

Uweinat oasis, all the deserts of the country including that of Sinai, Red Sea coastal strip, Gebel Elba and the surrounding mountainous region (3).

3. Part used for medicinal purposes

Herbs (3).

4. Major chemical constituents

- **Flavonoids:** Quercetin, kaempferol, and isorhamnetin, flavonol glycosides, flavones (methoxylated flavones and flavone glycosides) (4-10).

- **Terpenes:** Sesquiterpenes, diterpenes and triterpenes (11- 14).

- **Essential oil:** Aerial parts main constituents of *C. droserifolia* oil are (E)-3,7, 11-trimethyl-1,6,10-decatrien, carotol, *δ*-cadinene, *β*-eudesmol, and benzyl isothiocyanate (15, 16).

- **Others:** Saponins, coumarins, alkaloids, sterols and docosanoic acid (1, 3, 10, 17).

5. Traditional medicinal uses (18)

A. Treatment of hyperglycemia.
B. Accelerate wound healing especially for *diabetes mellitus* patients.
C. Open sores and cuts.
D. Allergy, dermatitis, inflammation, scabies, as antimicrobial agent and antibiotic for wounds and burns.

E. Bee stings.

***C. droserifolia* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (18)

A. **1.** Decoction: Half of a teaspoonful of the air-dried leaves powder is added to a cup of water, boiled, and taken in the morning before breakfast (North eastern desert, red sea coast area and north Sinai).

2. Powder (Halaib triangle area).

B. **1.** Paste, Infusion or powder of Leaves and Shoot.

2. The leaves powder is oven dried and added on wounds as powder.

C. Grind leaves, boil them in milk butter, strain, cool and apply to wound.

D. **1.** Decoction of boiled leaves.

2. Infusion.

E. **1.** Add the ground leaves in cold water.

2. Infusion: Add the ground leaves in warm water.

7. Posology and method of administration correlated to medicinal use (18)

A. Orally

1. Drinking the extract of boiled leaves in water in the morning before breakfast (North eastern desert and red sea coast area, north Sinai).
2. A dose of 5g of powder is taken before meal (Halaib triangle area).

B. Topically

C. Topically

D. **1- Orally:** Drinking the decoction.
2- Topically: Washing of body with the infusion.

E. **1- Orally:** Add the ground leaves in cold water and drink (0.5 glass).
2- Topically: Wash the sting with the leaves' infusion.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The plant is very toxic if given intraperitoneally (1, 3).
- Monitoring of blood glucose level should be done regularly.

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation

-Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

-No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- None known.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

14. Overdose

No case of overdose has been reported.

15. Relevant biological activities

- The antidiabetic activities of the aqueous and ethanolic extracts of *C. droserifolia* (Forssk.) Del., were tested in cultured C2C12 skeletal muscle cells and 3T3-L1 adipocytes. The chloroform and ethyl acetate fractions of *C. droserifolia* aqueous extract were found to have significant insulin-like effects in peripheral tissues, namely the stimulation of basal glucose uptake in skeletal muscle cells and glitazone-like enhancement of adipogenesis (19).
- The evaluation of the possible protective effects of *C. droserifolia* methanolic extract (CDE) against pancreas *β*-cells' damage and antioxidant defense systems in alloxan induced diabetic rats was studied. The increase in blood glucose and MDA levels

with the decrease in GSH content and in enzymatic activities were the salient features observed in diabetic rats. Administration of CDE (0.31g/kg bw/day, orally) for 30 days caused a significant reduction in blood glucose and MDA levels in alloxan treated rats when compared with diabetic rats. Furthermore, diabetic rats treated with CDE showed a significant increase in the activities of both enzymatic and non-enzymatic antioxidants when compared to those of diabetic rats. Degenerative changes of pancreatic *β*-cells in alloxan treated rats were minimized to near normal morphology by administration of CDE as evidenced by histopathological examination. Results clearly indicated that *C. droserifolia* treatment exerts a therapeutic protective nature in diabetes by decreasing oxidative stress and pancreatic *β*-cells' damage which may be attributed to its antioxidative potential (10, 20).

- Investigation of the antidiabetic as well as the effect on lipid peroxidation of three different doses (50, 100, and 200 mg/kg) of *C. droserifolia* aerial parts methanolic extract in comparison with glibenclamide in alloxan-induced diabetic rats was done. Oral administration of 100 and 200mg/kg of the methanolic extract for 3 weeks significantly *(P < 0.05)* restored the blood glucose level, plasma malondialdehyde and urine sugar to near the physiological values whereas the effect of 50mg/kg was not significant (21).
- The antibacterial activities of essential oil from *C. droserifolia* were investigated against a selection of Gram-positive and Gram-negative bacteria by the agar-well diffusion and the micro-dilution methods. The study showed that the oil exerted marked growth inhibitory effects. Most bacterial species tested were suppressed, despite the varying degrees of inhibition observed (15).
- The aerial parts of the *C. droserifolia* shrub had strong antioxidant, antimicrobial and immunomodulatory activities, which can improve the overall health status and seem to be related to its impressive range of biologically active phenolic compounds (22).

16. Additional information:

-

17. Date of compilation/last revision

06/08/2022.

References

1	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
2	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
3	Hammouda, F. M. and Hassan, A. H. (2018). *Cleome droserifolia*. In: Egyptian Encyclopedia of Wild Medicinal Plants, **6**, 71-79. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Nassar, M. I., and Gamal-Eldeen, A. H. (2003). Potential antioxidant activity of flavonoids from *Hypericum triquetrifolium* Turra and *Cleome droserifoila* (Forssk) Del. *Bulletin of the Faculty of Pharmacy* (Cairo University), **41**, 107–115.
5	Yang, S. S., Mabry, T. J., El-Fishawy, A. M., El-Kashoury, E. A., Abdel-Kawy, M. A and Soliman, F. M. (1990). Flavonoids of *Cleome droserifolia*. *Egyptian Journal of Pharmaceutical Sciences*, **31**, 443–446.
6	Shinji, F., Yoji, H., Javzan, B., Fumihide, T., Singab, A. and Toru, O. (1999). Flavonoids from *Cleome droserifolia* suppress NO production in activated macrophages *in vitro*. *Journal of Natural Products*, **65**, 404–407.
7	Aboushoer, M. I., Fathy, M., Abdel-Kader, S., Goetz, G. and Omar, A. A. (2010). Terpenes and flavonoids from an Egyptian collection of *Cleome droserifolia*. *Natural Product Research*, **24**, 687–696.
8	Seif El-Nasr, M. M., Youssef, M. M. and Helmy, M. (1984). Flavonoids of *Cleome droserifolia*. *Fitoterapia*, **55**, 231–232.
9	Sharaf, M., Mansour, R. M. A. and Saleh, N. A. M. (1992). Exudate flavonoids from aerial parts of four *Cleome* species. *Biochemical Systematics and Ecology*, **20**, 443–448.
10	Helal, E. G. E., Abou Aouf, N., Abdallah, I. Z. A. and Khattab, A. M. (2015). Hypoglycemic and antioxidant effects of *Cleome droserifolia* (Samwah) in alloxan-induced diabetic rats. *The Egyptian Journal of Hospital Medicine*, **58**, 39-47.
11	El-Askary, H. (2005). Terpenoids from *Cleome droserifolia*. *Molecules*, **10**, 971–977.
12	Hussein, N. S., Ahmed, A. A. and Darwish, F. M. (1994). Sesquiterpene from *Cleome droserifolia*. *Pharmazie*, **49**, 76–77.
13	Fathy, H. M., Aboushoer, M. I., Harraz, F. M., Omar, A. A., Goetz, G. and Tabacchi, R. (2008). Dolabellane diterpene from *Cleome droserifolia*. *Natural Products Communication*, **3**, 1479–1482.
14	Fushiya, S., Kishi, Y., Hattori, K., Batkhuu, .J, Takano, F., Singab, A. N. and Okuyama, T. (1999). Flavonoids from *Cleome droserifolia* suppress NO production in activated macrophages *in vitro*. *Planta Med.*, **65**, 404–407.
15	Muhaidat, R., Al-Qudah, M. A., Samir, O., Jacob, J. H., Hussein, E., Al Tarawneh, I. N., Bsoul, E. and Abu Orabi, S. T. (2015). Phytochemical investigation and *in vitro* antibacterial activity of essential oils from *Cleome droserifolia* (Forssk.) Delile and *C. trinervia* Fresen. Cleomaceae .*South African Journal of Botany,* **99**, 21–28.

16	Abd EI-Kawy, M. A., EI-Deib, S., Hanna, R. A., EI-Khyat, Z. and Mikhail, Y. A. (2000). Chemical and biological studies of *Cleome droserifolia* (Forssk.) Del. Part—II. *Egyptian Journal of Biomedical Sciences,* **6**, 219–232.
17	Singh, H., Mishra, A. and Mishra, A. K. (2018). The chemistry and pharmacology of *Cleome* genus: A review. *Biomed. Pharmacother.,* **101**, 37–48.
18	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
19	Abdel Motaal, A., Ezzat, S. M. and Haddad, P. S. (2011). Determination of bioactive markers in *Cleome droserifolia* using cell-based bioassays for antidiabetic activity and isolation of two novel active compounds. *Phytomedicine*, **19**, 38– 41.
20	Nagy, M. A. and Mohamed, S. A. (2014). Antidiabetic effect of *Cleome droserifolia* (Cleomaceae). *American Journal of Biochemistry*, **4**(4), 68-75.
21	El Naggar, E. M. B., Bartosikova, L., Zemliika, M., Svajdlenka, E., Rabiskova, M., Strnadova, V. and Necas, J. (2005). Antidiabetic effect of *Cleome droserifolia* aerial parts: Lipid peroxidation–induced oxidative stress in diabetic rats. *ACTA VET. BRNO.*, **74**, 347–352.
22	Hashem, N. M. and Shehata, M. G. (2021). Antioxidant and antimicrobial activity of *Cleome droserifolia* (Forssk.) Del. and its biological effects on redox status, immunity and gut microflora. *Animals*, **11**, 1929. https://doi.org/10.3390/ ani11071929.

Egyptian Herbal Monograph

Traditional wild medicinal plants

Cymbopogon proximus Hochst. ex A. Rich. حلفابر

1. Names & Synonyms

***Cymbopogon proximus* Hochst. ex A. Rich**. (1, 2).

Family: Gramineae (Poaceae) (2, 3).

Syns.: (3)

- *Andropogon proximus* Hochst.
- *Andropogon sennarensis* Hochst.
- *Andropogon jwarancusa* Jones var. *proximus* Hochst. ex A. Rich.
- *Andropogon jwarancusa* Jones var. *sennarensis* Hochst.
- *Cymbopogon sennarensis* Hochst.

Arabic: Halfa bar حلفابر, Mahareb محاريب (1, 4).
English: Camel grass, camel's hay, geranium grass, Scenanth (1, 2).

2. Geographical distribution

Confined to the desert east of the Nile including that of the Sinai Peninsula (3), the southern eastern desert and Gebel Elba (1).

3. Parts used for medicinal purposes

Aerial parts of the plant (1).

4. Major chemical constituents

-Essential Oil (4, 5): Piperitone, *β*-elemol, *α*-eudesmol, *β*-eudesmol, *β*-elemene, eudesm-7(11)-en-4-ol, D-limonene,2-, *α*-terpineol, *τ*-cadinol, terpinolene, *β*-selinenol, 3-cyclohexen-1-one, 2-isopropyl-5-methy, 4-carene, shyobunol, cadina-1(10), 4-diene, (−)-guaia-6,9-diene and *β*-caryophyllaneare are the main components, where other minor components also considered such as thymol and camphene.

-Sesquiterpenoids: Bicyclic sesquiterpene diol (proximadiol) is the main bioactive metabolite in addition to 5*α*-hydroxy-*β*-eudesmol, 1*β*-hydroxy-*β*-eudesmol, 1*β*-hydroxy-*α*-eudesmol, 5*α*-hydroperoxy-*β*-eudesmol and 7*α*, 11-dihydroxycadin-10(14)-ene(6, 1).

5. Traditional medicinal uses

A. Diuretic (5, 6).
B. Antispasmodic (5, 6).
C. Renal colic pain killer (7, 8).
D. Removal of small stones from the urinary tract (7).
E. Antipyretic in fevers (7).

***C. proximus* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use

1. **Weak infusion in the form of "teas"** (1, 8):
   Pour freshly boiled water on 2 teaspoonful of the herb in a cup; cover the cup with the lid and infuse for 5 minutes. Drink it sweetened if desired.
2. **Decoction:**
   Pour cold water on 2 teaspoonful of the entire dried herb or dried leaves and boil, simmer for 10 minutes. Pour into a cup and drink it sweetened if desired (5, 8).
3. **Herbal extract in a pharmaceutical dosage form:**
   The pharmaceutical form should be described by the Pharmacopoeia full standard term.

7. Posology and method of administration correlated to medicinal use

Preparation 1,2: 3 cups daily (8).

Preparation 3: 3 times daily.

Method of administration: oral use.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation

-*C. proximus* is not recommended during pregnancy <<see section 15. Relevant biological activities >>.

-Safety during lactation has not been established. In the absence of sufficient data, the use during lactation is not recommended.

-No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

-None known.

-If adverse reactions occur, a doctor or a pharmacist should be consulted.

14. Overdose

No case of overdose has been reported.

15. Relevant biological activities

- The aqueous extract (5%) of *C. proximus* (CP) was injected in male Wistar albino rats at a dose of 1.5 ml/100 g body weight/day for 10 days. The results obtained suggest that CP has a significant protective effect against ethylene glycol-induced nephrolithiasis in rats (9).
- New herbal beverages from *Foeniculum vulgare* and *C. proximus* were tested for inhibiting or preventing calcium oxalate crystals formation. The results indicate that the inhibition efficiency of formulated beverages from *F. vulgare* and *C. proximus* on calcium oxalate renal stone formation in rats increased gradually through rising the ratio of *C. proximus*. Therefore, it was recommended that intake two or three cups of beverages D or E (0.5:1.5% and 0.0:2.0% from *F. vulgare* and *C. proximus*, respectively) will adjust the levels of urinary risk factors, marker enzymes, and kidney functions when divided into two or three times a day (10).

- The prophylactic effect of *C. proximus* on Sulfadimidine (200mg/kg) induced urolithiasis in rabbits was investigated. *C. proximus* alcoholic and aqueous extracts (330mg/kg) were given orally for 10 days. Blood and urine samples were collected from rabbits on the 10th day. The results recorded a significant decrease in serum creatinine, urea, uric acid and crystalluria in *C. proximus* groups

compared to sulfadimidine treated group. It was concluded that *C. proximus* have a nephroprotective and antiurolithiatic effects against sulfadimidine induced crystalluria (11).

- Evaluation of the congenital malformation of proximol in pregnant albino rats during gestation period was done. The virgin female rats were mated with male rats and the pregnant rats were orally administered a human equivalent dose (0.05mg/kg) of Proximol from 5th-20th gestation day. At day 20 of pregnancy, all rats were anesthetized to obtained maternal and fetal data. The treatment group displayed some disorders, which can be summarized as growth retardation, external anomalies, embryonic resorption, and skeletal malformation. It was concluded that the oral administration of Proximol resulted in embryonic abnormalities and skeletal malformations (12).
- During admistration of Proximol (*C. proximus*) (0.05mg/ kg) as herbal drug to the pregnant albino rats during the gestation period, the drug will pass to embryos through placenta causing several implications (13).
- The 70% ethanolic extract and its fractions (petroleum ether, chloroform and ethyl acetate) were evaluated for their antispasmodic effect. The most potent fraction is petroleum ether which produced full inhibition by the least dose. Based on the results obtained, the presence of specific sesquiterpene in *C. proximus* justified the use of this plant as antispasmodic, nephrolithiasis, renal colic, helmenthiasis, diuresis, inflammation of prostate and as antipyretic (14).

16. Additional information:

Presence of moisture, ash, crude fiber, crude protein, crude lipid and total carbohydrates (11).

17. Date of compilation/last revision

06/08/2022.

References

1	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
2	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
3	Saleh, I. A. and Hegazy, M. E. F. (2018). *Cymbopogon proximus*. In: Egyptian Encyclopedia of Wild Medicinal Plants, **6**, 390-399. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Malin, M. A., Ali, M. M. and Ramadhani, A. M. (2018). GC-MS analysis and antimicrobial activities of *Cymbopogon proximus* essential oil and phytochemical screening of its crude extracts. *Journal of Medicinal Plants Studies*, **6**(4), 117-122.
5	El-Tahir, K. E. H. and Abdel Kader, M. S. (2008). Chemical and pharmacological study of *Cymbopogon proximus* volatile oil. *Research Journal of Medicinal Plants*, **2**, 53-60.
6	El-Askary, H. I., Meselhy, M. R., Galal, A. M. (2003). Sesquiterpenes from *Cymbopogon proximus*. *Molecules*, **8**, 670-677.
7	Selim, S. A. (2011). Chemical composition, antioxidant and antimicrobial activity of the essential oil and methanol extract of the Egyptian lemongrass *Cymbopogon proximus* Stapf. *Grasasy Aceites*, **62**(1), 55-61.
8	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
9	Warrag, N. M., Tag Eldin, I. M. and Ahmed, E. M. (2014). Effect of *Cymbopogon proximus* (Mahareb) on ethylene glycol-induced nephrolithiasis in rats. *African Journal of Pharmacy and Pharmacology,* **8**(17), 443-450.
10	Ibrahim, F. Y. and El-Khateeb, A. Y. (2013). Effect of herbal beverages of *Foeniculum vulgare* and *Cymbopogon proximus* on inhibition of calcium oxalate renal crystals formation in rats. *Annals of Agricultural Science*, **58**(2), 221–229.
11	El-Nabtity, S. M., Abdllatief, S. A., Al-Attar, S. R. and Taha, S. M. (2019). Antiurolithiatic effect of *Cymbopogon proximus, Alhagi Maurorum, on* Sulfadimidine induced urolithiasis in male New Zealand rabbits. *Mansoura Veterinary Medical Journal,* **20**(1), 14-21.
12	Abdelrahman, H. A., Omar, A. R. and Salah EL-Din, E. Y. (2017). The impact of Proximol (*Cymbopogon proximus*) intake on pregnant albino rats and their fetuses during gestation period. *Int. J. Morphol*., **35**(2), 500-505.
13	Omar, A. R., Salah El-Din, E. Y. and Abdelrahman, H. A. (2016). Implications arising from the use of *Cymbopogen proximus;* proximal on placenta of pregnant Albino rats. *Brazilian Archives of Biology and Technology,* **59**, e16160165. https://doi.org/10.1590/1678-4324-2016160165
14	Khalafalla, E. B., Sami, Z. A. and Khalid, A. (2015). Chromatographic profiling of *Cymbopogon proximus* antispasmodic fraction(s). Conference: 16th NAPRECA Symposium, Arusha, Tanzania.

Egyptian Herbal Monograph

Traditional wild medicinal plants

***Cyperus rotundus* L.** السعد

1. Names & Synonyms (1, 2)

***Cyperus rotundus* L.**

Family: Cyperaceae.

Arabic: Se'ed سعد

English: Nut grass, nutsedge, purple nutsedge (North Africa, IUCN).

Two varieties occur in Egypt:

a. var. ***rotundus***

Syns. *Cyperus tuberosus* Rottb., *C. hexastachyos* Rottb., *C. comosus* Sibth. & Sm., *C. subcapitatus* C. B. Clarke.

b. var. ***fenzelianus***

Syns. *Cyperus fenzelianus* Steud., *C. ochreoides* Steud., *C. pallescens* Boiss.

2. Geographical distribution (2)

a. var. ***rotundus*:** Common in nearly all the phytogeographical regions of the country.
b. var. ***fenzelianus*:** The Nile region, the oases of the western desert as well as the Mediterranean region and all the deserts of the country.

3. Parts used for medicinal purposes

Rhizomes, tubers, leaves and the herb (2-4).

4. Major chemical constituents

- **Volatile oil:** The chemical constituents of the volatile oil obtained from *C. rotundus* rhizomes growing in Bahtim, Egypt includes two monoterpenes, eight oxygenated monoterpenes, eight sesquiterpenes, seventeen oxygenated sesquiterpenes, and two hydrocarbons. The oil contained a high percentage of oxygenated sesquiterpenes followed in decreasing order by oxygenated monoterpenes then monoterpenes, sesquiterpenes and hydrocarbons. Major compounds are humulene

epoxide, caryophyllene oxide, lα,7α,10α gaia- 4,11(13)-dien-3-one, β-pinene, α-pinene, *trans*-(-) pinocarveol and oxo-α-ylangene (5).

Volatile oil of *C. rotundus* tubers collected from Giza, Egypt constituted mainly of oxo-α-ylangene, α-cyperone, *trans*-pinocarveol, cyperene, 2(H)-Naphthalenone, 2(H)-naphthalenone, 4a,5,6,7,8,8a hexahydro-7-isopropyl,4a β, 8a β-dimethyl and aristolone (6).

Among the chemical composition of volatile oil of *C. rotundus* parts from around the world are: α-cyperone, cyperene, cyperotundone and β-selinene as major compounds, along with other constituents such as, α-copaene, valerenal, caryophyllene oxide, patchoulenyl acetate and sugeonyl acetate. In addition, α- and β-pinenes, limonene and 1,8-cineole are the minor components. The oil chemical composition changes considerably according to its geographical origin (7- 11).

- **Flavonoids:**

The main flavonoids are: apigenin, luteolin, tricin and quercetin and their glycosides, myricetin, kaempferol, rutin, isorhamnetin, rhamnetin3-(4-rhamnosylrhamnoside), biflavones (amentoflavone, ginkgetin, isoginkgetin and sciadopitysin). The flavonol derivative; cyperaflavoside (myricetin 3,3',5'-trimethyl ether 7-*O*-β-D-glucopyranoside) and five flavonoids (vitexin, orientin, cinaroside, quercetin 3-*O*-β-D-glucopyranoside, and myrcetin 3-*O*-β-D-glucopyranoside) were reported (12-16).

- **Nitrogenous constituents**

The main compounds are: rotundine A and B, octopamine, 6,7-dihydro-2, 3-dimethyl-5-cyclopentapyrazine, adenosine, uridine and tryptophan α-D-fructofuranoside (17).

- **Others:**

Tannins(Afzelechin, catechin), phenolic acids (e.g. salicylic, protocatechuic, caffeic, *p*-coumaric and ferulic acids), sterols, saponins, coumarins, chromones (visnagin, khellin, ammiol and Khellol-β-Dglucopyranoside), steroids (steroidal glycoside, sitosteryl-(6'-hentriacontanoyl)-β-D-galactopyranoside), phenylpropanoids (isoaragoside, chionoside A and helioside C) and iridoid glycosides (Rotunduside A & B), as well as quinones (cyperaquinones, scabiquinones, berviquinones and alkenylhdroxy of quinones), carbohydrates, starch, protein, amino acids and fatty acids (linolenic, linoliec, oleic, myristic and stearic acids) were reported. The molasses extracted from the tubers of *C. rotundus* contains D- glucose, D- fructose and non-reducing sugars (9, 17).

5. Traditional medicinal uses

A. Stops body hair growth (3).

B. Aphrodisiac, anthelmintic, diuretic, carminative, tonic and stimulant. Also, it is used as a remedy for renal colic and dysentery (18).

C. Aromatic, stomachic, sedative and as analgesic (3).

***C. rotundus* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to traditional medicinal uses

1. The herb is boiled with water till it becomes thick, then rub the hairy body areas (3).
2. **Anthelmintic** (4):
   - **2.1. Tablet:** Grind the leaves of *C. rotundus* (or the herb of *C. rotundus*) into a paste and make it in tablets.
   - **2.2. Paste:** The rhizome is made into a paste.
3. Rhizome, in the form of ellipsoid tubers (3).

7. Posology and method of administration correlated to traditional medicinal uses

Preparation 1

Indication A

Rub the preparation into the body hairy areas to stop hair growth (3).

Method of administration: Topical use.

Preparation 2

Indication: Anthelmintic (4):

2.1. Take one tablet orally, thrice a day for one or two days.

2.2. 10 - 20g of the paste is eaten 3 times a day, 2-3 days. Children dose is usually halved.

Method of administration: Oral use.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use (19, 20)

-If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

-Bleeding disorders: *C. rotundus* might slow blood clotting. This might increase the risk of bruising or bleeding in people with bleeding disorders.

-Slow heart rate (bradycardia): *C. rotundus* might slow down the heartbeat. This could be a problem in people who already have a slow heart rate.

-Diabetes: *C. rotundus* might lower blood sugar levels. People with diabetes should monitor their blood glucose levels regularly.

-Gastrointestinal tract blockage: *C. rotundus* might cause "congestion" in the intestines. This might cause problems in people who have a blockage in their intestines.

-Lung conditions: *C. rotundus* might increase fluid secretions in the lung. There is a concern that this could worsen lung conditions such as asthma or emphysema.

-Surgery: *C. rotundus* might lower blood sugar or slow blood clotting. Stop taking *C. rotundus* at least 2 weeks before a scheduled surgery.

10. Interactions with other medicinal products and other forms of interaction (20)

- **Cholinergic drugs:** Various medications used for glaucoma and other conditions.
- **Drying medications (anticholinergic drugs):** *C. roduntus* might decrease the effects of drying medications including atropine, scopolamine and some medications used for allergies (antihistamines) and depression (antidepressants).
- **Medications for Alzheimer's disease:** *C. rotundus* might increase the effects of Alzheimer's medications, e.g. Acetylcholinesterase (AChE) inhibitors.
- **Antidiabetic medications:** *C. rotundus* might decrease blood sugar; monitor your blood sugar regularly.
- **Anticoagulant/Antiplatelet drugs:** Taking *C. rotundus* along with medications that slow clotting e.g. warfarin and aspirin, might increase the chances of bruising and bleeding.

11. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- None known.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

14. Overdose

No case of overdose has been reported.

15. Relevant biological activities

- In an open-label pilot study, the author prospectively evaluated the efficacy of *C. rotundus* essential oil, compared with the Alexandrite laser (GentleLase; Candela Laser Corp, Wayland, Massachusetts) and saline, for reducing unwanted axillary hair. Eligible participants (n = 65) with unwanted axillary hair were assigned randomly to 1 of 3 study groups: topical *C. rotundus* oil (group 1), saline (group 2), and Alexandrite laser (group 3). Sixty patients completed the entire study. Three methods were used to evaluate the results: hair counts, observations of independent professionals and patient self-assessments. Overall results did not differ significantly between *C. rotundus* oil and the Alexandrite laser (p>0.05). However, statistically significant differences were noted with respect to decreased growth of white hair (p>0.05), favoring the oil. This finding was evident by all 3 methods of assessment. No side effects were detected. *C. rotundus* essential oil is as effective as the Alexandrite laser for decreasing the growth of axillary hair (both dark and white) (21).
- The efficacy and safety of application of Egyptian *C. rotundus* essential oil in comparison to 0.9% saline on androgenic hair was evaluated. Ninety one female patients with Androgenic hair (hirsutism and axillary hair) completed the study. They were randomly assigned to two groups: group I (active group) (n=47) and group II (control group) (n=44). Patients used topical *C. rotundus* essential oil for six months and were evaluated on the 6th month. The topical oil was significantly more effective (p<0.05) than the placebo without side effects. This result was proven by three assessment methods; difference in hair count, independent observer assessment and patients' self-assessment. The topical Egyptian *C. rotundus* essential oil is an effective method in treating moderate degrees of hirsutism and axillary hair without affecting serum testosterone (22).
- The essential oil of the *C. rotundus* tubers had antibacterial activity against several foodborne Pathogens. The antibacterial effects of essential oil were greater against Gram-positive bacteria as compared to Gram-negative bacteria, and the antibacterial effects were significantly influenced by incubation time and concentration. These results may provide biological evidence for the practical

application of the *C. rotundus* rhizomes essential oil in food and pharmaceutical industries (8).

- The antimicrobial activity of the essential oil and its fractions from the *C. rotundus* tubers were evaluated using the disc diffusion method against six foodborne pathogens. The essential oil and its fractions exhibited notable antibacterial activity against all the bacteria species tested. The Gram (+) bacteria was more sensitive than Gram (-). *Staphylococcus aureus* was the most sensitive bacterium, *Salmonella* was the most inhibited Gram (-) bacterium while *Eschirichia coli* was the most resistant strain at the same essential oil concentration. . *C. rotundus* essential oils can be used instead of antibiotic (10).
- The antibacterial activity of *C. rotundus* oil was studied for various microorganisms *(Staphylococcus aureus, Klebsiella pneumoniae, Proteus vulgaris, Streptococcus pyogenes, Eschirichia coli and Pseudomonas aeruginosa)* using inhibition zone method (Aromatogram). The oil of *C. rotundus* showed a remarkable activity against Gram-positive bacteria, less antibacterial activity was found against Gram–negative bacteria and no activity was observed with the oil against *Pseudomonas aeruginosa* and *Proteus vulgaris* (23).
- The antibacterial properties of *C. rotundus* root extracts (petroleum ether, acetone, methanol and water) was investigated against three Gram-positive and two Gram-negative bacteria causing respiratory tract infections. Results showed that methanol extract was the most active as comparison to other extract. The maximum inhibition was noted against *H. influenzae* followed by *S. pyogenes*, *P. aeruginosa* and *S. pneumoniae* and the minimum activity was recorded against *S. aureus* (15.3±0.05mm) (24).
- The methanol extract of *C. rotundus* rhizome, given orally at the doses of 250 and 500mg/kg b.w., showed significant antidiarrhoeal activity in castor oil induced diarrhoea in mice. Among the fractions, tested at 250mg/kg, the petroleum ether fraction and residual methanol fraction were found to retain the activity, the latter being more active as compared to the control. The ethyl acetate fraction did not show any antidiarrhoeal activity (25).
- An aqueous extract of tubers of *C. rotundus* (ACR) was tested for its antidiarrhoeal and antispasmodic activity. Antidiarrhoeal effect of ACR was evaluated in castor oil induced diarrhea in mice and antispasmodic effect was evaluated by charcoal meal test in mice at a dose of 125, 250, 500mg/kg. The % inhibition of diarrhoea was 30.36%, 37.90%, 45.45% and 92.45% for ACR 125, 250, 500mg/kg orally and loperamide 2mg/kg dose orally respectively. ACR 125, 250, 500mg/kg orally and atropine sulphate 2mg/kg dose orally produced 24.35%, 31.48%, 36.75% and 55.94% inhibition of intestinal transit respectively (26).
- Study the biflavone constituents in *C. rotundus* L., investigation of the effect and mechanism of amentoflavone on inhibition of uterine tumors was carried out. Four

biflavone constituents were isolated and obtained. . Amentoflavone could markedly reduce the uterine coefficient in model rats, lower serum estrogen levels in rats with uterine fibroids, improve the pathological conditions of uterine tissues. It concludes that amentoflavone has a significant inhibitory effect on uterine tumors in rats. Its mechanism may be by elevating Bax protein expression, down-regulating Bcl-2 expression, forming homodimers Bax/Bax, and reducing plasma estradiol and progesterone to promote apoptosis of uterine fibroid cells (14).

- Analgesic activity of *C. rotundus* essential oil was evaluated. Swiss albino rats were injected with 0.05 ml of 2.5% formalin in the sub plantar of right hind paw to induce pain 30 min after the oral administration of essential oils (250, 500mg/kg), indomethacin (10mg/kg) and 1% CMC. The neurogenic and inflammatory responses were evaluated. Essential oils of *C. rotundus* were found to inhibit both neurogenic and inflammatory pain at higher dose, whereas at lower dose only inflammatory pain was inhibited. This shows that essential oils of *C. rotundus* have analgesic activity (27).
- The petroleum ether extract of *C. rotundus* was reported to possess analgesic activity (28).
- Aqueous, ethyl acetate, methanol and total oligomers flavonoid-enriched extracts of *C. rotundus* (300, 150, and 50μg/ml) were evaluated for their analgesic and anti-inflammatory activities in mice. The tested extracts were able to decrease the mouse ear oedema induced by xylene and reduced the number of abdominal contractions caused by acetic acid, revealing the peripheral analgesic activity of these extracts. No toxicity was recorded in mice treated with doses up to 300mg/kg b.w. (29).
- Cyperaflavoside (myricetin 3,3',5'-trimethyl ether 7-*O*-β-D-glucopyranoside), vitexin, orientin, cinaroside, quercetin 3-*O*-β-D-glucopyranoside, and myrcetin 3-*O*-β-D-glucopyranoside were assessed for their 5- lipoxygenase inhibitory potential. All compounds possessed 5-lipoxygenase inhibitory. The results supported the traditional uses of *C. rotundus* in treating inflammation and its related symptoms (16).
- The analgesic and anti-inflammatory activities of methanol, chloroform and ethyl acetate extracts of *C. rotundus* were investigated. All the extract displayed significant analgesic effect in acetic acid and hot plate pain models in a dose dependent manner. The ethyl acetate extract (500mg/kg) was the most effective in the analgesic test and it showed significantly inhibiting pain. Similarly, carrageenan-induced paw volume was significantly reduced by ethyl acetate extract (500mg/kg) (30).
- The alcoholic extract of *C. rotundus* showed significant (p<0.001) antipyretic activity against pyrexia induced in rats by the subcutaneous injection of suspension of dried Brewer's yeast in gum acacia in normal saline (31).

- The sedative-hypnotic and antidepressant effect of the methanolic extract of *C. rotundus* were evaluated. The sedative and hypnotic activity were studied performing hole board and open field tests in albino mice model at the doses of 100 and 200mg/kg body weight of the extract. Diazepam at the dose of 1mg/kg was utilized as a standard drug in both experiments. Similarly, antidepressant activity test was also performed using forced swimming test and tail suspension test. The study suggested that the plant extract do not possess notable sedative-hypnotic and antidepressant or neurobehavioral properties (32).
- The gastroprotective effect of the methanolic extract of *C. rotundus* rhizome was studied. Damage of gastric mucosa was induced by ischemia and reperfusion in male Wister albino rats. The extract was given at the dose of 100 and 200 mg/kg. The rats treated with the extracts were subjected to 30-min ischemia followed by 60-min reperfusion. The mean ulcer index of *C. rotundus* extract treated rats were significantly lower than that of control rats. The increased antioxidant activity of GSH-Px and decreased MDA levels were found in the *C. rotundus* rhizome extract treated rats when compared to the decreased antioxidant activity in untreated rats. The results showed that the *C. rotundus* extract has a profound gastroprotective effect against the gastric mucosal damage (33).
- The rhizome of *C. rotundus* was assessed for its cytoprotective effects against ethanol induced gastric damage. Decoctions of Rhizoma Cyperi were given orally (1.25, 2.5, 4.0g crude drug/kg) to rats 30 min before ethanol (40% v/v, 10mL/kg) was administered. The decoction showed an ulcer inhibitory effect in a dose dependent manner. Moreover, the activity was also observed when the decoction was given subcutaneously (0.3-0.6g/kg), suggesting that the herb possessed systemic effects on protecting the stomach. Compared with controls, gastric motility of the ethanol-treated rats was delayed significantly by either oral (2.5-4.0 g/kg) or subcutaneous (0.3g/kg) administration of the decoction. Pretreatment of rats with indomethacin (5 mg/kg) significantly reduced the gastric protective action of *C. rotundus* (34).
- The ulcer-preventive role of *C. rotundus* was studied in rats treated with non-steroidal anti-inflammatory drugs. Oral administration of different doses of *C. rotundus* rhizome methanolic extract (250 and 500mg/kg) significantly inhibited aspirin-induced gastric ulceration in animals in a dose-dependent manner (49.32% and 53.15%, respectively), which was also comparable with the standard gastric ulcer drug ranitidine. Administration of *C. rotundus* rhizome methanolic extract also significantly increased the activity of superoxide dismutase, cellular glutathione and glutathione peroxidase, and inhibited the lipid peroxidation in the gastric mucosa of ulcerated animals in a dose-dependent manner (35).
- The assessment of anti-inflammatory, antiulcer and neuropharmacological activities of the ethanolic extract of *C. rotundus* was evaluated. In experimental design, inflammation was produced by carrageenan in rats and compared with

saline treated and Aspirin treated group. The plant exhibited significant property to act as an anti- inflammatory agent. Simultaneously, the drug was also observed for its antiulcer response and found effective enough. These two activities were observed at the dosage of 300mg/kg and 500mg/kg of *C. rotundus* ethanolic extract. The anti-ulcer activity was observed (41.2% inhibition) at a dosage of 500mg/kg. Neuropharmacological activities were also observed at 300 and 500mg/kg of *C. rotundus* extract. The ethanolic extract showed mild decreased in all test and exhibited slight muscle relaxant effect (36).

- The effects of *C. rotundus* tuber extract on the microorganisms of the urinary tract infection were investigated. Ethanol extracts of the tuber was prepared by maceration. Antimicrobial effect of these extracts on the isolated strains was determined by disk diffusion and broth microdilution methods. Results revealed a growth inhibitory concentration greater than 0.5mg/ml of the ethanol extract on all the examined microorganisms of the urinary tract infection. It was thus concluded that the plant has a significant antimicrobial property with a potentially important role in the treatment of the urinary tract infection (37).
- The *in vitro* anthelmintic activity of methanolic extract of *C. rotundus* leaves at two different concentrations was studied (20, 50mg/ml). The extract was taken for anthelmintic activity against Indian earthworm *Pheretima posthuma*. The results were expressed in terms of time required for paralysis and death of *Pheretima posthuma*. Albendazole was used as a standard control group. The plant extract showed the significant activity at higher concentrations when compared to a standard control group (Albendazole) (38).
- The effect of hydroalcoholic extract of *C. rotundus* rhizomes in nephrolithiatic male Sprague Dawley rats was evaluated. The results showed that test extract has significant antilithiatic effect in terms of solute balance, reduction in crystal numbers and improvement in renal cell derangement (39).
- The behavioral studies on mice indicated CNS depressant activity of the ethanol extract of *C. rotundus* was evaluated. The ethanol extract of *C. rotundus* significantly potentiated the sleeping time of mice induced by standard hypnotics (pentobarbitone sodium, diazepam and meprobamate) in a dose dependent manner (40).

16. Additional information

- The antiplatelet activities the ethanolic extract of *C. rotundus* and eight of its constituent compounds were evaluated by examining their effects on rat platelet aggregations *in vitro* and *ex vivo*, and on mice tail bleeding times. The extract showed significant and concentration dependent inhibitory effects on collagen-, thrombin-, and/or arachidonic acid (AA)-induced platelet aggregation prolonged bleeding times. *C. rotundus* can also improve all hemorrheological indexes, such as

the whole blood specific viscosity, the plasma specific viscosity, erythrocyte electrophoresis, *etc.* (41).

- The antidiabetic activity of hydro-ethanolic extract of *C. rotundus* rhizomes in alloxan induced diabetes in rats was carried out. Oral daily administration of 500 mg/kg of the extract (once a day for seven consecutive days) significantly lowered the blood glucose levels. This antihyperglycemic activity can be attributed to its antioxidant activity as it showed the strong DPPH radical scavenging action *in vitro* (42).

17. Date of compilation/last revision

05/04/2022.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Ahmed, S. S. and Ibrahim, A. E. (2018). *Cyperus rotundus* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **6**, 457-470. Academy of Scientific Research and Technology, Cairo, Egypt.
3	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
4	Sofia, H. N., Walter, T. M., Merish, S., Tamizhamuthu, M. (2014). An overview of nut grass (*Cyperus rotundus*) with special reference to Ayush. *World Journal of Pharmaceutical Research*, **3**(6), 1459-1471.
5	Samra, R. M., Soliman, A. F., Zaki, A. A., El-Gendy, A., Hassan, M. A. and Zaghloul, A. M. (2020). Chemical composition, antiviral and cytotoxic activities of essential oil from *Cyperus rotundus* growing in Egypt: Evidence from chemometrics analysis. *Journal of Essential Oil Bearing Plants,* **23**(4), 648-659. DOI: 10.1080/0972060X.2020.1823892.
6	EL-Gohary, H. M. (2004). 14- Study of essential oils of the tubers of *Cyperus rotundus* L. and *C. alopecuroides* rottb. *Bulletin of Faculty of Pharmacy*, Cairo University, **42**(1), 157-163.
7	Lawal, O. A. and Oyedeji, A. O. (2009). Chemical Composition of the Essential Oils of *Cyperus rotundus* L. from South Africa. *Molecules*, **14**, 2909-2917.
8	Hu, Q. P., Cao, X. M., Hao, D. L. and Zhang, L. L. (2017). Chemical composition, antioxidant, DNA damage, protective, cytotoxic and antibacterial activities of *Cyperus rotundus* rhizomes essential oil against foodborne pathogens. *Scientific Reports*, **7**, 45231. DOI: 10.1038/srep45231.
9	Al-Snafi, A. E. (2016). A review on *Cyperus rotundus.* A potential medicinal plant. *IOSR Journal of Pharmacy*, **6**(7), 32-48.
10	Essaidi, I., Koubaier, H. B., Snoussi, A., Casabianca, H., Chaabouni, M. M. and Bouzouita, N. (2014). Chemical composition of *Cyperus rotundus* L. tubers essential oil from the south of Tunisia, antioxidant potentiality and antibacterial activity against foodborne pathogens. *Journal of Essential Oil-Bearing Plants,* **17**(3), 522 - 532.
11	Aghassi, A., Naeemy, A., Feizbakhsh, A. (2013). Chemical composition of the essential oil of *Cyperus rotundus* L. from Iran. *Journal of Essential Oil-Bearing Plants*, **16**(3), 382-386.
12	Harbone, J. B., Williams C. A. and Wilson, K. L. (1985). Flavonoids in leaves and inflorescences of Australian Cyperaceae. *Phytochemistry*, **24**, 751-677.
13	Al-Jumaily, E. F. A. and Al-Isawi, J. K. T. (2014). Composition and aAntioxidant potential of polyphenol compounds of *Cyperus rotundus* L. rhizomes. *American Journal of Phytomedicine and Clinical Therapeutics*, **2**(11), 1277-1286.
14	Ju, Y. and Xiao, B. (2016). Chemical constituents of *Cyperus rotundus* L. and their inhibitory effects on uterine fibroids. *African Health Sciences*, **16**(4), 1000.
15	Peerzada, M., Ali, H. H., Naeem, M., Latif, M., Bukhari, A. H. and Tanveer, A. (2015). *Cyperus rotundus* L.: Traditional uses, phytochemistry, and pharmacological activities. *Arslan Journal of Ethnopharmacology*, **174**, 540–560.

16	Ibrahima, S. R. M., Mohamed, G. A., Alshalie, K. Z., Al Haidaria, R. A., El-Kholyf, A. A. and Zayed, M. F. (2018). Lipoxygenase inhibitors flavonoids from *Cyperus rotundus* aerial parts. *Brasileira de Farmacognosia*, **28**(3), 451-456.
17	Gamal, M. A., Hani, K. M. K., Sameh, E. S. and Sabrin, I. R. M. (2015). A review: Compounds isolated from *Cyperus* species (Part I): Phenolics and nitrogenous. *International Journal of Pharmacognosy and Phytochemical Research*, **7**(1), 51-67.
18	Boulos, L. and El-Hadidi, M. N. (1984). The Weed Flora of Egypt, Cairo: The American University in Cairo Press.
19	https://www.webmd.com/vitamins/ai/ingredientmono-1297/purple-nut-sedge
20	https://www.rxlist.com/purple_nut_sedge/supplements.htm
21	Mohammed, G. F. A. (2014). Topical *Cyperus rotundus* oil: A new therapeutic modality with comparable efficacy to Alexandrite Laser Photo-Epilation. *Aesthetic Surgery Journal*, **34**(2), 298–305.
22	Mohammed, G. F. A. (2012). Role of *Cyperus rotundus* oil in decreasing hair growth. *J. Intercult. Ethnopharmacol.,* **1**(2), 111-118.
23	Nima, Z. A., Jabier, M. S., Wagi, R. I., Hussain, H. A. (2008). Extraction, identification and antibacterial activity of *Cyperus* oil from Iraqi *C. rotundus*. *Eng. Technol.*, **26**(10), 1156-1159.
24	Kumar, S., Kumar, K. and Gautam, S. S. (2014). Antibacterial evaluation of *Cyperus rotundus* Linn. root extracts against respiratory tract pathogens. *African Journal of Pharmacology and Therapeutics*, **3**(3), 95-98.
25	Uddina, S. J., Mondala, K., Shilpia, J. A. and Rahman, M. T. (2006). Antidiarrhoeal activity of *Cyperus rotundus*. *Fitoterapia*, **77**(2), 134-136.
26	Shamkuwar, P. B., Hoshamani, A. H. and Indrajeet, D. (2012). Antispasmodic effect of *Cyperus rotundus* L (Cyperaceae) in diarrhoea. *Der Pharma Letter*, **4**, 522-524.
27	Biradar, S., Kangralkar, V. A., Mandavkar, Y., Thakur, M. and Chougule, N. (2010). Anti-inflammatory, anti-arthritic, analgesic and anticonvulsant activity of *Cyperus* essential oils. *Int. J. Pharm. Pharm. Sci.*, **2**, 112–115.
28	Gupta, M. B., Palit, T. K., Singh, N. and Bhargava, K. P. (1971). Pharmacological studies to isolate the active constituents from *Cyperus rotundus* possessing anti-inflammatory, anti-pyretic and analgesic activities. *Indian Journal of Medical Research*, **59**, 76–82.
29	Soumaya, K. J., Dhekra, M., Fadwa, C., Zied, G., Ilef, L., Kamel, G. and Leila, C. G. (2013) Pharmacological, antioxidant, genotoxic studies and modulation of rat splenocyte functions by *Cyperus rotundus* extracts. *BMC Complement Altern Med*, **13**, 28.
30	Rajamanickam, M. and Rajamanickam A. (2016). Analgesic and anti-inflammatory activity of the extracts from *Cyperus rotundus* Linn rhizomes. *J. App. Pharm. Sci*., **6**(9), 197-203.
31	Singh, N., Kulshrestha, V. K., Gupta, M. B. and Bhargava, K. P. (1970). A pharmacological study of *Cyperus rotundus*. *Indian J. Med. Res.*, **58**, 103-109.
32	Kabir, I., Biswas, S., Asaduzzaman, M., Molla, M. and Rafe, M. (2019). Neurobehavioral activity study of methanolic whole plants extract of *Cyperus rotundus* Linn. *Journal of Pharmaceutical Negative*, **10**(1), 36-40.

33	Muhammet, E., Guldur, A., Ibrahim, O. H., Kilic, O., Sogut, M., Ozaslan, M., Yalcin, B. M., Musa, D. (2010). Gastroprotective effect of *Cyperus rotundus* extract against gastric mucosal injury induced by ischemia and reperfusion in rats. *Int. J. Pharmacol.*, **6**, 104–110.
34	Zhu, M., Luk, H. H., Fung, H. S. and Luk, C. T. (1997). Cytoprotective effects of *Cyperus rotundus* against ethanol induced gastric ulceration in rats PTR. *Phytotherapy Research*, **11**(5), 392-394.
35	Thomas, D., Govindhan, S., Baiju, E. C., Padmavathi, G., Kunnumakkara, A .B. and Padikkala, J. (2015). *Cyperus rotundus* L. prevents non-steroidal anti-inflammatory drug-induced gastric mucosal damage by inhibiting oxidative stress. *J. Basic Clin. Physiol. Pharmacol.*, **26**(5), 485-490.
36	Ahmad, M., Rookh, M., Bin Rehman, A., Muhammad, N., Younus, M. and Wazir, A. (2014). Assessment of anti-inflammatory, anti-ulcer and neuropharmacological activities of *Cyperus rotundus* Linn. *Pak. J. Pharm. Sci*., **27**(6), 2241-2246.
37	Dadooka, M., Mehrabianb, S. and Irianc, S. (2019). Antimicrobial effect of *Cyperus rotundus* tuber extract on the microorganisms of the urinary tract infection. *J. Bacteriol. Mycol.*, **6**(4), 2471-2472.
38	Kasala, S., Ramanjaneyulu, K., Himabindhu, J., Alluri, R. and Babu, R. R. (2016). Preliminary phytochemical screening and *in vitro* anthelmintic activity of *Cyperus rotundus* (L). *Journal of Pharmacognosy and Phytochemistry*, **5**(5), 407-409.
39	Jahan, N., Bano, H., Makbul, S. A., Kumar, B. N. and Mushir, A. (2019). Effect of hydroalcoholic extract of *Cyperus rotundus* L. rhizome against ethylene glycol and ammonium chloride-induced urolithiasis in male sprague-dawley rats. *Urol. Sci.*, **30**, 99-106.
40	Pal, D., Dutta, S. and Sarkar, A. (2009). Evaluation of CNS activities of ethanol extract of roots and rhizomes of *Cyperus rotundus* in mice. *Acta Pol. Pharm.*, **66**(5), 535-541.
41	Xue, J. X., Jiang, Y. and Yan, Y. Q. (1993). Effects of the combination of *Astragalus membranaceus* (Fisch.) Bge. (AM), tail of *Angelica sinensis* (Oliv.) Diels. (TAS), *Cyperus rotundus* L. (CR), *Ligusticum chuanxiong* Hort. (LC) and *Paeonia veitchii* Lynch (PV) on the hemorrheological changes in normal rats. *Zhongguo Zhong Yao Za Zhi*, **18**(10), 621-623.
42	Raut, N. A. and Gaikwad, N. J. (2006). Antidiabetic activity of hydro-ethanolic extract of *Cyperus rotundus* in alloxan induced diabetes in rats. *Fitoterapia*, **77**(7-8), 585-588.

Egyptian Herbal Monograph

Traditional wild medicinal plants

Moringa peregrina (Forssk.) Fiori حب اليسار

1. Names & Synonyms

Moringa peregrina (Forssk.) Fiori (1,2).
Family: Moringaceae (3).
Syns. *Hyperanthera peregrina* Forssk.
Moringa aptera Gaertn., Fruct.
Moringa arabica Pers., Syn. (3).
Arabic: Yasaar يسار , El-Baan البان , Habb El-Yasaar (seeds) حب اليسار (البذور) (3).
English: Ben-oil tree, Horse radish tree, Ben nut (seed), Moringa (1, 3).

2. Geographical distribution

Desert east of the Nile including that of Sinai, Red Sea region and Gebel Elba (1, 3).

3. Parts used for medicinal purposes

All parts of the plant (seeds, leaves, stems and tubers) (1, 3).

4. Major chemical constituents (3)

- *M. peregrina* leaves contained numerous bioactive phyto-constituents belonging to various classes such as tannins, glycosides, alkaloids, flavonoids, steroids, sterols/ triterpenes and saponins (4).

- **Fatty Acids:** Oleic acid was identified as the major one, palmitic, stearic, behenic, palmitoleic, arachidic, eicosenoic, lingnoceric, linoleic, margaric, myristic, margaroleic and linolenic acids were also detected. Furthermore, sterol composition analysis of the oil showed that β-sitosterol was the major one followed by stigmasterol, campesterol and Δ-5-avenasterol (5).

- **Phenolic Compounds:** Gallic, protocatechuic, 4-hydroxybenzoic, caffeic, syringic, trans *p*-coumaric, chlorogenic and trans- ferulic acids as well as catechin (6).

- **Triterpenoids:** Lupeol acetate, β-amyrin and α-amyrin.

- **Flavonoidal compounds:** Quercetin, chrysoeriol-7-O-rhamnoside, apigenin, rhamnetin, Quercetin-3-*O*-rutinoside, rhamnetin-3-*O*-rutinoside and 6-methoxy-acacetin-8-C-β-glucoside (7).

- **Isothiocyanates:** Benzyl isothiocyanate, 2-propyl isothiocyanate, 2- butyl isothiocyanate, 2-methylpropyl isothiocyanate, 4(a-L-rhamnosyloxy) benzyl isothiocyanate, 4-(4′-O-acetyl-a-L-rhamnosyloxy benzyl isothiocyanate, glucosinolate and 5,5-dimethyloxazolidine- 2-thione from the seeds (8).

- **Nitrile glycosides:** Niazirin, niazirinin and 4-(4′-*O*-methyl-α-L-rhamnosyloxy benzyl nitrile).

5. Traditional medicinal uses (9, 10)

Ancient Egyptians were using *M. peregrina* for thousands of years to maintain their skin health and mental fitness.

A. Increasing appetite and to treat slimness.
B. Anti-constipation.
C. Headache, fever, abdominal pain, burns, back and muscle pains and during labor.
D. Soothe rash.

***M. peregrina* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (10)

1. Jam of several constituents cooked in black honey.
2. Decoction: add 2 teaspoonful of seeds in a pot, pour cold water, boil and simmer for 10 minutes then pour into a cup and drink it.
3. The seed oil.
4. The seed oil.
5. The leaf extract.

7. Posology and method of administration correlated to medicinal use (10)

Method of administration: Oral use**.**
M. peregrina hot decoction is taken in the morning before breakfast.

Method of administration: Topical use.
The leaf extract and oil are rubbed over the skin.

Duration of use:
If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- None known.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

14. Overdose

No case of overdose has been reported.

15. Relevant biological activities

- The antimicrobial potential of *M. peregrina* seed oil was studied (11). The results indicated that the oil was effective against all the tested microorganisms (bacterial and fungal strains). Antimicrobial activity of ethanol extract of leaves, seed coat and endosperm of the plant were also studied. The leaf extract of *M. peregrina* showed good antibacterial activity, followed by seed coat and endosperm. The ethanolic leaf extract also showed good antifungal activity (12). Aqueous extract of *M. peregrina* seeds was investigated for antibacterial activity against clinically isolated multidrug resistant Salmonella species. The results showed that the extracts exhibited good antibacterial activity against the multidrug resistant Salmonella isolates (13).

- The anti-spasmodic potential of hydroalcoholic extract from the leaves and seeds of *M. peregrina* was studied by ileum contractions induced by 80mM KCl, 250µM of acetylcholine (ACh) and electrical field stimulation (EFS). Both the extracts have an inhibitory potential on ileum contractions. The seeds extract of *M. peregrina* had more potential inhibitory effect of ileum contraction (14).
- Ethanol and aqueous extracts of *M. peregrina* were studied for anti-inflammatory potential using fresh egg albumin induced inflammation (oedema) in rats. The results revealed that the aqueous and ethanol extracts significantly reduced the acute inflammation induced by fresh egg albumin. At a dose level of 300 mg/kg, aqueous and ethanol extracts reduced the inflammation by 72.96 and 81.01%, respectively at the third hour after the oedema was induced. Whereas, the control drug diclofenac at the dose level of 100 mg/kg reduced the inflammation by 100% at the third hour (15).
- The neuroprotective effect of aqueous extract from the leaves of *M. peregrina* was investigated and reported by studying the learning capacity and memory in mice. Based on the results, it was concluded that the aqueous extract of *M. peregrina* enhanced the memory function of scopolamine induced amnesia in mice (16).
- Various extracts of *M. peregrina* were studied for their antioxidant potential. The results showed that *M. peregrina* extracts exhibited antioxidant activity in all tests and the extracts could be considered as a source of natural antioxidants (15, 17-19).

16. Additional information:

The seeds contained 24.1% crude protein, 53.5% fat, 2.6% ash and 2.4% moisture. The mineral analysis indicated high potassium (630.2 mg/100 g) and phosphorus (620.5 mg/100 g) content. Moringa protein was rich in arginine (15.3%), leucine (9%), glycine (8.4%) and proline (8.2%), while essential amino acids comprised approximately 56% of the moringa protein. The seeds oil was found to contain high level of unsaturated fatty acids (83.5%) and in particular oleic acid (74.8%). palmitic (8.9%), stearic (3.1%) and behenic (2.6%) acids were found to be the predominant saturated fatty acids. The seeds oil was also found to contain high levels of *β*-sitosterol (28.3%), stigmasterol (24.54%), campesterol (23.7%) and Δ-5-avenasterol (16.1%) (5).

17. Date of compilation/last revision

05/04/2022.

References

1	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
2	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
3	Ahmed, S. S. and Sabry, R. M. (2018). *Moringa peregrina* (Forssk.) Fiori, In: Egyptian Encyclopedia of Wild Medicinal Plants, **8**, 418-432. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Akbar, S. and Al-Yahya, M. A. (2011). Screening of Saudi plants for phytoconstituents, pharmacological and antimicrobial properties. *Australian Journal of Medical Herbalism*, **23**(2), 76-87.
5	Al-Dabbas, M. M., Ahmad, R., Ajo, R. Y., Abulaila, K., Akash, M. and Al-Ismail, K. (2010). Chemical composition and oil components in seeds of *Moringa peregrina* (Forssk) Fiori. *Crop Res*., **40**, 161-167.
6	Al-Owaisi, M., Al-Hadiwi, N. and Khan, S. A. (2014). GC-MS analysis, determination of total phenolics, flavonoid content and free radical scavenging activities of various crude extracts of *Moringa peregrina* (Forssk.) Fiori leaves. *Asian Pac. J. Trop. Biomed.*, **4**(12), 964-970.
7	El-Alfy, T. S., Ezzat, S. M., Hegazy, A. K., Amer, A. M. and Kamel, G. M. (2011). Isolation of biologically active constituents from *Moringa peregrina* (Forssk.) Fiori. (Family: Moringaceae) growing in Egypt. *Pharmacogn. Mag*., **7**(26), 109-115.
8	Kær, A., Malver, O., El-menshawi, B., and Reischt, J. (1979). Isothiocyanates in myrosinase-treated seed extracts of *Moringa peregrina*. *Phytochem*., **18**, 1485-1487.
9	Senthilkumar, A., Karuvantevida, N., Rastrelli, L., Kurup, S. S. and Cheruth, A. J. (2018). Traditional uses, pharmacological efficacy and phytochemistry of *Moringa peregrina* (Forssk.) Fiori. - A review. *Front. Pharmacol*., **9**, 465. doi: 10.3389/ fphar.2018.00465.
10	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
11	Lalas, S., Gortzi, O., Athanasiadis, V., Tsaknis, J. and Chinou, I. (2012). Determination of antimicrobial activity and resistance to oxidation of *Moringa peregrina* seed oil. *Molecules*, **17**, 2330-2334.
12	Hajar, A. S., and Gumgumjee, N. M. (2014). Antimicrobial activities and evaluation of genetic effects of *Moringa peregrina* (Forsk.) Fiori using molecular techniques. *Int. J. Plant Anim. Environ. Sci.,* **4**, 65–72.
13	Saleh, N. M., Mabrouk, M. I., Salem-Bekhit, M. M. and Hafez, E. H. (2017). Challenge of *Moringa peregrina* Forssk. as an antimicrobial agent against multi-drug-resistant Salmonella Spp. *Med. Biotechnol*., **31**, 380–386.
14	Sadraei, H., Asghari, G., and Farahnaki, F. (2015). Assessment of hydroalcoholic extract of seeds and leaves of *Moringa peregrina* on ileum spasm. *Res. Pharm. Sci*., **10**, 252–258.

15	Koheil, M. A., Hussein, M. A., Othman, S. M., and El-Haddad, A. (2011). Antiinflammatory and antioxidant activities of *Moringa peregrina* seeds. *Free Radical Antioxidants,* **1**, 49–61. doi: 10.5530/ax.2011.2.10.
16	Elsaey, M. A., Sallam, A. E. D., Hassaneen, E., and Zaghloul, M. S. (2016). Circadian phase modulates the enhancing effect of the Egyptian *Moringa peregrina* extract on learning and memory in mice. *Biol. Rhythm Res.,* **47**, 703–715.
17	Marwah, R. G., Fatope, M. O., Al Mahrooqi, R., Varma, G. B., Al Abadi, H. and Al-Burtamani, S. K. S. (2007). Antioxidant capacity of some edible and wound healing plants in Oman. *Food Chem*., **101**, 465–470.
18	Dehshahri, S., Wink, M., Afsharypuor, S., Asghari, G. and Mohagheghzadeh, A. (2012). Antioxidant activity of methanolic leaf extract of *Moringa peregrina* (Forssk.) Fiori. *Res. Pharm. Sci.,* **7**, 111–118.
19	Moustafa, S. M. A., Menshawi, B. M., Wassel, G. M., Mahmoud, K. and Mounier, M. M. (2014). Screening of some wild and cultivated Egyptian plants for their free radical scavenging activity. *Int. J. PharmTech. Res*., **6**, 1271–1278.

Egyptian Herbal Monograph

Traditional wild medicinal plants

***Origanum syriacum* L.** زعتر ، بردقوش

1. Names & Synonyms (1-3)

Family: Labiatae (Lamiaceae).

Syn. *Origanum maru* L. var. *sinaicum* Boiss.

Arabic: Bardaqoush بردقوش ، Za'atar زعتر.

English: Syrian oregano, Lebanese oregano, or the hyssop of the Bible (4).

2. Geographical distribution (1-3)

Confined to Sinai (endemic).

3. Parts used for medicinal purposes (3)

The leaves, the flower heads and the total herb.

4. Major chemical constituents (3)

- Essential Oil: Thymol, carvacrol, *p*-cymene, thymoquinone and *γ*-terpinene were identified as major constituents of *O. syriacum* oil. Other identified constituents were octan-3-ol, caryophyllene oxide, *β*-caryophyllene, *cis*-sabinene hydrate, terpinen-4-ol and *α*-terpinene (5-10). Only in one case the bicyclic *cis*-sabinene hydrate was described as a major compound in this species (7).

- Flavonoids: Luteolin, luteolin-6-C-glucoside, luteolin-3_-methylether-6-C-glucoside, luteolin-7,4_-dimethyether-6-C-glucoside, apigenin, apigenin-7-methylether-6-C-glucoside, apigenin-7-O-glucoside, diosmetin-7-O-glucoside, acacetin-7-O-glucoside, quercitrin, rutin, acacetin-7-O-rutinoside and acacetin-7-O-[2-O-*α*-L-rhamnopyranosyl-6-O-*β*-D-glucopyranosyl]-*β* -D-glucopyranoside (11, 12).

- Phenolics: Catechol, catechinic acid and pyrogallol. Other polyphenol components were chrysin, syringic, gallic, vanillic, coumaric, hydroxybenzoic, chlorogenic, caffeic and rosmarinic acids (12).

- Carotenoid: as *β*-carotene (12).

5. Traditional medicinal uses

Stomach troubles:

- Stomach and digestive disorders (13).

Origanum is also used as a stimulant, analgesic, antitussive, expectorant, sedative, antiparasitic and antihelminthic, but mostly for gastrointestinal complaints (7).

***O. syriacum* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (13)

*** Decoction:**

Pour cold water on 2 teaspoonful of *O. syriacum* leaves and boil, simmer for 10 minutes. Pour into a cup and drink it sweetened if desired.

7. Posology and method of administration correlated to medicinal use

***Oral:**

Drinking the extract of the boiled leaves 3 cups/day.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Monitoring of blood glucose level should be done regularly (13, 14).

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during lactation is not recommended.
- No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- None known.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

14. Overdose

No case of overdose has been reported.

15. Relevant biological activities

- Both cultivated and wild *O. syriacum* essential oil showed anti-bacterial and anti-fungal activities (15-19). The essential oil showed *in vitro* anti-oxidant and anti-microbial properties (20, 21). In addition, the aqueous extract showed anti-oxidant properties (22).
- Ethanol crude extract of the plant showed anti-proliferative activity. The hydrodistilled essential oil and aqueous extract did not show any cytotoxic activity (23).
- The essential oil exhibited some properties relevant to anti-inflammatory action. Moreover, even at very small concentrations, an interesting inhibitory activity on acetylcholinesterase (AchE) and butyrylcholinesterase (BchE), key enzymes in the pathogenesis of Alzheimer's disease was observed (24).
- The anthelminthic and insecticidal potential of the leaf essential oil of *O. syriacum* against the L3 larvae of the parasitic nematode *Anisakis simplex* and larvae and adults of the mosquito *Culex quinquefasciatus* was determined through the oil impact as AchE inhibitor (LC_{50} of 0.087 and 0.067mg mL-1 after 24 and 48h treatment, respectively). The essential oil was also highly effective on both larvae and adults of *C. quinquefasciatus*, showing LC_{50} values of 32.4mg L^{-1} and 28.1μg cm^{-2}, respectively (25) These results support the folk usage of *O. syriacum* as an antiparasitic agent, providing new insights about its utilization for developing new effective and eco-friendly nematocidal and insecticidal products.
- The essential oil of *O. syriacum* was evaluated for its AchE, nitric oxide production inhibitory activities, and antioxidant properties. The oil inhibited oxidation of linoleic acid after 30min and 60min of incubation, with IC_{50} values of 46.9 and 58.9lg/ml, respectively. AchE and BchE inhibition was also assessed. The data suggest that *O. syriacum* oil could be used as a valuable new flavor with functional

properties for food or nutraceutical products with particular relevance to supplements for the elderly (24).

- The hepatoprotective and therapeutic effects of *O. syriacum* aqueous methanolic extract of defatted aerial parts on paracetamol induced liver cell damage in mice with respect to antioxidant status, was investigated. Mice were treated with the extract in saline solution (0.5ml of 1/10 extract LD50/day/ 5days) and silymarin in recommended dose (25mg/kg for 5days prepared in 0.5ml saline solution) after or before paracetamol administration (400mg/ kg/ day). The results proved sufficient activity of *O. syriacum* extract in hepatic protection against administration of paracetamol and showed the role of *O. syriacum* extract in liver amelioration of mucopolysaccharide content in hepatocytes and in cells of renal tissue. It was more effective than sylimarin as hepatoprotective. Also, the plant extract was sufficient to decrease the oxidative stress on liver as mentioned in magnification of glutathione-antioxidant system (26).
- The anti-ulcer activity of the essential oil and the ethanol extract of *O. syriacum* L. was evaluated in indomethacin-induced rats (150-170g). Both essential oil and the ethanol extract showed significant reduction of ulcers in a dose-dependent manner and significantly decreased the gastric secretion, total acidity on gastric and the effects were compared with omeprazole (27).
- Antioxidant, anti-inflammatory, antinociceptive and antipyretic activities, of the total ethanol extract, were evaluated in rats at doses of 250, 500 and 1000mg/kg. The plant extract possessed antioxidant, anti-inflammatory and antinociceptive activities in a dose dependent manner. No antipyretic activity was detected at the used doses (28).
- The methanolic extract of *O. syriacum* leaves was tested against three opportunistic microorganisms by determining the minimum inhibitory concentration. The extract was also evaluated for its ability to suppress the release of the pro-inflammatory cytokine IL-6 while not suppressing the release of the anti-inflammatory cytokine IL-10 from peripheral blood mononuclear cells using ELISA. The extract exhibited high antimicrobial activity for the three microorganisms and inhibited the expression of the pro-inflammatory cytokine IL-6 with apparent dose-dependent responses and attenuated the secretion of the anti-inflammatory cytokine IL-10. This shows that *O. syriacum* may contribute to the reduction of inflammation and microbial growth and may also be preventive against various infections, including those related to the oral cavity (29).
- In a randomized double-blind controlled trial, the activity of a spray containing essential oils of *Eucalyptus citriodora, E. globulus, Mentha x piperita, Origanum syriacum, and Rosmarinus officinalis* was studied in patients with URTI. 34 patients in the test group used this spray 5 times a day (4 spraying each time) for 3 days. Then the change of the most debilitating symptoms (sore throat, hoarseness or

cough) was assessed in patients. 20 minutes after the use of the spray, participants in the test group reported a greater improvement in symptoms compared to participants in the control group. There was no difference in symptom severity between the two groups after 3 days of treatment. Based on these results, authors suggested the local, rather than systemic, effect of this spray on the upper respiratory tract (30).

16. Additional information

In Palestinian folk medicine, *O. syriacum* is used for the treatment of skin fungal diseases, abdominal pain, throat infection and cough. Similar therapeutic uses of *O. syriacum* have been reported from neighboring countries as Jordan, Syria and Lebanon (31-35).

O. syriacum oil was evaluated for its antifungal activity against *Aspergillus niger, Fusarium oxysporum,* and *Penicillium* species. The oil exhibited strong inhibitory action against the three fungi tested. The minimum inhibitory concentration of the oil was found to be 0.1μ/ml of yeast extract sucrose broth for the fungi tested (36).

The assessment of the antimicrobial activity of plant essential oil against *Candida albicans* and six pathogenic bacteria revealed that *O. syriacum* oil showed moderate antimicrobial activity with minimal inhibitory concentrations varying from 400 to 1200μg/ml (19).

17. Date of compilation/last revision

05/04/2022.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Hammouda, F. M., Abdel-Azim, N. S, and Shams, K. A. (2018). *Origanum syriacum* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **8**, 474-489. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Mesmar, J., Abdallah, R., Badran, A., Maresca, M. and Baydoun, E. (2022). *Origanum syriacum* phytochemistry and pharmacological properties: A comprehensive review. *Molecules*, **27**, 4272. https://doi.org/10.3390/molecules27134272.
5	Kamel, M. S., Assaf, M. H., Hasanean, H. A., Ohtani, K., Kasai, R. and Yamasaki, K. (2001). Monoterpene glycosides from *Origanum syriacum. Phytochemistry*, **58**(8), 1149-1152.
6	Zgheib, R., Chaillou, S., Ouaini, N., Kassouf, A., Rutledge, D., Azzi, D. and El Beyrouthy, M. (2016). Chemometric tools to highlight the variability of the chemical composition and yield of Lebanese *Origanum syriacum* L. essential oil. *Chem. Biodivers.*, **13**, 1326-1347.
7	Baser, K. H. C., Kurkcuoglu, M., Demirci, B. and Ozek, T. (2003). The essential oil of *Origanum syriacum* L. var. *sinaicum* (Boiss.) letswaart. *Flavour Fragrance J.,* **18**, 98-99.
8	Halim, A. F., Mashaly, M. M., Zaghloul, A. M., Abd El-Fattah, H. and De-Pooter, H. L. (1991). Chemical constituents of the essential oils of *Origanum syriacum* L. and *Stachys aegyptiaca*. *Int. J. Pharmacogn.*, **29**, 183-187.
9	Soliman, F. M., Yousif, M. F., Zaghloul, S. S., Okba, M. M. and El-Sayed, E. M. (2007). Seasonal variation in the essential oil composition of *Origanum syriacum* L. subsp. *sinaicum* greuter and burdet; evaluation of its tocolytic activity. *Egypt. J. Biomed. Sci.,* **23**, 121-134.
10	Shamseddine, L. and Chidiac, J. J. (2020) Composition's effect of *Origanum syriacum* essential oils in the antimicrobial activities for the treatment of denture stomatitis. *Odontology*, **109**(2), 327-335. doi: 10.1007/s10266-020-00547-3.
11	Samy K. El-Desoukya et al (2009) Phytochemical constituents and biological activities of *Origanum syriacum. Z. Naturforsch.*, **64b**, 447–451.
12	Afify, M. R. A., Esawy, S. H., El-Hadidy, E. M. and Abdel-Salam, M. A. L. (2014). Antioxidant content and cytotoxicity of *Origanum syriacum* L. *Advances in Food Sciences*, **36**(2), 58-64.
13	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.
14	https://www.drugs.com/npc/oregano.html
15	Daouk, R. K., Dagher, S. M. and Sattout, E. J. (1995). Antifungal activity of the essential oil of *Origanum syriacum* L. *Journal of Food Protection*, **58**(10), 1147-1149.

16	El Gendy, A. N., Leonardi, M., Mugnaini, L., Bertellonic, F., Ebanic, V. V., Nardonic, S., Manciantic, F., Hendawy, S., Omer, E. and Pistelli, L. (2015). Chemical composition and antimicrobial activity of essential oil of wild and cultivated *Origanum syriacum* plants grown in Sinai, Egypt. *Ind. Crops Prod*., **67**, 201-207.
17	Ramadan, A., Afifi, N. A., Fathy, M. M., El-Kashoury, E. A. and El-Naeneey, E. V. (1994). Some pharmacodynamic effects and antimicrobial activity of essential oils of certain plants used in Egyptian folk medicine. *Veterinary Medical Journal*, **42**(1B), 263-270.
18	Ibrahim, L., Karaky, M., Ayoub, P., El Ajouz, N. and Ibrahim, S. (2012). Chemical composition and antimicrobial activities of essential oil and its components from Lebanese *Origanum syriacum* L. *The Journal of Essential Oil Research*, **24**(4), 339-345.
19	Al Hafi, M., El Beyrouthy, M., Ouaini, N., Stien, D., Rutledge, D. and Chaillou, S. (2016). Chemical composition and antimicrobial activity of *Origanum libanoticum, Origanum ehrenbergii* and *Origanum syriacum* growing wild in Lebanon. *Chem. Biodivers*., **13**, 555-560.
20	Alma, M. H., Mavi, A., Yildirim, A., Digrak, M. and Hirata, T. (2003). Screening chemical composition and *in vitro* antioxidant and antimicrobial activities of the essential oils from Origanum syriacum L. growing in Turkey. *Biol. Pharm. Bull.*, **26**(12), 1725-1729.
21	Tepe, B., Daferera, D., Sokmen, M., Polissiou, M. and Atalay, S. (2004). The *in vitro* antioxidant and antimicrobial activities of the essential oil and various extracts of *Origanum syriacum* L. var. *bevanii*. *J. Sci. Food Agric*., **84**, 1389-1396.
22	Dorman, H. J., Bachmayer, O., Kosar, M. and Hiltunen, R. (2004). Antioxidant properties of aqueous extracts from selected Lamiaceae species grown in Turkey. *J. Agric. Food Chem*., **52**(4), 762-770.
23	Al-Kalaldeh, J. Z., Abu-Dahab, R. and Afifi, F. U. (2010). Volatile oil composition and antiproliferative activity of *Laurus nobilis, Origanum syriacum, Origanum vulgare* and *Salvia triloba* against human breast adenocarcinoma cells. *Nutrition Research*, **30**, 271-278.
24	Loizzo, M. R., Menichini, F., Conforti, F., Tundis, R., Bonesi, M., Saab, A. M., Statti, G. A., Cindio, B., Houghton, P. J., Menichini, F. and Frega, N. G. (2009). Chemical analysis, antioxidant, antiinflammatory and anticholinesterase activities of *Origanum ehrenbergii* Boiss and *Origanum syriacum* L. essential oils. *Food Chemistry,* **117**, 174–180.
25	López, V., Pavela R., Gómez-Rincón, C., Les, F., Bartolucci, F., Gali, V., Petrelli, R., Cappellacci, L., Maggi, F., Canale, A., Otranto, D., Sut, S., Dall'Acqua, S. and Benelli, G. (2019). Efficacy of *Origanum syriacum* essential oil against the mosquito Vector *Culex quinquefasciatus* and the gastrointestinal parasite *Anisakis simplex*, with insights on acetylcholinesterase inhibition. *Molecules*, **24**, 2563.
26	Ibrahim, A. Y., Shaffie, N. M. and Motawa, H. M. (2010). Hepatoprotective and therapeutic activity of *Origanum syriacum* aqueous extract in paracetmol induced cell damage in albino mice. *Journal of American Science*, **6**(11), 449-458.
27	Afify, A. M. R., Esawy, S. H., El-Hadidy, E. M. and Abdel-Salam, M. A. L. (2012). Anti-ulcer activity of oregano (*Origanum syriacum* l.) against gastric ulcer in rats. *Advances in Food Sciences*, **34**(3), 145-149.

28	Awaad, A. S., El-meligy, R. M., Qenawy, S. A., Atta, A. H. and Soliman, G. A. (2011). Anti-inflammatory, antinociceptive and antipyretic effects of some desert plants. *Journal of Saudi Chemical Society*, **15**, 367-373.
29	Assaf, A. M., Amro, B. I., Mashallah, S. and Haddadin, R. N. (2016). Antimicrobial and anti-inflammatory potential therapy for opportunistic microorganisms. *J. Infect. Dev. Ctries.*, **10**(5), 494-505.
30	Ben-Arye, E., Dudai, N., Eini, A., Torem, M., Schiff, E. and Rakover, Y. (2011). Treatment of upper respiratory tract infections in primary care, A randomized study using aromatic herbs. *Evid. Based Complement. Alternat. Med*., 690346. doi: 10.1155/2011/690346.
31	Shehadeh, M., Silvio, S., Ghadeer, A., Darwish, R. M., Giangaspero, A., Vassallo, A., Lepore, L., Oran, S. A., Hammad, H. and Tubaro, A. (2014). Topical anti-inflammatory potential of six *Salvia* species grown in Jordan. *Jordan J. Pharm. Sci*., **7**(2), 153–161.
32	Shehadeh, M., Suaifan, G. and Darwish, R. (2017). Complementary and alternative modalities, a new vein in weight control and reduction interventions. A pilot study in Jordan. *Int. J. Biol. Biomed.*, **2**, 1–5.
33	Aburjai, T., Hudaib, M., Tayyem, R., Yousef, M. and Qishawi, M. (2007). Ethnopharmacological survey of medicinal herbs in Jordan, the Ajloun Heights region. *J. Ethnopharmacol.,* **110**(2), 294–304.
34	Ali-Shtayeh, M. S., Yaniv, Z. and Mahajna, J. (2000). Ethnobotanical survey in the Palestinian area: a classification of the healing potential of medicinal plants. *Journal of Ethnopharmacology*, **73**, 221-232.
35	Husein, A. I., Ali-Shtayeh, M. S., Jamous, R. M., Zaitoun, S. Y. A., Jondi, W. J. and Zatar, N. A. A. (2014). Antimicrobial activities of six plants used in traditional Arabic Palestinian herbal medicine. *Afr. J. Microbiol. Res*., **8**(38), 3501–3507.
36	Daouk, R. K., Dagher, S. M. and Sattout, E. J. (1995). Antifungal activity of the essential oil of *Origanum syriacum* L. *Journal of Food Protection*, **58**(10), 1147-1149.

Egyptian Herbal Monograph

Traditional wild medicinal plants

Silybum marianum L. Gaertn. شوك الجمل

1. Names & Synonyms (1)

***Silybum marianum* L. Gaertn.** (2).

Family: Compositae (Asteraceae) (2).

Syns.: Carduus marianus L. (2).

Arabic: Shawk Sennari شوك سناري, Shok El-Gamal شوك الجمل (3).

English: Milk thistle and St. Mary's thistle (3).

2. Geographical distribution

Nile region, Oases of the Western Desert as well as the Mediterranean coastal strip and Sinai (3).

3. Parts used for medicinal purposes

Dried ripe fruits, freed from the pappus (1).

4. Major chemical constituents (2-6)

- Flavonolignans: Silymarin mixture mainly (silybin A, silybin B, isosilybin A, isosilybin B, silychristin, isosilychristin, silydianin).

- Flavonoids: Taxifolin, apigenin, kaempferol and their derivatives.

- Fixed oil: Linoleic, oleic, palmitic and stearic acids.

- Sterols: Tocopherol (vitamin E) and phospholipids.

- Others: Mucilage, sugars, amines and saponins.

5. Traditional medicinal uses (7, 8)

A. Symptomatic relief of digestive disorders, sensation of fullness and indigestion.

B. Support the liver function, after serious conditions have been excluded by physician.

***S. marianum* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (7)

1. Comminuted herbal substance as herbal tea for oral use.
2. Powder herbal substance.
3. Dry extracts (using acetone/ ethyl acetate / ethanol/ water or mixture of ethanol: water in different concentration).
4. Silymarin.

Herbal preparations (2-4) are in a pharmaceutical dosage form. The pharmaceutical form should be described by the pharmacopoeia full standard term.

7. Posology and method of administration correlated to medicinal use

General Dosages
140 - 600 mg of silymarin (calculated as silibinin/silybin) per day; Not to exceed 200 mg per single dose (7).

Adults and elderly (8):

Preparation 1
Single dose: 3-5 g in 100 ml of boiling water, daily dose: 2 or 3 times daily, before meals.

Preparation 2
Single dose: 300–600 mg, daily dose: 2-3 times daily, up to 1800 mg daily, before meals.

Preparation 3
- Extraction solvent acetone:
Single dose: 82-239 mg dry extract, daily dose: 2-3 times daily, up to 478 mg, before meals.

-Extraction solvent ethyl acetate:
Single dose: 123-250 mg dry extract, daily dose: 3-4 times daily.

- Extraction solvent ethanol 96% (V/V) or hydroalcoholic:
Single dose: 200 mg dry extract, daily dose: 200 mg dry extract.

Preparation 4
140-600 mg (calculated as silibinin/silybin) per day; Not to exceed 200 mg per single dose (7).

Duration of use: *S. marianum* should be used at least 3 weeks to see beneficial effects (7).

Method of administration: Oral use (7,8).

8. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Hormone-sensitive conditions such as breast, uterine and ovarian cancers, endometriosis or uterine fibroids (9, 10).

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children and adolescents under 18 years of age is not recommended (7, 8,11).
- If icterus or a change in colour of urine or stool appears, a doctor should be consulted immediately (8).

10. Interactions with other medicinal products and other forms of interaction

None reported (8).

11. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (8-10).
- No fertility data available (8).

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (8).

13. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Adverse effects are mainly transient, non-serious, gastrointestinal complaints. It is stated that silymarin may occasionally produce a mild laxative effect (2).

14. Overdose

No case of overdose has been reported (8).

15. Relevant biological activities

-The Clinical outcome, biochemical profile and the antiperoxidative effects of silymarin MZ-80 during 6 months treatment were investigated in sixty consecutive patients with alcoholic liver cirrhosis. The patients were randomized to receive either silymarin MZ-80 (S) (150 mg *t.i.d.* per day) or placebo (P) for periods of 6 months. Silymarin is well-tolerated and produces a small increase in glutathione and a decrease in lipid peroxidation in peripheral blood cells in patients with alcoholic liver cirrhosis. Despite these effects no changes in routine liver tests were observed during therapy (12).

-A comparative study was performed in patients (pts) with chronic hepatitis C and alcoholic liver disease. In addition, the effects of a flavonolignan drug silymarin were assessed. 10 pts with chronic hepatitis C, 5 pts with alcoholic hepatitis and 13 pts with alcoholic cirrhosis have been investigated. Biochemical liver tests were determined. Silymarin treatment of one month duration resulted in normalization of serum bilirubin in 55% of treated pts, AST became normal in 45%, and RBC hemolyzate MDA level normalized in similar rate. A significant increase in both GSH and retinoids was found. Alterations in oxidative stress and antioxidant defense system were shown in chronic hepatitis C, not only in alcoholic liver disease (13).

-The hepatoprotective activity of the nanoemulsion formulation of silymarin against carbon tetrachloride (CCl4))-induced hepatotoxicity on Wistar rats was assessed by determining biochemical parameters and histopathological properties. The nanoemulsion-treated group showed significant decreases in glutamate oxaloacetate transaminase, pyruvate transaminase, alkaline phosphotase, total bilirubin and tissue lipid peroxides and increased total protein, albumin, globulin and tissue glutathione as compared to toxicant. The results indicate an excellent potential of the nanoemulsion formulation for the reversal of CCl4-induced liver toxicity in rats as compared to standard silymarin (14).

-The alterations in sulfur containing amino acid metabolism induced by silymarin in association with its effects on the antioxidant capacity of liver were determined on male mice which treated with silymarin (100 or 200 mg/kg, p. o.) every 12 h for a total of 3 doses and sacrificed 6 h after the final dosing. The results demonstrate that silymarin enhances hepatic glutathione generation by elevating cysteine availability via an increment in cysteine synthesis and an inhibition of its catabolism to taurine, which may subsequently contribute to the antioxidant defense of liver (15).

-The in vitro antioxidative and oxidative DNA, protein and lipid damage protective effects of milk thistle (Silybum marianum) seed ethanol extract was investigated. The extract was found to have protective effect against DNA, protein and lipid oxidation induced by hydroxyl radical and it can protect DNA from damage. The inhibitory activity of seed extract against hydroxyl radical-induced DNA, protein and lipid damage may be mainly responsible for the cancer chemoprevention and hepatoprotection effects (16).

- Silymarin is a natural antioxidant, and this action is believed to contribute to the hepatoprotective effects of milk thistle (MT) preparations. Natural antioxidants have been shown to have beneficial effects in the preclinical models of NAFLD as well as in the pilot clinical trials. It has been reported that silymarin markedly increases the expression of superoxide dismutase in the patients with nonalcoholic steatohepatitis and decreases the oxidative stress in the *β*-thalassemia patients. Silymarin has no direct effect on ethanol metabolism and has no role in reducing ethanol levels or on the rate at which ethanol is removed from the body but the results suggest that antitoxic effects of MT are likely due to its antioxidant and free radical scavenging properties (17).

-Silymarin is a suitable candidate to treat drug-induced and toxic liver injury. It exerts a regulatory action on cellular and mitochondrial membrane permeability in association with an increase in membrane stability against the xenobiotic injury. Also, silymarin can prevent the absorption of toxins into the hepatocytes by occupying the binding sites as well as by inhibiting many transport proteins at the cell membrane (17).

-Silymarin exerts anti-inflammatory actions and attenuates autoimmune and immune-mediated liver diseases, possibly via suppression of oxidative and nitrosative immunotoxicity and T-lymphocyte function (18, 19).

- Anti-inflammatory activities of silymarin or MT extracts have been observed in a number of rat/mouse models of liver diseases, including cholestatic liver injury, restraint stress-induced acute liver, the stelic animal model of steatohepatitis, zidovudine/isoniazid-induced liver toxicity and, finally, a model of steatohepatitis induced by a methionine and choline deficient diet (20).

-A number of studies have shown that silymarin exerts anti-inflammatory action via suppression of the release of cytokines such as tumor necrosis factor-*α* (TNF-*α*), adhesion molecules, such as E-selectin, as well as via suppression of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-*κ*B) signaling, nitric oxide and 5-lipoxygenase pathways (20).

- Specifically, silymarin inhibits/suppresses: (a) the TNF-*α*-induced activation of mitogen-activated protein kinase and c-Jun N-terminal kinase and as well as the TNF-*α*-induced cytotoxicity and caspase activation, (b) both the kappa B motif of NF-*κ*B DNA binding activity and its dependent gene expression in hepatoma cells as well as the translocation of NF-*κ*B p65 protein through phosphorylation to the nucleus without affecting its ability to bind the DNA, and (c) lipopolysaccharides (LPS)-induced production of NO in isolated mouse peritoneal macrophages. A recent relevant study has shown that the NAD+/SIRT2 pathway is an important mediator through which silybin prevents the NLRP3 inflammasome activation in mice with liver steatosis (20).

-Milk thistle (MT) extracts, silymarin, and active components such as silybin have been shown to stimulate hepatic regeneration in partially hepatectomized rat livers. In several preclinical studies, silybin stimulated ribonucleic acid (RNA) polymerase-I and ribosomal RNA, leading to a more rapid formation of ribosomes, which, in turn, accelerate protein synthesis. The stimulating effect of silybin on ribosome formation can have therapeutic implications in the repair of damaged hepatocytes and the restoration of normal liver functions (17).

-The Hepatoprotective effects of silymarin in non-human primates (twelve baboons) with alcoholic liver disease was assessed. The baboons were fed alcohol with or without silymarin for 3 years with a nutritionally adequate diet. The results were showed that silymarin opposed the alcohol-induced oxidative stress and retards the development of alcohol induced hepatic fibrosis in baboons (20).

- The properties of an optimized dose of encapsulated crude Silymarin (SMR) extracted by the milk thistle seeds (SMR) on antidiabetic activity and liver fibrosis induced by paracetamol in male albino rat have been assessed. Hepatic fibrosis was assessed by measuring liver enzymes. According to the optimized study, the long-term induction of SMR (300 mg/kg) significantly amplified survival time of rats with paracetamol induced hepatic injuries. the results suggest that SMR acts as a hepatoprotective agent by inhibiting the fibrogenesis and apoptosis in liver, as well as insulin resistance (21).

-Non-alcoholic steatohepatitis (NASH) is a progressive form of non-alcoholic fatty liver disease (NAFLD characterized by hepatocellular injury and initial fibrosis severity has been suggested as an important prognostic factor of NASH. Silymarin was investigated whether it could suppress the activation of hepatic stellate cell (HSCs) in NASH induced by methionine- and choline-deficient (MCD) diet fed to insulin-resistant rats. The study demonstrates the possible protective effect of silymarin against diet induced NASH by disturbing the role of the inflammatory cytokine, TNF-α, and suppressing the activation of HSCs (22).

-The mechanisms regulating the anti-fibrogenic and anti-inflammatory activity of Silybin were assessed. Experiments were performed on hepatic stellate cells (HSC) isolated from human liver and activated by culture on plastic. The results of the study provide molecular insights into the potential therapeutic action of Silybin in chronic liver disease. This action seems to be mostly related to a marked inhibition of the production of pro-inflammatory cytokines, a clear antioxidant effect and a reduction of the direct and indirect pro-fibrogenic potential of HSC (23).

- Animal studies have shown that in the early stages of the fibrotic process, silymarin is able to inhibit the fibrogenetic mechanisms and the progression of the initial liver fibrosis. In these studies, a reduction of collagen and pro-collagen III content after biliary obstruction in the rat by 30% with 50 mg/kg/day of silymarin have been observed. Experiments aiming at investigating the mode of action have shown that

silymarin (a) suppresses the expression of pro-fibrogenic pro-collagen-α1 and TIMP-1, most likely via down-regulation of TGF-β1 mRNA, inhibits NF-κB; (b) retards the activation of HCS; and (c) alters the expression of genes involved in cytoskeleton organization and mitochondrion electron-transfer chain. Silymarin is also able to ameliorate liver fibrosis induced by carbon tetrachloride in rats in combination with sitagliptin, a dipeptidyl peptidase-4 inhibitor clinically used as an oral antidiabetic agent. Interestingly, silymarin prevents liver fibrosis in a juvenile model of nonalcoholic steatohepatitis, which can have clinical relevance in the light of the increasing incidence of NAFLD in adolescents. The antifibrotic action of silymarin could be improved with new formulations of silymarin as nanoparticles. Indeed, a special formulation silymarin-loaded Eudragit® RS100 nanoparticles has been shown to resolve cholestasis-induced liver fibrosis by restoring hepatic regenerative capabilities (17).

-A study retrospectively tracked and analyzed the data of 602 patients, out of which 230 were alcohol induced; 131 with alcohol-induced liver damage (ALD), 13 with liver cirrhosis, and 86 with fatty liver; to assess the effects of water soluble Silymarin (Liverubin™) (a patented, water-soluble liver formulation, with 140 mg of silymarin per tablet) on important hepatic biochemical parameters. Liverubin™ treatment is found to bring about effective lowering of abnormally elevated hepatic biochemical parameters and is observed to be a promising safe and effective drug in cases of alcoholic liver disease (24).

16. Additional information:

- The bioavailability of silymarin could be increased by Phospholipids (25-27).
- Silymarin is poorly soluble in water, teas have been analyzed with about 10% original levels of silymarin from the fruits. Thus, for hepatic benefits, the concentrated extract is recommended (28).

17. Date of compilation/last revision

17/05/2022.

References

1	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **2**, 300-316.
2	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
3	Hassan, N. M. and Abdallah W. E. (2020). *Silybum marianum* (L.) Gaertn. In: Egyptian Encyclopedia of Wild Medicinal Plants, **10**, 8-33. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Kroll, D. J., Shaw, H. S. and Oberlies, N. H. (2007). Milk Thistle nomenclature: Why it matters in cancer research and pharmacokinetic studies. *Integrative Cancer Therapies,* **6**(2), 110–119.
5	Graf, T. N., Cech, N. B., Polyak, S. J. and Oberlies, N. H. (2016). A validated UHPLC-tandem mass spectrometry method for quantitative analysis of flavonolignans in milk thistle (*Silybum marianum*) extracts. *J. Pharm. Biomed. Anal.*, **126**, 26-33.
6	Chambers, C. S., Holečková, V., Petrásková, L., Biedermann, D., Valentová, K., Buchta, M. and Křen, V. (2017). The silymarin composition… and why does it matter? *Food Res. Int.,* **100**(3), 339-353.
7	http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=138&lang=eng
8	European Union Herbal Monograph on *Silybum marianum* (L.) Gaertn., fructus (2018). EMA/HMPC/294187/2013. Committee on Herbal Medicinal Products (HMPC).
9	https://www.rxlist.com/consumer_milk_thistle_carduus_marianum/drugs-condition.htm
10	https://www.webmd.com/vitamins/ai/ingredientmono-138/milk-thistle
11	Mosby's Handbook of Herbs and Natural Supplements, 4th ed., ISBN: 978-0-323-05741-7.
12	Lucena, M. I., Andrade, R.J ., de la Cruz, J. P., Rodriguez-Mendizabal, M., Blanco, E. and Sánchez de la Cuesta, F. (2022). Effects of silymarin MZ-80 on oxidative stress in patients with alcoholic cirrhosis. Results of a randomized, double-blind, placebo-controlled clinical study. *Int. J. Clin. Pharmacol. Ther*., **40**(1), 2-8. doi: 10.5414/cpp40002.
13	Pár, A., Róth, E., Rumi, G. Jr., Kovács, Z., Nemes, J. and Mózsik, G. (2000). Oxidatív stressz és antioxidáns védelem alkoholos májbetegségben és krónikus C hepatitisben [Oxidative stress and antioxidant defense in alcoholic liver disease and chronic hepatitis C]. *Orv Hetil*., **141**(30), 1655-1659.
14	Parveen, R., Baboota, S., Ali, J., Ahuja, A., Vasudev, S. S. and Ahmad, S. (2011). Effects of silymarin nanoemulsion against carbon tetrachloride-induced hepatic damage. *Arch. Pharm. Res*., **34**(5), 767-74. doi: 10.1007/s12272-011-0510-8.
15	Kwon, D. Y., Jung, Y. S., Kim, S. J., Kim, Y. S., Choi, D. W. and Kim, Y. C. (2013). Alterations in sulfur amino acid metabolism in mice treated with silymarin: a novel mechanism of its action involved in enhancement of the antioxidant defense in liver. *Planta Med*., **79**(12), 997-1002. doi: 10.1055/s-0032-1328704.
16	Serçe, A., Toptancı, B. Ç., Tanrıkut, S. E., Altaş, S., Kızıl, G., Kızıl, S. and, Kızıl, M. (2016). Assessment of the antioxidant activity of *Silybum marianum* seed extract and its protective effect against DNA oxidation, protein damage and lipid peroxidation. *Food Technol. Biotechnol*., **54**(4), 455-461. doi: 10.17113/ftb.54.04.16.4323.

17	Abenavoli, L., Izzo, A. A., Milić, N., Cicala, C., Santini, A. and Capasso, R. (2018). Milk thistle (*Silybum marianum*): A concise overview on its chemistry, pharmacological, and nutraceutical uses in liver diseases. *Phytother. Res.*, **32**(11), 2202-2213. doi: 10.1002/ptr.6171.
18	Esmaeil, N., Anaraki, S. B., Gharagozloo, M. and Moayedi, B. (2017). Silymarin impacts on immune system as an immunomodulator: One key for many locks. *International Immunopharmacology*, **50**, 194–201.
19	Milic, N., Milosevic, N., Suvajdzic, L., Zarkov, M. and Abenavoli, L. (2013). New therapeutic potentials of milk thistle (*Silybum marianum*). *Natural Product Communications*, **8**, 1801–1810.
20	Lieber, C. S., Leo, M. A., Cao, Q., Ren, C. and Leonore M., DeCarli, L. M. (2003). Silymarin retards the progression of alcohol-induced hepatic fibrosis in Baboons. *J. Clin. Gastroenterol.*, **37**(4), 336–339.
21	Mukhtar, S., Xiaoxiong, Z., Qamer, S., Saad, M., Mubarik, M. S., Mahmoud, A. H. and Mohammed, O. B. (2021). Hepatoprotective activity of silymarin encapsulation against hepatic damage in albino rats. *Saudi J. Biol. Sci.*, **28**(1), 717-723. doi: 10.1016/j.sjbs.2020.10.063.
22	Kim, M., Yang, S. G., Kim, J. M., Lee, J. W., Kim, Y. S. and Lee, J. I. (2012). Silymarin suppresses hepatic stellate cell activation in a dietary rat model of non-alcoholic steatohepatitis: analysis of isolated hepatic stellate cells. *Int. J. Mol. Med.,* **30**(3), 473-9. doi: 10.3892/ijmm.2012.1029.
23	Trappoliere, M., Caligiuri, A., Schmid, M., Bertolani, C., Failli, P., Vizzutti, F., Novo, E., di Manzano, C., Marra, F., Loguercio, C. and Pinzani, M. (2009). Silybin, a component of sylimarin, exerts anti-inflammatory and anti-fibrogenic effects on human hepatic stellate cells. *J. Hepatol.*, **50**(6), 1102-11. doi: 10.1016/j.jhep.2009.02.023.
24	Nanda, V., Gupta, V., Sharma, S. N., Pasricha, A., Karmakar, A. K., Patel, A., Bhatt, V. M., Kantroo, B. L., Kumar, B., Paul, N. K. and Attam, R. (2014). Effect of Liverubin™ on hepatic biochemical profile in patients of alcoholic liver disease: a retrospective study. *Minerva Med.*, **105**(6 Suppl 2), 1-8.
25	Méndez-Sánchez, N., Dibildox-Martinez, M., Sosa-Noguera, J., Sánchez-Medal, R. and Flores-Murrieta, F. J. (2019). Superior silybin bioavailability of silybin-phosphatidylcholine complex in oily-medium soft-gel capsules versus conventional silymarin tablets in healthy volunteers. *BMC Pharmacol Toxicol.*, **20**(1), 5. doi: 10.1186/s40360-018-0280-8. Erratum in: *BMC Pharmacol Toxicol.*, **20**(1), 14. Erratum in: *BMC Pharmacol Toxicol.*, (2021), **22**(1), 37.
26	Morazzoni, P., Magistretti, M. J., Giachetti, C. and Zanolo, G. (1992). Comparative bioavailability of Silipide, a new flavanolignan complex, in rats. *Eur. J. Drug Metab. Pharmacokinet.*, **17**(1), 39-44. doi: 10.1007/BF03189986. Erratum in: *Eur. J. Drug Metab. Pharmacokinet.,* **17**(2), 165.
27	Filburn, C. R., Kettenacker, R. and Griffin, D. W. (2007). Bioavailability of a silybin-phosphatidylcholine complex in dogs. *J. Vet. Pharmacol. Ther.*, **30**(2), 132-138. doi: 10.1111/j.1365-2885.2007.00834.x.
28	Blumenthal, M., Goldberg, A., and Brinckmann, J., editors (2000). Milk Thistle Fruit. In: Herbal Medicine: Expanded Commission E Monographs. Newton, MA: Integrative Medicine Communications, 257–263.

Egyptian Herbal Monograph

Medicinal Plants Used Traditionally in Egypt

***Tribulus terrestris* L.** ضريس

1. Names & Synonyms (1)

***Tribulus terrestris* L.**

Family: Zygophyllaceae.

Syns. *Tribulus lanuginosus* L., *Tribulus robustus* Boiss. & Noê in Boiss.

Arabic: Dreiss ضريس, Glaya جلاية

English: Caltrops, Land caltrops.

2. Geographical distribution (1)

All the phytogeographical regions of the country except that of the oases of the Western Desert.

3. Parts used for medicinal purpose

Dried fruits (1-4).

4. Major chemical constituents

Steroidal saponins: Protodioscin, prototribestin, pseudoprotodioscin, dioscin, tribestin and tribulosin (5,6).
Flavonoids: Kaempferol, kaempferol 3-*O*-rutinoside, quercetin, rutin, astragalin, tribuloside (6).
Phenolic acids and esters: Ferulic acid, feruloyloctopamine, caffeoyltyramine, coumaroyltyramine, 5-*p*-*trans*-coumaroylquinic acid and 5-*p*-*cis*-coumaroylquinic acid (6).
Others: Tribulusamides A and B, harmane and norharmane (6).

5. Traditional medicinal uses

A. Diuretic and help relieve difficult/painful urination (2,7).

B. Aphrodisiac to increase libido and enhances sexual function (2-4,7).

T. terrestris **is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use

1. Comminuted dried fruits as herbal tea in the form of decoction (2,3).
2. Powdered fruits (2).
3. Dry extract (ethanol 70-95% or water as solvent) (3,4).

Herbal preparations (2 and 3) are in a pharmaceutical dosage form. The pharmaceutical form should be described by the pharmacopoeia full standard term.

7. Posology and method of administration correlated to medicinal use

Preparations 1
20 – 30 g, daily (2).
3 – 9 g, daily, in divided doses (3).

Preparations 2
3 – 6 g, daily (2).

Preparations 3
750 – 1200 mg, daily (8).

Duration of use:

Occasional use only (2).

Method of administration: Oral use (2,3).

8. Contraindications

- Hypersensitivity to the active substances and to other plants of the same family.
- In hypotension and liver diseases (2).
- People with androgen-sensitive tumours (4).

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

- Patients should avoid excessive exposure to sunlight and use a sunscreen with a high sun protection factor (SPF 30+), due to the possibility of phototoxic reactions (3).

- The use in children under the age of 12 years is not recommended (3).

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (3).
- No fertility data available (3).

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Gastrointestinal disturbance may occur in sensitive individuals due to the saponin content (4).
- Except for diuretic effect, increased urination may occur (2).

14. Overdose

No case of overdose has been reported.

15. Relevant biological activities

- Administration of the aqueous extract of the fruit (at an intragastric dose of 5.0 g/kg b.w. in saline) induced diuresis in rats and was slightly more effective than furosemide. The sodium, potassium and chloride ion concentrations in the urine of treated rats were also increased. Addition of the extract to the bath medium of guinea-pig ileum induced contractile activity (9).
- In the anaesthetized dogs, the ether extract of the fruits of *T. terrestris* produced diuresis and increased the creatinine renal clearance, which suggest increase in the glomerular filtration rate. However, the ether extract did not significantly increase the chloride clearance which excludes inhibition of tubular chloride reabsorption. The aqueous extract of the fruits produced no significant effect on the urine volume or on the creatinine or the chloride renal clearance (10).
- The ethanol extract was tested for activity against artificially induced urolithiasis in albino rats. The extract was administered orally at 25, 50 and 100 mg/kg daily for 4 months. It exhibited dose dependent antiurolithiatic activity and almost completely

inhibited stone formation. Other biochemical parameters in urine and serum which were altered during the process of stone formation were normalized by the plant extract in a dose dependent manner (11).

- The effect of an aqueous extract of *T. terrestris* administered orally at a dose of 5 g/kg body weight was studied in rats with induced hyperoxaluria (intraperitoneal injection of 4 –OH proline at a dose of 2.5 g/kg body weight for three successive days) and maintained by sodium glycolate, twenty-four hours urine was collected and analyzed for creatinine and oxalate. The oxalate excretion reversed to normal from 1.97 + 0.314 to 0.144 + 0.004 mg/mg creatinine ($p<0.01$) within 21 days of administration of *T. terrestris* extract and remained so until 15 days after withdrawal of extract and sodium glycolate (12).

- A study was conducted to investigate the effect of oral treatment of *T. terrestris* extract on the isolated corpus carvenosal tissue of rabbits to determine the mechanism by which protodioscin (PTN) a constituent of *T. terrestris* exerted its pharmacological activity. The animals were treated with extracts at different dose levels that is, 2.5, 5, 10 mg/kg body weight which was administered orally, once daily for a period of 8 weeks. The penile tissue from the sacrificed animals was subjected for responses to both contractions and relaxing pharmacological agents and electrical field stimulation (EFS). The results indicating the relaxant responses to acetylcholine, nitroglycerine and EFS by more than 10, 24 and 10%, respectively compared to their control values and the lack of such effect on the contractile response to noradrenaline and histamine indicated that PTN had a proerectile activity. The enhanced relaxant effect was attributed to the increase of nitric oxide from the endothelium and nitrergic nerve endings, which may account for its claims as an aphrodisiac (13).

- The decoction of root and fruit of Gokshura showed an increased amount of excreted urine volume and root decoction showed more Na^+, K^+ and Cl^- excretion as compared to fruit decoction. Diuretic action of both root and fruit is similar in terms of urine volume but the root is more effective in the basis of ionic excretion. Hence, while treating patients suffering from ionic imbalance, it is better to use the fruits for protecting the ionic balance during diuresis. In all other conditions, root can be used for diuretic activity (14).

- Comparative diuretic effects of the whole plant and fruits of *Tribulus terrestris* Linn. in Wistar albino rats were investigated. Eight groups of 6 Wistar albino rats in each were used. Watery extract of three different doses (300 mg/kg, 500 mg/kg and 700 mg/kg) for each whole plant and fruits were used to test diuretic effect. Control group was given 0.9% sodium chloride solution and furosemide was used as the standard drug. After fasting, the animals were given watery extract orally and put into metabolic cages. Then urine was collected for 5 hours. Urinary sodium and potassium concentrations were measured by atomic absorption spectrophotometer. When analysing the results, as compared with control, there was no significant diuretic effect in whole plant extract but only fruit extract showed significant diuretic effect (15).

- A comparative study to evaluate and compare the effect of *Tribulus terristris* on urine volume and electrolytes with furosemide was performed. The duration of study was two weeks. 24 rabbits of mixed breed were used. They were fed on grass, grain, seasonal vegetables and water *ad libitum*. Animals were weighed for calculation of dosage of herb. They were divided into three equal groups randomly. Group Tt was given *Tribulus terristris* while Group F was given furosemide, while group C was not given any drug. Tt vs F: the change in 24 hours urine volume was found statistically significant $p<0.05$ on day 01 and day 15. Serum Na^+, K^+ levels were also found statistically significant $p<0.05$ throughout the study period. The results revealed that the plant has diuretic properties but is less efficacious than furosemide. Keeping in view, the result of our study, we recommend that the use of this herb may be promoted as diuretic agent; it may be helpful in pulmonary oedema and other oedematous conditions (16).

- The preventive and curative urolithiatic efficacy in experimentally induced nephrolithiatic Wistar rats, along with preclinical toxicity was evaluated following oral administration of statistically optimized aqueous extract of *T. terrestris*. Treatment showed augmented renal function, restoration of normal renal architecture and increase in body weight. Microscopic analysis of urine revealed excretion of small sized urinary crystals, demonstrating that treatment potentially modulated the morphology of renal stones. Tissue enzymatic estimation affirmed the antioxidant efficacy of treatment with reduced free radical generation. Significant upregulation of p38MAPK at both the gene and protein level was noted in hyperoxaluric group and interestingly treatment reversed it. Acute oral toxicity study established the Median Lethal Dose (LD50) to be greater than 2000 mg/kg body weight (b.wt.). No observed adverse effect level by repeated oral toxicity for 28 days at 750 mg/kg b.wt. was noted (17).

- The influence of hydroalcoholic extract of *T. terrestris* on cisplatin (CIS) induced renal tissue damage in male mice was evaluated. Thirty mice were divided into five groups (n = 6). The first group (control) was treated with normal saline (0.9% NaCl) and experimental groups with CIS (E1), CIS + 100 mg/ kg extract of *T. terrestris* (E2), CIS + 300 mg/kg extract of TT (E3), CIS + 500 mg/kg extract of *T. terrestris* (E4) intraperitoneally. The kidneys were removed after 4 days of injections, and histological evaluations were performed. The data were analysed using one-way analysis of variance followed by Tukey's post-hoc test, paired-sample *t*-test, Kruskal–Wallis and Mann–Whitney tests. In the CIS treated group, the whole kidney tissue showed an increased dilatation of Bowman's capsule, medullar congestion, and dilatation of collecting tubules and a decreased in the body weight and kidney weight. These parameters reached to the normal range after administration of fruit extracts of *T. terrestris* for 4 days. The results suggested that the oral administration of *T. terrestris* fruit extract at dose 100, 300 and 500 mg/kg body weight provided protection against the CIS induced toxicity in the mice (18).

- An extract of the fruit of *Tribulus terrestris* containing protodioscin was investigated in both normal and castrated rats to determine aphrodisiac effects. The treatments

were distilled water, testosterone and extract. Compared to the castrated control animals, treatment of castrated rats with either testosterone or the extract led to a mild to moderate improvement of the sexual behaviour parameters as demonstrated by an increase in mount frequency and intromission frequency and a decrease in mount latency, intromission latency and post-ejaculatory interval (19).

- Rats were fed a standard diet treated with *Mucuna pruriens*, *T. terrestris* (TT), and Ashwagandha (300 mg/kg) for 8 weeks. These herbs are potent of enhancers of sexual function and behaviour by increasing the testosterone levels and regulating the NF-κB and Nrf2/HO–1 pathway in male. The results indicated that the extract of TT was comparatively more potent than the other two. (20).

- The hormonal effects of *T. terrestris* (TT) were evaluated in primates, rabbits and rats to identify its usefulness in the management of erectile dysfunction (ED). Blood samples were analysed for testosterone (T), dihydrotestosterone (DHT) and dehydroepiandrosterone sulphate (DHEAS) levels using a radioimmunoassay. TT increased some of the sex hormones, which is possibly due to the presence of protodioscin in the extract (21).

Clinical trials:

- A double-blind clinical trial was done on 45 men with infertility due to oligoasthenoteratozoospermia. Thirty-six men were treated with 500 mg purified extract of the fruits containing protodioscin, orally 3 times daily for 3 months. The nine men in the control group were given a placebo for the same period of time. Spouses of eight of the men in the treated group became pregnant after treatment of their husbands, whereas no pregnancies occurred in the spouses of the men in the control group. An improvement in the sperm morphology, acrosome morphology and reaction seemed to account for the increased fertility after treatment. In addition, the extract was shown to increase the level of dehydroepiandrosterone and might also have contributed to the activation of cell membrane receptors and the production of weak androgens (22).

- A clinical trial involving 30 men with erectile dysfunction, but not diabetes, 30 with neither erectile dysfunction nor diabetes and 15 men with both diabetes and erectile dysfunction was performed to assess the relationship between dehydroepiandrosterone sulfate and erectile dysfunction. The men were given an extract of the *T. terrestris* fruits at a dose of 3 × 250 mg per day for 3 weeks. The results of the study showed a significant increase of dehydroepiandrosterone sulfate levels in subjects with and without diabetes after treatment, and a significant increase in the frequency of successful intercourse of 60% in subjects with or without diabetes and with or without erectile dysfunction (23).

- A clinical trial was conducted on 30 consecutive male patients presenting to Kasr-Al Ainy Andrology outpatient clinic complaining of manifestations of partial androgen deficiency in aging males. In this study, 750 mg/day of *T. terrestris* fruit extract in 3 divided doses, each of 250 mg, as an endogenous testosterone enhancer had been tried for a duration of 3 months and the evaluation of its effect had been monitored

for each patient concerning its effect on serum testosterone (total and free) and luteinizing hormone (LH), as well as its impact on erectile function, which was evaluated by the International Index of Erectile Function-5 (IIEF-5) questionnaire for those patients. Results showed a statistically significant difference in the level of testosterone (total and free) and IIEF-5, but no statistically significant difference in the level of LH before and after treatment. Also, the study showed statistically significant correlation between testosterone (total and free) and IIEF-5, but no statistically significant correlation between the level of LH and the IIEF-5 before and after treatment (24).

- The efficacy and safety profiles of *Tribulus terrestris* in aging males with partial androgen deficiency who suffered from erectile dysfunction and lower urinary tract symptoms were evaluated. A total of 70 randomized aging patients with erectile dysfunction and lower urinary tract symptoms were recruited from June 2017 to March 2018 from the andrology outpatient clinic. Thirty-five patients (group A) received *T. terrestris* 3 times daily for 3 months and the other 35 patients (group B) received placebo. The mean of aspartate transaminase was elevated in group A after 3 months of receiving *T. terrestris* (26.5 (before), 27.8 (after), respectively, p = 0.03). Moreover, there were significant elevations in the means of both total testosterone together with the score of the validated Arabic index of erectile function (5-item version of the International Index of Erectile Function) (2.2, 10.7 (before), 2.7, 16.1 (after), p<0.001, p<0.001, respectively). Finally, the mean of the total prostate-specific antigen was elevated in this group (1.4 (before), 1.7 (before), p = 0.007, respectively). Interestingly, there were no worsening of the lower urinary tract symptoms in group A as there was no change in the mean score of the international prostate symptom score, which was used to assess these symptoms before and after treatment (mean 14.4 (before), 14.6 (after), p = 0.67, respectively). In sum, this study replicates the findings of previous reports about the robust effect of this herbal medicine in elevating the testosterone level and improving the sexual function of patients who suffered from erectile dysfunction with partial androgen deficiency (25).

16. Additional information

---

17. Date of compilation/last revision

12/07/2023.

References

1	Hussein, S. R., Marzouk, M. M. and El Negomy, S. (2020), In: Egyptian Encyclopedia of Wild Medicinal Plants, **10**, 285 - 294. Academy of Scientific Research and Technology, Cairo, Egypt.
2	Natural Health Product, Tribulus – *Tribulus terrestris* (2019). Health Canada. https://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=1900
3	WHO monographs on selected medicinal plants (2010). Monographs on selected medicinal plants, **4**, 323– 334.
4	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements - An evidence-based guide. 3rd edition, Churchill Livingstone. ISBN: 978 0 7295 3910 4.
5	Dinchev, D., Janda, B., Evstatieva, L., Oleszek, W., Aslani, M. R. and Kostova, I. (2007). Distribution of steroidal saponins in *Tribulus terrestris* from different geographical regions. *Phytochemistry,* **69**(1), 176-186. doi: 10.1016/j.phytochem.2007.07.003.
6	Ştefănescu, R., Tero-Vescan, A., Negroiu, A., Aurică, E. and Vari, C-E. (2020). A comprehensive review of the phytochemical, pharmacological, and toxicological properties of *Tribulus terrestris* L. *Biomolecules*, **10**(5), 752. https://doi.org/10.3390/biom10050752.
7	Duke, J. A. (2002). Handbook of Medicinal Herbs. 2nd ed. CRC Press. ISBN 978084931284.
8	www.webmed.com
9	Al-Ali, M., Wahbi, S., Twaij, H. and Al-Badr, A. (2003). *Tribulus terrestris*: Preliminary study of its diuretic and contractile effects and comparison with *Zea mays*. *J. Ethnopharmacol*., **85**(2-3), 257-260. doi:10.1016/s0378-8741(03)00014-x.
10	Singh, R. C. P. and Sisodia, C. S. (1971). Effect of *Tribulus terrestris* fruit extracts on chloride and creatinine renal clearances in dogs. *Ind. J. Physiol. & Pharmac.,* **15**(3), 93-96.
11	Anand, R., Patnaik, G. K., Kulshreshtha, D. K. and Dhawan, B. N. (1994). Activity of certain fractions of *Tribulus terrestris* fruits against experimentally induced urolithiasis in rats. *Int. J. Exp. Biol*., **32**, 548-552.
12	Sangeeta, D., Sidhu, H., Thind, S. K., Nath, R. and Vaidyanathan, S. (1993). Therapeutic response of *Tribulus terrestris* (Gokhru) aqueous extract on hyperoxaluria in male adult rats. *Phytother. Res*., **7**, 116-119.
13	Adaikan, P. G., Gauthaman, K., Prasad, R. N. and Ng, S. C. (2000). Projectile pharmacological effects of *Tribulus terrestris* extract on the rabbits corpus carvenosum. *Ann. Acad. Med. Singapore*, **29**(1), 22-26.
14	Sudheendran, A., Shajahan, M. A. and Premlal, S. A. (2021). Comparative diuretic evaluation of fruit and root of Gokshura (*Tribulus terrestris* Linn.) in albino rats. *AYU*, **42**, 52 -56.
15	Maw, A. M., Phyu, K. P., Kyaw, P. P. M., Mar, K. K., San, K.., Thura, A., Aye, N. N., Oo, K. T. and Myint, Y. Y. (2016). Comparative diuretic effects of the whole plant and fruits of *Tribulus terrestris* Linn. in Wistar albino rats. *44th Myanmar Health Research Congress*, Abstract Book, 19-20.

16	Jabbar, A., Nazir, A., Khalil, J., Ansari, N. I., Qureshi, K. M. and Javed, F. (2012). To compare the Effects of *Tribulus terristris* with Furosemide on urine volume and electrolytes. *Annals*., **18**(2), 196-200.
17	Kaushik, J., Tandon, S., Bhardwaj, R., Kaur, T., Singla, S. K., Kumar, J. and Tendon, C. (2019). Delving into the antiurolithiatic potential of *Tribulus terrestris* extract through *in vivo* efficacy and preclinical safety investigations in Wistar rats. *Scientific Reports*, **9**, 15969. https://doi.org/10.1038/s41598-019-52398-w.
18	Raoofi, A., Khazaei, M. and Ghanbari, A. (2015). Protective effect of hydroalcoholic extract of *Tribulus terrestris* on Cisplatin induced renal tissue damage in male mice. *International Journal of Preventive Medicine*, **6**, 11, DOI: 10.4103/2008-7802.151817.
19	Gauthaman, K., Adaikan, P. G. and Prasad, R. N. (2002). Aphrodisiac properties of *Tribulus terrestris* extract (Protodioscin) in normal and castrated rats. *Life Sci.*, **71**(12), 1385-1396. doi: 10.1016/s0024-3205(02)01858-1.
20	Sahin, K., Orhan, C., Akdemir, F., Tuzcu, M., Gencoglu, H., Sahin, N., Turk, G., Yilmaz, I., Ozercan, I. H. and Juturu, V. (2016). Comparative evaluation of the sexual functions and NF-κB and Nrf2 pathways of some aphrodisiac herbal extracts in male rats. *BMC Complement. Altern. Med*., **16**(1), 318. doi: 10.1186/s12906-016-1303-x.
21	Gauthaman, K. and Ganesan, A. P. (2008). The hormonal effects of *Tribulus terrestris* and its role in the management of male erectile dysfunction- an evaluation using primates, rabbit and rat. *Phytomedicine*, **15**(1-2), 44-54. doi: 10.1016/j.phymed.2007.11.011.
22	Adimoelja, A., Setiawan, L. and Djojotananjo, T. (1995). *Tribulus terrestris* (protodioscin) in the treatment of male infertility with idiopathic oligoasthenoteratozoospermia. In*: Proceedings of the First International Conference of Medical Plants for Reproductive Medicine*. Taipei, Taiwan, Province of China.
23	Adimoelja, A. and Adaikan, P. G. (1997). Protodioscin from herbal plant *Tribulus terrestris* L. improves the male sexual functions, probably via DHEA. In: Proceedings of the 6th Biennial Asian-Pacific Meeting on Impotence in Kuala Lumpur, Malaysia. *International Journal of Impotence Research*, **9**(Suppl 1), 20.
24	Roaiah, M. F., El Khayat, Y. I., GamalEl Din, S. F. and Abd El Salam, M. A. (2016). Pilot study on the effect of botanical medicine (*Tribulus terrestris*) on serum testosterone level and erectile function in aging males with partial androgen deficiency (PADAM). *J. Sex Marital Ther*., **42**(4), 297-301. doi: 10.1080/0092623X.2015.1033579.
25	GamalEl Din, S. F., Abdel Salam, M. A., Mohamed, M. S., Ahmed, A. R., Motawaa, A. T., Saadeldin, O. A. and Elnabarway, R. R. (2018). *Tribulus terrestris* versus placebo in the treatment of erectile dysfunction and lower urinary tract symptoms in patients with late-onset hypogonadism: A placebo-controlled study. *Urologia Journal*, **86**(2), 74-78. doi: 10.1177/0391560318802160.

Egyptian Herbal Monograph

Volume 2

Pharmacopoeial wild medicinal plants

Egyptian Drug Authority (EDA)

2023

Preface

As it is intended to enable the appropriate use of wild medicinal plants and help manufacturers prepare the registration scientific files for their products, this volume on wild Pharmacopoeial medicinal plants is considered to be a continuation of the previous one. The seven pharmacopoeial plants discussed in this volume include those that are frequently utilised in Egypt, and for each, there is adequate scientific justification. Therapeutic uses are categorized as well-established uses (those specified mainly in the Egyptian Pharmacopoiea: E.P. 1953-2005) and traditional uses (those described in Egyptian folk medicine). It is predicted that this chapter would undergo another revision soon in accordance to Egyptian Pharmacopoeia's update.

Egyptian HerbalMonograph

Pharmacopoeial wild medicinal plants

***Ammi majus* L.** خلة شيطاني / خلة بري

1. Names & Synonyms (1 - 3)

***Ammi majus* L.**

Family: Umbelliferae (Apiaceae).

Syns. *Apium ammi* Crantz.

Arabic: Khella sheitaani خلة شيطاني/ Khella barri خلة برى

English: Bishop's weed, Amee.

2. Geographical distribution (1 - 3)

Nile region, Oases of the Western Desert, Mediterranean region as well as Sinai Peninsula.

3. Parts used for medicinal purpose (1 - 3)

The fruits and leaves.

4. Major chemical constituents

- **Furanocoumarins:** Xanthotoxin (known as methoxsalen, 8-methoxypsoralen and ammoidin), imperatorin (ammidin) isoimperatorin, bergapten (known as heraclin, majudin and 5-methoxypsoralen), marmesin, heraclenin, pimpinellin, isopimpinellin, majurin, saxalin, pabulenol, marmesinin and xanthotoxol (4, 5).
- **Other coumarins:** Umbelliprenin, 6- hydroxy-7-methoxy-4 methyl coumarin, 6-hydroxy-7-methoxy coumarin (6) and umbelliferone (7).
- **Flavonoids**:
  - **Fruits:** Quercetin, isoquercetin, quercetin-7-O-glucoside, kaempferol, kaempferol-7-O-glucoside and luteolin glycosides (8, 9).
  - **Leaves:** Quercetin and its glycosides, isorhamnetin-3-O-glucoside, isorhamnetin-3-O-rutinoside, and luteolin glycosides (10).

- **Aerial parts**: Acetylated flavonol triglycosides (kaempferol and isorhamnetin 3-O-[2"-(4"'-acetylrhamnosyl) -6"-glucosyl] glucosides) and glycosides (isorhamnetin-3-O-rutinoside, kaempferol-3-O-glucoside and isorhamnetin-3-O-glucoside (11).

- **Fatty acids:** Linoleic, oleic, palmitic and linolenic acids as main fatty acids, in addition to hexanoic, carylic capric, lauric, myristic, pentadecanoic, margaric, stearic, elaidic, arachidic, behenic, tricosnoic and tetracosanoic acids as minors (5, 12).

- **Essential oil**
  - **Fruits:** The major identified monoterpenes are carvone, 1,8-cineole, α- terpinyl acetate, *trans*-pinocarveol and citronellal, while the major sesquiterpenes are globulol and nerolidol. Non-terpenic volatiles included high boiling hydrocarbons and bergapten (13).

- **Diterpenes:**
  - **Aerial parts:** Ammi majanes, phytol, isophytol and isoelemicin (14).

- **Other constituents**: Vitamin E, resin, mucilage (7), tannin, oleoresin, acrid oil, fixed oil, proteins (4), oleanolic acid, mannitol (15) and furoquinoline alkaloids (14, 16).

5. Medicinal uses

Well-established use (17-21)

Vitiligo

Traditional use (6, 21)

A. For skin disorders (Psoriasis, Vitiligo and Leprosy)
B. As emmenagogue
C. For Urinary Tract Disorders:

- Diuretic.
- Lithotriptic agent (to break up renal stones).
- Urinary tract infections.

***A. majus* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (17-21)

1. Powdered dried fruits
2. Decoction

7. Posology and method of administration correlated to medicinal use

Average daily dose: 0.02–0.04 g in divided doses (17-21).

Method of administration: Oral use.

8. Contraindications (4, 17, 19 - 21)

- Hypersensitivity to active substances and to other plants of the same family.
- Diseases associated with photosensitivity.
- Cataract.
- Invasive squamous-cell cancer and known sensitivity to xanthotoxin (psoralens).
- Tuberculosis.
- Liver and kidney diseases.
- Human immunodeficiency virus (HIV) infections and other autoimmune diseases.
- Children under the age of 12 years.

9. Special warnings and precautions for use (21)

- Care should be taken where there is a familial history of sunlight allergy or chronic infections.
- Avoid direct and indirect sunlight for up to 8 hours after oral and 12–48 hours after following oral therapy, sunglasses must be worn for 24 hours.
- Avoid the ingestion of foods that contain furanocoumarins, such as limes, figs, parsley, celery, cloves, lemons, mustard and carrots (19).
- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

10. Interactions with other medicinal products and other forms of interaction

- The toxicity of *A. majus* fruits may be increased when the fruits are administered with other photosensitizing agents such as coal tar, dithranol, griseofulvin, nalidixic acid, phenothiazines, sulfanilamides, tetracyclines and thiazides (19-21).
- Avoid the ingestion of foods that contain furanocoumarins, such as limes, figs, parsley, celery, cloves, lemons, mustard and carrots (19, 21).

11. Fertility, pregnancy and lactation (4)

- The fruits are contraindicated in pregnancy and nursing mothers (21).
- No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Patients, after the first exposures, developed bullous reactions of more or less severe but in constant degree similar to burns, nervousness and insomnia nausea and gastric burning. However, itching, edema, hypotension, vertigo, depression, painful blistering, burning and peeling of the skin, pruritus, freckling, hypopigmentation, rash, cheilitis and erythema were also recorded with xanthotoxin therapy (4, 19, 21, 22).

14. Overdose

- Prolonged use or overdose may cause nausea, vertigo, constipation, lack of appetite, headache, allergic symptoms and sleeplessness (21, 23).
- Clinical treatment requires management by a physician (21).

15. Relevant biological activities

Toxicology

- Chronic toxicity in the form of a decrease in the red blood cell count and haemoglobin A concentration was observed in mice after administration of 100.0 mg/kg bw of a 95% ethanol extract of the fruits in drinking water (21).
- Toxicities by photosensitizing furanocoumarins contained in *A. majus* fruits are reports in many animal species (4, 21).

Treatment of vitiligo, psoriasis and hypopigmentation tinea versicolor

Numerous clinical trials have assessed the efficacy of *A. majus* fruits and xanthotoxin for the treatment of vitiligo, psoriasis and hypopigmentation and tinea versicolor (4):

-- Experimentation with *A. majus* extracts for the treatment of leucodermia was started in Egypt by El Mofti (24, 25).

-- *A. majus* Linn was used in six patients with vitiligo, five men and one woman. Their ages were from 30 to 50 years. *A. majus* was used (a) by oral administration, (b) by local topical application at the affected sites followed by sun or ultraviolet lamp exposure, or, (c) by a combination of (a) and (b). Three of patients were subjected to the combined treatment, two only to topical treatment and one to treatment by mouth for 5 months, and then to the combined treatment. The re-pigmentation appeared in all patients as pigmented minute macules with hair follicles in their center (22).

-- The powdered fruits of *A. majus* was administered orally to leukodermic patients, who then exposed the affected patches to direct sunlight for 1 hour. The patients

subsequently developed symptoms of itching, redness, oedema, vesiculation and oozing in the leukodermic patches. A few days later the affected skin gradually started to display deep brown pigmentation (26).

-- In two small groups of patients (eight patients each) with leukodermia treated with oral (0.05 g of *A. majus* three time daily) or liniment 1 g/100 ml, applied to the skin, with daily exposure of leukodermic areas to the sun for 0.5 hour or to UV light for 2 minutes, gradually increasing to 10 minutes, the leukodermic skin areas were inflamed and vesiculated, and the leukodermic areas began to show normal pigmentation (27).

-- *A. majus* and its furanocoumarins constituents (xanthotoxin) showed good results in many clinical studies for the treatment of psoriasis, vitiligo and tinea versicolor (28-32).

Antimicrobial activity

-- All crude extracts of *A. majus* fruits (methanol, hexane, chloroform, ethyl acetate and butanol extracts) displayed moderate antimicrobial activity against one Gram positive bacteria, *Staphylococcus aureus,* and three Gram negative bacteria, namely *Escherichia coli, Haemophilus influenzae* and *Proteus spp.* with growth inhibition zone of 0–15 mm (33).

-- *A. majus* coumarins were evaluated for their anti-viral activity by means of the end titration technique that depends on the ability of plant extract dilutions to inhibit the produced cytopathogenic effect and expressed as reduction factor of the viral titer. *A. majus* coumarins exerted antiviral activity against vesicular stomatitis virus (VSV) in a concentration dependent manner at complete non-toxic concentration range 10-100 µg/ml. *A. majus* coumarins found to have no reliable antiviral activity against herpes simplex virus (HSV) (6).

-- Furanocoumarins from *A. majus* have bactericidal, fungicidal, insecticidal, larvicidal, moluscicidal, nematicidal, ovicidal, viricidal and herbicidal activities (34, 35).

Antihyperlipidemic, anti-inflammatory, analgesic and antipyretic activities

-- The evaluation of the antihyperlipidemic, anti-inflammatory, analgesic, and antipyretic activities of the alcoholic extract of the *A. majus* fruits on albino rats and mice was done. After 2 months of administration, both the doses (50 and 100 mg/kg body weight [bwt], respectively) resulted in a significant decrease in the concentrations of cholesterol, triglycerides, and low-density lipoprotein and increase in the concentration of high-density lipoprotein. The extract was found to inhibit the rat paw edema at both the doses, which means that it exerts a significant anti-inflammatory activity compared with control-untreated groups at the intervals of 30 and 60minutes post-treatment. The antipyretic effect of the extract was quite obvious;

it showed that 100 mg/kg bwt was more potent in lowering body temperature starting after 1 hour of treatment than the lower dose (50mg/kg bwt) (36).

--*A. majus* coumarins were evaluated for anti-inflammatory activity by the carrageenan induced rat paw edema method. They possessed anti-inflammatory effects at a dose of 0.01 mg/100 g (6).

The efficacy and dose- response effect of *A. majus* alcoholic extract (2, 4, 8, 16, and 32 mg/rat) were assessed using formalin to induce paw edema in rats as a model of chronic inflammation. The tested extract and control were given orally before induction of inflammation. Paw edema was measured by using vernier caliper after 7 days for chronic inflammation. The result indicated that *A. majus* alcoholic extract significantly lower paw edema (p<0.05) compared to standard and control, while the dose 16mg/rat also lower the paw edema compared with other tested groups but less compared with the dose 32mg/rat. *A. majus* alcoholic extract possessed anti-inflammatory activity in animal's model of chronic inflammation and the effect increased with increasing the dose (37).

Antioxidant activity

-- Determined by 1,1-diphenyl-2-picrylhydrazyl (DPPH). The highest antioxidant activity was observed in case of chloroform crude extract which indicates the presence of polyphenolic compounds whereas the lowest activity corresponded to methanol crude extract (33).

16. Additional Information

The crystalline extracts of *A. majus* L. have been used and proved to be of remarkable specific effect in treating leueoderma. This has been shown in two previous papers on the subject (26, 27) and by other workers (22, 38). Experiments with this drug showed that a high percentage of cases of vitiligo promptly responded and completely recovered or greatly improved within relatively short periods—either during or immediately after treatment. *A. majus* L. has been used (a) by oral administration, (b) by local topical application at the affected sites followed by sun or ultraviolet lamp exposure, or, (c) by a combination of (a) and (b).

The best results were obtained when all the crystalline constituents of *A. mujus* L., were given orally, and the areas painted and exposed to ultraviolet rays (22, 39).

17. Date of compilation/last revision

27/8/2023.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Hassan, N, M, and Abdelmohsen, M. M. (2017). *Ammi majus* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **2**, 107-120. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Al-Snafi, A. E. (2013). Chemical constituents and pharmacological activities of *Ammi majus* and *Ammi visnaga*. A review. *Int. J. Pharm & Ind. Res*., **03** (03), 257 – 265.
5	Sajadi, K. P., Moghadamnia, A. A., Bakhshi, D. and Sefidgar, A. A. (2017). A study of phytochemical properties of various extracts of *Ammi majus* fruit using GC-MS technique. *Eco. Env. & Cons.*, **23** (1), 150-155.
6	Selim, Y. A. and Ouf, N. H. (2012). Anti-inflammatory new coumarin from the *Ammi majus* L. *Medicinal Chemistry Letters*, **2**, 1-4.
7	Curini, M., Cravotto, G., Epifano, F. and Giannone, G. (2006). Chemistry and biological activity of natural and synthetic prenyloxycoumarins. *Curr. Med. Chem.,* **13**(2), 199-222.
8	Mishaal, A. S., Nawwar, M. A., Nofal, Z., Elsherbiny, A. and Abu– Mustafa, E. A. (1981). Int. Conf. Chem. Biotechnol. *Biol. Act. Nat. Prod.* (proc.), **3**, 111.
9	Abdul-Jalil, T. Z., Saour, K. and Nasser, A. (2010). A Phytochemical study of some flavonoids present in the fruits of two *Ammi* L. species wildly grown in Iraq. *Iraqi J. Pharm. Sci.*, 19(1): 48-57.
10	Rizk, A. M. (1986). The Phytochemistry of the Flora of Qatar. Scientific and Applied Research Center, University of Qatar, Doha, Qatar.
11	Singab, A. N. (1998). Acetylated flavonol-triglycosides from *Ammi majus* L. *Phytochem*., **49**(7), 2177-2180.
12	Hussain, I., Khan, S., Khan, Ur Rehman, I. and Ahmad, M. (2012). Investigation of fatty acid composition of *Ammi majus* seed oil by gas chromatography mass spectrometry. *J. Chinese Chem. Soc*., **59**(5), 655-658.
13	Akhtar, P., Kaskoos, A. R., Mir, R. Sh., Ali, M. and Sharma, M. P. (2009). Composition of volatile oil of fruits of *Ammi majus* Linn. *J. Essent. Oil Bear. Plants*, **12**(4), 490-493.
14	Abraham, W. R., Löwenstein, C., Stahl-Biskup, E., Hanssen, H.P. and Sinnwell, V. (1996). *Ammi majus:* Novel volatile diterpenes from *Ammi majus* L. (Apiaceae). *J. Essent. Oil Res*., **8**(5), 507-511.
15	El-Gamal, M. H. A., Shalaby, N. M. M., Duddeck, H. and Hiegemann, M. (1993). Coumarins and coumarin glycosides from the fruits of *Ammi majus* L. *Phytochem*., **34**(3), 819-823.
16	Mohammed, M. M. and El-Sharkawy, E. R. (2017). Cytotoxic new furoquinoline alkaloid isolated from *Ammi majus* L. growing in Egypt. *Nat. Product Res*., **31**(6), 645-652.
17	Egyptian Pharmacopoeia (1972). 2rd ed. General Organization for Government Printing, Cairo.

18	Egyptian Pharmacopoeia (1984). 3th ed. General Organization for Government Printing, Cairo,
19	Lacy, C., Armstrong, L. L., Goldman, M. P. and Lance L. L. (2000). Drug Information Handbook, 6th ed. Lexi-Comp, Hudson, OH.
20	Wagner, H. and Wisenauer, M. (1995). Phytotherapie [Phytotherapy.] Stuttgart, Gustav Fisher.
21	WHO monographs on selected medicinal plants (2007). Fructus *Ammi Majoris*, **3**, 9-22.
22	Sidi, E. and Bourgeois, J. (1951). The treatment of vitiligo with *Ammi majus* Linn. *J. Invest. Dermatology*, **3**, 391-395.
23	Bisset, N. G. (1994). Herbal Drugs and Phytopharmaceuticals. Boca Raton, FL, CRC Press.
24	El-Mofty, A. M. (1952). Further study on treatment of leucodermia with *Ammi majus* Linn. *J. Egypt Med. Assoc.*, **35**, 1–19.
25	El-Mofty, A. M. (1984). A preliminary clinical report on the treatment of leucodermia with *Ammi majus* Linn. *J. Egypt Med. Assoc.*, **31**, 651–665.
26	Hakim, R. E. (1969). Rediscovery of a treatment for vitiligo. *Clio Medica*, **4**, 277–289.
27	Fahmy, I. R. and Abu-Shady, H. (1984). The isolation and properties of ammoidin, ammidin and majudin and their effect in the treatment of leukodermia. *Q. J. Pharm. Pharmacol.*, **21**, 499–503.
28	El-Mofty, A. M., El-Sawalhy, H. and El-Mofty, M. (1994). Clinical study of a new preparation of 8-methoxypsoralen in photochemotherapy. *Int. J. Dermatol*, **33**, 588–592.
29	Parsad, D., Saini, R. and Verma, N. (1998). Combination of PUVAsol and topical calcipotriol in vitiligo. *Dermatology*, **197**, 167–170.
30	Collins, P. (1996). 8-MOP PUVA for psoriasis: a comparison of minimal phototoxic dose-based regimen with a skin-type approach. *British Journal of Dermatology*, **135**, 248–254.
31	Kavli, G. and Volden, G. (1984). Phytophotodermatitis. *Photodermatology*, **1**, 65–75.
32	Becker, S. W. (1967). Psoralen phototherapeutic agents. *Journal of the American Medical Association*, **202**, 422–424.
33	Al-Hadhrami, R. M. S. and Hossain, M. A. (2016). Evaluation of antioxidant, antimicrobial and cytotoxic activities of seed crude extracts of *Ammi majus* grown in Oman. *Egyptian Journal of Basic and Applied Sciences*, **3**, 329-334.
34	Joy, P. P., Thomas, J., Mathew, S. and Skaria, M. (1998). Medicinal Plants. Kerala Agricultural University, India.
35	Duke, J. A. (1988). Bishops weed (*Ammi majus* L., Apiaceae). *Econ. Bot.*, **42** (3), 442-445.
36	Koriem, K. M. M., Asaad, G. F., Megahed, H. A., Zahran, H. and Arbid, M. S. (2012). Evaluation of the antihyperlipidemic, anti-inflammatory, analgesic, and antipyretic activities of ethanolic extract of *Ammi majus* seeds in albino rats and mice. *International Journal of Toxicology,* **31**(3), 294-300.
37	Mutlag, S. H. (2012). Dose dependent anti-inflammatory effect of *Ammi majus* alcoholic extract in rat: Chronic Study. *Iraqi J. Pharm. Sci.*, **21**(1), 82-86.
38	Tzanck, A., Sidi, E. and Boubgeois-Gavardin, J. (1952). Traitement du vitiligo par *l'ammi majus* linn. *Bull. Soc. Med*. Hop. Paris, **67**, 1400.
39	El-Mofty, A. M. (1952). Observations on the use of *Ammi majus* Linn. in vitiligo. *The British Journal of Dermatology*, **64**, 434-441.

Egyptian Herbal Monograph

Pharmacopoeial wild medicinal plants

Ammi visnaga L. خلة بلدي

1. Names & Synonyms (1 - 3)

***Ammi visnaga* L.**

Family: Umbelliferae (Apiaceae).

Syn. *Daucus visnaga* L.

Arabic: Khella baladi خلة بلدى , Khella خلة, Gazar sheitani جزر شيطاني, Kammon habashi كمون حبشي.

English: Pick-tooth, Tooth pick and Bishop's weed (3).

2. Geographical distribution (1 - 3)

Confined to the Nile valley and Mediterranean region.

3. Parts used for medicinal purpose (1 - 3)

The fruits and leaves.

4. Major chemical constituents

- **Furanochromone derivatives (*Y*-Pyrones):** Khellin, visnagin, khellinol, ammiol, visammiol, khellol, khellinin, khellinone, visnaginone (4) and visamminol.
- **Coumarins**: Pyranocoumarins/visnagans mainly as samidin, dihydrosamidin and visnadin (4), and furanocoumarins mainly as xanthotoxin, ammoidin, bergapten, and psoralen (5-12).
- **Flavonoids:** Quercetin, kaempferol, rhamnocitrin, rhamnetin and rhamnazin. Flavonoidal glycosides include quercetin-3-O-glucoside, kaempferol-3-O-glucoside and isorhamnetin 3-O-glucoside as well as rhamnetin-3-O-glucoside, isorhamnetin-3-O-glucoside, rhamnazin-3-O-glucoside, isorhamnetin-7-O-glucoside, quercetin-7,3,3'-O-triglucoside, quercetin-3-O-rutinoside, kaempferol-3-rutinoside and isorhamnetin-3-O-rutinoside. *A. visnaga* is also considered a rich source of flavonoidal sulfates including quercetin 3-sulfate, rhamnocitrin 3-sulfate, rhamnetin, and isorhamnetin-3-sulfate (13).

- **Essential Oil:** Major oxygenated monoterpenes are linalool and thymol, while monoterpene hydrocarbons are α-thujene, α-pinène, β-pinene, and β-myrcene (13). Major nonterpene derivatives are isoamyl 2-methylbutyrate, isoamyl isobutyrate, isobutyl 2-methylbutyrate, 2-methylbutyl 2-methylbutyrate, 2-methylbutyl isobutyrate, and isoamyl isovalerate (14, 15).
- **Sterols and Fatty acids:** β-Sitosterol and β-sitosterol-glucoside (16), in addition to palmitic, palmitoleic, stearic, petroselinic, linoleic, linolinic, arachidic and tetracosanoic acids (13).

5. Medicinal uses

Well-established use (17, 19)

A. Muscle relaxant as an antispasmodic.
B. Dilate coronary vessels and the ureter.

Traditional use (13, 18, 19)

C. For mild anginal symptoms.
D. For Urinary Tract Disorders:

- Diuretic
- Renal colic
- In postoperative treatment of conditions associated with the presence of urinary calculi.
- Lithotriptic agent (to break up renal stones).

E. Supportive treatment for mild obstruction of the respiratory tract in asthma or spastic bronchitis.
F. For skin disorders (psoriasis and vitiligo).
G. As emmenagogue to regulate menstruation.
H. Treatment of gastrointestinal cramps and painful menstruation.

***A. visnaga* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (19)

1. Powdered dried fruits.
2. Decoction / infusion.

7. Posology and method of administration correlated to medicinal use

Average daily dose from *A. visnaga* fruit: 0.05 to 0.15 g in divided doses (20).

Method of administration: Oral use.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

- During treatment with *A. visnaga* and its constituents, the exposure to sun or other sources of ultraviolet light should be avoided, in order to minimize photosensitivity (19, 21).

- Khella has been associated with the development of severe ophthalmologic changes, particularly pigmentary retinopathy. Patients receiving khella or its extracts should be monitored for ophthalmologic changes (22, 25).

- Intake of *A. visnaga* is not recommended at all along with blood thinners such as coumadin, heart drugs called calcium channel blockers or other drugs that lower blood pressure (18).

- Monitoring of blood glucose level should be done regularly.

10. Interactions with other medicinal products and other forms of interaction

None reported.

11. Fertility, pregnancy and lactation

- *A. visnaga* should be avoided during pregnancy (19).

- Safety during lactation has not been established. In the absence of sufficient data, the use during lactation is not recommended.

- No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects (19,21)

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Side effects like pseudoallergic reactions, reversible cholestatic jaundice.

14. Overdose

- Long term use or overdose of the drug can lead to queasiness , dizziness , loss of appetite , headache, nausea, vertigo, sleep disorders and with very high dosage (corresponding to over 100 mg khellin) , it caused reversible elevation in the levels of liver enzymes (transaminases and γ-glutamyltransferase) (19, 21, 24).

15. Relevant biological Activities

Kidney diseases

- Evaluation whether oral administration of an aqueous extract prepared from the fruits of *A. visnaga* could prevent crystal deposition in stone-forming rats was done. Hyperoxaluria was induced in male Sprague-Dawley rats by giving 0.75% ethylene glycol (EG) and 1% ammonium chloride (NH_4Cl) via the drinking water. The Khella extract (KE; 125, 250 or 500 mg/kg) was orally administered for 14 days. The histopathological examination of the kidneys revealed that KE significantly reduced the incidence of calcium oxalate crystal deposition. In addition, KE significantly increased urinary excretion of citrate along with a decrease of oxalate excretion (25).

- The effect of *A. visnaga* and its two major constituents (khellin and visnagin) on renal epithelial injury was evaluated using LLC-PK1 and Madin-Darby-canine kidney cells. It was found that *A. visnaga* extract as well as khellin and visnagin could prevent renal epithelial cell damage caused by oxalate and calcium oxalate monohydrate and could therefore play a potential role in the prevention of stone formation associated with hyperoxaluria (26).

- The effect of *A. visnaga* fruits was investigated in animal model for urolithiasis. When oxalate nephrolithiasis was induced by 3% glycolic acid given for 4 weeks, it was found that daily oral treatment with *A. visnaga* (500 mg/kg) could inhibit the formation of kidney stones by lowering the deposition of calculi in kidney. The prophylactic effect of *A. visnaga* was attributed to its diuretic activity (27).

- The inhibitory effect of *A. visnaga* extract (aqueous extract of whole plant and its fruits) was studied on the oxalocalcic crystallization in human urine. Even this study revealed the efficacy of extracts of the *A. visnaga* fruits in inhibiting the crystallization of calcium oxalate. Further, it was found that the extracts reduced oxalate calcium crystallization and specially monohydrate oxalate calcium (28).

Antispasmodic and vasodilating effects

- The vasodilating properties of *A. visnaga* have been investigated by several researches:

- It has been established as a bronchodilator and coronary medication in the treatment of angina pectoris due to its peripheral and coronary vasodilator activity (29).

- In addition to being an antiasthmatic and a vasodilator, as well as an effective muscle relaxant agent without affecting blood pressure (30, 31).

- The vasodilating properties of *A. visnaga* are associated with its two major γ-pyrones, khellin and visnagin, along with the pyranocoumarin, visnadin. Both khellin and visnadin have been proven to possess calcium antagonistic activity, which, in turn, yields vasodilating activities. Visnadin has been shown to possess both peripheral and coronary vasodilator activities, and is thus used for the treatment of angina pectoris. It preferentially inhibits the contractile responses mediated by Ca2+ entry through L-type Ca2+ channels, and at high concentrations, it may also interfere with other sites involved in vascular smooth muscle contraction (32-37).

- The vasodilating effect of visnagin is a result of inhibiting the vascular smooth muscle contractility at multiple sites, and weakly inhibiting the hydrolytic activity of the cyclic nucleotide phosphodiesterase (PDE) isozymes (38- 40).

Smooth muscle relaxant effects (41)

- Visnadine caused nonspecific inhibition of vascular smooth muscle. It was selectively inhibited the contractile response in the rat isolated aortic ring and portal vein segment (33, 38, 40).

- Aqueous extract of *A. visnaga* fruits induced relaxant effect on contractibility of small intestine of rabbit (42).

- *A. visnaga* induced relaxation of smooth muscle, including that of the ureter and coronary arteries, in a variety of animal species (43).

Antimicrobial effects (41)

- The antimicrobial effects of the ethanolic and aqueous extract of *A. visnaga* were tested against eight pathogenic microorganisms. The most active extract against Gram-positive bacteria was ethanol extract with a minimal inhibitory concentration (MIC) value of (5mg/ml) against *Enterococcus faecalis*. In addition, the same extract exerted antimicrobial activity against the Gram-negative bacteria *Escherichia coli, Klebsiella pneumoniae* with an MIC value of 12.5mg/ml. In yeast, a high concentration of extract was needed to cause inhibition (44).

- The essential oil of *A. visnaga* was tested against *Escherichia coli* ATCC 25922 and different other types of bacteria. The essential oil exhibited the best antibacterial activity against *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 43300 *and Pseudomonas aeruginosa* ATCC 27853, the diameter of the inhibitory zones were 29, 25, 25 and 25 mm; respectively (45).

- An aqueous extract of the fruits of *A. visnaga* (2–10 mg/ml) inhibited growth and aflatoxin production of *Aspergillus flavus*. The effects were dose-dependent (46).

- The aqueous and hydroalcoholic extract of the fruits and stem of *A. visnaga* showed a good antibacterial activity against *Streptococcus mutans, Streptococcus salivarius and Streptococcus sanguis* oral pathogens (47).

- The 95% ethanol extract of the fruits exhibited antibacterial activity, inhibiting the growth of *Mycobacterium tuberculosis* H37RVTMC 102 even in a very low concentration (dilution of 1:40). Similarly, 50% acetone, 50% aqueous or 95% ethanol extract of *A. visnaga* inhibited fungal growth (*Neurospora crassa*) *in vitro* (18).

Cardiovascular effects (41)

- A chloroform, and methanol extract (1mg/ml) of the fruits inhibited the potassium chloride induced contractions of the rabbit and guinea-pig aorta *in vitro* (32, 48, 49).

- Visnadin, 60.0 µg/ml or 120.0 µg/ml, increased coronary blood flow in isolated guinea-pig hearts by 46% and 57% respectively (49).

- Samidin and khellol glucoside induced positive inotropic effects on heart (50).

- In coronary vasospasm and myocardial ischaemia induced in dogs by daily intramuscular injections of vasopressin, visnadin, dihydrosamidin, khellin and samidin effectively normalized the electrocardiogram when given in a dose of 4.7 mg/kg/day intramuscularly for 7 days (50).

- Immediately after the rapid intravenous administration of 20-30 mg of khellin to the dogs, the blood pressure drops to about 50 mm Hg, the heart beats considerably slower, and the respiration is momentarily arrested. The entire effect lasts for only a short time, within a minute or two (51).

- According to the results obtained by different researchers, Khella seems to improve blood supply to smooth muscles and makes myocardial metabolism more efficient. It dilated the coronary vessels, and increased the capacity of the heart without increasing the heart rate or affecting blood pressure (43).

- A clinical trial of khellin in 38 cases of angina pectoris and in 8 cases of coronary thrombosis was performed. Continuous treatment, by the oral or intramuscular routes or by both, gave favorable results in 35 out of 38 cases of angina pectoris. Continuous administration of khellin for several weeks to eight patients after coronary thrombosis appeared favorable (50).

- A clinical study was carried out on 20 non-obese, normolipaemic male subjects to determine the effects of orally administered 50 mg khellin four times daily for 4 weeks on the plasma lipids. Plasma total cholesterol and triglyceride remained unchanged, but high-density-lipoprotein cholesterol concentration was significantly elevated during the treatment and till one week after cessation of treatment (52).

- In a comparison with glyceryl trinitrate, khellin (3 ml containing 150 mg of khellin; alcoholic extract standardized to contain 50 mg/ml) was used in twelve patients for

prevention of angina of effort and the electrocardiographic changes that may accompany it. Khellin was less potent but longer acting than glyceryl trinitrate, and it did not cause any unpleasant side effects (53).

Melanoprotective activity (13)

- A study on 60 people revealed that the combination of *A. visnaga* and natural sun exposure caused re-pigmentation in 76.6% of the treatment receiving group (54).

- A subsequent placebo-controlled study on 36 patients of vitiligo revealed that a topical *A. visnaga* gel plus UVA caused re-pigmentation in 86.1% of the treated cases compared to 66.6% in the placebo group (55).

-In a study on 28 patients with vitiligo, a new photo-chemotherapeutic course of therapy using *A. visnaga*, a furanochromone (as photosensitizer) and ultraviolet A (UVA) irradiation was used. More than 70% re-pigmentation was achieved in 41% of the patients who received 100 to 200 treatments (56).

-A pilot study was conducted on 33 patients to evaluate the effectiveness of local khellin and UVA (KUVA) and systemic psoralens and UVA (PUVA) therapy for vitiligo and to compare them in terms of the degree of re-pigmentation, duration of treatment, number of procedures, total UVA dose and side effects. The results revealed that local KUVA effectively induced re-pigmentation of vitiligo-affected skin areas to an extent comparable to a degree comparable to that achieved when using systemic PUVA, provided that treatment duration is long enough (57).

- In a study on 19 patients with vitiligo disease, who did not respond to khellin in liposomes and ultraviolet light (KLUV) treatment for no less than a year were treated with Blister Roof Transplantation (BRT) followed by KLUV. Around 75% of the patients were satisfied with the cosmetic results and more than 75% re-pigmentation of the vitiligo areas was noted in 47% of the patients (58).

Hypoglycemic activity

-The effect of the aqueous extract of *A. visnaga* on blood glucose levels was investigated in fasting normal and streptozotocin (STZ) induced diabetic rats after single and repeated oral administration. The aqueous extract of *A. visnaga* at a dose of 20 mg/kg significantly reduced blood glucose in normal rats six hours after a single oral administration ($p < 0.005$) and nine days after repeated oral administration ($p<0.05$). This hypoglycaemic effect is more pronounced in STZ diabetic rats ($p<0.001$). These findings suggest that the aqueous extract of *A. visnaga* possess significant hypoglycemic effect in both normal and STZ diabetic rats (59).

-An aqueous extract of *A. visnaga* was shown to possess a significant hypoglycemic effect when given to both normal and streptozotocin diabetic rats. Additionally, a decoction prepared from the fruits of the *A. visnaga* had the ability to reduce blood glucose level by 51% in normoglycemic rats, compared to an oral hypoglycemic agent (Tolbutamide®) (13).

Antioxidant effects

- The antioxidant activity of the butanol extract of *A. visnaga* was determined by 2,2-Diphenyl-1picryl-hydrazyl (DPPH) method. The butanol extract of *A. visnaga* was markedly quenched the DDPPH radical by 78.7 % at a concentration of 200 g/ml (60).

Neuroprotective activity

- Visnagin which is an active principle of was investigated for neuroprotective effect against kainic acid (KA) -induced neuronal cell death. Visnagin administration (100 mg/kg, p.o. or i.p.) not only inhibited microglial and astroglial activation but also attenuated the inflammatory marker expressions concomitantly, suggesting that visnagin exerts its neuroprotective effects via an anti-inflammatory mechanism in KA model (61).

16. Additional information

Worldwide, many pharmaceutical products are containing *A. visnaga* extract as active principal (13).

17. Date of compilation/last revision

27/8/2023.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Hassan, N. M. and Abdelmohsen, M. M. (2017). *Ammi visnaga* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **2**, 121-136. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Hashim, S., Jan, A., Marwat, K. B. and Khan, M. A. (2014). Phytochemistry and medicinal properties of *Ammi visnaga* (Apiacae). *Pak. J. Bot.*, **46**(3), 861-867.
5	Abou-Mustafa, E. A., Saleh, N. A. M., Elgamal, M. H. A., Shalaby, N. M. M. and Duddeck, H. (1990). A further contribution to the γ-pyrone constituents of *Ammi visnaga* fruits. *Planta Medica*, **56**, 134.
6	Martelli, P., Bovalini, L., Ferri, S. and Franchi, G. G. (1984). Rapid separation and quantitative determination of Khellin and Visnagin in *Ammi visnaga* (L.) Lam Fruits by high performance liquid-chromatography. *J. Chromato.*, **301**, 297-302.
7	Eldomiaty, M. M. (1992). Improved high-performance liquid-chromatographic determination of khellin and visnagin in *Ammi visnaga* fruits and Pharmaceutical formulations. *J. Pharm. Sci.*, **81**, 475-478.
8	Zgorka, G., Dragan, T., Głowniak, K. and Basiura, E. (1998). Determination of furanochromones and pyranocoumarins in drugs and *Ammi visnaga* fruits by combined solid-phase extraction, high-performance liquid chromatography and thin layer chromatography. *J. Chromato. A,* **797**(1-2), 305-309.
9	Balbaa, S. I., Hilal, S. H. and Zaki, A. Y. (1976). Medicinal Plant Constituents. 2nd edition, Central Agency for University and School Books, Cairo, Egypt.
10	El-Gamal, M. H., Shalaby, N. M., El-Hagrassy, A. M., Toth, G., Simon, A. and Duddeck, H. (1998). A further contribution to some gamma-pyrone constituents of *Ammi visnaga*. *Fitoterapia*, **69**(6), 549-550.
11	Sonnenberg, H., Kaloga, M., Eisenbach, N. and Frömming, K. K. (1995). Isolation and characterization of an angular-type dihydro-pyrano-coumarin-glycoside from the fruits of *Ammi visnaga* (L.) LAM. (Apiaceae). *J. Naturforsch*, **50**(9-10), 729-731.
12	Razzaghi-Abyaneh, M., Shams-Ghahfarokhi, M., Rezaee, M.B. and Sakuda, S. (2010). Natural Aflatoxin Inhibitors from Medicinal Plants. In Mycotoxins in Food, Feed and Bioweapons; Rai, M., Varma, A., eds.; Springer: Berlin/Heidelberg, Germany, 329–352.
13	Khalil, N., Bishr, M., Desouky, S. and Salama, O. (2020). *Ammi visnaga* L., a potential medicinal plant: A review. *Molecules*, **25**, 301.
14	Zrira, S., Elamrani, A., Pellerin, P., Bessiere, J. M., Menut, C. and Benjilali, B. (2008). Isolation of Moroccan *Ammi visnaga* oil: comparison between hydrodistillation, steam distillation and supercritical fluid extraction. *J. Essent. Oil Bear. Plants*, **11**, 30–35.
15	Abdul-Jalil, T.Z., Saour, K. and Nasser, A. A. (2010). Phytochemical study of some flavonoids present in the fruits of two *Ammi* L. species wildly grown in Iraq. *Iraqi J. Pharma. Sci.*, **19**, 48–57.

16	Keddad, A., Baaliouamer, A. and Hazzit, M. (2016). Chemical composition and antioxidant activity of essential oils from umbels of Algerian *Ammi visnaga* (L.). *J. Essent. Oil Bear. Plants*, **19**, 1243–1250.
17	Egyptian Pharmacopoeia (1984). 3th ed. General Organization for Government Printing, Cairo.
18	Alam, S., Anjum, N., Akhtar, J. and Bashir, F. (2018). Pharmacological investigations on khella-(*Ammi visnaga* L.). *World Journal of Pharmaceutical Research*, **7**(13), 212-224.
19	WHO monographs on selected medicinal plants (2007). Fructus *Ammi Visnagae*, **3**, 23-32.
20	Egyptian Pharmacopoeia (1972). 2rd ed. General Organization for Government Printing, Cairo,
21	Blumenthal, M., and Busse, W. R. (1998). *The complete German Commission E monographs.* Austin, Texas: Boston, American Botanical Council.
22	Shlosberg, A., Egyed, M. N. and Eilat, A. (1974). The comparative photosensitizing properties of *Ammi majus* and *Ammi visnaga* in goslings. *Avian Dis.*, **18**(4), 544–550.
23	Shlosberg, A. and Egyed, M. N. (1983). Examples of poisonous plants in Israel of importance to animals and man. *Arch. Toxicol. Suppl.*, **6**, 194–196.
24	PDR for Herbal Medicines (1998). Medical Economic Co. Montvale, New Jersey, 639. ISBN 1563633612, 9781563633614.
25	Vanachayangkul, P., Chow, N., Khan, S.R. and Butterweck, V. (2011). Prevention of renal crystal deposition by an extract of *Ammi visnaga* L. and its constituents khellin and visnagin in hyperoxaluric rats. *Urol. Res.*, **39**(3), 189–195.
26	Vanachayangkul, P., Byer, K., Khan, S. and Butterweck, V. (2010). Aqueous extract of *Ammi visnaga* fruits and its constituents khellin and visnagin prevent cell damage caused by oxalate in renal epithelial cells. *Phytomed.*, **17**, 653-658.
27	Khan, Z. A., Assiri, A. M., Al-Afghani, H. M. and Maghrabi, T. M. (2001). Inhibition of oxalate nephrolithiasis with *Ammi visnaga* (AI-Khillah). *Int. Urol. Nephrol.*, **33**, 605-608.
28	Charafi, S., Kzaiber, F., Hafid, A., Berkani, M. and Oussama, A. (2012). Study of *Ammi visnaga* Lam on oxalocalcic crystallization. *M. Global J. Trad. Med. Sys.*, **1**, 7-12.
29	Balandrin, M. F., Kinghorn, A. D. and Farnsworth, N. R. (1993). Plant-Derived Natural Products in Drug Discovery and Development, In: Human Medicinal Agents from Plants; American Chemical Society: Washington, DC, USA.
30	Chevallier, A. (1996). The Encyclopedia of Medicinal Plants, Dorling Kindersley, London, UK.
31	Al-Snafi, A. E. (2016). A review of medicinal plants with broncho-dilatory effect- Part1. *Sch. Acad. J. Pharm.*, **5**, 297–304.
32	Rauwald H. W., Brehm, O. and Odenthal, K. P. (1994). The involvement of a Ca^{2+} channel blocking mode of action in the pharmacology of *Ammi visnaga* fruits. *Planta Med.*, **60**, 101–105.
33	Duarte, J., Vallejo, I., Perez-Vizcaino, F., Jimenez, R., Zarzuelo, A. and Tamargo, J. (1997). Effects of visnadin on rat isolated vascular smooth muscles. *Planta Med.*, **63**, 233–236.
34	Venugopala, K. N., Rashmi, V. and Odhav, B. (2013). Review on natural coumarin lead compounds for their pharmacological activity. *BioMed. Res. Inter.*, 1–14, doi: 10.1155/2013/963248.
35	Ubeda, A., Tejerina, T., Tamargo, J. and Villar, A. (1991). Effects of khellin on contractile responses and 45 Ca^{2+} movements in rat isolated aorta. *J. Pharm. Pharmacol.*, **43**, 46–48.
36	Campos-Toimil, M., Orallo, F., Santana, L. and Uriarte, E. (2002). Synthesis and vaso relaxant activity of new coumarin and furocoumarin derivatives. *Bioorg. Med. Chem. Lett.*, **12**, 783–786.
37	Tripathi, Y. and Pandey, A. (2017). Bioprospecting of phytodiversity for new therapeutic products: Trends, potential and challenges. *Org. Med. Chem.*, **2**, 1–7.

38	Duarte, J., Perez-Vizcaino, F., Torres, A. I., Zarzuelo, A., Jimenez, J. and Tamargo, J. (1995). Vasodilator effects of visnagin in isolated rat vascular smooth muscle. *Eur. J. Pharm*., **286**, 115–122.
39	Duarte, J., Lugnier, C., Torres, A. I., Pérez-Vizcaino, F., Zarzuelo, A. and Tamargo, J. (1999). Effects of visnagin on cyclic nucleotide phosphodiesterases and their role in its inhibitory effects on vascular smooth muscle contraction. *Gen. Pharm. Vasc. Sys.*, **32**, 71–74.
40	Duarte, J., Torres, A. I. and Zarzuelo, A. (2000). Cardiovascular effects of visnagin on rats. *Planta Med.*, **66**, 35–39.
41	Al-Snafi, A. E. (2013). Chemical constituents and pharmacological activities of *Ammi majus* and *Ammi visnaga*. A review. *Int. J. Pharm & Ind. Res*., **03** (03), 257 – 265.
42	Jawad, A. A. D., Khuon, O. S. and Ali, N. A. (2006). Spasmolytic activity of *Ammi visnaga* seeds on isolated rabbit jejunum. *Basrah Journal of Scienec*, **24**(1), 47-58.
43	Altinterim, B (2012). The effect of khella seed (Umbelliferae, *Ammi majus* L.) on smooth muscles. *Nevşehir Üniversitesi Fen Bilimleri Enstitü Dergisi*, 60-64.
44	Ghareeb, A. M., Zedan, T. H. and Gharb, L. A. (2011). Antibacterial and antifungal activities of *Ammi visnaga* extracts against pathogenic microorganisms. *Iraqi Journal of Science*, **52**(1), 30-36.
45	Khalfallah, A., Labed, A., Semra, Z., Al Kaki, B. and Kabouche, R. (2011). Antibacterial activity and chemical composition of the essential oil of *Ammi visnaga* L. (Apiaceae) from Constantine, Algeria. *Int. J. Med. Arom. Plants*, **193**, 302-305.
46	Mahmoud, A. (1999). Inhibition of growth and aflatoxin biosynthesis of *Aspergillus flavus* by extracts of some Egyptian plants. *Letters in Applied Microbiology*, **29**, 334–336.
47	Semyari, H., Owlia, P., Farhadi, S. and Saeed, T. M. (2011). Evaluation of antimicrobial effect of *Ammi visnaga* against oral streptococci. *Journal of Microbiology and Antimicrobials*, **3**(5), 126-129.
48	Rauwald, H. W., Brehm, H. and Odenthal, K. P. (1994). Screening of nine vasoactive medicinal plants for their possible calcium antagonist activity. Strategy of selection and isolation for the active principles of *Olea europaea* and *Peucedanaum ostruthium*. *Phytotherapy Research*, **8**, 135-140.
49	Erbring, H., Uebel, H., Vogel, G. and Chemie, Z. (1967). Pharmakologie und voxicologie von visnadin [Chemistry, pharmacology, and toxicology of visnadine]. Arzneimittelforschung, **17**, 283-287.
50	Galal, E. E., Kandil, A. and Latif, M. A. (1975). Evaluation of cardiac inotropism of *Ammi visnaga* principles by the intra-ventricular technique. *Journal of Drug Research of Egypt*, **7**, 45–57.
51	Anrep, G. V., Barsoum, G. S., Kenawy, M. R. and Misrahy, G. (1945). *Ammi vinaga* in the treatment of angina syndrome. *Gazette of the Faculty of Medicine*, Cairo: **13**, 39.
52	Harvengt, C. and Desager, J. P. (1983). HDL-cholesterol increase in normolipaemic subjects on khellin: a pilot study. *International Journal of Clinical Pharmacology Research*, **3**, 363–366.
53	Dewar, H. A. and Grimson, T. A. (1950). Khellin in the treatment of angina of effort. *Br. Heart J.*, **12**, 54-60.
54	Abdel-Fattah, A., Aboul-Enein, M. N. and Wassel, G. M. (1982). An approach to the treatment of vitiligo by khellin. *Dermatologicia*, **165**, 136– 140.
55	Orecchia, G., Sangalli, M. E. and Gazzaniga, A. (1998). Topical photochemotherapy of vitiligo with a new khellin formulation: preliminary clinical results. *J. Dermatol. Treat.*, **9**, 65–69.

56	Ortel, B., Tanew, A. and Hönigsmann, H. (1988). Treatment of vitiligo with khellin and ultraviolet A. *J. Am. Acad. Dermatol.*, **18**, 693-701.
57	Valkova, S., Trashlieva, M. and Christova, P. (2004). Treatment of vitaligo with local khellin and UVA: Comparison with systemic PUVA. *Clin. Exp. Dermatol.*, **29**, 180-184.
58	Leeuw, J.D., Assen, Y. J., Beek, N.V.D., Bjerring, B. and Neumann, H. M. (2011). Treatment of vitiligo with khellin liposomes, ultraviolet light and blister roof transplantation. *J. Eur. Acad. Derm. Vener.*, **25**, 74-81.
59	Jouad, H., Maghrani, M. and Eddouks, M. (2002). Hypoglycemic effect of aqueous extract of *Ammi visnaga* in normal and streptozotocin-induced diabetic Rats. *Journal of Herbal Pharmacotherapy*, **2**(4), 19-29.
60	Bencheraiet, R., Kherrab, H., Kabouche, A., Kabouche, Z. and Jay, M. (2011). Flavonols and antioxidant activity of *Ammi visnaga* L. (Apiaceae). *Rec. Nat. Prod.*, **5**(1), 52-55.
61	Kwon, M. S., Lee, J. K., Park, S. H., Sim, Y. B., Jung, J. S., Won, M. H., Kim, S. M. and Suh, H. W. (2010). Neuroprotective effect of visnagin on kainic acid-induced neuronal cell death in the mice Hippocampus. *Korean J. Physiol. Pharmacol.*, **14**(5), 257-263.

Egyptian Herbal Monograph

Pharmacopoeial wild medicinal plants

***Citrullus colocynthis* L.** حنظل – حنضل

1. Names & Synonyms (1-3)

***Citrullus colocynthis* L.**

Family: Cucurbitaceae.

Syns. *Cucumis colocynthis*

Colocynthis vulgaris.

Arabic: Hanzal حنظل - Handal حنضل.

English: Colocynth, Bitter apple, Bitter gourd.

2. Geographical distribution

Common in nearly all the phytogeographical regions of the country (3).

3. Parts used for medicinal purpose

Colocynth; Pulp of the peeled fruit (dried unripe, but fully grown fruit deprived of its seeds and hard outer part of pericarp) (4, 5); seeds, leaves, and roots are also used (2, 6).

4. Major chemical constituents (3)

- **Cucurbitacins and its glycosides** (7): Cucurbitacin A, B, C, D, E, I, J, K and L (8-13), 2-O-*β*-D-glucopyranosyl-cucurbitacin I, 2-O-*β*-D-glucopyranosyl-cucurbitacin L (14), colocynthein, colocynthetin (15), and Cucurbitane-type triterpenoid glycoside (saponin) (16) as colocynthosides A and B (11) are major constituents in the fruit.
- **Flavonoids**: Quercetin (leaf, stem, fruit, root), flavone-C-glucoside (Isovitexin), isoorientin and isoorientin 3′-O-methylether (fruit), C-*p*-hydroxybenzyl derivatives as 8-C-*p*-hydroxybenzylisovitexin, 6-C-*p*-hydroxybenzylvitexin, 8-C-*p*-hydroxybenzylisovitexin 4′-O-glucoside (aerial parts) (14, 17,18), kaempferol (19), catechin, myricetin (19-21), isoscoparin and isosaponarin (14).

- **Phenolic acids**: Gallic (20), *p*-hydroxybenzoic, chlorogenic, caffeic, vanillic acid, *p*-coumaric, sinapic and ferulic acids from fruit pulp (19), and 3-O-caffeoylquinic acid from the leaves (22).
- **Alkaloids**: Alkaloids from the whole fruit and pulp (13, 23- 26); choline from fruit pulp (24), 2-(nonan-8-one) -(1H)-4-quinolone and 2-(nonan-8-one) 4-methoxy-quinoline from the aerial parts (27).
- **Fatty acids**: Linoleic, oleic, palmitic, stearic, myristic, linolenic (17, 28-31) and arachidic acids from seeds (20).
- **Amino acids:** Arginine (in pulp), aspartic acid (in rind) and glutamic acid (in seeds) (32).
- **Others**: (17)
  - Protein: rich in lysine, leucine, sulfo-amino acids as methionine.
  - Vitamins: Vitamin B (Thiamine, Riboflavin and Niacin).
  - Minerals: Ca, Mg, Mn, K, P, Fe and Zn .
  - Tocopherols and Carotenes: α-Tocopherol (20), γ-tocopherol and β-carotene from fruit seed oil (33).
  - Volatile compounds (fruit pulp): 2-Methyl, 4-heptanone, 3-methyl, 2-heptanone, trimethylsilyl methanol and 1-propoxy pentane (34).

5. Medicinal uses

A. Well-established

Oral: Purgative (4-5).

B. Traditional use

Externally: Rheumatic disease (low back, knee and joints pain) (35-37).

***C. colocynthis* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use

1. Oral dried fruits powder (4-5).
2. Topical Poultice (with warm cooking oils) (35-37).

7. Posology and method of administration correlated to medicinal use

Preparation 1
Indication A
Oral: 0.1 – 0.3g of dried fruits powder as purgative (4-5).

Preparation 2
Indication B
Externally: Poultice is made of colocynth with warm cooking oils to place it topically on the joint for rheumatic pain (35-37).

Method of administration: Oral and external use.

8. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

9. Special warnings and precautions for use

- Colocynth should be used under medical supervision and in proper dose as it is severely poisonous. It has a strongly irritating and painful effect on mucous membranes due to its content of cucurbitacin glycosides, out of which cucurbitacins are released in watery environments (38).
- **Diabetes**: Colocynth might lower blood sugar levels. Blood glucose levels should be regularly monitored in diabetics (39).
- **Surgery**: Colocynth might interfere with blood sugar control during and after surgery. Colocynth should be stopped at least 2 weeks before a scheduled surgery (39).
- Encouraging use of seeds (containing no saponin) instead of the whole fruit or pulp (40).

10. Interactions with other medicinal products and other forms of interaction (39)

- **Digoxin**

Colocynth is a stimulant laxative which can decrease potassium levels in the body therefore can increase the risk of side effects of digoxin.

- **Warfarin**

Colocynth can work as a laxative. In some people colocynth can cause diarrhea which can increase the effects of warfarin and increase the risk of bleeding.

- **Diuretic drugs**

Colocynth is a laxative agent and can decrease potassium in the body. Diuretic drugs can also decrease potassium in the body. Accordingly, concomitant use with diuretic drugs might severly decrease potassium in the body. Some diuretic drugs that can decrease potassium include chlorothiazide, chlorthalidone, furosemide, hydrochlorothiazide, and others.

11. Fertility, pregnancy and lactation

Colocynth is not recommended in pregnancy and breast-feeding (39) <<see section 15; Relevant biological activities>>.

Long term exposure to *C. colocynthis* L. may cause adverse effects on the reproductive system and fertility (41) <<see section 15; Relevant biological activities >>.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Gastrointestinal disorders such as diarrhea, painful cramp (42), colitis (43, 44); intestinal damage (45); the dried fruit pulp is irritating to the eye and powdered colocynth pulp causes severe pain if it meets the nasal mucous membrane (46-47); leucocytosis (48-49).

14. Overdose

- Vomiting, bloody diarrhea, colic, and kidney irritation following the intake of toxic dosages (0.6 to 1 g), and then increased diuresis that progresses to anuria. Lethal dosages (starting at 2 g) lead to convulsions, paralysis and, if untreated, lead to death through circulatory collapse. The treatment of poisonings should proceed symptomatically following gastric lavage (38).
- In case of poisoning, a dilute tannic acid solution should be taken, followed by large quantities of drinks that contain eggs (albuminous drinks) (39).

15. Relevant biological activities

Analgesic, anti-inflammatory and antinociceptive

- Carrageenan-induced edema in a rat hind paw was carried out to evaluate the topical anti-inflammatory effect of the *C. colocynthis* (*CC*) fruit extract cream (2–8%) and the tissue levels of IL-6 and TNF-α were estimated by using a commercial ELISA kit. Also the topical antinociceptive activity of the CC cream (2–8%) was evaluated in rat formalin test. The study indicated that topical application of *CC* cream possesses significant anti-inflammatory and antinociceptive activities in animal models, which were probably mediated by opioid receptors and the suppression of pro-inflammatory cytokines (TNF-α and IL-6) (50).

- *C. colocynthis* aqueous extracts of the plant different parts were screened for analgesic and anti-inflammatory activities using the acetic acid writhing test in mice and the carrageenan-induced paw edema assay in rats, respectively. All extracts displayed analgesic and anti-inflammatory activities at different doses without inducing acute toxicity. The best results were obtained with immature fruits followed by seeds. The stem and root extracts were shown to possess the less significant inhibitory activity against the analgesic and anti-inflammatory models used (51). Also, the same assessment was carried out on the immature fruit and seeds organic extracts (petroleum ether, chloroform, ethyl acetate, acetone and finely methanol extract). All extracts displayed an important analgesic and anti-inflammatory activities at different doses without inducing any side effects. Experiment results provide scientific insight into the ancient practice of utilizing *CC* as analgesic and as anti-inflammatory agents (52).

- The extract of the dried pulp of the plant fruits was studied for its effects through inhibition of inflammatory cytokines secreted in obesity conditions on male mice. The fed animals received 50 mg/kg of hydroalcoholic extract by gavage for 42 days. TNF-α, IL-6 and IL-10 in serum were assayed by ELISA technique after every two weeks. The extract dramatically decreased expression of TNF-α 44.83 (***$p < 0.001$), IL-6 30.23 (***$p < 0.001$) and marginally increased IL-10 5.31 (ns-$p > 0.05$) in obese mice. This study demonstrated that, although the extract did not show anti-obesity effects, it could have an anti-inflammatory effect through down regulation of obesity-associated pro-inflammatory cytokines (53).

- The effect of ethanol extract of the roots at dose of 20 ng/ml on inflammatory cytokine expression in inflamed cells with LPS20 both cartilage cells/macrophage was examined. The results indicated that the ethanol extract of root can reduce expression levels of pro-inflammatory cytokines in inflamed cells caused by situation same as that of osteoarthritis (54).

- Sodium carboxymethyl cellulose (5%) topical gel formulations containing 3% of Colocynth extract, hydrolyzed extract, or acetylated extract were studied for their release through cellophane membrane and their permeability through hairless mouse skin and, for the *in vivo* anti-inflammatory activity of the different types of colocynth extract using the carrageenan induced paw edema model in albino rats in comparison with the commercial Voltarin Emulgel®. The acetylated extract gel showed comparatively rapid permeability through hairless mouse skin, with low release rate through cellophane membrane. The pharmacological screening revealed that the percent reduction of edema produced by colocynth extract was 45.39%, the hydrolyzed extract produced 54.11% inhibition and the acetylated extract produced 64.95%, while Voltarin Emulgel® produced 63.35%. This means that acetylated colocynth extract can be used as an effective local anti-inflammatory agent (55).

- Fruit extracts in methanol were subjected to check anti-inflammatory activity against carrageenan induced paw edema, serotonin induced edema and prostaglandin E1-induced paw edema in albino rats. Extracts showed anti-inflammatory activity against all types of edema but the most significant results were seen against prostaglandin E1-induced paw edema (56).

Toxicity

- The study was undertaken to determine the acute median lethal dose of the methanol extract of the fruit of *C. colocynthis* and to evaluate the toxic effects of this extract at a single daily oral dose (131mg/kg) in 50 Albino rats. Liver, kidney and bone marrow function test were assessed using standard techniques. The acute median lethal dose of the extract was found to be 1311.45 mg/kg. The plasma ALT, AST, urea, and creatinine levels were significantly affected, an indication that the extract is hepato-nephrotoxic. The results obtained for hematological parameters reflect that methanol extract at a dose of 131 mg/kg did not affect quantitatively but disrupted qualitatively some functions of the bone marrow. The study also showed that the intake of extract of ripe *C. colocynthis* fruit presented some adverse effects on the functions of the liver, kidney, and bone marrow in rats (57).

- The toxic effects of *C. colocynthis* on male rabbits were investigated. Test animals were treated with 100 or 200 mg/kg/day of either pulp or seed extract. One month later, surviving animals were sacrificed and specimens of small intestine, kidney, and liver were prepared for morphological evaluation. No animals treated with 200 mg/kg/day of pulp extract survived. Animals treated with 100 mg/kg/day of pulp extract displayed sever lesions in the small intestine, kidney, and liver. Interestingly, animals treated with either 100 or 200 mg/kg/day of seed extract displayed only minor intestinal insult. In contrast to seeds extract, pulp extract of *C. colocynthis* can be fatal to rabbits. Therefore, seeds extract may be the preferred route for therapeutic application (45).

- The toxic effect of alcoholic extract of *C. colocynthis* on rat Liver was investigated with a single daily dose of (50, 100, 200, 400 g/kg) administered intraperitoneally. The results indicated that there is a morphological change in liver cells including karyrrhexis, chromatolysis, and granulation of the cytoplasm. Additionally, collagen and reticular fibers were evident in liver parenchyma in high doses. *C. colocynthis* can have toxic effects on liver cells which may induce hepatocyte necrosis and liver fibrosis. These effects were dose dependent (58).

- The acute toxicity studies of the methanolic extract of dried fruit pulp of *C. colocynthis* (Cucurbitaceae) in albino mice NMRI indicated the highly toxic nature of the colocynth. A very significant decrease in body weight of test animals was noted at $p < 0.05$. The LD_{50} was calculated as 1000mg/kg body weight. Within four days of experimentation, mortality was 100%. Histopathological studies confirmed the toxic

nature of extract. Gross changes in histology of heart, liver and kidneys were noted. Section of spleen did not exhibit any abnormality (59).

- Ethanolic extract of the plant fruits was investigated for its sub-chronic toxicity on Sprague Dawley (SD) rats, to develop safe doses, 30 male rats were used with 0, 12.5 and 25 mg/kg of the extract twice per week for 8 weeks. The raw extract of the fruits at dose of 12.5 mg and 25 mg/kg induced significant increase in level of creatinine and total protein and increased non-significantly levels of glucose and blood urea while reduced level of triglycerides, total cholesterol, and high-density lipoprotein-cholesterol significantly when compared with control group. Histopathological examination revealed that kidney of rat treated with *C. colocynthis* at dose of 12.5 mg/ kg show interstitial chronic inflammatory cell infiltrate while kidney of SD-rat treated with *C. colocynthis* at dose of 25 mg/kg showed interstitial fibrosis stained with Mallory trichrome stain. While liver showed lytic necrosis replaced by leukocyte infiltration at dose of 12.5 mg/kg of raw extract and rat treated with 25 mg/ kg show interstitial fibrosis stained with Mallory trichrome stain. Raw extract of the fruits had adverse effect on liver and kidney while in improving lipid profile and hematology in a novel manner in SD rats at selected dosed (60).

Case Presentations

- Four patients with colocynth intoxication are presented. The main clinical feature was acute rectorrhagia preceeded by mucosal diarrhea with tenesmus, which gradually progressed to bloody diarrhea and overt rectorrhagia within 3 to 4 hours. The only colonoscopic observation was mucosal erosion which was completely resolved in follow-up colonoscopy after 14 days.

The membranolytic activity of some *C. colocynthis* ingredients is responsible for the intestinal damage. Patients and herbalists should be acquainted with the proper use and side effects of the herb. Clinicians should also be aware of *C. colocynthis* as a probable cause of lower GI bleeding in patients with no other suggestive history, especially diabetics (40).

- Three examples were reported of toxic acute colitis which occurred after ingestion of *C. colocynthis* for ritual purposes. The prominent clinical feature was dysenteric diarrhea; colonoscopic changes included congestion and hyperaemia of the mucosa with abundant exudates but no ulceration or pseudopolyp formation. A causal relationship between colonic injury and the intake of colocynth was supported by the following features: (1) the pharmacology of the colocynth extract ingested; (2) the temporal relationship between colocynth intake and clinical onset (eight to 12 h); (3) the rapid recovery within three to six days, with normal endoscopy at day 14; (4) the absence of other possible causes for the observed patterns, except in one case, in which a concomitant intestinal infection with *Clostridium perfringens* Type A was discovered; (5) the specific pathological features. Colonic biopsies taken 27, 44, and 72

h after colocynth intake showed: erosions with fibrino-purulent exudate, early fibrosis of the lamina propria, hyaline thickening of the superficial epithelial basal membrane. These pathological features completely disappeared within 14 days in all three cases (61).

Pregnancy and Lactation

In Ayurvedic medicine, the fruit pulp has a reputation of causing miscarriage, when administered to pregnant women (62) and colocynth has also been used for this purpose in Europe (49, 63). Such activity could arise indirectly from congestion in the pelvic region as a manifestation of the cathartic action (62). It should be added, however, that on several occasions colocynth was ineffective as an abortive agent, even though it produced serious poisoning (63).

Fertility

- An ethanolic extract of *C. colocynthis* seeds, administered at an oral dose of 200 mg/kg for 2 days, did not inhibit copper acetate induced ovulation in rabbits to such an extent that further research seemed warranted (64). Different extracts of *C. colocynthis* were screened for anti-implantation activity by feeding female rats with each extract from day 1 to day 7 of their pregnancy. Acetone and methanolic root extracts in doses of 150 mg/kg prevented implantation in 3 and 4 of 7 test animals, respectively, whereas 200 mg/kg of an ethanolic leaf extract and 150 mg/kg of a benzene leaf extract inhibited implantation in 4 of 6 rats (65). The spermatotoxicity was observed in mice treated with an alcoholic extract of *C. colocynthis* fruit in daily oral doses of 0.1 g/kg body weight for 3 months (48). Early textbooks claim that *C. colocynthis* is excreted into breast milk and should therefore not be given to nursing women (66-68).

The short and long effects of *C. colocynthis* L. (400 mg/kg/body weight) on the reproductive system after administration to female Sprague-Dawley rats were investigated. The rats were intraperitoneally injected in dose of 400 mg/kg/body weight. First group received treatment for 4 weeks and a second group received the same dose of treatment for a period of 12 weeks. Female rats were allowed mating with males after 10 days prior to the last administration dose. Several parameters were determined including: number of pregnant rats, body and reproductive organ weight, number of implantation sites, viable fetuses and resorption sites. The results indicate that long-term exposure of female rats to *C. colocynthis* L. causes adverse effects on the reproductive system and fertility (41).

16. Additional Information

Colocynth has a drastic purgative and irritant action and has been superseded by less toxic laxatives. It is used in homoeopathic medicine (69).

C. colocynthis has showed wide range of pharmacological activities including:

- Antidiabetic, hypoglycemic and antihyperglycaemic activities (30, 70-85).
- Peripheral neuropathy (86).
- Antioxidant activity (19, 87-90).
- Hair growth effect (91, 92).
- Anti-microbial activity (13, 25, 93-98).
- Anthelmintic activity (99-103).
- Cytotoxic activity (87, 104-106).
- Hypolipidemic effect /antihyperlipidemic (89, 107,108).
- Hepatoprotective effect (109-111).

17. Date of compilation/last revision

30/8/2023.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Hassan, N. M and Omer, E. A. (2018). *Citrullus colocynthis* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **6**, 18-36. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Egyptian Pharmacopoeia (1984). 3rd edition. General Organization for Government Printing. Cairo.
5	Egyptian Pharmacopoeia (2005). 4th edition. General Organization for Government Printing. Cairo.
6	Hammouda, F. M., Ismail, S. I., Abdel-Azim, N. S. and Shams, K. A. (2005). A Guide to Medicinal Plants in North Africa (Batanouny K. H., editor). IUCN Centre for Mediterranean Cooperation. Malaga.
7	Hussain, A. I., Rathore, H. A., Sattar, M. Z. A., Chatha, S. A. S., Sarker S. D. and Gilani, A. H. (2014). *Citrullus colocynthis* (L.) Schrad (bitter apple fruit): A review of its phytochemistry, pharmacology, traditional uses and nutritional potential. *J. Ethnopharmacol*., **155**, 54-66.
8	Adam, S. E. I., Al-Yahya, M. A. and Al-Farhan, A. H., (2001). Response of Najdi sheep to oral administration of *Citrullus colocynthis* fruits, *Neriumo leander* leaves or their mixture. *Small Ruminants Research*, **40**, 239–244.
9	Chen, J. C., Chiu, M. H., Nie, R. L., Cordell, G. A. and Qiu, S. X. (2005). Cucurbitacins and cucurbitane glycosides: structures and biological activities. *Natural Product Reports*, **22**(3), 386–399.
10	Tannin-Spitz, T., Grossman, S., Dovrat, S., Gottlieb, H. E. and Bergman, M. (2007). Growth inhibitory activity of cucurbitacin glucosides isolated from *Citrullus colocynthis* on human breast cancer cells. *Biochemical Pharmacology*, **73**, 56–67.
11	Yoshikawa, M., Morikawa, T., Kobayashi, H., Nakamura, A., Matsuhira, K., Nakamura, S. and Matsuda, H. (2007). Bioactive saponins and glycosides, XXVII. Structures of new cucurbitane-type triterpene glycosides and antiallergic constituents from *Citrullus colocynthis*. *Chemical and Pharmaceutical Bulletin*, **55**, 428–434.
12	Torkey H. M., Abou-Yousef H. M., Azeiz, A. and Farid, H. E. A. (2009). Insecticidal effect of cucurbitacin E glycoside isolated from *Citrullus colocynthis* against *Aphis craccivora*. *Australian Journal of Basic and Applied Sciences,* **3**, 4060–4066.
13	Ali, A. A., Alian, M. A. and Elmahi, H. A. (2013). Phytochemical analysis of some chemical metabolites of Colocynth plant (*Citrullus colocynthis* L.) and its activities as antimicrobial and antiplasmidial. *Journal of Basic and Applied Scitific Research*, **3**, 228–236.
14	Delazar, A., Gibbons, S., Kosari, A., Nazemiyeh, H., Modarresi, M., Nahar, L. and Sarker, S. (2006). Flavone c-glycosides and cucurbitacin glycosides from *Citrullus colocynthis*. *DARU J. Pharmaceut. Sci.*, **14**(3), 109-114.

15	Pravin, B., Tushar, D., Vijay, P. and Kishanchnad, K. (2013). Review on *Citrullus colocynthis*. *International Journal of Research in Pharmacy and Chemistry (IJRPC)*, **3**(1), 46-53.
16	Song, F., Dai, B., Zhang, H., Xie, J., Gu, C. and Zhang, J. (2015). Two new cucurbitane-type triterpenoid saponins isolated from ethyl acetate extract of *Citrullus colocynthis* fruit. *Journal of Asian Natural Products Research*, **17**(8), 1-6.
17	Gurudeeban, S., Satyavani, K. and Ramanathan, T. (2010). Bitter apple (*Citrullus colocynthis*): an overview of chemical composition and biomedical potentials. *Asian Journal of Plant Sciences*, **9**, 394–401.
18	Maatooq, G. T., El-Sharkawy, S. H., Afifi, M. S. and Rosazza, J. P. N. (1997). C-p-hydroxybenzoyl glycoflavones from *Citrullus colocynthis*. *Phytochemistry*, **44**, 187-190.
19	Hussain, A. I., Rathore, H. A., Sattar, M. Z. A., Chatha, S. A. S., Ahmad, F., Ahmad, A. and Johns, E. J. (2013). Phenolic profile and antioxidant activity of various extracts from *Citrullus colocynthis* (L.) from the Pakistani flora. *Industrial Crops and Products*, **45**, 416–422.
20	Al-Snafi, A. E. (2016). Chemical constituents and pharmacological effects of *Citrullus colocynthis* - A review. *IOSR Journal of Pharmacy,* **3**(6), 57-67.
21	Meena, M. C. and Patni, V. (2008). Isolation and identification of flavonoid "Quercetin" from *Citrullus colocynthis* (Linn.) Schrad. *Asian Journal of Experimental Sciences,* **22**, 137-142.
22	Shawkey A. M., Rabeh M. A. and Abdellatif A. O. (2014). Biofunctional molecules from *Citrullus colocynthis*: An HPLC/MS analysis in correlation to antimicrobial and anticancer activities. *Advances in Life Science and Technology,* **17**, 51-61.
23	Lahfa, F. B., Azzi, R., Mezouar, D. and Djaziri, R. (2017). Hypoglycemic effect of *Citrullus colocynthis* extracts. *Phytothérapie*, **15**, 50-56 .
24	Sayed, D. M., Balbaa, S. I. and Afifi, M. S. A. (1973). Nitrogenous bases of the different organs of *Citrullus colocynthis*. *Planta Medica*, **24**(3), 260–265.
25	Najafi, S., Sanadgol, N., Nejad, B. S., Beiragi, M. A. and Sanadgol, E. (2010). Phytochemical screening and antibacterial activity of *Citrullus colocynthis* (Linn.) Schrad against *Staphylococcus aureus*. *Journal of Medicinal Plants Research*, **4**(22), 2321-2325.
26	Mukherjee, A. and Patil, S. D. (2012). Effects of alkaloid rich extract of *Citrullus colocynthis* fruit on Artemia salina and human cancerous (MCF-7andHEPG-2) cells. *Journal of Pharma Sci. Tech.,* **1**, 15–19.
27	Salama, H. M. H. (2012). Alkaloids and flavonoids from the air dried aerial parts of *Citrullus colocynthis*. *Journal of Medicinal Plants Research*, **6**(38), 5150-5155.
28	Sawaya, W. N., Daghir, N. J. and Khan, P. (1983.) Chemical characterization and edibility of the oil extracted from *Citrullus colocynthis* seeds. *Journal of Food Science*, **48**, 104–106.
29	Sadou, H., Sabo, H., Alma, M. M., Saadou, M. and Leger, C. L. (2007). Chemical content of the seeds and physico-chemical characteristic of the seed oils from *Citrullus colocynthis, Coccinia grandis, Cucumis metuliferus* and *Cucumis prophetarum* of Niger. *Bulletin of the Chemical Society of Ethiopia,* **21**, 323–330.

30	Sebbagh, N., Cruciani-Guglielmacci, C., Ouali, F., Berthault, M. F., Rouch, C., Sari, D. C. and Magnan, C. (2009). Comparative effects of *Citrullus colocynthis,* sun flower and olive oil-enriched diet in streptozotocin-induced diabetes in rats. *Diabetes and Metabolism*, **35**, 178–184.
31	Sayed, M. D., Balbaa, S. I. and Afifi, M. S. (1973b). The lipid content of the seeds of *Citrullus colocynthis. Planta Medica*, **24**, 41-45.
32	Abudayeh Z. H. M., Lamazian H. R., Sereda P., Chekman I., Al Khalifa I. I., Al Azzam K. M. and Hassouneh L. K. M. (2016). Comparative study of amino acid composition in the seeds, pulp and rind from *Citurllus colocynthis* fruits. *International Journal of Pharmacognosy and Phytochemical Research*, **8**(3), 433-437.
33	Kalhoro, M. A., Afza, N., Saleem, M. and Malik, A. (2002). Pharmacochemical studies of the oil, aerial parts, pulp and peel of *Citrullus colocynthis*. *Journal of Chemical Society of Pakistan*, **24**, 274–276.
34	Gurudeeban, S., Ramanathan, T. and K. Satyavani. (2011). Characterization of volatile compounds from bitter apple (*Citrullus colocynthis*) using GC-MS. *International Journal of Chemical and Analytical Science*, **2**(8), 108-110.
35	Conservation and sustainable use of medicinal plants in Egypt, National Surveys (2016). UNDP, GEF, ASRT and NRC, Volumes 1-5.
36	Bailey, C. and Danin, A. (1981). Bedouin plant utilization in Sinai and the Negev. Economic Botany, **35**(2), 145-162.
37	Mahmoud, T. and Gairola, S. (2013). Traditional knowledge and use of medicinal plants in the Eastern Desert of Egypt: a case study from Wadi El-Gemal National Park. *Journal of Medicinal Plants Studies,* **1**(6), 10-17.
38	PDR for Herbal Medicines (1998). Medical Economic Co. Montvale, New Jersey, 639. ISBN 1563633612, 9781563633614.
39	https://www.webmd.com/vitamins/ai/ingredientmono-921/jimson-weed
40	Reza, H. J., Davoudi, A., Davoudi, F., Valizadegan, G., Goodarzi, H., Mahmoodi, S., Reza. M. G. and Faraji, M. (2013). *Citrullus colocynthis* as the cause of acute rectorrhagia. *Case Reports in Emergency Medicine*, Article ID 652192, 5. doi: 10.1155/2013/652192.
41	Qazan, W. S. H., Almasad, M. M. and Daradka, H. (2007). Short and long effects of *Citrullus colocynthis* L. on reproductive system and fertility in female Sprague Dawley rats. Pak. *J. Biol. Sci.,* **10**(16), 2699-2703.
42	Barghamdi, B., Ghorat, F., Asadollahi, K., Sayehmiri, K., Peyghambari, R. and Abangah, G. (2016). Therapeutic effects of *Citrullus colocynthis* fruit in patients with type II diabetes: A clinical trial study. *J. Pharm. Bioallied Sci.,* **8**(2), 130–134.
43	Jouad, H., Haloui, M., Rhiouani, H., El Hilaly, J. and Eddouks, M. (2001). Ethnobotanical survey of medicinal plants used for the treatment of diabetes, cardiac and renal diseases in the North centre region of Morocco (Fez-Boulemane). *Journal of Ethnopharmacology*, **2-3** (77), 175–182.
44	Khan, S. A., Shelleh, H. H., Bhat, A. R. and Bhat, K. S. (2003). Colocynth toxicity. A possible cause of bloody diarrhea. *Saudi Medical Journal*, **8** (24), 904–906.

45	Shafaei, A., Esmaeili, H. Rad, S., Delazar, A. and Behjati, M. (2012). *Citrullus colocynthis* as a medicinal or poisonous plant: a revised fact. *JMPR*., **35** (6), 4922–4927.
46	Mitchell, J. and Rook, A. (1979). Botanical Dermatology: Plants and Plant Products Injurious to the Skin. Greengrass, Vancouver, Canada. ISBN:0889780471, 9780889780477.
47	Blacow, N., Wade, W. and Red, A. (1972). Martindale: The Extra Pharmacopoeia. 26th ed. London: *The Pharmaceutical Press,* l627-1628.
48	Shah, A. H., Qureshi, S., Tariq, M. and Ageel, A. M. (1989). Toxicity studies on six plants used in the traditional Arab system of medicine. *Phytother. Res.,* **3**, 25-29.
49	Harnmarsten, G. and Lindgren, G. (1941-43). Ein Fall von Koloquinten-Vergiftung. Vergiftungsfalle **12**, A919: 107-110.
50	Pashmforosh, M., Vardanjani, H. R., Vardanjani, H. R., Pashmforosh, M. and Khodayar, M. J. (2018). Topical anti-inflammatory and analgesic activities of *Citrullus colocynthis* extract cream in rats. *Medicina*, **54**, 51- 61.
51	Marzouk, B., Marzouk, Z., Haloui, E., Fenina, N., Bouraoui, A. and Aouni, M. (2010). Screening of analgesic and anti-inflammatory activities of *Citrullus colocynthis* from southern Tunisia. *Journal of Ethnopharmacology*, **128**(1), 15-19.
52	Marzouk, B., Marzouk, Z., Fenina, N., Bouraoui, A. and Aouni, M. (2011). Anti-inflammatory and analgesic activities of Tunisian *Citrullus colocynthis* Schrad. Immature fruit and seed organic extracts. *Eur. Rev. Med. Pharmacol. Sci.,* **15**(6), 665-672.
53	Sanadgol, N., Najafi, S., Ghasemi, L. V., Motalleb, G and Estakhr, J. (2011). A study of the inhibitory effects of *Citrullus colocynthis* (CCT) using hydro-alcoholic extract on the expression of cytokines: TNF-and IL-6 in high fat diet-fed mice towards a cure for diabetes mellitus. *J. Pharmacognosy & Phytotherapy*, **3**(6), 81-88.
54	Akhzari, M., Mirghiasi, S., Vassaf, M., Bidgoli, M. and Tari, Z. (2015). The effect of *Citrullus colocynthis* on the reduction of inflammatory agents in osteoarthritis. *Mol. Biol*., **4**(4), 33- 38.
55	Aly, A. M. and Naddaf, A. (2006). Anti-inflammatory activities of Colocynth topical gel. *J. Med. Sci.,* **6**, 216-221.
56	Rajamanickam, E., Gurudeeban, S., Ramanathan, T. and Satyavani, K. (2010). Evaluation of anti-inflammatory activity of *Citrullus colocynthis*. *Int. J. Cur. Res*., **2**, 67-69.
57	Soufane, S., Bedda, A., Mahdeb, N. and Bouzidi, A. (2013). Acute toxicity study on *Citrullus colocynthis* fruit methanol extract in albino rats. *Journal of Applied Pharmaceutical Science,* **3**(6), 88-93.
58	Dehghani, F. and Panjehshahin, M. R. (2006). The toxic effect of alcoholic extract of *Citrullus colocynthis* on rat liver. *Iranian Journal of Pharmacology & Therapeutics*, **5**, 117-119.
59	Shaikh, J., Shaikh, D., Bin Rahman, A. and Shafi, S. (2016). Antimicrobial and toxicological studies on fruit pulp of *Citrullus colocynthis* L. *Pak. J. Pharm. Sci*., **29**(1), 9-15.
60	Elalfy, M. M., Farag, A., Helmy, A. A., Metwaly, Z. E. and Ali, F. R. (2019). Hematological, biochemical and cytotoxic effect of ethanolic raw extract of Egyptian *Citrullus colocynthis* in sprague dawley rats. *Enz. Eng*., **8**, 165.

61	Goldfain, D., Lavergne, A., Galian, A., Chauveinc, L. and Prudhomme, F. (1989). Peculiar acute toxic colitis after ingestion of colocynth: a clinicopathological study of three cases. *Gut*, **30** (10), 1412-1418.
62	Banerjee, S. P. and Dandiya, P. C. (1967). Smooth muscle and cardiovascular pharmacology of α-elaterin-2-D-glucopyranoside glycoside of *Citrullus colocynthis*. *J. Pharm. Sci*., 56:1665-1667.
63	Lewin, L. (1962). Gifte und Vergiftungen. Lehrbuch der Toxikologie. Fiinfte unveranderte Ausgabe. UImIDonau: Karl F. Haug Verlag, 722-723.
64	Vohora, S. B., Khan, M. S. Y. and Afaq, S. H. (1973). Antifertility studies on Unani herbs. Part 2. Antiovulatory effects of 'hanzal', 'halun', 'kalonji' and 'sambhalu'. *Indian J. Pharm.,* **35**, 100-102.
65	Prakash, A. O., Saxena, V., Shukla, S., Tewari, R. K., Mathur, S., Gupta, A., Sharma, S. and Mathur, R. (1985). Anti-implantation activity of some indigenous plants in rats. *Acta Eur. Fertil*., **16** (6), 441-448.
66	Osol, A. and Farrar, G. E. (1955). The Dispensatory of the United States of America. 25th ed. Philadelphia: J.B. Lippincott Company, 359-360.
67	Anonymous. (1941). The Extra Pharmacopoeia - Martindale. 22nd ed. London: The-Pharmaceutical Press.
68	Sollmann, T. (1957). A Manual of pharmacology and its applications to therapeutics and toxicology. 8th ed. Philadelphia: W.B. Saunders Company, 216.
69	Sweetman, S. C. (Ed). (2007). Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version, London.
70	Agarwal, V., Sharma, A. K., Upadhyay, A., Singh, G. and Gupta, R. (2012). Hypoglycemic effects of *Citrullus colocynthis* roots. *Acta Po.l Pharm*., **69**(1), 75-79.
71	Huseini, H. F., Darvishzadeh, F., Heshmat, R., Jafariazar, Z., Raza, M. and Larijani, B. (2009). The clinical investigation of *Citrullus colocynthis* (L.) schrad fruit in treatment of Type II diabetic patients: a randomized, double blind, placebo controlled clinical trial. *Phytother. Res*., **23**(8), 1186-1189.
72	Benariba, N., Djaziri, R., Zerriouh, B. H., Boucheri1, K., Louchami, K., Sener, A. and Willy, J. M. (2009). Antihyperglycemic effect of *Citrullus colocynthis* seed aqueous extracts in streptozotocin-induced diabetic rats. *Metabolic and Functional Research on Diabetes*, **2**, 71-77.
73	Jayaraman, P. N. N., Arihara, S., Anitha, T. and Joshi, V. D. (2009). Antidiabetic effect of petroleum ether extract of *Citrullus colocynthis* (L.) Schrad. fruits against streptozotocin-induced hyperglycemic rats. *Rom. J. Biol.-Plant Biol*., **54**, 127–134.
74	Nmila, R., Gross, R., Rchid, H., Roye, M., Manteghetti, M., Petit, P., Tijane, M., Ribes, G. and Sauvaire, Y. (2000). Insulinotropic effect of *Citrullus colocynthis* fruit extracts. *Planta Medica*, **66**(5), 418-423.
75	Esmaeel, E., Somaieh, B., Mahmoud, H., Ghorban, M. Z., Saeed, S., Javad, J. (2016). Effect of hydroalcoholic leaves extract of *Citrullus colocynthis* on induction of insulin secretion from isolated rat islets of Langerhans. *Asian Pacific Journal of Tropical Disease,* **8**(6), 638-641.

76	Atole, S., Jangde, C., Philip, P., Rekhe, D., Aghav, D., Waghode, H. J. and Chougule, A. M. (2009). Safety evaluation studies of *Citrullus colocynthis* for diabetes in rats. *Veterinary World,* **2**(11), 423-425. .
77	Nikbakht, M. and Gheatasi, I. (2006). Evaluation of the effect of hydroalcoholic extract of *Citrullus colocynthis* in normoglycemic and streptozocine (STZ) induced diabetic male rats. *Armaghane Danesh Bimonthly Journal*, **11**(2), 63-71.
78	Huseini, H. F., Zaree, A., Heshmat, R., Larijani, B., Fakhrzadeh, H., Rezaii Sharifabadi, R., Naderi, G. A., Zaringhalam, J. and Shikh Samani, A. H. (2006). The effect of *Citrullus colocynthis* (L.) Schrad. Fruit on oxidative stress parameters in type II diabetic patients. *Journal of Medicinal Plants*, **1**(17), 55-60.
79	Karimabad, M. N., Niknia, S., Golnabadi, M. B., Poor, S. F., Hajizadeh, M. R. and Mahmoodi, M. (2020). Effect of *Citrullus colocynthis* extract on glycated hemoglobin formation (*in vitro*). *The Eurasian Journal of Medicine*, **52**(1), 47-51.
80	Benariba, N., Djaziri, R., Zerriouh, B. H., Bellakhdar, W., Hupkens, E., Boucherit, Z. and Malaisse, W. J. (2012). Short-and long-term effects of various *Citrullus colocynthis* seed extracts in normal and streptozotocin-induced diabetic rats. *International Journal of Molecular Medicine*; **30**(6), 1528-36.
81	Amin, A., Tahir, M. and Lone, K. P. (2017). Effect of *Citrullus colocynthis* aqueous seed extract on beta cell regeneration and intra-islet vasculature in alloxan induced diabetic male albino rats. *JPMA The Journal of the Pakistan Medical Association*, **67**(5), 715-721.
82	Li, Y., Zheng, M., Zhai, X., Huang, Y., Khalid, A., Malik, A., Shah, P., Karim. S., Azhar. S. and Hou X. (2015). Effect of - *Gymnema sylvestre*, *Citrullus colocynthis* and *Artemisia absinthium* on blood glucose and lipid profile in diabetic human. *Acta. Pol. Pharm.*, **72**, 981-985.
83	Pooladvand, V., Taghavi, S., Mahmoodi, M., Tavakolian, F. V. and Hosseini, Z. M. (2011). Histological alterations due to the consumption of different doses of *Citrullus colocynthis* fruit in normal and diabetic male rats. *J .Mazandaran Univ. Med. Sci.*, **21**(82), 63-71.
84	Amin, A. and Tahir, M. (2016). Alpha cells a 'therapeutic target': effect of *Citrullus colocynthis* on alpha cell count in healthy and alloxan induced diabetic male albino rats. *World Journal of Pharmaceutical Research*, **11**(5), 329-339.
85	Abdel-Hassan, A., Abdel-Barry, J. A. and Mohammed, T. S. (2000). The hypoglycaemic and antihyperglycaemic effect of *Citrullus colocynthis* fruit aqueous extract in normal and alloxandiabetic rabbits. *J. Ethnopharmacol*, **71**, 325–330.
86	Ostovar, M., Akbari, A., Anbardar, M. H., Iraji, A., Salmanpour, M., Hafez, G. S., Heydari, M. and Shams, M. (2020). Effects of *Citrullus colocynthis* L. in a rat model of diabetic neuropathy. *Journal of Integrative Medicine*, **18**(1), 59-67.
87	Bourhia, M., Messaoudi, M., Bakrim, H., Mothana, R. A., Sddiqui, N. A., Almarfadi, O. M., El Mzibri, M., Gmouh, S., Laglaoui, A. and Benbacer, L. (2020). *Citrullus colocynthis* (L.) Schrad: Chemical characterization, scavenging and cytotoxic activities. *Open Chemistry*, **18**, 986–994.
88	Jayaraman, R. and Christina, A. J. M. (2013) Evaluation of *Citrullus colocynthis* fruits on *in vitro* antioxidant activity and *in vivo* DEN/PB induced hepatotoxicity. *Int. J. Applied Res. in Nat. Pro*., **6**(1), 1-9.

89	Dallak, M. (2011). *In vivo*, hypolipidemic and antioxidant effects of *Citrullus colocynthis* pulp extract in alloxan induced diabetic rats. *Afr. J. Biotech.*, **10**(48), 9898-9903.
90	Gill, N. S., Kaur, S, Arora, R. and Bail, M. (2011). Screening of antioxidant and antiulcer potential of *Citrullus colocynthis* methanolic seed extract. *Res. J. Phytochemistry*, **5**(2), 98- 106.
91	Roy, R. K., Thakur, M. and Dixit, V. K. (2007). Effect of *Citrullus colocynthis* on hair growth in albino rats. *Pharma Bio.*, **45**(10), 739-744.
92	Dhanotia, R., Chauhan, N. S., Saraf D. K. and Dixit, V. K. (2011). Effect of *Citrullus colocynthis* Schrad fruits on testosterone-induced alopecia. *Nat. Prod. Res.*, **25**(15), 1432-1443.
93	Gurudeeban, S., Ramanathan, T. and Satyavani, K. (2010). Antioxidant and radical scavenging activity of *Citrullus colocynthis*. *Inventi Rapid: Nutracuticals*, **1**, 38.
94	Rodge, S. V. and Biradar, S. D. (2012). Preliminary phytochemical screening and antimicrobial activity of *Citrullus colocynthis* (Linn.) Shared. *Indian J. Plant Sci.*, **2**(1), 19- 23.
95	Eidi, S., Azadi, H. G., Rahbar, N. and Mehmannavaz, H. R. (2015). Evaluation of antifungal activity of hydroalcoholic extracts of *Citrullus colocynthis* fruit. *Journal of Herbal Medicine*, **5**(1), 36-40.
96	Archana, M., Garima, S., Sumita, K., Meenakshi, S. and Kothari, S. L. (2013). Antimycobacterial activity of *Citrullus colocynthis* (L.) Schrad. against drug sensitive and drug resistant Mycobacterium tuberculosis and MOTT clinical isolates. *J. Ethnopharm.*, **149**(1), 195-200.
97	Al-hejjaj, M. Y., Alhurba, Y. A. and Mohamad, S. A. (2010). Study of alkaloid extract from *Citrullus colocynthis* fruit and its antimicrobial activity screening. *J. Basrah. Res. (Sciences)*, **36**(4), 42-47.
98	Memon, U., Brohi, A. H., Ahmed, S. W., Azhar, I. and Bano, H., (2003). Antibacterial screening of *Citrullus colocynthis*. *Pak. J. Pharm. Sci.,* **16**(1), 1-6.
99	Menaria, K., Swarnakar, G. and Kumawat, A. (2020). Anthelmintic effect of *Citrullus colocynthis* on the tegument of *Cotylophoron cotylophorum* by light microscope. *IJPSR*, **11**(8), 4029-4038.
100	Swarnakar, G. and Kumawat, A. (2014). *In vitro* anthelmintic effect of *Citrullus colocynthis* on tegument of amphistome *Orthocoelium scoliocoelium* (Trematoda: Digenea). *Int. J. Curr. Microbiol. App. Sci.*, **3**(6), 571-582.
101	Ahmed, C. N., Hamad, K. K. and Qadir, F. A. (2019). *Haemonchus contortus* as a model in assessing activity of *Citrullus colocynthis* fruit extract to control benzimidazole-resistant parasitic nematodes. *ZJPAS*, 31(5): 61-70.
102	Damor, R. and Swarnakar, G. (2018). In vitro anthelmintic effects of fruit extracts of *Citrullus colocynthis* on liver fluke *Fasciola gigantica* in buffaloes. *International Journal of Innovative Research and Revie.,* **6** (1), 1-11.
103	Talole, B. B., Baheti, D. G. and More, P. A. (2013). *In vitro* helmintholytic activity of leaves of *Citrullus colocynthis*. *International Journal of Research in Pharmacy and Chemistry,* **3**(2), 240-243.
104	Grossman, S., Dovrat, S., Gottlieb, H. E. and Bergman, M. (2007). Growth inhibitory activity of cucurbitacin glucosides isolated from *Citrullus colocynthis* on human breast cancer cells. *Biochem. Pharmacol.*, **73**(1), 56-67.

105	Shokrzadeh, M., Chabra, A., Naghshvar, F. and Ahmadi, A. H. (2013). The mitigating effect of *Citrullus colocynthis* (L.) fruit extract against genotoxicity induced by cyclophosphamide in mice bone marrow cells. *The Scientific World Journal*, Article ID 980480: 8.
106	Ayyad, S. E1. , Abdel-Lateff, A., Alarif, W. M., Patacchioli, F. R., Badria, F. A. and Ezmirly, S. T. (2011). *In vitro* and *in vivo* study of cucurbitacins-type triterpene glucoside from *Citrullus colocynthis* growing in Saudi Arabia against hepatocellular carcinoma. *Environmental toxicology and pharmacology*, **33**(2), 245-251.
107	Sari, M., Nemmiche, S., Benmehdi, H., Amrouche, A., Hamadi, A. and Sari, D. C. (2019). Hypolipidemic and antioxidant effects of *Citrullus colocynthis* seeds oil in high-fat diets induced obese rats. *Phytotherapie*, **17**(6), 310-320.
108	Yazit, S. M., Nemmiche, S., Amamou, F., Meziane, R. K. and Chabane-Sari, D. (2020). Anti-hyperlipidemic effect of fatty acids methyl esters (FAMEs) of *Citrullus colocynthis* in high-fat diet induced obesity in rats. *Phytothérapie*, **18**, 131-139.
109	Vakiloddin, S., Fuloria, N., Fuloria, S., Dhanaraj, S. A., Balaji, K. and Karupiah, S. (2015). Evidence of hepatoprotective and antioxidant effect of *Citrullus colocynthis* fruits in paracetamol induced hepatotoxicity. *Pak. J. Pharm. Sci*., **28**(3), 951-957.
110	Iqbal, A. D., Sharma, V., Saxena, R. C. and Bansal, S. K. (2011). Hepatoprotective activity of *Citrullus colocynthis* Linn. *Inventi Rapid: Ethnopharmacolog,* **2** (2): ISSN 0976-3805.
111	Iqbal, A. D., Saxena, R. C. and Bansal, S. K. (2012). Hepatoprotection: A Hallmark of *Citrullus colocynthis* L. against paracetamol induced hepatotoxicity in swiss albino rats. *American Journal of Plant Sciences*, **7**, 1022-1027.

Egyptian Herbal Monograph

Pharmacopoeial wild medicinal plants

***Datura stramonium* L.** داتورا

1. Names & Synonyms (1 - 4)

***Datura stramonium* L.**
Family: Solanaceae
Syns.: *Datura tatula* L.
Arabic: Datura داتورا , Tatura طاطورا.
English: Thorn-apple, Devil's apple, Jimson Weed, Stramonium.

2. Geographical distribution

Confined to Nile region (3).

3. Parts used for medicinal purpose

All parts possess medicinal value, though seeds and dried leaves with or without flowering tops are most widely used (2, 5-7).

4. Major chemical constituents

- **Tropane alkaloids**:
  - Hyoscyamine and hyoscine (scopolamine) (9).
  - 3-(hydroxyacetoxy) tropane, 3-hydroxy-6-(2-methylbutyryloxy)tropane, 3α-tigloyloxy-6-hydroxytropane, 3,7-dihydroxy-6-tigloyloxytropane, 3-tigloyloxy-6- propionyloxytropane, 3-phenylacetoxy-6,7-epoxytropane, 3-phenylacetoxy-6-hydroxytropane, aponorscopolamine, 3α,6 α -ditigloyloxytropane, 7-hydroxyhyoscyamine (10-14), 3-phenylacetoxy-6, 7-epoxynortropane, and 7-hydroxyapoatropine (15).
- **Steroids**:
  - Datura lactones (withanolides): withastramonolide (16), withatatulin and several others with anolides (17).
  - Ergostane-type sterols (18), stigmasterol and campesterol (19).
- **Essential oil:**
  Leaf oil: Phytol, diterpenes and oxygenated monoterpenes (9).
- **Other Constituents:**

Phenolic acids: Caffeic, *p*-coumaric, and ferulic acids; Flavonoids: chrysin, quercetin and their esters; Coumarins: umbelliferone, fraxetin, scopoletin, scopolin, umckalin; Amino acids: asparagines and glutamine; Fatty acids: daturic acid; Terpenes: hyoscyamilactol, daturaolone, daturadiol. *N-trans*-feruloyl tryptamine, tyramine, *N-trans*-ferulicacyl-tyramine; Coumarinolignoid: cleomiscosin A; Carbolines: 1-acetyl-7-hydrox-*β*-carboline and 7-hydroxy-*β*-carbolinel-propionic acid (19, 20); saponin and tannins (21).

5. Medicinal uses

A. Well-established (5)

- Spasmolytic
- Anti-asthmatic

B. Traditional use

- Rheumatic disease (7)

***D. stramonium* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use

1. Powdered herbal substances
   1.1 Leaves (7)
   1.2 Seeds (4).
2. Fluid extracts from leaves or seeds, tincture from leaves, powdered extract using the same amount of the stabilized standardized powdered drug (7).
3. Poultice (7).

7. Posology and method of administration correlated to medicinal use

Preparation 1
Indication A
1.1. A single dose of 50-100mg of stabilized powdered leaves (up to 3 times a day); maximum daily dose: 600mg in divided doses (4).
1.2. A single dose of 50mg of stabilized powdered seeds; maximum daily dose: 600mg in divided doses (4).

Preparation 2
Indication A
Equivalent to stabilized standardized powdered drug:

*Stabilized powdered leaves standardized to contain 0.23 to 0.27% of tropane alkaloids, calculated as hyoscyamine (22).
*Stabilized powdered seeds standardized to contain 0.4 to 0.6% of tropane alkaloids, calculated as hyoscyamine (4).

Preparation 3
Indication B
Leaves have been used as poultice (with some oil) for rheumatic pain (7).

Note: *D. stramonium* is to be dispensed by prescription only (a prescription drug). It is considered to be potentially harmful if not used under medical supervision.

Method of administration: Oral and topical use.

8. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Congestive heart failure; acute pulmonary edema; Constipation; Down syndrome; Seizures; Esophageal reflux; Fever; Stomach ulcer; Stomach and intestinal infections; Hiatal hernia; Glaucoma; Rapid heartbeat (tachycardia); Toxic megacolon; Ulcerative colitis; Obstructive digestive tract disorders (as atony, paralytic ileus, and stenosis); Urinary retention; Enlarged prostate (prostatic hypertrophy) (4); thyrotoxicosis; Asthma; Acute haemorrhage; hepatic disease; myocardial ischemia; CNS disorders (as myasthenia gravis); hyperthyroidism; hypertension; renal disease (23).

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Children, patients with urine retention or coronary sclerosis should not use *D. stramonium* (4).
- Rubbing skin and eyes after contact with this plant is dangerous (2).

10. Interactions with other medicinal products and other forms of interaction

D. stramonium will have an additive effect when taken with other anticholinergic medications; co-administration of *D. stramonium* with other anticholinergic drugs may increase the frequency and/or severity of anticholinergic side effects (such as dry mouth, constipation, drowsiness, and others).

With drugs:

- *D. stramonium* will have an additive effect when taken with other anticholinergic drugs (drying medications) as atropine, scopolamine, some antihistamines and antidepressants; Together with these medications might cause side effects as dry skin, dizziness, low blood pressure, fast heartbeat, and other serious side effects. (4, 24).
- Antacids: decrease action of Jimsonweed (23).
- Phenothiazines: *D. stramonium* decreases the action of Phenothiazines (23).

With herbs:

Aloe, Buckthorn, Cascara, Chinese Rhubarb, Senna: *Stramonium* increase action in case of chronic use or abuse (23).

11. Fertility, pregnancy and lactation

- The use should be avoided during pregnancy and lactation as atropine component crosses the placenta and excreted in breast milk (23).
- *D. stramonium* may cause impotence (23).

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects (23)

- If adverse reactions occur, a doctor or a pharmacist should be consulted
- **Central nervous:** Headache, dizziness, confusion, anxiety, flushing, drowsiness, insomnia, weakness, involuntary movements, decreased sweating, increased/decreased body temperature, coma, seizures, death (plant ingestion).
- **Cardiovascular:** Hypotension, paradoxical bradycardia, angina, premature ventricular contractions, hypertension, tachycardia, ectopic ventricular beats.
- Blurred vision, photophobia, eye pain, pupil dilatation, nasal congestion.
- **Gastrointestinal:** Nausea, vomiting, anorexia, dry mouth, abdominal pain, constipation, abdominal distention, altered taste.
- **Genitourinary:** retention, hesitancy, impotence, dysuria.
- **Integumentary:** hypersensitivity reactions, rash, urticaria, contact dermatitis, dry skin, flushing.

14. Overdose (4, 25)

- The intake of very high dosages leads to central excitation (restlessness, compulsive speech, hallucination, delirium, manic episodes), followed by exhaustion and sleep. The four early warning symptoms of poisoning are skin reddening, dryness of the mouth, tachycardia and mydriasis. Accommodation disorders, heat build-up through decline in sweat secretion, miction disorders and severe constipation can occur as side effects, particularly with overdosages.
- *D. stramonium* (in an oral dose of 1gm powdered leaves) acts as a narcotic.
- Lethal dosages (for adults starting at 100 mg atropine, depending upon atropine content, 15 to 100 g of the leaf drug, 15 to 25 g of the seeds, considerably less for children) carry with them the danger of asphyxiation.
- Treatment for poisoning include stomach emptying, temperature-lowering measures with wet cloths (no antipyretics), oxygen respiration for respiratory distress, intubation, parenteral physostigmine salts as antidote, diazepam for spasms and chlorpromazine for severe excitation.

15. Relevant biological activities

Antimicrobial effect

- The antimicrobial activity of *D. stramonium* (leaf ethanolic extract) was assessed against pathogenic bacteria. The plant showed significant antibacterial activity against the tested pathogens (26-29).

- Aerial parts (mainly stem and bark) of *D. stramonium's* aqueous and ethanolic extract were investigated for their antimicrobial effect on *Eschericia coli, Salmonella typhi, Staphylococcus aureus, Klebsiella pneumonia, Shigella and Neisseria gonorrhea*. The stem bark extract exhibited different inhibitory activities on the tested microorganisms. Ethanol extract exhibited the highest inhibitory activity against *K. pneumonia* followed by *S. aureus. S. typhi*. The aqueous extract showed activity only on *S. aureus*, while *N. gonorrhea* was resistant to both extracts (30).

- *D. stramonium* phytochemicals were investigated for their *in-vitro* activity against bacterial pathogens by disk diffusion method. *D. stramonium* leaf extracts exhibited a considerable antibacterial activity even at low concentrations. Of various fractions obtained from leaf, methanol extracts showed maximum inhibitory effect (31).

- The antibacterial activity was detected by agar well diffusion method against *Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus.* The zones of inhibitions obtained were recorded and analyzed against standard control of Ampicillin. The methanolic extract showed higher antibacterial activity against *E. coli* and least antibacterial activity against *P. aeruginosa* (21).

- The plant extracts were tested on Gram negative bacteria *Escherichia coli* and on Gram positive bacteria *Staphylococcus aureus*. Both tested strains showed resistance but for *E. coli* a higher inhibition was observed at all samples containing *D. stramonium* extract (32).

- The antibacterial activity of aqueous extracts of different parts of *D. stramonium* (root, stem, leaf, seed and fruit coat) studied against five human pathogenic bacteria viz. *B. megaterium, B. cereus, E. coli, S. typhi and S. aureus*. The results indicated that aqueous extract of leaf were most effective against all the tested pathogens (33).

- The antimicrobial activities of *in-vitro* grown callus and *D. stramonium* methanolic extracts of root, stem, leaves, fruits, were studied against *E. coli, S. aureus and P. aeruginosa.* The methanolic leaf extract exhibited better antimicrobial activity against *S. aureus, E. coli, P. aeruginosa*. In the metabolite rich fraction (flavonoids, phytosterols and alkaloids), greatest bactericidal activity was exhibited by flavonoids against *P. aeruginosa* (34).

- The antibacterial activity of *D. stramonium* branches and leaves samples in three different solvents benzene, chloroform and ethanol was studied against *Enterobacter, Micrococcus luteus, Pseudomonas aeruginosa, E. coli, S. aureus and K. pneumonia*. All the solvent extracts showed significant antibacterial activity against tested pathogens. Comparative minimum inhibitory concentration of benzene, chloroform and ethanol extract determined that benzene extract was very effective against all bacterial strains (35).

- The methanolic extract of *D. stramonium* was screened for antimicrobial assay against different bacterial. Standard antibiotic (Azithromycin) and methanol were used as a positive and negative respectively. Leaf extract showed strong antimicrobial activity against bacterial species like *Bacillus thuringiensis, Pseudomonas aeruginosa, Agrobacterium tumefaciens and Klebsiella pneumoniae* (36).

-The fungicidal effects of the acetone extracts indicate the potential of *D. stramonium* seeds as natural source of antifungal agent. The MIC of *D. stramonium* extracts ranges from 1.25- 2.50mg/ml (37).

Antiasthmatic activity

- In 12 asthmatic patients with mild airway obstruction, the effect on specific airway resistance (sRaw) of inhaling the smoke of one *D. stramonium* cigarette was measured. In 11 patients sRaw decreased substantially after the cigarette, the mean maximal decrease being 40% at the 30th minute. Minor side effects were observed in six patients after the cigarette (38).

- The regular use of antiasthmatic cigarettes ever cannot be recommended for the following reasons: (1) the duration of action seems rather short. This could therefore lead to repeated inhalations and tachyphylaxis might occur. The risk of addiction from

overuse has also been suggested (2) the total composition of the smoke is not known. It may contain unwanted alkaloids, particles that may cause chronic mucosal inflammation, or even carcinogenic agents (38).

- The exposure of *D. stramonium* to the fetus when a mother uses it for asthma will cause a continuous release of acetylcholine, resulting in the desensitizing of nicotinic receptors, which could ultimately result in permanent damage to the fetus (39).

Anticholinergic activity

The alkaloids found in *D. stramonium*, are organic esters used clinically as anticholinergic agents. The anticholinergic syndrome results from the inhibition of central and peripheral muscarinic neurotransmission (40 - 43).

The antioxidant effect

- The antioxidant activity of methanolic extract of *D. stramonium* seeds was studied. The methanolic extract reduced the concentration of DPPH free radical with an efficacy near to that of standard antioxidant gallic acid, but less than butylated hydroxytoluene (BHT) (21).

- The methanolic extract of *D. stramonium* seeds is a potential source of natural antioxidants and significantly inhibit free radicals dose-dependently. The difference in the antioxidant activity may be ascribed to their different group of phenolic and flavonoid compounds. The extract showed higher phenolic content contributes to the higher antioxidant activity. Based on the results obtained, it can be concluded that the plant contains essential phytochemical constituents and possess antioxidant property (44).

Anticancer activities

- The evaluation of the cytotoxic effect of aqueous extract of *D. stramonium* leaves extract on different human cancer cell lines *in-vitro*. Breast (MDA-MB231), head, neck (FaDu), and lung (A549) cancer cell lines were treated with 1 mg/ mL of *D. stramonium* aqueous extract for 24 and 48 hours. The results may suggest therapeutic potential of *D. stramonium* aqueous leaf extract for the treatment of different types of cancer (45).

- *In-vitro* cytotoxic activity for breast cancer cell line (MCF7) was studied by MTT reagent assay method using the methanolic extract of *D. stramonium* seeds. The study do confirm that extracts exhibit cytotoxic effect on MCF-7 (44).

- Experiment on the cytotoxicity of methanol extracts of *D. stramonium* seeds on human breast adenocarcinoma cells (MCF-7) showed increasing cytotoxicity with increasing concentrations of extract and the viable cells detected by MTT assay (46).

Analgesic activity

The analgesic effect of alcoholic extract of *D. stramonium* seeds extract was evaluated in acute and chronic pain using hot plate and formalin tests. The extracts when administrated intraperitoneally administrated to the animals, the extract alleviated the pain dose dependently (ED_{50} values of 25 and 50mg/ kg in hot plate and formalin tests, respectively) (47).

Organophosphate poisoning

- *D. stramonium* contains atropine and other anticholinergic compounds, it is a useful remedy for the central cholinergic symptoms of organophosphate (OP) poisoning. The seeds were heated in water to make 2mg/ml atropine solution and administrated to male rats as a single intraperitoneal injection 5min before the subcutaneous injection of 25mg/kg of Dichlorvos . Pretreatment with *D. stramonium* seed extract significantly increased survival in a rat model of severe OP (48).

Antiepileptic effects

- According to Peredery and Persinger (2004), rats were continuously administrated once of three herbal treatments *S. lateriflora, G. sempervirens* and *D. stramonium* through water supply for 30 days, one week after the induction of status epilepticus by a single injection of lithium (3mEq/kg) and pilocarpine (30g/kg). The number of spontaneous seizures per day during a 15min observation interval was recorded for each rat during the treatment period and during an additional 30 days when only tap water was given. Rats that received a weak solution of the three herbal fluid extracts displayed no seizures during treatment. However, when this treatment was removed, the rats displayed numbers of spontaneous seizures comparable to the controls (49).

Anti-inflammatory activity

The ethanolic extract of *D. stramonium* leaves showed significant anti-inflammatory activity comparable to the standard drug Diclofenac sodium against carrageenan induced paw edema in rats. 39.43% inhibition of the edema was observed after 3 hours of oral administration of 200mg/kg extracts. Maximum activity was observed when the extract was administered in doses of 3-hours intervals (50).

Wound healing activity

The hydro-alcoholic extract of *D. stramonium* leaves was investigated for wound healing potential in rats. The leaves were dried, crushed and the hydro-alcoholic extract was obtained and turned to 10% ointment form. In the course of this study, 18 male wistar albino rats weighing approximately 150- 180g were used. Group 1 as negative control group, Group 2 as reference group were treated topically with Povidone-Iodine ointment USP, Group 3 as test control were treated with 10% *D. stramonium* ointment. Wound healing was monitored on days 4, 8, 12, 16 and

histopathological evaluation was carried out on the samples. Leaf extract of *D. stramonium* promotes wound healing via bactericidal activity (51).

Vibriocidal activity

Water, ethanol and acetone extracts of *D. stramonium* leaves were tested for their vibriocidal activity. A simple *in-vitro* screening assay was employed for the standard strain of *Vibrio cholerae*, 12 isolates of *Vibrio cholerae* non-O1, and *Vibrio parahaemolyticus*. The extracts were investigated by using the disk diffusion method. The results indicated that *D. stramonium* served as broad-spectrum vibriocidal agents (52).

Toxicity studies

- Due to *D. stramonium* anticholinergic activity, it has been reported as a drug of abuse and has been involved in the accidental poisoning of humans and animals. Symptoms of acute *D. stramonium* poisoning included dryness of the mouth and extreme thirst, dryness of the skin, pupil dilation and impaired vision, urinary retention, rapid heartbeat, confusion, restlessness, hallucinations, and loss of consciousness (53 - 55).

- Two doses of 50 and 200 mg/kg of the leaves ethanolic extract were administered to the rats for five weeks. Parameters studied were the indices of liver and kidney function and some biochemical and haematological parameters. Feed intake, final body weight, serum AST, ALT, billurubin, total protein, urea and the electrolyte studied were not affected by the extract administration. Serum creatinine levels were, however, significantly raised in the rats administered with the ethanolic extract at the dose of 200 mg/kg body weight. The biochemical and haematological parameters were also affected (56).

- Ingestion of *D. stramonium* seeds at concentrations of 0.5% or more in the diet have reported to produce adverse physiological changes in rats (57).

- The effects of acute, subacute and chronic administration of alkaloids atropine and scopolamine, the main active principle of *D. stromonium*, with toxic properties, were studied in male Albino Wistar rats. After acute *i.p.* administration of dose 100mg/kg of total alkaloids of the seeds of *D. stramonium*, there were no remarkable changes in general appearance and no deaths occurred in any experimental group. Twenty-four hours after administration of total alkaloids of seeds, a significant reduction in indices of liver, spleen, brain and kidney function and some biochemical and haematological parameters were observed. The red blood cells, hematocrit, hemoglobin and white blood cells were significantly higher in the treated groups than the control group. Subacute study for four weeks showed no resulting mortality or signs of toxicity. In chronic study, the synthetic alkaloids administered *i.p.* at daily doses of 4.2 mg/kg of atropine and 1.6 mg/kg of scopolamine, did not produce death. However, diarrhea and hypoactivity were observed. The relative weight of liver was significantly less than that of the control group (58).

Administration of scopolamine in drinking water to pregnant rabbits on days 10-14 of gestation led to fetal deformities of eye. These malformations were observed in all living fetuses present in six different animals (59).

-Various cases of toxic delirium and psychiatric symptoms have been reported after ingestion of *D. stramonium*. Careful consideration of the toxicity of the plant is required before its use. Its ingestion induces characteristic symptoms such as dry mouth, intense thirst, blurred vision, mydriasis and increased heart rate followed by hallucinations, delirium and loss of motor coordination leading to comma and ultimately to death by respiratory failure (55, 60 - 63).

16. Additional information

- Store *D. stramonium* in airtight containers. Protect from moisture and light (22).
- The atropine component is well absorbed, metabolized by the liver, and excreted by the kidneys (23).
- *D. stramonium* has also been smoked in cigarettes or burnt in powder and the fumes inhaled but the irritation produced by the fumes may aggravate bronchitis (22).
- Toxicity varies from season to season and depends on the manner in which the plant is ingested *i.e.* chewed, drank as an extract or smoked (64).

17. Date of compilation/last revision

30/8/2023.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Hassan, N. M. and Abdelmohsen, M. M. (2018). *Datura stramonium* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, 7, 17-29. Academy of Scientific Research and Technology, Cairo, Egypt.
4	PDR for Herbal Medicines (1998). Medical Economic Co. Montvale, New Jersey, 639. ISBN 1563633612, 9781563633614.
5	Egyptian Pharmacopoeia (1984). 3rd edition. General Organization for Government Printing. Cairo.
6	Egyptian Pharmacopoeia (2005). 4th edition. General Organization for Government Printing. Cairo.
7	Hammouda, F. M., Ismail, S. I., Abdel-Azim, N. S. and Shams, K. A. (2005). A Guide to Medicinal Plants in North Africa (Batanouny K. H., editor). IUCN Centre for Mediterranean Cooperation. Malaga.
8	Khare, C.P. (2007). Indian Medicinal Plants. Delhi: Rajkamal Electric Press, 203.
9	Aboluwodi, A. S., Avoseh, O. N., Lawal, O. A., Ogunwande, I. A. and Giwa, A. A. (2017). Chemical constituents and anti-inflammatory activity of essential oils of *Datura stramonium* L. *Journal of Medicinal Plants Studies*, **5**(1), 21-25.
10	Miraldi, E., Masti, A., Ferri, S. and BarniComparini, I. (2001). Distribution of hyoscyamine and scopolamine in *Datura stramonium*. *Fitoterapia*, **72**(6), 644-648.
11	Bazaoui, A., Bellimam, M. and Soulaymani, A. (2011). Nine new tropane alkaloids from *Datura stramonium* L. identified by GC/MS. *Fitoterapia*, **82**, 193-197.
12	Ademiluyi, A., Ogunsuyi, O. and Oboh, G. (2016). Alkaloid extracts from Jimson weed (*Datura stramonium* L.) modulate purinergic enzymes in rat brain. *NeuroToxicology*, **56**, 107-117.
13	Al-Snafi, A. E. (2017). Medical importance of *Datura fastuosa* (syn: *Datura metel*) and *Datura stramonium* -A review. *IOSR Journal of Pharmacy*, **7**(2), 43-58.
14	Berkov, S., Zayed, R. and Doncheva, T. (2006). Alkaloid patterns in some varieties of *Datura stramonium. Fitoterapia*, **77**(3), 179-182.
15	Mukhtar, Y., Tukur, S. and Bashir, R. A. (2019). An Overview on *Datura stramonium* L. (Jimson weed): A notable psychoactive drug plant. *American Journal of Natural Sciences*, **2**(1), 1-9.
16	Tursunova, R. N., Maslennikova, V. A. and Abubakirov, N. K. (1978). Withanolids of *Datura stramonium*. II. Withastramonolide. *Khim. Prir. Soedin*., **1**, 91-95.
17	Manickam, M., Awasthi, S. B., Sinha Bagchi, A., Sinha, S. C. and Ray, A. B. (1996). Withanolides from *Datura tatula*. *Phytochemistry*, **41**(3), 981-983.
18	Fang, S. T., Liu, X., Kong, N. N., Liu, S. J. and Xia, C. H. (2013). Two new withanolides from the halophyte *Datura stramonium* L. *Nat. Prod. Res*., **27**(21), 1965-1970.

19	Singh, L.R. and Singh, O.M. (2013). *Datura stramonium*: An overview of its phytochemistry and pharmacognosy. *Research J. Pharmacognosy and Phytochemistry*, **5**(3), 143-148.
20	Li, J., Lin, B., Wang, G., Gao, H. and Qin, M. (2012). Chemical constituents of *Datura stramonium* seeds. *Zhongguo Zhong Yao Za Zhi*, **37**(3), 319-322.
21	Waza, S. A., Anthony, P. and Dar, S. (2015). Phytochemical analysis, antioxidant and antimicrobial activities of methanolic extract of *Datura stramonium* seeds. *International Journal of Pharmaceutical Sciences and Research*, **6**(7), 3021-3026.
22	Martindale: The Complete Drug Reference (2007). Pharmaceutical Press. Electronic version, London.
23	Skidmore-Roth (2010). Mosby's Handbook of Herbs and Natural Supplements. St. Louis: Mosby, 4th ed. ISBN: 978-0-323-05741-7.
24	https://www.webmd.com/vitamins/ai/ingredientmono-921/jimson-weed
25	https://www.rxlist.com/jimson_weed/supplements.htm
26	Reddy, B. U. (2009). Antimicrobial activity of *Datura stramonium* L. and *Tylophora indica* (Burm.f.) Merr. *Pharmacology online*, **1**, 1293-1300.
27	Reddy, B. U. (2010). Enumeration of antibacterial activity of few medicinal plants by bioassay method. *E- Journal of Chemistry*, **7**(4), 1449-1453.
28	Banso, A. and Adeyemo, S. (2006). Phytochemical screening and antimicrobial assessment of *Abutilon mauritianum*, *Bacopa monnifera* and *Datura stramonium*. *Int. J. Exp. Boil.*, **18**(1), 39-44.
29	Gachande, B. D. and Khillare, E. M. (2013). *In-vitro* evaluation of Datura species for potential antimicrobial activity. *Biosci. Discov.,* **4**(1), 78-81.
30	Shagal, M. H., Modibbo, U. U. and Liman, A. B. (2012). Pharmacological justification for the ethnomedical use of *Datura stramonium* stem-bark extract in treatment of diseases caused by some pathogenic bacteria. *Int. Res. Pharm. Pharmacol.*, **2**(1), 16-19.
31	Sreenivasa, S., Vinay, K. and Mohan, N.R. (2012). Phytochemical analysis, antibacterial and antioxidant activity of leaf extract of *Datura stramonium*. *International Journal of Science Research*, **1**(2), 83-86.
32	Carpa, R., Dumitru, D. V., Burtescu, R. F., Maior, M. C., Dobrotă, C. and Neli-Kinga, O. (2017). Bio-chemical analysis of *Datura stramonium* extract *studia universitatis babeș-bolyai biologia, LXII*, **2**, 5-19.
33	Jamdhade, M. S., Survase S. A. 2, Kare, M. A. and Bhuktar, A. S. (2010). Antibacterial activity of genus *Datura* L. in Marathwada, Maharashtra. *J. of Phytol*, **2**(12), 42-45.
34	Sharma, R., Sharma, P. and Yadav, A. (2013). Antimicrobial screening of sequential extracts of *Datura stramonium* L. *Int. J. Pharm. Pharm. Sci.*, **5**(2), 401-404.
35	Gul, H., Qaisrani, R., Khan, M., Hassan, S. and Younis, N. (2012). Antibacterial and antifungal activity of different extracts of *Datura stramonium* (branches and leaves sample). *E3 J. Biotechnol. Pharm. Res.*, **3**(9), 141-148.
36	Mdee, L. K., Masoko, P. and Eloff, J. N. (2009). The activity of extracts of seven common invasive plant species on fungal phytopathogens. *South African Journal of Botany*, **75**(2), 375-379.

37	Deshmukh, A. S., Shelke, P. D., Palekar, K. S., Pawar, S. D. and Shinde, H. S. (2015). Antimicrobial investigation of *Datura stramonium* leaf extract against different microorganisms. *Journal of Environmental Science, Toxicology and Food Technolog,* **9**(9), 17-19.
38	Charpin, D., Orehek, J. and Velardocchio, J. M. (1979). Bronchodilator effects of antiasthmatic cigarette smoke (*Datura stramonium*). *Thorax*, **34**(2), 259-261.
39	Pretorius, E. and Marx, J. (2006). *Datura stramonium* in asthma treatment and possible effects on prenatal development. *Environ.Toxicol. Pharmacol*., **21**(3), 331-337.
40	Taha, S. A. and Mahdi, A.W. (1984). *Datura* intoxication in Riyadh. *Trans. R. Soc. Trop. Med. Hgy*., **78**, 134–135.
41	Diker, D., Markovitz, D., Rothman, M. and Sendovski, U. (2007). Coma as a presenting sign of *Datura stramonium* seed tea poisoning. *Eur. J. Int. Med*., **18**(4), 336–338.
42	Boumba, A., Mitselou, A. and Vougiouklakis, T. (2005). Fatal poisoning from ingestion of *Datura stramonium* seeds. *Vet. Human Toxicol*., **46**, 81–82.
43	Alberto, K., Claudia, S., Ludmilla, K. and Arnon, B. (2001). Toxic delirium due to *Datura stramonium. Israel Med. Asso. J.,* **3**, 538-539.
44	Iqbal, S., Sivaraj, C. and Gunasekaran, K. (2017). Antioxidant and anticancer activities of methanol extract of seeds of *Datura stramonium*. *Free Radicals and Antioxidants*, **7**(2), 184-189.
45	Ahmad, I. M., Abdalla, M. Y., Mustafa, N. H., Qnais, E. Y. and Abdulla, F. A. (2009). *Datura* aqueous leaf extract enhances cytotoxicity via metabolic oxidative stress on different human cancer cells, *Jordan Journal of Biological Sciences*, **2**(1), 9-14.
46	Ferrari, M., Fornasiero, M. C. and Isetta, A. M. (1990). MTT colorimetric assay for testing macrophage cytotoxic activity *in-vitro*. *J. Immunological Methods*, **131**(2), 165-170.
47	Khalili, N. M. and Atyabi, S. M. (2004). Evaluation of analgesic of *Datura stramonium* seed extract in hot plate and formalin tested on male rats. *Iranian Journal of Medicinal and Aromatic Plants,* **20**(3), 309-322.
48	Theodore, C. B., Jasan, C., Dallas, B. and Melanie, O. (2004). Jimson weed extract as a protective agent in severe organophosphate toxicity. *Acad. Emerg. Med*., **11**(4), 335–338.
49	Peredery, O. and Persinger, M. A. (2004). Herbal treatment following post seizure induction in rat by lithium pilocarpine: *Scutellaria lateriflora* (Skullcap), *Gelsemium sempervirens* (Gelsemium) and *Datura stramonium* (Jimson Weed) may prevent development of spontaneous seizures. *Phytother. Res*., **18**(9), 700-705.
50	Gupta, S., Raghuvanshi, M. and Jain, D. (2010). Comparative studies on anti-inflammatory activity of *Coriandrum Sativum, Datura stramonium and Azadirachta Indica. Asian J. Exp. Biol. Sci*., **1**(1), 151–154.
51	Shekhar, P., Joshi, A., Malviya, S. and Kharia, A. (2017). Wound healing activity of the hydro-alcoholic extract of *Datura stramonium* leaves in wistar albino rats. *Journal of Drug Delivery & Therapeutics*, **7**(7), 214-215.
52	Sharma, A., Patel, V. K. and Chaturvedi, A. N. (2009). Vibriocidal activity of certain medicinal plants used in Indian folklore medicine by tribals of Mahakoshal region of central India. *Indian J. Pharmacol*., **41**(3), 129-133.

53	Sever, M. and Cekin, M. (2007). Anticholinergic intoxication due to *Datura stramonium*: three pediatric cases. *ARALIK*, **5**, 28-30.
54	Adesanya, O., Adewale, B., Aremu, P., Akintayo, A. and Alonge, A. (2020). *Datura stramonium* consumption causing severe anticholinergic toxicity in an adolescent male: a case report and review of the literature*. J. Pharmacol Clin. Toxicol.*, **8**(1), 1140.
55	Oberndorferk, S., Grisold, W., Hinterholzer, G. and Rosner, M. (2002). Coma with focal neurological signs caused by *Datura stramonium* intoxication in a young man. *J. Neurol. Neurosurg Psychiatr.,* **73**(4), 458-459.
56	Giadado, A., Zainab, A., Hadiza, M. U., Serah, D. P., Anas, H. Y. and Milala, M. A. (2015). Toxicity studies of ethanol extract of the leaves of *Datura stramonium* in rats. *African J. Biotech.*, **6**(8), 1012–1015.
57	Dugan, G. M., Gumbmann, M. R. and Friedman, M. (1989). Toxicological evaluation of Jimson weed (*Datura stramonium*) seed. *Food Chem Toxicol*., **27**(8), 501-510.
58	Bouzidi, A., Mahdeb, N. and Kara, N. (2011). Toxicity studies of alkaloids of seeds of *Datura stramonium* and synthesis alkaloids in male rats. *J. Med. Plants Res*., **5**(15), 3421-3431.
59	Sharma, P. C., Yelne, M. B. and Dennis, T. J. (2001). Database on Medicinal Plants Used in Ayurveda. New Delhi: CCRAS, Ministry of AYUSH.
60	Chang, S. S., Wu, M. and Deng, J. F. (1999). Poisoning by *Datura* leaves used as edible wild vegetables. *Vet. Hum. Toxicol*., **41**, 242–245.
61	Spina, S. P. and Taddei, A. (2007). Teenagers with Jimson weed (*Datura stramonium*) poisoning. *CJEM*., **9**(6), 467-468.
62	Kurzbaum, A., Simsolo, C., Kvasha, L. and Blum, A. (2001). Toxic delirium due to *Datura stramonium. Isr. Med. Assoc. J*., **3**(7), 538-539.
63	Karadaş, S., Selvi, Y., Şahin, M., Selvi, F., Öncü, R. and Özgökçe, F. (2011). *Datura stramonium* intoxication: report of a case with psychiatric symptoms. Düşünen Adam: *J. Psychiatry Neuro Sci.*, **24**(2), 152-154.
64	Trancă, S., D., Szabo, R. and Cociş, M. (2017). Acute poisoning due to ingestion of *Datura stramonium*- a case report. *Rom. J. Anaesth Intensive Care*, **24**, 65-68.

Egyptian Herbal Monograph

Pharmacopoeial wild medicinal plants

***Plantago afra* L.** قاطونة

1. Names & Synonyms (1-3)

***Plantago afra* L.**

Family: Plantaginaceae.

Syns.: *Plantago psyllium* L.

Plantago parviflora Desf.

Arabic: Qatoona قاطونة, Hab El-baragheet حب البراغيث

Seeds are known as Bizr qatoona بذر قاطونة.

English: Flea-wort.

2. Geographical distribution (1-3)

Desert east of the Nile including that of Sinai as well as the Red Sea and Gebel Elba.

3. Parts used for medicinal purposes (1-3)

Ripe seeds.

4. Major chemical constituents

- **Polysaccharides:** Mucilage (4) mainly composed of arabinoxylan (hemicellulose) (5).
- **Phenylpropanoid glycosides**:

  Acetoside (Verbascoside) and isoacetoside (isoverbascoside) (seeds) (6).
- **Fatty acids:**

  Tritriacontanoic acid (synonyms: psyllic acid, ceromelissic acid) (husk) (7, 8).
- **Iridoids:** aucubin (seeds) (9).

5. Medicinal uses

Well-established

A. Emollient, demulcent (10) and in chronic constipation (10, 11).

B. Bulk-forming laxative to provide gentle relief of constipation (for the treatment of habitual constipation) (12).

C. In conditions where easy defecation with soft stool is desirable, *e.g.* in cases of painful defecation after rectal or anal surgery, fissures and haemorrhoids, following rectal examinations and pregnancy (9, 12, 13, 15).

D. In conditions which need an increased daily intake of fiber, *e.g.* irritable bowel syndrome (12, 16)**.**

Traditional use (2, 17)

E. Emollient.

F. Bulk forming laxative for chronic constipation.

***P. afra* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (2)

1. Seeds.
2. Decoction of seeds.

7. Posology and method of administration correlated to medicinal use

Adults and children over 12 years of age: as laxative, 4-16g orally (11), 1-3 times daily depending of the individual response (13).

Children 6-12 years: as laxative, half of the adult dose (9).

Duration of use

Continued use for 2 to 3 days is needed for maximum laxative benefit (13).

Method of administration: Oral use.

A sufficient amount of liquid (water, milk, fruit juice or similar aqueous liquid) should always be taken *e.g*. 30 ml of water per 1 g of herbal substance (12). The medicinal product can be mixed with the liquid and then swallowed as quickly as possible after stirring briskly, and then adequate fluid intake has to be maintained (9). The effect starts 12 - 24 hours later (12).

8. Contraindications

- Hypersensitivity to active substances or to other plants of the same family.
- Patients who have difficulty in swallowing or any throat problems (9, 11, 14, 18).
- Patients suffering from abnormal constrictions (12, 19) or inflammatory illness in the gastro-intestinal tract (19).
- In case of intestinal obstruction, potential or existing intestinal blockage (ileus) (12, 13, 19, 20).
- Patients with diseases of the esophagus and cardia (12).
- Paralysis of the intestine or megacolon (12).
- Patients experiencing a sudden change in bowel habits that has persisted for more than 2 weeks (9, 12).
- Patients with fecal impaction (12).
- Patients with undiagnosed rectal bleeding, or failure to defaecate following the use of another laxative product (9, 12, 13, 21).
- Diabetic patients who have difficulty managing their blood sugar level (9, 12, 13, 14, 17, 18, 19, 21).

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- It should always be taken with sufficient fluid *e.g*. 30 ml of water per 1 g of herbal substance (12), as there is a risk of intestinal or esophageal obstruction and fecal impaction, especially if it is swallowed dry (12, 13, 19, 22).
- When taken with inadequate fluid amounts, bulk forming agents can cause obstruction of the throat and esophagus with choking and intestinal obstruction. Symptoms can be chest pain, vomiting, or difficulty in swallowing or breathing (12).
- It should not be taken immediately before going to bed (22).
- In patients who are confined to bed, do little physical exercise, debilitated patients or elderly patients, a medical examination may be necessary prior to treatment with the drug (12, 13).
- It should be taken at least half an hour after other medications to prevent delayed absorption of the latter (13).
- If taken with medicinal products known to inhibit peristaltic movement (*e.g*. opioids) a medical supervision is necessary in order to decrease the risk of gastrointestinal obstruction (ileus) (12).
- Treatment should be stopped and medical advice sought, in case of bleeding , or if no response occurs after ingesting the drug, or in cases of any irregularity of feces,

(12, 13, 23); symptoms such as abdominal pain, nausea and vomiting can be signs of potential or existing intestinal blockage (ileus) (12).

- It is not recommended to be used for children under 6 years of age due to insufficient data on efficacy (12).
- Laxative bulk producers should be used before using other purgatives if change of nutrition is not successful (12).
- In patients with diabetes taking oral agents or insulin to achieve glycemic control, blood glucose levels should be monitored more closely when initiating or adjusting doses of the latter can lower blood glucose level and impair carbohydrate absorption (24).
- In the case of insulin dependent diabetics, if the product is taken together with meals, it may be necessary to reduce the insulin dose (25, 26).
- Bulking agents have been reported to diminish the absorption of concomitantly some administered medicines (13).
- Psyllium seed should be used concomitantly with thyroid hormones only under medical supervision. The dose of the thyroid hormones may have to be adjusted (12).

Warning on hypersensitive reactions concerning powder formulations:

- Allergic sensitization may occur due to inhalation of the airborne dust upon using the powder of Psyllium seeds or in individuals with continued occupational contact to powder (*i.e.* healthcare workers, caregivers). This sensitization usually leads to hypersensitivity reactions which could be serious (12). To minimize the potential allergic reaction, users should spoon the product from the container directly into a drinking glass and then add liquid (23) and the health professionals who frequently dispense powdered should avoid inhaling airborne dust while handling these products (13). It is recommended to assess clinically the possible sensitization of individuals at risk. In case of proven sensitization leading to hypersensitivity reactions, exposure to the product should be stopped immediately and avoided in the future (12).

10. Interactions with other medicinal products and other forms of interaction

- **Oral medicinal products** (9, 12, 13, 20, 24, 25, 28-30): Enteral absorption of concomitantly administered medicines may be delayed such as:
    - Minerals (*e.g.* calcium, magnesium, copper and zinc)
    - Vitamins (B 12)
    - Cardiac agents (beta-blockers, calcium channel blockers and cardiac glycosides)

- Coumarin derivatives
- Lithium salts
- Carbamazepine

- **Antidiabetic agents:** If the product is taken together with meals in the case of insulin dependent diabetics it may be necessary to reduce the insulin dose (9, 12, 13, 20, 25, 26).
- **Thyroid hormones:** It should be used concomitantly with thyroid hormones only under medical supervision because the dose of the thyroid hormones may have to be adjusted (9, 12).
- **Peristaltic movement inhibitor agents:** In order to decrease the risk of gastrointestinal obstruction (ileus), it should only be used under medical supervision together with medicinal products known to inhibit the peristaltic movement (*e.g.* Morphinomimetics and Loperamide) (9, 12).
- **Sodium picosulfate:** Mild interactions (31).
- **Food:** It may decrease nutrient absorption (20).
- **Lab Test:** Psyllium may decrease blood glucose testing (theoretical), may decrease total cholesterol, LDL, HDL ratio test results and may cause a false increase in serum digoxin (20).

11. Fertility, pregnancy and lactation

- It can be used during pregnancy and lactation (9, 32). A risk is not to be expected since the constituents of Psyllium seed are not absorbed and have no systemic effects (9).
- No fertility data available (13).

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Hypersensitivity reactions such as rhinitis, conjunctivitis, bronchospasm and in some cases, anaphylaxis; cutaneous symptoms such as exanthema and/or pruritus have also been reported (9, 12- 14, 18, 19, 33-35).
- Flatulence may occur with the use of the product (9, 12, 13, 18, 20, 26). These side-effects may be reduced by gradually increasing fiber intake, starting at one dose per day and gradually increasing to three doses per day and may be reduced by

decreasing the amount of Psyllium taken for a few days (13, 26) with generally disappears in the course of the treatment (9, 12).

- Abdominal distension and risk of intestinal or esophageal obstruction and fecal impaction may occur, particularly if swallowed with insufficient fluid. The frequency is not known (9, 12, 20).
- Nausea, vomiting, anorexia, diarrhea (20).

14. Overdose

Overdose may cause abdominal discomfort and flatulence, or even intestinal obstruction. Adequate fluid intake should be maintained, and management should be symptomatic (9, 12).

15. Relevant biological activities

Laxative effect

-A preparation made from "*Plantago psyllium*" was administered (3 times 3.4 g daily) to 63 patients suffering from chronic functional constipation for a period of 20 days. The tolerance of the preparation was satisfactory in 55 patients (87%), including 49 (89%), who reported a favorable effect, i.e. problem-free defecation and regression or disappearance of meteorism. A statistically significant decline of serum cholesterol occurred. In 14 patients (25%) a weight loss of more than 1 kg was observed. The results concluded that the preparation can be considered suitable for the treatment and probably also the prevention of chronic functional constipation and as an adjuvant in the treatment of hyperlipoproteinaemia type II, in particular when associated with obesity (36).

-The therapeutic value of "Psyllium" for the treatment of constipation among others was discussed: 'There is a scientific basis for Psyllium working as a mild laxative. This evidence, combined with the available research in humans, suggests that Psyllium decreases the time necessary to pass bowel movements, increases the number of bowel movements per day and increases the amount of stool passes (37).

-Psyllium has been shown to have the paradoxical property of both improving constipation by increasing stool weight (38) and ameliorating chronic diarrhea (39).

-The hypothesis that a gel-forming fraction of Psyllium escapes microbial fermentation and is responsible for the characteristics that enhance laxation were tested. Fifteen healthy adults consumed controlled diets for two 7-d periods, one of which included 8.8 g dietary fiber provided by 15 g/d of a Psyllium seed husk preparation. All stools were collected and evaluated and diet was monitored throughout. Psyllium significantly increased the apparent viscosity of an aqueous stool extract, stool moisture, and wet and dry stool weights. A very viscous fraction, not present in low-

fiber stool and containing predominantly 2 sugars: xylose (64%) and arabinose (27%), the same two sugars that account for the majority (79%) of the carbohydrate in Psyllium. The results concluded that in contrast with other viscous fibers that are fermented completely in the colon, a component of Psyllium is not fermented. This gel provided lubrication that facilitated propulsion of colon contents and produced a stool that was bulkier and moister than were stools resulting with use of comparable amounts of other bowel-regulating fiber sources (40).

-Psyllium has been reported to increase stool frequency, weight and decrease stool consistency in constipated patients. These effects are not associated with significant changes in colorectal motility. The clinical parameters were not significantly affected by treatment with Psyllium although there was a significant decrease in transit time (41-45).

16. Additional information

It has lipid- and glucose-lowering effects (46-50).

17. Date of compilation/last revision

15/9/2023.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Hassan, N. M and Abdallah, W. E. (2020). *Plantago afra* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **9**, 112-121. Academy of Scientific Research and Technology, Cairo, Egypt.
4	https://arzneipflanzenlexikon.info/en/medicinal-plants/psyllium-plantain.php.
5	Kumar, D., Pandey, J., Kumar, P. and Raj, V. (2017). *Psyllium* mucilage and its use in pharmaceutical field: An overview. *Curr. Synthetic Sys. Biol.,* **5**, 134.
6	Li, L., Rong, T., Zhiqiang, L., Shuying, L., Raymond, Y., Christopher, J. Y., Honghui, Z., Zeyuan, D., Mingyong, X. and Zhihong, F. (2005). Isolation and purification of acteoside and isoacteoside from *Plantago psyllium* L. by high-speed counter-current chromatography. *Journal of Chromatography A*, **1063**, 161–169.
7	https://pubchem.ncbi.nlm.nih.gov/compound/Tritriacontanoic-acid.
8	Kawashty, S. A., Gamal-El-Din, E., Abdalla, M. F. and Saleh, N. A. M. (1994). Flavonoids of *Plantago* species in Egypt. *Biochemical Systematics and Ecology*, **7**(22), 729-733.
9	ESCOP Monographs (2017). Psyllii Semen - *Psyllium* Seed. European Scientific Cooperative on Phytotherapy. Simon Mills and Roberta Hutchins, editors. Thieme, Stuttgart. Online series, IBN 978-1-901964-48-6.
10	Egyptian Pharmacopoeia (2005). 4th edition. General Organization for Government Printing. Cairo.
11	Egyptian Pharmacopoeia (1984). 3rd edition. General Organization for Government Printing. Cairo.
12	Community Herbal Monograph on *Plantago afra* L. et *Plantago indica* L., semen (2013). EMA/HMPC/599747/2012. Committee on Herbal Medicinal Products (HMPC).
13	WHO Monographs on Selected Medicinal Plants (1999). Monographs on Selected Medicinal Plants, **1**, 202-212.
14	Blumenthal, M., Goldberg, A. and Brinkmann, J. (2000). Herbal Medicine: Expanded Commission E Monographs. Psyllium Seed, Black. Boston (MA): Integrative Medicine Communications.
15	Food and Drug Administration (2007). Rules and Regulations Federal Register, **60**(27), 14669-14674.
16	Ford, A. C., Moayyedi, P., Chey, W. D., Harris, L. A., Lacy, B. E., Saito, Y. A. and Quigley, E. M. M. (2018). ACG Task force on the management of functional bowel disorders. American College of Gastroenterology monograph on the management of irritable bowel syndrome and chronic idiopathic constipation. *Am. J. Gastroenterol.,* **118** (suppl 2): 1-18. doi: 10.1038/s41395-018-0084-x.
17	Conservation and sustainable use of medicinal plants in Egypt, National Surveys (2016). UNDP, GEF, ASRT and NRC, Volumes **1-5**.

18	Bradley, P. R. (1992). British Herbal Compendium: A Handbook of Scientific Information on Widely Used Plant Drugs, volume **1**. Bournemouth (UK): British Herbal Medicine Association.
19	PDR for Herbal Medicines (1998). Medical Economic Co. Montvale, New Jersey, 639. ISBN 1563633612, 9781563633614.
20	Skidmore-Roth (2010). Mosby's Handbook of Herbs and Natural Supplements. St. Louis: Mosby, 4th ed. ISBN: 978-0-323-05741-7.
21	Bradley, P.R., ed. (1983). British herbal compendium, volume **1**. Bournemouth, British Herbal Medicine Association, 199–203.
22	Martindale: The Complete Drug Reference (2007). Pharmaceutical Press. Electronic version, London.
23	Physicians' Desk Reference. (1991). 45th ed. Montvale, NJ, Medical Economics Company، 1740–1741.
24	https://www.drugs.com/npp/capers.html.
25	Cummings, J. H. (1978). Nutritional implications of dietary fiber. *Am. J. Clin. Nutr*., **31**, S21-9.
26	Kay, R. M. and Strasberg, S. M. (1978). Origin, chemistry, physiological effects and clinical importance of dietary fiber. *Clin. Invest. Med*., **1**, 9-24.
27	Bräutigam, M. (2007). In: Blaschek W., Ebel, S., Hackenthal, E., Holzgrabe, U., Keller, K., Reichling, J. and Schulz, V., editors. Plantago. In: Hagers Enzyklopadie der Arzneistoffe und Drogen, Par-Pol. Stuttgart: Springer-Verlag, 6th ed., **12**, 936-959.
28	USP Dispensing Information, (1994). 14th ed. Laxatives (local). In: (I): Drug information for the health care professional. Rockville M. D.: The United States Pharmacopoeial Convention, 1703-1709.
29	Brunton, L. L. (1996). Agents affecting gastrointestinal water flux and mortility, Emesis and antiemetics; bile acids and pancreatic enzymes. In: Hardman J. G., Limbird, L. E., Molinoff, P. B., Ruddon, R. W. and Gilman, A. G., editors. Goodman & Gilman's. The Pharmacological Basis of Therapeutics, 9th ed. New York: McGraw-Hill, 917-936.
30	Drews, I. M., Kies, C. and Fox, H. M. (1979). Effect of dietary fiber on copper, zinc and magnesium utilization by adolescent boys. *Am. J. Clin. Nutr*., **32**, 1893-1897.
31	https://www.rxlist.com/consumer_psyllium_metamucil/drugs-condition.htm
32	Lewis, J. H. and Weingold, A. A. B. (1985). The use of gastrointestinal drugs during pregnancy and lactation. *Am. J. Gastroenterol*, **80**, 912-923.
33	Hulbert, D. C., Thorpe, P. J., Winning, A. J. and Beckett, M. W. (1995). Fatal bronchospasm after oral ingestion of ispaghula. *Postgraduate Medical Journal,* **71**, 305–306.
34	Freeman, G. L. (1994). *Psyllium* hypersensitivity. *Annals of allergy*, **73**, 490–492.
35	Knutson, T. W., Bengtsson, U., Dannaeus, A., Ahlstedt, S., Stålenheim, G., Hällgren, R. and Knutson, L. (1993). Intestinal reactivity in allergic and nonallergic patients; an approach to determine the complexity of the mucosal reaction. *Journal of Allergy and Clinical Immunology*, **91**, 553–559.

36	Weis, M. (1996). *Plantago psyllium* - přírodní rostlinné projímadlo a vliv na hladiny cholesterolu a triacylglycerolu. [*Plantago psyllium* – natural plant laxative and its effect on cholesterol and triacylglycerol levels]. Ceska a Slovenska Gastroenterologie, **50**(2), 45-47.
37	Singh, B. (2007). *Psyllium* as therapeutic and drug delivery agent. *Int. J. Pharm.*; **4**, 334(1-2), 1-14.
38	Kumar, A., Kumar, N., Vij, J. C., Sarin, S. K. and Anand, B. S. (1987). Optimum dosage of Ispaghula husk in patients with irritable bowel syndrome: correlation of symptom relief with whole gut transit time and stool weight. *Gut,* **28**, 150–155.
39	Qvitzau, S., Matzen, P. and Madsen, P. (1988). Treatment of chronic diarrhoea: loperamide versus ispaghula husk and calcium. Scand. *J. Gastroenterol*, **23**, 1237–1240.
40	Marlett, J. A., Kajs, T. M. and Fischer, M. H. (2000). An unfermented gel component of *psyllium* seed husk promotes laxation as a lubricant in humans. *Am. J. Clin. Nutr.*, **72**, 784–789.
41	Mamtani, R., Cimino, J. A., Cooperman, J. M. and Kugel, R. (1990). Comparison of total costs of administering calcium polycarbophil and psyllium mucilloid in an institutional setting. *Clin. Ther.*, **12**, 22–25.
42	Heaton, K. W., Radvan, J., Cripps, H., Mountford, R. A., Braddon, F. E. and Hughes, A. O. (1992). Defecation frequency and timing and stool form in the general population: a prospective study. *Gut*, **33**, 818–824.
43	Lederle, F. A. (1995). Epidemiology of constipation in elderly patients. Drug utilisation and cost-containment strategies. *Drugs Aging,* **6**, 465–469.
44	Karaus, M. and Wienbeck, M. (1991). Colonic motility in humans—a growing understanding. *Baillieres Clin. Gastroenterol.*, **5**, 453–478.
45	Bassotti, G., Gaburri, M., Imbimbo, B. P., Morelli, A. and Whitehead, W. E. (1994). Distension-stimulated propagated contractions in human colon. *Dig. Dis. Sci.*, **39**, 1955–1960.
46	Frati-Munari, A. C., Flores-Garduño, M. A., Ariza-Andraca, R., Islas-Andrade, S. and Chávez N. A. (1989). Effect of different doses of *Plantago psyllium* mucilage on the glucose tolerance test. **20**(2), 147-152.
47	Rodríguez-Morán, M., Guerrero-Romero, F. and Lazcano-Burciaga, G. (1998). Lipid- and glucose-lowering efficacy of *Plantago psyllium* in type II diabetes. *Journal of Diabetes and its Complications,* **5**(12), 273-278.
48	Frati Munari, A. C., Benítez, P. W., Raúl A. A. and Casarrubias, M. (1998). Lowering glycemic index of food by acarbose and *Plantago psyllium* mucilage Summer, **29**(2), 137-141.
49	Eun, Y. J., Yang, H. H., Un, J. C. and Hyung, J. S. (2016). Anti-obese effects of chitosan and *Psyllium* husk containing vitamin C in Sprague-Dawley (SD) rats fed a high fat diet. *Progress in Nutrition*, **2**(18), 152-160.
50	Frati-Munari, A. C., Fernández-Harp, J. A., Becerril, M., Chávez-Negrete, A. and Bañales-Ham, M. (1983). Decrease in serum lipids, glycemia and body weight by *Plantago psyllium* in obese and diabetic patients. *Arch. Invest. Med. (Mex),* **14**(3), 259-268.

Egyptian Herbal Monograph

Pharmacopoeial wild medicinal plants

***Senna alexandrina* Mill.** سنا مكي

1. Names & Synonyms (1-3)

***Senna alexandrina* Mill.**

Family: Leguminosae (Caesalpinioideae).

Syns.: *Cassia acutifolia* Delile, *Cassia senna* L., *Cassia lanceolata* Forssk.

Arabic: Sanna Mekki سنا مكى , Salamekki سلامكى.

English: True Senna, Alexandrian Senna.

2. Geographical distribution

The Nile region, desert east of the Nile including that of Sinai as well as the Red Sea and Gebel Elba regions (3).

3. Parts used for medicinal purposes

Leaves and pods (3).

4. Major chemical constituents

- **Anthraquinones**: Sennosides A and B, sennosides C and D (4), gluco aloe-emodin, rhein-8-monoglucoside, rhein 8-diglucoside, sennidin (5-7).
- **Naphthalene glucoside:** 6-Hydroxymusicin glucoside (8).
- **Flavonoids:** Mostly as mono- and di-*O*-glycosides of quercetin, kaempferol and isorhamnetin (5).

5. Medicinal uses

Well-established uses

A. Purgative (9) for short term use in occasional constipation (10).

Traditional medicinal uses

B. Stimulant laxative (11).

***S. alexandrina* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparation correlated to medicinal use

1. Liquid extract (alcoholic 30%) (12).
2. Infusion (13).
3. Decoction, dried extract, elixir, granules (pharmaceutical), oral solution, powder, rectal suppositories and tablets (14-15).
4. The boiled tea of leaves, sweetened with black honey, is taken in the morning before breakfast for treatment of constipation (11).

7. Posology and method of administration correlated to medicinal use

Adult oral dose:

- **Powdered drug:** 0.5-3gm (12).
- **Liquid extract:** 0.5-3ml (12).
- **Senna preparations expressed in terms of total sennosides calculated as sennoside B:** The usual adult dose is 15 to 30 mg given by mouth once or twice daily (15).

Children younger than 12 years of age: under medical supervision (14).

- Children over 6 years of age: one-half the adult dose (15).
- Children aged 2 to 6 years: one-quarter the adult dose (15).
- Not to be used by children younger than 2 years of age (15).

Elderly patients: Should initially take half of the normal prescribing dose (13).

8. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Children younger than 2 years of age (13).
- It should not be used by persons with intestinal obstruction, ulcerative colitis, gastrointestinal bleeding, appendicitis, nausea, vomiting, congestive heart failure, or an acute condition in the abdomen caused by surgery (14).
- Patients with suspected stricture, inflammatory bowel disease, or impending obstruction should not receive a bowel stimulant, to reduce the risk of colonic perforation (15).
- Senna should not be given to patients with undiagnosed abdominal pain (15).
- Prolonged use should generally be avoided (15).

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Hypersensitivity reactions manifesting as asthma and rhinoconjunctivitis have been reported in those manufacturing or dispensing Senna products (15).
- It should not be used for longer than 1-2 weeks without medical advice (14).
- Children younger than 12 years of age should not be used unless prescribed by a physician (14).

10. Interactions with other medicinal products and other forms of interaction (14)

- Cardiac glycosides (digoxin): Chronic use of Senna may potentiate cardiac glycosides.
- Disulfiram: Do not use Senna with disulfiram.
- Laxatives /stimulant laxative herbs: Avoid the concurrent use of Senna with other laxatives; additive effect can occur.
- Jimson weed (*Datura stramonium* L.): The action of Jimson weed is increased in cases of chronic use or abuse of Senna.

11. Fertility, pregnancy and lactation

- The use of Senna should be avoided during pregnancy (13) and lactation due to its content of anthraquinones (16) which is distributed into breast milk (15).
- No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Senna may cause mild abdominal discomfort such as colic or cramps (15), nausea, vomiting, anorexia, cramping, diarrhea, flatulence, hypocalcemia, enteropathy, alkalosis and hypokalemia (14).

14. Overdose

- Prolonged use or over dosage can result in diarrhoea with excessive loss of water and electrolytes, particularly potassium; there is also the possibility of developing an atonic non-functioning colon. Anthraquinone derivatives may colour the urine yellowish-brown at acid pH, and red at alkaline pH. Reversible melanosis coli has been reported following chronic use (15).
- Prolonged use or abuse of Senna laxatives has been associated with reversible finger clubbing, hypokalaemia and tetany, hypertrophic osteoarthropathy, intermittent urinary excretion of aspartylglucosamine, hypogammaglobulinaemia, reversible cachexia, and hepatitis or hepatic failure (15).

15. Relevant biological activities

-The laxative action and the laxative potency of Alaxandria and Tinnevelley senna in mice were studied using a standardized procedure. The results indicated that the laxative potency of various grades have been found to be reasonably uniform, the variations in potency not exceeding 25 per cent of the mean (17-18).

- The effect of repeated administration of the doses of Alexandria or Tinnevelly senna on mice over many weeks were studied. Two sets of experiments were conducted. In the first set of experiments no tolerance to either Tinnevelly or Alexandria senna developed. In the second set of experiments, 31 out of 40 mice survived the twenty-three-week period. It would therefore seem that mice may be used once a week for quantitative assay of laxative activity of senna and the repeated administration of the doses over many weeks did not cause any tolerance (19).

-Intravenous and intraperitoneal injections of Senna infusion produced negligible cathartic response compared to the same dose after oral administration (20).

- The effect of repeated administration of the doses of Alexandria Senna on mice over many weeks was studied. It would therefore seem that mice may be used once a week for quantitative assay of laxative activity of Senna and the repeated administration of the doses over many weeks did not cause any tolerance (19).

-Purgative action of Senna depends on the amount of hydroxyanthraquinone existing in the plant (21-22) but the effect is not due to the presence of sennoside A and B only (23), rather a synergistic action of different components (24), because Senna extracts are more potent laxatives than the pure active principles (25). Oral Senna-pod extract reverses net absorption of water, sodium and chloride to net secretion, and increases potassium secretion and stimulates output of PGE2 into the colonic lumen (26). The purgative action of Senna has been attributed, in part, to the release of histamine in the gut (27).

- Senna extract (SE) causes diarrhea and enhances gastrointestinal motility through digestive tract administration. Long-term gastric administration of SE induces inflammatory changes and cell damage in the whole gastrointestinal tract. The differential proteins screened from the colonic tissues of the model mice might mediate the enhancing effect of SE on gastrointestinal motility (28).

16. Additional information

Senna preparations may be used for bowel evacuation before investigational procedures or surgery, prior to X-ray examination or in mechanical preparation in the evening before elective colonic or rectal resection, as a colon cleansing, for elective colonoscopy (15, 29-32).

- The *β-O*-linked glycosides (e.g. sennosides and rhein 8-*O*-glucoside) are neither absorbed in the upper gut nor split by human digestive enzymes. They are converted by the bacteria of the large intestine into the ultimately active metabolite (rheinanthrone) (10, 33). The Aglycones are absorbed in the upper gut.

- Animal experiments with radio-labeled rheinanthrone administered directly into the caecum demonstrated absorption < 10%. In contact with oxygen, rheinanthrone is oxidised into rhein and sennidins, which can be found in the blood, mainly in the form of glucuronides and sulphates.

- After oral administration of sennosides, 3 - 6% of the metabolites are excreted in urine; some are excreted in bile (10). However, most of the sennosides (ca. 90%) are excreted in faeces as polymers (polyquinones) together with 2 - 6% of unchanged sennosides, sennidins, rheinanthrone and rhein. (10.)

- In human pharmacokinetic studies with Senna pods powder (20 mg sennosides), administered orally for 7 days, a maximum concentration of 100 ng rhein/ml was found in the blood, but an accumulation of rhein in blood was not observed. Small amounts of rhein pass into breast milk (10).

- Animal experiments demonstrated that placental passage of rhein is low.

17. Date of compilation/last revision

15/09/2023.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Hassan, N. M. and Abdelmohsen, M. M. (2020). *Senna alexandrina* Mill. In: Egyptian Encyclopedia of Wild Medicinal Plants, **9**, 473-480. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Dave, H. and Ledwani, L. (2012). A review on anthraquinones isolated from Cassia species and their applications. *Indian Journal of Natural Products and Resources*, **3**(3), 291-319.
5	Farag, M. A., Porzel, A., Mahrous, E. A., El-Massry, M. M. and Wessjohann, L. A. (2015). Integrated comparative metabolite profiling via MS and NMR techniques for Senna drug quality control analysis. *Anal. Bioanal. Chem.*, **407**, 1937–1949. https://doi.org/10.1007/s00216-014-8432-1.
6	Agarwal, V. and Bajpai, M. (2010). Pharmacognostical and biological studies on *Senna* and its products: An overview. *International Journal of Pharma and Bio Sciences*, **6**(2), 1-10.
7	Rastogi, R. P. and Mehrotra, B. N. (1990). Compendium of Indian Medicinal Plants, Publication and Information Directorate, CSIR, New Delhi, **1**, 81-83.
8	Franz, G. (1993). The senna drug and its chemistry. *Pharmacology*, **47**(1), 2-6. doi: 10.1159/000139654. PMID: 8234429.
9	Egyptian Pharmacopoeia (2005). 4th edition. General Organization for Government Printing. Cairo.
10	European Union Herbal Monograph on *Senna alexandrina* Mill. (*Cassia senna* L.; *Cassia angustifolia* Vahl), fructus (2018). EMA/HMPC/228761/2016. Committee on Herbal Medicinal Products (HMPC).
11	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys (2016). UNDP, GEF, ASRT and NRC, volumes 1-5.
12	Egyptian Pharmacopoeia (1972). 2nd edition. General Organization for Government Printing. Cairo.
13	PDR for Herbal Medicines (1998). Medical Economic Co. Montvale, New Jersey, 639. ISBN 1563633612, 9781563633614.
14	Skidmore-Roth (2010). Mosby's Handbook of Herbs and Natural Supplements. St. Louis: Mosby, 4th ed. ISBN: 978-0-323-05741-7.
15	Martindale: The Complete Drug Reference (2007). Pharmaceutical Press. Electronic version, London.
16	Joint Formulary Committee (2008) British National Formulary. 55th ed., London: British Medical Association and Royal Pharmaceutical Society of Great Britain.
17	Grote, I.W. and Woods, M. (1944). Laxative action in mice of Tinnevelley and *Alexandria senna*, and of several botanically related plants. *J. Am. Pharm. Assoc. (Sci. edi),* **33**, 266–270.
18	Grote, I. W. and Woods, M. (1951). The laxative activity in mice of the various parts of the *Senna* plant. *J. Am. Pharm. Assoc.*, **40**, 52–53.

19	Woods, M. and Grote, I.W. (1951). The repeated administration of Tinnevelly and Alexandria senna to mice. *J Am Pharm Assoc. (Sci. edi.)*, **40**, 198–202.
20	Hazleton, L. W. and Talbert, K. D. (1945). Factors influenceing the cathartic activity of *Senna* in mice. *J. Am. Pharm. Assoc. (Sci. edi)*, **34**, 260–264.
21	Auterhoff, H. (1953). Anthraquinone. III. The pharmacological action of anthraquinone derivatives. *Arzneimittel-Forsch*., **3**, 23–25.
22	Caravaggi, A. and Manfredi, A. (1937). Laxative action of active principles extracted from some commonly used plants. *Boll. Chim. Farm.*, **76**, 117–123.
23	Fairbairn, J. W. and Saleh, M. R. I. (1951). Vegetable purgatives containing anthracene derivatives. V. A third active glycoside of *Senna*. *J. Pharm. Pharmacol.*, **3**, 918–925.
24	Ploss, E. (1975). Synergism and potassium substitution as preferences in vegetable laxatives. *Dtsch. Apoth. -Ztg.,* **28**, 336–338.
25	Marvola, M., Koponen, A., Hiltunen, R. and Hieltala, P. (1981). The effect of raw material purity on the acute toxicity and laxative effect of sennosides. *J. Pharm. Pharmacol.*, **33**, 108–109.
26	Beubler, E. and Kollar, G. (1985). Stimulation of PGE2 synthesis and water and electrolyte secretion by *Senna* anthraquinones is inhibited by indomethacin. *J. Pharm. Pharmacol.*, **37**, 248–251.
27	Erspamer, E. and Paolini, A. (1946). Histamine a positive conditioner of the purgative action of some drastic agents. *Experientia*, **2**, 455–458.
28	Wang, X., Zhong, Y.X. and Lan, M. (2002). Screening and identification of proteins mediating Senna-induced gastrointestinal motility enhancement in mouse colon. *World J. Gastroenterol.*, **8**, 162–167.
29	Sitiris G. (1970). A new laxative, X-preparation: to be used as a bowel evacuant prior to X-ray examination. *Tidsskr Nor Laegeforen*, **90**, 1477–1478.
30	Shavakhi, A., Kianinia, M., Torabi, G., Nemati, A., Saeidian, B., Hoseinzadeh, M., Madjlesi, F., Navaei, P., Rashidinejad, F. and Minakari, M. (2011). High dose Senna or polyethylene glycol (PEG) for elective colonoscopy preparation: a prospective randomized investigator-blinded clinical trial. *J. Res. Med. Sci.*, **16**(2), 149–155.
31	Arezzo, A. (2000). Prospective Randomized Trial Comparing Bowel Cleaning Preparations for Colonoscopy. *Surg. Laparosc. Endosc. Percutan. Tech.*, **10**(4), 215-217.
32	Valverd, A., Hay, J., Fingerhut, A., Boudet, A., Petroni, R., Pouliquen, X., Msika, S. and Flamant, Y. (1999). Senna *vs* polyethylene glycol for mechanical preparation the evening before elective colonic or rectal resection. A multicenter controlled trial. *Arch. Surg.*, **134**(5), 514-519. doi:10.1001/archsurg.134.5.514.
33	Meselhy, R. M., Nishimoto, E., Akao, T. and Hattori M. (2001). Human intestinal Bacteroides spp. RHEIN-I and RHEIN-II capable of transforming rhein to rheinanthrone, induce rhein-dependent diarrhea in rats. *J. Trad. Med*. **18**, 169-176.

Egyptian Herbal Monograph

Pharmacopoeial wild medicinal plants

Drimia maritima (L.) Stearn بصل العنصل

1. Names & Synonyms (1)

***Drimia maritima* (L.) Stearn**
Family: Asparagaceae (formerly the family Hyacinthaceae/Liliaceae)
Syns: *Charybdis maritima* (L.) Speta, *Ornithogalum maritimum* (L.) Lam., *Ornithogalum squilla* Ker Gawl., *Scilla maritima* L., *Squilla maritima* (L.) Steinh., *Stellarisscilla* Moench, *Urginea maritima* (L.) Baker, *Urginea scilla* Steinh.

Arabic: Basal Far'aon بصل فرعون , Onsol عنصل , Basal Onsol بصل عنصل , Ashkil اشقيل , Askil أسقيل , Askal أسقال (2)

English: Sea onion, Squill, Medicinal squill, White squill.

2. Geographical distribution

Mediterranean coastal strip and Sinai (3).

3. Parts used for medicinal purposes

The dried fleshy scales of the bulbs of *U. maritima* (4) collected after withering of leaves; known as white squill (2) [Not to be confused with red squill used as rodenticide].

4. Major chemical constituents

Cardiac glycosides "Bufadienolides" (bulb):

- Scillaren A, proscillaridin A, scilliroside, scillaridin A, scilliglaucoside, scillipheoside, glucoscillipheoside, scillicyanoside, glucoscillaren A, scillarenin (5-7).

- Forty-one compounds were isolated from the Egyptian squill from which sixteen were glycosides; 16*β* hydroxy-scillarenin, 16*β* -*O*-acetyl-scillarenin, 12*β*-hydroxy-5 *α*-4,5-dihydro-scillirosidin, 16*β* - hydroxy-5*α*-4,5-dihydro-scillirosidin, 16*β* -*O*-acetyl-5*α* -4,5- dihydro-scillirosidin, 12*β*-hydroxy-scillirubrosidin, 16*β*-*O*-acetyl-scillirubrosidin, 9-hydroxy-scilliphaeosidine, and 12*β* -hydroxy-desacetyl-scillirosidin (8).

Other constituents:

- Flavonoids (5) (vitexin, isovitexin, orientin, isoorientin, scoparin, vicenin-2, quercetin-3-monoglucoside, dihydroquercetin, dihydroquercetin-4'-monoglucoside), calcium oxalate (5,7,9), xanthoscillide (5), dihydro-benzofuran-type neolignan glucoside and free amino acids (L-azatidine-2-carboxilic acid was the predominant one) (7).

5. Medicinal uses

Well-established uses (4)

A. Expectorant.

Traditional medicinal uses (2,10)

B. Expectorant.

U. maritima **is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparation correlated to medicinal use (11)

1. Infusion.
2. Liquid extract (Alcoholic 70%).
3. Vinegar.
4. Tincture.

7. Posology and method of administration correlated to medicinal use (11)

Preparation 1: 60-200 mg of dried bulb powder as infusion, three times daily; with maximum daily dose of 500mg (2).

Preparation 2: 0.06-0.2 ml (12).

Preparation 3: 0.6-2.0 ml (12).

Preparation 4: 0.3-2.0ml (12).

8. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.

- The drug and pure glycosides, among others, should not be administered in the presence of second- or third-degree atrioventricular block, hypercalcemia, hypokalemia, hypertrophic cardiomyopathy, carotid sinus syndrome, ventricular

tachycardia, thoracic aortic aneurysm or Wolff-Parkinson-White (WPW) syndrome (13).

- It is not recommended for patients with impaired hepatic or renal function (11).

- It is not recommended for children under 12 years old (11).

- It is not recommended in stomach or bowel problems, as it can irritate the stomach and intestine (11).

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

- Squill contains cardiac glycosides with a narrow therapeutic range, thus therapeutic doses may induce side effects in susceptible individuals (11).

-Contact with the juice of the fresh bulb can lead to skin inflammation (squill dermatitis) (11).

- Monitoring of blood glucose level should be done regularly when used for diabetics as squill had been used in traditional medicine for diabetes (2).

- Squill is to be dispensed by prescription only (a prescription drug). It is considered to be potentially harmful if not used under medical supervision.

10. Interactions with other medicinal products and other forms of interaction (11, 14, 15)

- Digoxin.
- Calcium supplements.
- Medications for inflammation (Corticosteroids).
- Quinidine.
- Stimulant laxatives.
- Water pills (Diuretic drugs).

11. Fertility, pregnancy and lactation

- Squill must be avoided during pregnancy and lactation. It has been reported to be an abortifacient and to affect the menstrual cycle (11, 16).
- No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- These include gastric irritation or hypersensitivity reactions (urticaria/hives, flushing or dermatitis), salt and water retention, low potassium levels in blood and irregular pulse (11).

14. Overdose (13)

Overdosage can lead to cardiac rhythm disorders, life-threatening ventricular tachycardia, atrial tachycardia with atrioventricular block, stupor, vision disorders, depression, confusion, hallucinations and psychosis. Fatal dosages lead to cardiac arrest or asphyxiation.

15. Relevant biological activities

Anti-asthmatic activity

-A preliminary evaluation of the efficacy and safety of an add-on Squill Oxymel treatment in patients with moderate to severe persistent asthma was done. In a 6-week, triple-blind, randomized, placebo-controlled trial, 60 patients with stable moderate to severe persistent asthma were randomly allocated to receive either 10 ml syrup of Squill Oxymel, simple oxymel, or a placebo 2 times a day, as an add-on to their routine treatment (inhaled corticosteroids and $\beta 2$ agonists). Spirometry and plethysmography were performed on patients to evaluate the effect of the treatment at baseline and end of intervention. The results showed significant improvement in spirometry parameters, especially FEV1 (1.54 ± .38 *vs.* 2.11 ± .49 l), in the Squill Oxymel group compared with the other groups. The increases in FEV1 liter, FEV1%, FEV1/FVC%, and MEF 25–75% during the intervention were significantly higher in the Squill Oxymel group than in the other groups ($p < .001$). However, the improvement of plethysmographic parameters showed no significant difference between the study groups ($p>.05$). The SGRQ scores (symptoms, activity, and total score) were significantly improved after intervention in both the Squill Oxymel and the simple honey oxymel groups ($p < .001$), but not in the placebo group. Nausea and vomiting was reported in 5 patients in Squill Oxymel and simple oxymel groups. No other serious adverse event was observed. The results of the study showed preliminary evidence for the efficacy and safety of the add-on treatment of Squill Oxymel in patients with moderate to severe persistent asthma (17).

Toxicity in human

-*U. maritima* led to death in 55 years-old woman who orally consumed two bulbs for arthritic pain. She was diagnosed with Hashimoto thyroiditis before ingestion of this plant and hypothyroidism may had associated with sever toxicity. Poisoning

symptoms were similar to digitals included vomiting, seizure, significant hyperkalemia, ventricular arrhythmias, atrioventricular block (18).

16. Additional information

U. maritima is the oldest drug used by human for cardiac problems (7). The glycosides present in the squill have digitalis like cardiotonic properties due to their aglycones. Action is faster but shorter-lasting than that of digitalis glycosides (19). Ingestion of squill is poisonous mainly due to its cardiac glycosides content (18).

17. Date of compilation/last revision

22/09/2023.

References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Bidak, L. M., Heneidy, S. Z. and Helmy, M. W. A. (2020). *Urginea-maritima* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, **10**, 309-323. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Egyptian Pharmacopoeia (1984). 3rd edition. General Organization for Government Printing. Cairo.
5	Ashutosh, K. (2008). Pharmacognosy and Pharmacobiotechnology, 2nd edition. Published by Anshan Publishers. ISBN 10: 1905740735, ISBN 13: 9781905740734.
6	Stoll, A. (1954). Sur les substances cardiotoniques de la scille maritime (*Scilla maritima* L.): Cardiotonic Substances of *Scilla maririma*. *Experientia*, **10**, 282- 297.
7	Bozorgi, M., Amin, G., Shekarchi, M. and Rahimi R. (2017). Traditional medical uses of *Drimia* species in terms of phytochemistry, pharmacology and toxicology. *J. Tradit. Chin. Med.*, **37**(1), 124-139.
8	Kopp , B., Krenn, L., Draxler, M., Hoyer, A., Terkola, R., Vallaster, P. and Robien, W. (1996). Bufadienolides from *Urginea maritima* from Egypt. *Phytochemistry*, **42**(2), 513-522.
9	Fernandez, M., Vega, F.A., Arrupe, T. and Renedo, J. (1972). Flavonoids of squill, *Urginea maritima*. *Phytochemistry*, **11**, 1534.
10	Conservation and sustainable use of medicinal plants in Egypt, National Surveys (2016). UNDP, GEF, ASRT and NRC, volumes 1-5.
11	Edwards, S. E., Rocha, I. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition, John Wiley & Sons, Ltd. ISBN: 978-1-118-54356-6.
12	The British Pharmaceutical Codex (BPC) (1973). Pharmaceutical Society of Great Britain, London. ISBN-10: 0853690847. ISBN-13: 978-0853690849.
13	PDR for Herbal Medicines (1998). Medical Economic Co. Montvale, New Jersey, 639. ISBN 1563633612, 9781563633614.
14	Williamson, E. M., Driver, S. and Baxter, K. (2013). Stockley's Herbal Medicines Interactions. 2nd edition. Pharmaceutical Press, London, UK.
15	https://www.rxlist.com/squill/supplements.htm
16	https://www.webmd.com/vitamins/ai/ingredientmono-743/squill
17	Nejatbakhsh, F., Karegar-Borzi, H., Amin, G., Eslaminejad, A., Hosseini, M., Bozorgi, M. and Gharabaghi, M. A. (2017). Squill Oxymel, a traditional formulation from *Drimia maritima* (L.) Stearn, as an add-on treatment in patients with moderate to severe persistent asthma: A pilot, triple-blind, randomized clinical trial. *Journal of Ethnopharmacology*, **196**, 186–192.
18	Tuncok, Y., Kozan, O., Cavdar, C., Guven, H., Fowler, J. (1995). *Urginea maritima* (squill) toxicity. *J. Toxicol. Clin. Toxicol.*, **33**(1), 83-86.
19	Hammouda, F. M., Ismail, S. I., Abdel-Azim, N. S. and Shams, K. A. (2005). A Guide to Medicinal Plants in North Africa (Batanouny K. H., editor). IUCN Centre for Mediterranean Cooperation. Malaga.

Annex

Dry extract: is a solid preparation obtained by evaporation of the solvent from a liquid/fluid extract. Dry extract can also be prepared by spray-drying with or without the use of an adsorbent (such as methyl cellulose), or by drying and milling to produce a powder. This may be further processed by compression or with use of a binding agent or granulation liquid to produce multiparticulate granules (1).

Elixir: are clear, flavored oral liquids containing one or more active ingreients dissolved in a vehicle that usually contains a high proportion of sucrose or a suitable polyhydric alcohol or alcohols and may also contain ethanol or a diluted ethanol (2).

Liquid extract (1): is a liquid preparation of herbal materials obtained using water, alcohol or other extraction solvents. Common preparations include:

- **Decoction**: is a water-based herbal preparation made by boiling herbal materials with water, and is commonly utilized in various traditional medicine contexts. In some cases, aqueous ethanol or glycerol can also be used to prepare decoctions. However, decoctions may be prepared by a programmable decocting machine that processes the herbal material at a specific temperature for a specific duration and then dispenses the decoction in hermetically sealed plastic pouches of a specified single-dosage volume that can be refrigerated for subsequent reheating and consumption. The amounts of herbal material and solvent used, as well as the length of the decocting process, should be specified.
- **Infusion**: is a dilute solution prepared by steeping the herbal materials in boiling water for a short time. Infusions prepared in edible oil or vinegar are also available.
- **Tincture**: As a general rule, a "tincture" is an alcoholic or hydroalcoholic extract of a herbal material, typically made up of 1 part herbal material and 5–10 parts solvent (for example, ethanol, vinegar, or glycerin). Tinctures can be prepared by extracting herbal materials usually with ethanol of a suitable concentration. The ratio of water to alcohol should be recorded.

Poultice: a paste of plant part or drug applied to the sore or inflamed part of the body to supply moisture or to act as a local stimulant (3).

References:

1	WHO Expert Committee on Specifications for Pharmaceutical Preparations. 51st Report. Geneva, 2017.
2	Egyptian Pharmacopoeia (2005). General Organization for Government Printing. Cairo, 4th edition.
3	Boulos, L. (1983). Medicinal Plants in North Africa. References publication Algonac, Michigan, ISBN 0917256166, 9780917256165.

Egyptian Herbal Monograph

Volume 3

Medicinal Plants used in Egypt

Egyptian Drug Authority (EDA)

2023

Preface

The third volume, which includes 54 monographs of medicinal plants widely used within the region and for a period of not less than 15 years in the Egyptian market, is seen of as a continuation of the earlier work of the Egyptian Herbal Monograph.

These monographs are meant to act as a manual and guide for creating the herbal medical product's scientific file, which is required upon registration for market authorization. They ease registration processes and offer scientific information on the quality, efficacy, safety, and appropriate use of medicinal plant products. The medicinal plants featured in this volume were selected as they are most commonly used in pharmaceutical industries in Egypt. The content was obtained by a systematic review of many international monographs as well as many other references. It is anticipated that this volume will be updated in the near future.

Egyptian HerbalMonograph

Medicinal Plants Used in Egypt

***Actaea racemosa* L.** كوهوش السوداء

1. Names & Synonyms (1)

***Actaea racemosa* L.**
Family: Ranunculaceae.
Syns.: *Botrophis serpentaria* Raf., *Cimicifuga racemosa* L. Nutt., *Cimicifuga serpentaria* Pursh, *Macrotrys racemosa* L. Sweet, *Megotrys serpentaria* Raf., *Thalictrodes racemosa* L. Kuntze.

Arabic: kuhush alsawda كوهوش السوداء.
English: Black cohosh, Black snakeroot (2-4).

2. Parts used for medicinal purpose

Dried rhizomes and/or roots (2-8).

3. Major chemical constituents

Rhizomes and roots

- **Triterpenoid glycosides**: Cimicifugoside, actein, and 23-epi-26-deoxyactein (3) beside the aglycones of actein, deacetylactein, and 23-epi-26-deoxyactein (9-17).
- **Phenylpropanoid derivatives**: Caffeic acid derivatives (caffeic, ferulic and isoferulic acids) (9-17), and its condensation products; cimicifugic acids (e.g. fukinolic acid) (3, 13).
- **Flavonoids:** Kaempferol, biochanin A and genestein 4′-methyl ether (3, 18).
- **Alkaloids:** Quinoline and quinolizidine-type; anagyrine, baptifoline, magnoflorine, methyl cystine and methyl serotonin (19).
- **Others:** Salicylic acid (3), tannins, resin and fatty acids (20).

4. Medicinal uses (Indications)

A. Relief of menopausal complaints such as hot flushes, profuse sweating, sleeping disorders, nervous irritability and depressive mood (2-8).
B. Relief the pain associated with menstruation, premenstrual symptoms and in dysmenorrhoea (2, 6).

5. Herbal preparations correlated to medicinal use

1. **Dry extract** (3)
   - **1.1.** Extraction solvent ethanol 58% (V/V).
   - **1.2.** Extraction solvent ethanol 60% (V/V).
   - **1.3.** Extraction solvent propan-2-ol 40% (V/V).

2. **Liquid (fluid) ethanolic extract** (3, 4, 6, 21).

3. **Tincture** (1: 10 in 60% ethanol) (3, 4, 21).

Herbal preparations are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

A standardized black cohosh extract at a dose of 40- 80 mg, daily (standardized to contain 1 mg of triterpenes calculated as 27-deozyacetein per 20 mg of extract)

Preparation 1
Indications A and B
Adults: Equivalent to 40 - 2,400 mg, daily (6).

Indication A
Preparation 1.1
Adults: Single dose: 2.8 mg, 2 times daily. Daily dose: 5.6 mg (3, 5).
Preparation 1.2
Adults: Single dose: 6.5 mg, one single daily dose. Daily dose: 6.5 mg (2, 5).
Preparation 1.3
Adults: Single dose: 2.5 mg or 5.0 mg, 1-2 times, daily. Daily dose: 5.0 mg (3, 5).

Preparation 2
Indications A and B
Adults: Equivalent to 40 - 2,400 mg per daily (6).
20 drops, twice daily (60% ethanol V/V; equivalent to 40mg dried herb daily) (21).

Preparation 3
Indications A and B
Adults: 0.4 - 2 ml, 1-3 times daily (3, 4, 21-23) up to 4 ml, 3 times daily (4, 23).

Duration of use: It should not be taken for more than 6 months without medical advice (5).

Method of administration (5, 6): Oral use.

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Not be used by individuals with hormone-sensitive condition, such as breast cancer, endometriosis, uterine fibroids, ovarian cancer or uterine cancer, (3, 24) and in patients with cholestasis and celiac disease (4).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Patients with a history of liver disorder or liver diseases should consult a physician prior taking *Cimicifuga racemosae* preparations (5, 6).
- Patients should stop taking *Cimicifuga racemosae* preparations and consult their doctor immediately if they develop signs and symptoms suggestive of liver injury (tiredness, loss of appetite, yellowing of skin and eyes, severe upper stomach pain with nausea and vomiting or dark urine) (5, 6).
- In case of vaginal bleeding or other unclear symptoms, patients should consult their doctor (5).
- Treatment with black cohosh is not recommended to exceed six months (5, 25).

9. Interactions with other medicinal products and other forms of interaction

- **Antihypertensives:** Black cohosh increases the action of anti-hypertensives; concurrent use should be avoided (4, 26).
- **Docetaxel, doxorubicin:** Black cohosh may increase the toxicity of docetaxel and doxorubicin; concurrent use should be avoided (4).
- **Hormonal contraceptives:** Black cohosh may increase the effects; concurrent use should be avoided (4).
- **Hormone replacement therapy:** Black cohosh may alter the effects of other hormone replacement therapies; use together cautiously (4).
- **Sedatives/hypnotics:** Black cohosh may increase the hypotension; concurrent use should be avoided (4).
- **Tamoxifen:** Black cohosh may augment the anti-proliferative properties of tamoxifen (4).

10. Fertility, pregnancy and lactation

- The use during pregnancy and lactation is not recommended (5).
- No fertility studies available (5).

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (5)

- If adverse reactions occur, a doctor or pharmacist should be consulted.
- **Hepatobiliary disorders**: Liver toxicity (including hepatitis, jaundice, disturbances in the liver function tests) is associated with the use of *Cimicifuga racemosae* containing products.
- **Skin and subcutaneous tissue disorders**: Allergic skin reactions (urticaria, itching, exanthema), facial oedema and peripheral oedema have been reported.
- **Gastrointestinal disorders**: Gastrointestinal symptoms (dyspeptic disorders, diarrhoea).

13. Overdose

- Large doses of black cohosh to be 5 g of the dried drug or 12 g of the fluid extract (27).
- Overdose has produced nausea and vomiting, vertigo and visual disturbances (23).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

06/09/2022.

References

1	https://powo.science.kew.org.
2	WHO monographs on selected medicinal plants (2002). Monographs on Selected Medicinal Plants, **2**, 55- 65.
3	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
4	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.
5	European Union herbal monograph on *Actaea racemosa* L. (2018). EMA/HMPC/48745/2017. Committee on Herbal Medicinal Products (HMPC).
6	Natural Health Product, *Actaea racemosa* L. (2018). Health Canada. http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=44.
7	ESCOP Monographs (2018). *Cimicifuga racemosa* L. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills..
8	Blumenthal, M., Brinckmann, J. and Wollschlaeger, B. (2003). The ABC Clinical Guide to Herbs, 1st ed., American Botanical Council, Austin, Texas, USA.
9	Shao, Y., Harris, A., Wang, M., Zhang, H., Cordell, G. A., Bowman, M. and Lemmo, E. (2000). Triterpene glycosides from *Cimicifuga racemosa*. *J. Nat. Prod.*, **63**, 905-910.
10	Wende, K., Mugge, C., Thurow, K., Schopke, T. and Lindequist, U. (2001). Actaeaepoxide 3-O-â-D-xylopyranoside, a new cycloartane glycoside from the rhizomes of *Actaea racemosa* (*Cimicifuga racemosa*). *J. Nat. Prod*., **64**, 986-989.
11	Bedir, E. and Khan, I. A. (2000). Cimiracemoside A: A new cyclolanostanol xyloside from the rhizome of *Cimicifuga racemosa*. *Chem. Pharm. Bull*., **48**, 425-427.
12	Bedir, E. and Khan, I. A. (2001). A new cyclolanostanol arabinoside from the rhizome of *Cimicifuga racemosa*. *Pharmazie*, **56**, 268-269.
13	Nikolić, D., Lankin, D. C., Cisowska, T., Chen, S. N., Pauli, G.F. and van Breemen, R. B. (2015). Nitrogen-containing constituents of black Cohosh: Chemistry, structure elucidation, and biological activities. *Recent Adv. Phytochem*., **45**, 31-75.
14	Chen, S. N., Li, W., Fabricant, D. S., Santarsiero, B. D., Mesecar, A., Fitzloff, J. F., Fong, H. H. and Farnsworth, N. R. (2002). Isolation, structure elucidation, and absolute configuration of 26-deoxyactein from *Cimicifuga racemosa* and clarification of nomenclature associated with 27-deoxyactein. *J. Nat. Prod*., **65**, 601-605.
15	Watanabe, K., Mimaki, Y., Sakagami, H. and Sashida, Y. (2002). Cycloartane glycosides from the rhizomes of *Cimicifuga racemosa* and their cytotoxic activities. *Chem. Pharm. Bull*., **50**, 121-125.
16	Kruse, S. O., Lohning, A., Pauli, G. F., Winterhoff, H. and Nahrstedt, A. (1999). Fukiic and piscidic acid esters from the rhizome of *Cimicifuga racemosa* and the in vitro estrogenic activity of fukinolic acid. *Planta Med*., **65**, 763-764.

17	Chen, S. N., Fabricant, D. S., Lu, Z. Z., Zhang, H., Fong, H. H. and Farnsworth, N. R. (2002). Cimiracemates A-D, phenylpropanoid esters from the rhizomes of *Cimicifuga racemosa*. *Phytochemistry*, **61**, 409-413.
18	McCoy, J. and Kelly, W. (1996). Survey of *Cimicifuga racemosa* for phyto-estrogenic flavonoids. In: 212th American Chemical Society National Meeting, Orlando, FL.
19	Mohapatra, S., Iqubal, A., Ansari, M.J., Jan, B., Zahiruddin, S., Mirza, M.A., Ahmad, S. and Iqbal, Z. (2022). Benefits of black cohosh (*Cimicifuga racemosa*) for women health: An up-close and in-depth review. *Pharmaceuticals*, **15**, 278. https://doi.org/10.3390/ ph15030278.
20	Barnes, J., Anderson, L. A. and Phillipson, J. D. (1996) Herbal Medicines: A Guide for Health-Care Professionals. The Pharmaceutical Press: London.
21	American Herbal Pharmacopoeia (1999). *Actaea racemosa* L. Analytical, Quality Control and Therapeutic Monograph. ISBN: 1-929425-04-X.
22	Pengelly, A. and Bennett, K. (2012). Appalachian Plant Monographs. Black cohosh, *Actaea racemosa* L. Published online at http://www.frostburg.edu/aces/appalachian-plants/.
23	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements - An evidence-based guide. 3rd edition, Churchill Livingstone. ISBN: 978 0 7295 3910 4.
24	https://www.webmd.verywellhealth.com/black-cohosh-888.
25	Blumenthal, M., Busse, W. R., Hall, T., Goldberg, A., Grünwald, J., Riggins, C. W. and Rister, R. S. (1998). The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines. Translator: Klein S. Boston: *Integ. Med. Comm*., 685 p. Translation of: German Kommission E.
26	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
27	List, P. H. and Hörhammer, L. (1973). Hagers Handbuch der Pharmazeutischen Praxis. Berlin: Springer.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Anethum graveolens* L.** شبت

1. Names & Synonyms (1)

***Anethum graveolens* L.**

Family: Apiaceae (Umbelliferae).

Syns: *Pastinaca anethum* Spreng., *Peucedanum graveolens* Benth. & Hook., *Selinum anethum* Roth.

Arabic: Shabat شبت

English: Dill.

2. Parts used for medicinal purposes

Dried ripe fruits (1).

3. Major chemical constituents

Essential oil: carvone, limonene, α-phellandrene, dihydrocarvone, dillapiole (2),

1,8-cineole, α-pinene and α-terpene (1).

4. Medicinal uses (Indications)

A. Carminative and spasmolytic in infantile colic (3).

B. For dyspepsia, gastritis, flatulence, stomachache (1) and as antispasmotic (4).

5. Herbal preparations correlated to medicinal use

1. Dill oil (as Dill water for infants) (5).
2. Dill oil (1,3,6).
3. Dill dry extract (using mixture of ethanol and water in different concentrations as solvent).
4. Dill powder (1,4,6).

Herbal preparations are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1(5)

Indication A

Dill water for infants: only for babies from 1 to 12 months old.
(Each 5 ml contain 2.3 mg dill water):
- 1-6 months old: 2.3 mg one teaspoonful during or after a feed.
- 6-12 months old: 2 teaspoonful during or after a feed.
Don't use more than 6 times in 24 hours.

Preparation 2-4

Indication B

Preparation 2

- **Adults:** Dill oil: 0.05-2 ml (3 times daily) (3,6) or 0.1-0.3 g daily in divided doses (1,3,6).
- **Children:** Pure essential oil should not be given to infants and young children (1) but it may be used in a pharmaceutical dosage form, under medical supervision and should not exceed the appropriate dose.

Preparation 3

-The appropriate dose of the extract depends on several factors such as the user's age, health, and several other conditions (7,8).

- Consult your physician or pharmacist before using (7,8).

Preparation 4

3 gm or equivalent (for other preparations) (1,4,6).

Method of administration: Oral use.

7. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

- Dill should not be given to children except under medical supervision (6).

- Persons with a fluid or electrolyte imbalance should not use this herb (6).

-Diabetes: Dill extract might lower blood sugar in people with diabetes so blood suger level should be monitored regularly (7,8).

-Surgery: Stop taking Dill extract at least 2 weeks before a scheduled surgery because dill extract might interfere with blood sugar control medications during and after surgery (7,8).

-Underactive thyroid (hypothyroidism): Taking Dill as a medicine seems to lower thyroid hormone levels. This might worsen symptoms in people with underactive thyroid (8).

9. Interactions with other medicinal products and other forms of interaction

None reported.

10. Fertility, pregnancy and lactation

-Dill should not be used during pregnancy and breastfeeding (1,6-8).

-Dill extract has been used as a contraceptive and to induce labour.

-Dill extract may have teratogenic effects (1).

- Dill can start menstruation and this might lead to a miscarriage (7,8).

-No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- May alter sodium balance and cause allergic reaction (6).

13. Overdose

No case of overdose has been reported.

14. Relevant biological properties

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

- There are two type of dill oil (dill seed oil & Terpenless dill seed oil).
- Terpenless dill seed oil is richer in carvone than dill seed oil.

16. Date of compilation/last revision

23/03/2022.

References

1	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, **3**, 33-41
2	Said-Al Ahl, H., Gendy, A. G. and Omer, E. A. (2016) Humic acid and indole acetic acid affect yield and essential oil of dill grown under two different locations in Egypt. *International Journal of Pharmacy and Pharmaceutical Sciences*, **8**, 146-157.
3	Wren, R. C. (1988). Potter's New Cyclopaedia of Botanical Drugs and Preparations. Completely revised by Elizabeth M. Williamson and Fred, J. Evans. C. W. Daniel Company, Ltd, Saffron Walden.
4	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
5	https://www.medicines.org.uk
6	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 978-0-323-05741-7.
7	https://www.rxlist.com/dill/supplements.htm#SpecialPrecautionsWarnings
8	https://www.webmd.com/vitamins/ai/ingredientmono-463/dill#

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Arctostaphylos uva-ursi* L.** عنب الدب

1. Names & Synonyms (1)

***Arctostaphylos uva-ursi* L.**

Family: Ericaceae.

Syns.: *Arbutus uva-ursi* L., *Arctostaphylos media* Greene, *Arbutus officinalis* Wimm., *Arbutus procumbens* Patzke, *Mairania uva-ursi* Desv., *Uva-ursi buxifolia* S.F. Gray, *Uva-ursi procumbens* Moench.

Arabic: Enab eddib عنب الدب.

English name: Bearberry, Uva ursi.

2. Parts used for medicinal purpose

Dried leaves (1-4).

3. Major chemical constituents

-Hydroquinone derivatives: Arbutin and methyl-arbutin (glycosides); galloyl arbutin, and hydroquinone (2, 5).
-Flavonoids: Myricetin, quercetin and their glycosides including hyperin, isoquercitrin, myricitrin and quercitrin; hyperoside; kaempherol (2,5,6).
-Polyphenols: Gallotannins, corilagin, catechin, anthocyanidin derivatives including cyanidin and delphinidin (2).
-Phenolic acids: Gallic, *p*-coumaric and syringic, salicylic acid, *p*-hydroxybenzoic, ferulic, caffeic and lithospermic acids (dimeric caffeic acid) (2).
-Terpenoids: α-Amyrin, α-amyrin acetate, β-amyrin, lupeol, uvaol, ursolic acid, and a mixture of mono- and di-ketonic α-amyrin derivatives (1,2,5).

4. Medicinal Uses (Indications)

Symptomatic treatment of mild recurrent lower urinary tract infections such as burning sensation during urination and/or frequent urination in women, after serious conditions have been excluded by a medical doctor (1-3).

5. Herbal preparations correlated to medicinal use (2)

1. **Comminuted herbal substances as herbal tea for oral use.**

   1.5-4 g (4) of the comminuted herbal substance in 150 ml of boiling water as a herbal infusion or a macerate (1,4).

2. **Powdered herbal substance.**

3. **Dry extract, extraction solvent ethanol 60% V/V**, containing 23.5-29.3% of hydroquinone derivatives calculated as anhydrous arbutin (spectrophotometry).

4. **Dry extract**, **extraction solvent water**, containing 20-28% of hydroquinone derivatives calculated as anhydrous arbutin (spectrophotometry).

5. **Liquid extract**, extraction solvent ethanol 25% V/V.

Herbal preparations (2-5) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use (2)

Adult and elderly females

Preparation 1
2 to 4 times daily. Maximum daily dose: 8 g.
The macerate should be used immediately after preparation.

Preparation 2: Single dose: 700 – 1050 mg, twice daily. Maximum daily dose: 1.75 g.

Preparation 3, 4
Single dose: the dose corresponding to 100–210 mg of hydroquinone derivatives calculated as anhydrous arbutin, 2–4 times daily.
Daily dose: the dose corresponding to 200–840 mg of hydroquinone derivatives calculated as anhydrous arbutin (3).

Preparation 5: Single dose: 1.5–4 ml, up to 3 times daily. Maximum daily dose: 8 ml.

Duration of use:

- Not to be used for more than one week.
- If the symptoms persist for more than 4 days during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (1-3).

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Kidney disorders (2).
- During pregnancy or lactation (1,3).
- Children under the age of 12 years (1,4), as hepatotoxicity may occur (4).

8. Special warnings and precautions for use

- If the symptoms worsen or if complaints such as fever, dysuria, spasms, or blood in urine occur during the use of the medicinal product, a doctor or a pharmacist should be consulted (2,3).
- It should not be used for prolonged periods (1-4).
- It should be used cautiously by persons with electrolyte imbalance, acidic urine, constipation, iron deficiency, anemia, malnutrition due to high tannin level, and disorders involving gastrointestinal irritation (4).
- It should not be administered with medicines or foods that acidify the urine, such as acidic fruits or fruit juice and should be administered with plenty of fluids (1,3).
- It may cause a greenish-brown coloration of the urine (1,2) that darkens on exposure to air due to the oxidation of hydroquinone (1).
- The use in children and adolescents under 18 years of age is not recommended without medical advice (2).
- The use in men is not recommended without medical supervision (2).

9. Interactions with other medicinal products and other forms of interaction (4)

- Concurrent use with diuretics can lead to electrolyte loss, primarily hypokalemia.
- Uva ursi may increase the effect of NSAIDs.

- Urine acidifiers may inactivate Uva ursi; concurrent use should be avoided.

10. Fertility, pregnancy and lactation

- The use during pregnancy and lactation should be avoided (1,4).
- No fertility data available (2).

11. Effects on ability to drive and use machines (2)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (2)

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Nausea, vomiting and stomachache.

13. Overdose (4)

Hepatotoxicity, cyanosis, tinnitus, vomiting, seizures, cardiovascular collapse, delirium, shortness of breath and feeling of suffocation.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

21/06/2022.

Referances

1	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **2**, 342-351.
2	Committee on Herbal Medicinal Products (HMPC) (2018). European Union Herbal monograph on *Arctostaphylos uva-ursi* (L.) Spreng., folium. EMA/HMPC/750269/2016. Committee on Herbal Medicinal Products (HMPC).
3	Natural Health Product – Bearberry - *Arctostaphylos uva-ursi* L. (2019). Health Canada, http://webprod.hc-sc.gc.ca/nhpidbdipsn/atReq.do?atid=arctostaphylos.uva.ursi&lang=eng
4	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs and Natural Supplements. St. Louis: Mosby. ISBN: 978-0-323-05741-7.
5	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
6	Sugier, P., Sęczyk, Ł., Sugier, D., Krawczyk, R., Wójcik, M., Czarnecka, J., Okoń, S., and Plak, A. (2021). Chemical characteristics and antioxidant activity of *Arctostaphylos uva-ursi* L. Spreng. at the southern border of the geographical range of the species in Europe. *Molecules,* **26**(24), 7692. https://doi.org/10.3390/molecules26247692.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Althaea officinalis* L.** الخطمية

1. Names & Synonyms (1, 2).

***Althaea officinalis* L.**
Family: Malvaceae.
Syns.: *Malva althaea* E. H. L. Krause, *Malva officinalis* (L.) K. F. Schimp. & Spenn. (3).
Arabic: Marshmallow مارشمالو, Al khatmia الخطمية ,الختمية, Al Khatmy الخطمى , Khairu خيرو (4).
English: Marshmallow, White-mallow (5).

2. Parts used for medicinal purpose

Peeled or unpeeled dried root (1, 2, 6- 8) and leaves (1, 5).

3. Major chemical constituents

- **Acidic polysaccharides**: Mucilage (galacturono–rhamnans, arabinans, glucans, arabinogalactans) (1, 9).
- **Flavonoids:** Hypolaetin-8-glucoside, isoquercitrin, kaempferol (10).
- **Phenolic acids:** Caffeic, *p*-coumaric, ferulic, *p*-hydroxybenzoic and syringic acids (1, 9).
- **Others**: Starch, pectin, asparagine, calcium oxalate, coumarins (scopoletin), sucrose, amino acids and tannins (1, 9, 10).

4. Medicinal uses (Indications)

- Demulcent preparation for the symptomatic treatment of oral or pharyngeal irritation associated dry cough (5, 6, 8).
- Demulcent preparation for the symptomatic relief of mild gastrointestinal discomfort (5, 6, 8).

5. Herbal preparations correlated to medicinal use (6)

1. **Comminuted herbal substance as herbal tea**

1.1 Roots.
1.2 leaves.

2. **Liquid extracts**
   - **2.1** extraction solvent water (roots).
   - **2.2** extraction solvent ethanol 25% (V/V).
     - **2.2.1** Roots.
     - **2.2.2** Leaves.
3. **Macerate for preparation of syrup** (roots)
   * To make a macerate pour 150 ml of water (max. temp. 40°C) over one dose of comminuted marshmallow roots. Steep for 30 min., stirring frequently. The filtered macerate should be used immediately after preparation (11).
4. **Dry extract,** extraction solvent water (roots).
5. **Tincture** (1:5) in 25% ethanol (roots) (8).

Herbal preparations (2-5) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1.1

Indication A

Adolescents, adults and elderly: 0.5 - 3 g in 150 ml of water as a macerate several times daily**.** Maximum daily dose: 15 g (5, 6, 11).

Children 6-11 years of age: 0.5–1.5 g in 150 ml of water as a macerate 3 times daily. Daily dose: 1.5 – 4.5 g (5, 6, 11).

Children 3-5 years of age

0.5 – 1.0 g in 150 ml of water as a macerate, 3 times daily

Daily dose: 1.5–3.0 g (5, 6, 11).

Indication B

Adolescents, adults and elderly: Herbal tea: 2 - 5 g in 150 ml of water as a macerate, 3 times daily. Maximum daily dose: 15 g (2, 5, 6, 11).

Preparation 1.2

Indications A and B

Adults: 2 - 15 g daily, not to exceed 5 g per a single dose (5).

Preparation 2.1
Indication A
Adolescents, adults and elderly:
Single dose: 4.6 g, 3 – 6 times daily. Daily dose: 13.8–27.6 g (6).
Children 6-11 years of age:
Single dose: 2.3 g, 5 times daily. Daily dose: 11.5 g (6).
Children 3-5 years of age:
Single dose: 1.9 g, 4 times daily. Daily dose: 7.6 g (6).

Preparation 2.2.1
Indications A and B
Adults and elderly:
Single dose: 2 – 5 ml, 3 times. Daily dose: 6–15 ml (1, 6).

Preparation 2.2.2
Indications A and B
Adults:
2 - 15 ml daily, not to exceed 5 ml per a single dose (5)
2 – 5 ml, 3 times daily (1).

Preparation 3
Indication A
Adolescents, adults and elderly
Single dose: 0.21 - 0.87 g of the herbal substance (10–15 ml of syrup), 3–5 times daily.
Daily dose: 0.63 - 2.9 g of the herbal substance (30–50 ml of syrup) (6).
Children 6-11 years of age
Single dose: 0.1 - 0.29 g of the herbal substance (5 ml of syrup) 3-5 times daily.
Daily dose: 0.32 - 1.45 g of the herbal substance (15–25 ml of syrup) (6).
Children 3-5 years of age
Single dose: 0.1 - 0.29 g of the herbal substance (5 ml of syrup), up to 4 times.
Daily dose: 0.21 - 1.16 g of herbal substance (10–20 ml of syrup), daily (6).

Preparation 4
Indication A
Adolescents, adults and elderly:
Single dose: corresponding to 0.5–3 g of herbal substance, several times daily.
Maximum daily dose: corresponding to 15 g of herbal substance (6).
Children 6-11 years of age
Single dose: corresponding to 0.5–1.5 g of herbal substance, 3 times daily
Daily dose: corresponding to 1.5–4.5 g of herbal substance (6).
Children 3-5 years of age
Single dose: corresponding to 0.5–1 g of herbal substance, 3 times daily
Daily dose: corresponding to 1.5–3 g of herbal substance (6).

Preparation 5 (8)
Indication A
Equivalent to 1-15 g dried root per day, not to exceed 5g per single dose (1:5; in 25% ethanol).

Method of administration (6):
Indication A: Oral or oromucosal use.
Indication B: Oral use

7. Contraindications

Hypersensitivity to the active substances and to other plants of the same family (6).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- For **indication A**, the use in children under 3 years of age requires medical advice before use (6).
- The use of **preparation 2.2** is not recommended in children and adolescents under 18 years of age (6).
- For **indication B**, the use of preparation 1 is not recommended in children under 12 years of age (6).
- The use of **the solid dosage form** in children under 6 years of age is not recommended because of the pharmaceutical form.
- Absorption of concomitantly administered medicines may be delayed. As a precautionary measure, the product should not be taken ½ to 1 hour before or after intake of other medicinal products (2, 6).
- If dyspnoea, fever or purulent sputum occurs during the use of the medicinal product, a doctor or a pharmacist should be consulted (6).

9. Interactions with other medicinal products and other forms of interaction

- **Oral medications:** Marshmallow may reduce the absorption of oral medications; concurrent use should be avoided (2, 11, 12).
- **Antidiabetics** and **Hypoglycemic herbs:** Marshmallow may increase hypoglycemic action (12).
- **Iron salts:** Marshmallow may reduce the absorption of iron salts; separate by two hours (12).
- **Lab Test** (12): **Blood glucose:** Marshmallow decreases blood glucose.

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available (6).

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (6).

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Hypoglycemia, nausea, vomiting, anorexia and hypersensitivity reactions (12).

13. Overdose

No case of overdose has been reported (6).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/last revision

31/8/2022.

References

1	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
2	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, **2**, 5-11.
3	http://www.powo.org.
4	Provençal, P. (2010). The Arabic Plant Names of Peter Forsskål's Flora Aegyptiaco-Arabica. The Royal Danish Academy of Sciences and Letters.
5	Natural Health Product, *Althaea officinalis* L. leaf. (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=2772&lang=eng.
6	European Union herbal monograph on *Althaea officinalis* L. (2016). EMA/HMPC/424583/2015. Committee on Herbal Medicinal Products (HMPC).
7	PDR for herbal medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
8	Natural Health Product, *Althaea officinalis* L. root. (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid bdipsn/atReq.do?atid=althaea.officinalis.root.racine&lang=eng.
9	Bonaterra, G. A., Bronischewski, K., Hunold, P., Schwarzbach, H., Heinrich, EU., Fink, C., Aziz-Kalbhenn, H., Müller, J. and Kinscherf, R. (2020). Anti-inflammatory and anti-oxidative effects of Phytohustil® and root extract of *Althaea officinalis* L. on macrophages *in vitro*. *Front. Pharmacol.,* **11**, 290. doi: 10.3389/fphar.2020.00290.
10	Ali, E. A. (2013). The pharmaceutical importance of *Althaea officinalis* and *Althaea rosea*: A review. *Int. J. Pharm Tech. Res*., **5**(3), 1378-1385.
11	ESCOP Monographs (2019). *Althaea officinalis* L. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills.
12	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Astragalus mongholicus Bunge. الأستراجالاس

1. Names & Synonyms (1, 2)

***Astragalus mongholicus* Bunge.**
Family: Fabaceae (Leguminosae).
Syns.: *A. membranaceus* (Fisch.) Bunge; *A. membranaceus* var. *mongholicus* (Bunge) P. G. Xiao.
Arabic: Astragalus الأستراجالاس.
English name: Astragalus root, Membranous milk vetch, Mongolian milk-vetch.

2. Parts used for medicinal purpose

Dried root (3, 4).

3. Major chemical constituents

- **Flavonoids** (5): Kaempferol and quercetin (and their glycosides) (6), astrasieversianin XV (II) (7).

- **Polysaccharides** (5): Gum (6), astragalan, astraglucan AMem-P (3) and mucilage (5).

- **Triterpenoid saponins**: Astragalosides I–X and isoastragalosides I–IV (3, 6).

- **Sterols**: Daucosterol and β-sitosterol (7).

- **Fatty acids:** Heptenoic, tetradecanoic, pentadecanoic, hexadecanoic, octadecenoic, octadecanoic, octadecadienoic, linoleic, linolenic, palmitic, stearic, eicosanoic, eicosenoic and docosanoic acids (7).

- **Amino acids:** Υ-L-glutamyl-Se-methyl-seleno-L-cysteine, Se-methylseleno-L-cysteine (7).

- **Minerals**: Ni and Cr (5).

4. Medicinal Uses (Indications)

A. As an adaptogen to help increase energy and resistance to stress (e.g. in case of mental and physical fatigue related to stress) (4).

B. Enhance the immune system (3, 8).

C. Treatment of common cold and other upper respiratory tract (3, 9).

5. Herbal preparations correlated to medicinal use (4, 8)

1. Comminuted herbal substances as herbal tea for oral use as infusion or decoction.

2. Powdered herbal substances.

3. Dry ethanolic extract.

4. Fluid ethanolic extract (1:1, 1:2 dilution).

5. Tincture.

Herbal preparations (2-5) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparations 1، 2
Indications A - C
Adults: 9 - 30 g, daily (2-4, 8, 9).

Preparation 3
Indication A
Adult: Equivalent to 2 - 4.8 g of dried root, daily (4).
Indication B
Adults: 100 - 150 mg, 3 times daily (8).

Preparation 4
Indications A and B
Adults: 4.5 - 8.5 ml in divided doses, daily (1:2 dilution) (8, 10).
2 - 4 ml, 3 times daily (1:1 dilution).
Equivalent to 2 - 4.8 g of dried root, daily (4).

Preparation 5
Indication A
Adults: Equivalent to 2 - 4.8 g of dried root, daily (4).
Indications A - C
Adults: 2 - 4 ml, 3 times daily (11).
Method of administration: Oral use (3, 4, 8).

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- It should not be used by persons with acute infections or in the presence of fever or inflammation (8).
- People with autoimmune diseases and who have had transplant surgery should not use it (2).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children and adolescents below 18 years of age is not recommended (4).

9. Interactions with other medicinal products and other forms of interaction (8)

Drugs

-Antihypertensives: Astragalus may decrease or increase the action of antihypertensives; concurrent use should be avoided.

- Cyclophosphamide: Astragalus may decrease the effect of cyclophosphamide.

- Immunosuppressants: Astragalus may interfere with immunosuppressant therapy.

- Interferon: The combination of interferon and Astragalus has been shown to prevent or shorten the duration of upper respiratory infections.

- Interleukin-2: Astragalus may increase the effect of drugs such as interleukin- 2 (IL-2). In contrast, other studies have shown that the effects of IL-2 can be decreased when combined with Astragalus.

- Since an extract showed remarkable inhibiting effects on the metabolism of CYP3A4 *in vitro* and *in vivo*, caution should be taken with drugs that also use this metabolic pathway (2).

Lab Test

- Semen specimen analysis: Astragalus may increase sperm motility *in vitro*.
- PT, INR: Astragalus may increase Prothrombin Time (PT) and International Normalized Ratio (INR).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (4, 8).
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Allergic reactions (rare) (8).

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of last compilation/last revision

23/08/2022.

References

1	http://www.powo.org.
2	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An evidence-based guide to herbal medicinal products. 1st edition. John Wiley & Sons, Ltd.
3	WHO monographs on selected medicinal plants (1999). Monographs on selected medicinal plants **1**, 50-58.
4	Natural Health Product, *Radix astragali* L. (2019). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=36.
5	Noreen, H., Rukhshanda, M., Khattak, Z. R., Minhas, A., Jan, M. and Hassan, W. (2019). Biochemical analysis and mineral composition of methanolic extract of *Astragalus gummifer*. *Biomed. J. Sci. and Tech. Res.*, **20**(1), 14736 – 14741.
6	Roman, L. and Roman, D. (2016). Pharmacology and ethnomedicine of the genus *Astragalus*. *International Journal of Pharmacology, Phytochemistry and Ethnomedicine*, **3**, 46-53.
7	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
8	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
9	American Herbal Pharmacopoeia (1999). Astragalus Root, *Astragalus membranaceus* and *Astragalus membranaceus* var. *mongholicus*. Analytical, Quality Control, and Therapeutic Monograph. ISBN: 1-929425-04-X.
10	Mills, S. and Bone, K. (2013). Principles and Practice of Phytotherapy: Modern Herbal Medicine. Churchill Livingstone, Edinburgh. ISBN: 9780443069925, 0443069921.
11	*Astragulus membranaceus* Monograph (2003). Alternative Medicine Review: *A journal of clinical therapeutic*, **8**(1), 72-77.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Boswellia serrata* Roxb.** لبان داكار

1. Names & Synonyms (1).

***Boswellia serrata* Roxb.**
Family: Burseraceae
Syns.: *Boswellia glabra* Roxb., *Libanotus asiaticus* Stackh., *Libanus thurifer* Colebr., *Chloroxylon dupada* Buch.
English: Boswellia, Indian Frankincense, Indian Olibanum (2,3).
Arabic: Luban لبان (4), luban dhakar لبان داكار (5).

2. Parts used for medicinal purpose

Dried oleogum resin (5-7).

3. Major chemical constituents

The content and composition of the oleogum resin may vary depending upon age, geographical conditions and quality of resin (8-9).

- **Triterpenoic acids:** *α*- and *β*-boswellic acids (BA), acetylated *α*- and-*β*-boswellic acids (ABA), 11-keto-*β*-boswellic acid (KBA), and 3-*O*-acetyl-11-keto-*β* -boswellic acid (AKBA) (8-10).

- **Essential oil:** mainly *α* –pinene, *α* -thujene, *trans*-verbenol, *β*-thujone, *p*-cymene, *m*-cymene and sabinene (11).

- **Carbohydrates:** disaccharides, oligo- and polysaccharides (9).

4. Medicinal uses (Indications) (5,6,12)

A. Management of Inflammatory Bowel Disease (IBD) (ulcerative colitis and Crohn's disease).

B. Management and treatment of rheumatism and arthritis.

C. Management of bronchial asthma and cough.

5. Herbal preparations correlated to medicinal use

1. **Dried resin** (2,6,12).
2. **Resin extracts** (2,5,12) using suitable solvents such as isopropanol, alcohol, methanol, hexane or mixtures of these solvents. The ratio of starting plant material to extract is approximately 6:1 (7).

6. Posology and method of administration correlated to medicinal use

Adolescence and Adults

Preparation 1

1-3 g daily (5,12).

Preparation 2

300-400 mg, 3 times daily (2,5,6) up to 1500 mg daily (13)

Duration of Use:

Indication1: 6 weeks (2).
Indication 2: 4-12 weeks (14).
Indication 3: 6 weeks (15).

Method of administration: Oral use

It should be taken with meals because food intake can significantly increase the bioavailability of boswellic acids (3).

7. Contraindications

- Hypersensitivity to the active substances and to other plants of the same family.
- Pre-existing gastritis (6).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use of the crude drug in children under the age of 12 years is not recommended (5).

9. Interactions with other medicinal products and other forms of interaction

Boswellia may interact with conventional drugs by inhibiting P-glycoprotein and/or cytochrome P450 isoenzymes (3).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No Fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Rare side effects may include retrosternal burning, nausea, abdominal fullness, epigastric pain, anorexia, dermatitis and skin rash (6,12).

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/last revision

18/05/2023.

References

1	www.powo.science.kew.org
2	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
3	Williamson, E.M., Driver, S. and Baxter, K. (2013). Stockley's Herbal Medicines Interactions. 2nd edition. Pharmaceutical Press, London, UK.
4	Sultana, A., Ur Rahman, K., Padmaja, A. R. and Shafeeq Ur Rahman, S. (2013). *Boswellia serrata* roxb. A traditional herb with versatile pharmacological activity: A review. *IJPSR*, **4**(6), 2106-2117.
5	WHO monographs on selected medicinal plants (2009). Monographs on Selected Medicinal Plants, **4**, 48-60.
6	Spiteri, M. (2011). Herbal Monographs including Herbal Medicinal Products and Food Supplements. Department of Pharmacy University of Malta. Set and printed by Print Right Ltd, Qormi.
7	The United States Pharmacopeial Convention (2011). *Boswellia serrata* extract, 1215-1217.
8	Sharma, N., Bhardwaj, V., Singh, S., Ali, S. A., Gupta, D. K., Paul, S., Satti, N. K., Chandra, S. and Verma, M. K. (2016). Simultaneous quantification of triterpenoic acids by high performance liquid chromatography method in the extracts of gum resin of *Boswellia serrata* obtained by different extraction techniques. *Chem. Cent. J.,* **10**, 49. doi: 10.1186/s13065-016-0194-8.
9	Tošić, N. G., Nikolić, V. D., Miljković, V. M. and Nikolić, L. B. (2022). *Boswellia serrata* resin isolates: Chemical composition and pharmacological activities (Review paper). *Advanced Technologies,* **11**(1), 76-87. DOI 10.5937/savteh2201076T.
10	Roy, N. K., Parama, D., Banik, K., Bordoloi, D., Devi, A. K., Thakur, K. K., Padmavathi, G., Shakibaei, M., Fan, L., Sethi, G. and Kunnumakkara, A. B. (2019). An update on pharmacological potential of boswellic acids against chronic diseases. *Int. J. Mol Sci.,* **20**(17), 4101. DOI: 10.3390/ijms20174101.
11	Ayub, M. A., Hanif, M. A., Blanchfield, J., Zubair, M., Abid, M. A. and Saleh, M. T. (2022). Chemical composition and antimicrobial activity of *Boswellia serrata* oleo-gum-resin essential oil extracted by superheated steam. *Natural Product Research*, **37**(14), 2451-2456. DOI: 10.1080/14786419.2022.2044327.
12	Duke, J. A. (2002). Handbook of Medicinal Herbs. 2nd ed. CRC Press. ISBN 978084931284.
13	https://www.healthline.com/health/boswellia#side-effects.
14	Yu, G., Xiang, W., Zhang, T., Zeng, L., Yang, K. and Li, J. (2020). Effectiveness of *Boswellia* and *Boswellia* extract for osteoarthritis patients: a systematic review and meta-analysis. *BMC Complement. Med. Ther*., **20**(1), 225. DOI: 10.1186/s12906-020-02985-6.
15	Gupta, I., Gupta, V., Parihar, A., Gupta, S., Lüdtke, R., Safayhi, H. and Ammon, H. P. (1998). Effects of *Boswellia serrata* gum resin in patients with bronchial asthma: results of a double-blind, placebo-controlled, 6-week clinical study. *Eur. J. Med. Res*., **3**(11), 511-514.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Camellia sinensis L. Kuntze شاي اخضر

1. Names & Synonyms

***Camellia sinensis* L. Kuntze**

Family: Theaceae.

Syns.: *Camellia thea* Link**,** *Thea sinensis* L., *Thea viridis* L. (1-3).

Arabic: Shai akhder شاى اخضر

English name: Green tea (2, 4, 5), Chinese tea (3).

2. Parts used for medicinal purpose

Dried leaves (4, 5).

3. Major chemical constituents

- **Catechins**: (-)-Epigallocatechin-3-gallate (EGCG), (-)-epigallocatechin (EGC), (-)-epicatechin-3-gallate (ECG),-and (-)-epicatechin (EC) (6, 7).
- **Phenolic acids:** Gallic acid, chlorogenic acid, theogallin, neochlorogenic acid, caffeoylquinic acid (4, 7, 8).
- **Alkaloids**: Caffeine (9), theobromine, and theophylline (4, 10)
- **Amino acids:** L-Theanine (7).
- **Flavonoids**: Quercitin-3-D-galactoside and kaempferol-3-glucoside (4, 7).

4. Medicinal Uses (Indications)

A. For relief of fatigue and sensation of weakness (4).

B. Weight reduction and management through following diet and increase physical activity during weight control programs (2).

5. Herbal preparations correlated to medicinal use

1. **Comminuted herbal substance as decoction or infusion** (2, 4).
2. **Powdered herbal substance** (4).
3. **Standardized extracts** (2, 5).
   - **3.1.** Dry extract.
   - **3.2.** Liquid extract.
4. **Tincture** (2).

Herbal preparations (2–4) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1
Indication A: 1.8 – 2.2 g of whole or comminuted herbal substance in 100 – 150 ml of boiling water, 3 – 5 times, daily (4).

Preparation 2
Indication A: 390 mg, 3 times daily (up to 5 times if necessary) (4).

Preparations 3 - 5
Indication B: 136 - 300 mg EGCG and 75 – 150 mg caffeine, daily (2).

Duration of use:
If the symptoms of fatigue or weakness persist longer than one week during the use of the medicinal product, a doctor or a pharmacist should be consulted (4).

Method of administration: Oral use (4).

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Gastric and duodenal ulcers, cardiovascular disorders such as hypertension and arrhythmia, hyperthyroidism, kidney inflammation, insomnia or increased intraocular pressure (4, 5).

8. Special warnings and precautions for use

- If symptoms worsen during the use of the medicinal products a doctor or pharmacist should be consulted.
- Use should be stopped and a doctor or pharmacist should be consulted if symptoms developed as liver trouble such as yellowing of the skin/eyes (jaundice), stomach pain, dark urine, sweating, nausea, unusual tiredness and/or loss of appetite (2).
- A doctor or pharmacist should be consulted if you have liver disorder or iron deficiency (2).
- The use in children and adolescents under 18 years of age is not recommended (4).
- Use is not rrecommended before bedtime as it may cause sleep disturbances (4).

9. Interactions with other medicinal products and other forms of interaction (5)

- **Beta-adrenergic blockers**: Green tea used with these agents may increased inotropic effects.
- **Bronchodilators, xanthines (theophylline)**: Large amounts of green tea increase the action of some bronchodilators, xanthines.
- **MAOIs**: Green tea used in large amounts with MAOIs can lead to hypertensive crisis, concurrent use should be avoided.
- **Ephedra**: Concurrent use of ephedra and caffeinated green tea may increase hypertension and CNS stimulation; concurrent use should be avoided.
- **Dairy products**: Dairy products may decrease the therapeutic effects of green tea.
- **Iron**: Green tea may decrease iron absorption.
- **Caffeine** containing preparations reduce sedative action and increase side effects caused by sympathomimetic drugs.
- The resorption of alkaline medications can be delayed because of chemical bonding with the tannins.
- **Lab Test**: Glucose, urine creatine, urine catecholamine: Green tea may increase these levels.

10. Fertility, pregnancy and lactation (4)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (4)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- None reported.
- If adverse reactions occur a doctor or a pharmacist should be consulted.

13. Overdose

- Anxiety, nervousness, insomnia, increased blood pressure, palpitations, irregular heartbeat, nausea, heartburn, increased stomach acid (3, 5).
- Quantities corresponding to more than 300 mg caffeine or 5 cups of tea can lead to restlessness, tremor and elevated reflex excitability. The first signs of poisoning are vomiting and abdominal spasm (4).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

–

16. Date of compilation/last revision

16/08/2022.

References

1	https://powo.science.kew.org.
2	Natural Health Product, Green Tea Extract (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=greentea_thevert&lang=eng.
3	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An evidence-based guide to herbal medicinal products. 1st edition. John Wiley & Sons, Ltd.
4	Community herbal monograph on *Camellia sinensis* (L.) Kuntze, non fermentatum folium (2013). EMA/HMPC/283630/2012. Committee on Herbal Medicinal Products (HMPC).
5	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
6	Lee, L. S., Kim, S. H., Kim, Y. B. and Kim, Y. C. (2014). Quantitative analysis of major constituents in green tea with different plucking periods and their antioxidant activity. Molecules, **19**(7), 9173 -9186.
7	Barreira, S., Carla, M., André, M. N. Silva, J. N., Ean-Jeong, S., Mohamed-Elamir, F. H., Thomas, E. and Lígia, R. G. (2021). Phytochemical characterization and biological activities of Green tea (*Camellia sinensis*) produced in the Azores, Portugal. *Phytomedicine Plus*, **1**(1), 100001.
8	Graham, H. N. (1992). Green tea composition, consumption, and polyphenol chemistry. *Prev. Med*., **21**, 334–350. DOI: 10.1016/0091-7435(92)90041-f.
9	De Oliveira, A. P., Guimarães, A. L., De Oliveira-Júnior, R. G., Quintans, J. S., De Medeiros, F. A., Barbosa-Filho, J. M., Quintans-Júnior, L. J. and Guedes da Silva Almeida, J. R. (2016). *Camellia sinensis* (L.) Kuntze: A Review of chemical and nutraceutical properties. In book: Natural Products: Research Reviews, **4**, 21-62. 1st edition. Publisher: Daya Publishing House, New Delhi. Editor: Gupta, V. K.
10	Chacko, S. M., Thambi, P. T, Kuttan, R. and Nishigaki, I. (2010). Beneficial effects of green tea: a literature review. *Chin. Med*., **6**(5), 13. doi: 10.1186/1749-8546-5-13.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Carum carvi* L.** كراوية

1. Names & Synonyms (1)

***Carum carvi* L.**

Family: Apiaceae (Umbelliferae).

Syns. *Carum velenovskyi* Rohlena.

Arabic: karawya كراوية

English: Caraway.

2. Parts used for medicinal purpose

Dried fruits (2, 3).

3. Major chemical constituents

- **Essential oil:** mainly carvone and limonene (5).
- **Fatty acids**: mainly unsaturated fatty acids as petroselinic, linoleic and oleic acids beside saturated fatty acids as myristic and palmitic acids (5, 6).
- **Flavonoids**: quercetin, kaempferol and their glycosides (quercetin-3-glucuronides, quercetin 3-*O*-caffeoylglucoside and kaempferol 3-glucoside) and isoquercitrin (5, 7).
- **Protein** (5).

4. Medicinal uses (Indications)

A. For the symptomatic relief of digestive disorders such as bloating, flatulence, and digestive spasms (2, 4).
B. To aid digestion and help stimulate appetite (stomachic) (8).
C. For relief of flatulent colic in infants and children (3).

5. Herbal preparations correlated to medicinal use

1. **Herbal substance or comminuted herbal substance as herbal tea for oral use** (2)

0.5-2 g of the herbal substance or comminuted herbal substance in 150 ml of boiling water as herbal infusion (2).

2. **Liquid extract** (8).
3. **Dry extract** (8).
4. **Essential oil** (3, 4, 8).

Herbal preparations (2-4) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1
Indications A, B
Adults: herbal tea for oral use 1-3 times daily (2).

Preparation 2, 3
Indications A, B
The equivalent extract of the following amount of the dried fruit (g/day) (8):

Adults 18 years and older	0.3-15 g
Adolescents 12-17 years	0.3-15 g
10-11 years	0.3-15g
4-9 years	0.3 -4 g
Children 1-3 years	0.3 -2 g
Infants 6-12 months	0.06 -1 g

Preparation 4
Indications A, B
Oral (3, 9):
Adults18 years and older: 3 – 6 drops (0.15-0.3 ml (4)) in divided doses daily.
Children above 4 years: 3 – 6 drops daily.
Children 1-3 years: 2 – 4 drops daily.
Children up to 1 year: 1–2 drops daily.

Indication C
External (3, 4):
Children and adolescents: an ointment (2% w/w) to be applied once daily in the evening as a thin layer on the abdominal area after bathing.

Adults: 10% in olive oil, rub 10-12 drops onto the stomach (10).

Method of administration: Oral and cutaneous use (2, 3, 8).

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- The use in patients with liver disease, cholangitis, achlorhydria, gallstones and any other biliary disorders are not recommended (4).
- The product should not be used on broken skin, around the eyes or on mucous membranes (4).
- Caraway should not be used in gastroesophageal reflux disease (11).

8. Special warnings and precautions for use

If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted (2, 4).

9. Interactions with other medicinal products and other forms of interaction

None reported (2, 4).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (2, 4, 8, 11).
- No fertility data available (2,4).

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (2, 4).

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Anorexia, diarrhea, skin redness, irritation and contact dermatitis (11).

13. Overdose

An intake of over dose of the volatile oil for extended periods can lead to kidney and liver damage (11, 12).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

31/05/2022.

References

1	Duke, J. A. (2002). Handbook of Medicinal Herbs. 2nd ed. CRC Press. ISBN 978084931284.
2	European Union Herbal Monograph on *Carum carvi* L., fructus (2015). EMA/HMPC/715092/2013. Committee on Herbal Medicinal Products (HMPC).
3	ESCOP Monographs (2019). *Carvi aetheroleum*, Caraway Oil. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills. ISBN 978-1-901964-65-3.
4	European Union Herbal Monograph on *Carum carvi* L., aetheroleum (2015). EMA/HMPC/715094/2013 Committee on Herbal Medicinal Products (HMPC).
5	Mahboubi, M. (2019). Caraway as important medicinal plants in management of diseases. *Natural Products and Bioprospecting*, **9**, 1–11. https://link.springer.com/content/pdf/10.1007/s13659-018-0190-x.pdf.
6	Laribi, B., Kouki, K., Bettaieb, T., Mougou, A., and Marzouk, B. (2013). Essential oils and fatty acids composition of Tunisian, German and Egyptian caraway (*Carum carvi* L.) seed ecotypes: A comparative study. *Ind. Crops Prod.*, **41**, 312–318.
7	Al-Snafi, A. E. (2015). The chemical constituents and pharmacological effects of *Carum carvi*- A review. *Indian Journal of Pharmaceutical Science & Research*, **5** (2), 72-82.
8	Natural Health Product Caraway – *Carum carvi* (2019). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=caraway.carvi&lang= eng.
9	Dorsch, W., Loew, D., Meyer-Buchtela, E. and Schilcher, H. (2002). In: Kinderdosierungen von Phytopharmaka. Kooperation Phytopharmaka GbR, Bonn, **51**.
10	Weiss, R and Fintelmann, V. (2000). In: Herbal Medicine (2nd Edition), Georg Thieme Verlag, Stuttgart, New York, 74-75.
11	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
12	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Chamaemelum nobile* L.** بابونج

1. Names & Synonyms

***Chamaemelum nobile* L.** (1).
Family: Asteraceae/Compositae (1).
Syns.: *Anthemis nobilis* L., Chamomile, *Ormenis nobilis* L. J. Gay ex Coss. & Germ. (1).
Arabic: Baboonig بابونج .
English name: Roman chamomile flower (2).

2. Parts used for medicinal purpose

Flowerheads (2-4).

3. Major chemical constituents

- **Essential oil**: Esters of angelic and tiglic acids, 1,8 cineole, 1-*trans*-pinocarveol, 1-*trans*-pinocarvone, chamazulene, farnesol, and nerolidol (1, 5).
- **Phenolic compounds**: **Flavonoids:** Apigenin, luteolin, quercetin and their glycosides. **Phenolic acids**: caffeic and ferulic acids. **Coumarins:** scopolin, umbelliferone and herniarin (1, 5).
- **Sesquiterpenes lactones:** Nobilin, 3-epinobilin, 1, 10-epoxynobilin and 3-dehydronobilin (1, 5).
- **Others**: Anthemic acid, fatty acids, phytosterols, choline and inositol (1).

4. Medicinal Uses (Indications)

A. Internal use: Symptomatic treatment of mild, spasmodic gastrointestinal complaints including bloating and flatulence (2-4).

B. External use: Minor inflammations of the oral mucosa and skin in wounds and abrasions; as an itch-relieving agent; for treatment to promote wound healing (4, 6).

5. Herbal preparations correlated to medicinal use

1. Comminuted herbal substance as herbal tea infusion or decoction for oral use, or herbal substance for external use (2, 3).
2. Liquid extract, extraction solvent ethanol 70% v/v (2, 4).

Herbal preparation (2) is in a pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1
Indication A
Adolescents, adults and elderly: 1-4 g in 100-150 ml of boiling water as herbal tea 3 times daily between the meals (1-4).

Indication B (4)

- 3% infusion in poultices or mouthwashes, 2 – 3 times daily.
- 5 - 15% of the drug or equivalent (as semi-solid preparations), as needed.

Preparation 2
Indication A
Adolescents, adults and elderly: 1 - 4 ml, 3 times daily (1, 2, 4).

Duration of use: If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor should be consulted (2).

Method of administration: Oral administration (1-4), oromucosal and topical applications (4).

7. Contraindications

Hypersensitivity to the active substance and to other plants of the same family.

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children under 12 years of age is not recommended (2, 4, 6).
- Roman chamomile may precipitate an allergic reaction or exacerbate existing symptoms in susceptible individuals (e.g. asthmatics) (1).

9. Interactions with other medicinal products and other forms of interaction (4)

- As a precaution, Roman chamomile should not be used concomitantly with aspirin, warfarin or other substances possessing anticoagulant activity

- Since apigenin is a ligand for the central benzodiazepine receptor, Roman chamomile should not be used concurrently with diazepam or other benzodiazepines, as this may potentiate their action
- Roman chamomile essential oil exhibited ≤ 40% inhibition of CYP3A4 activity.

10. Fertility, pregnancy and lactation

- Roman chamomile is a known abortifacient and should not be used during pregnancy and breastfeeding (4).
- No fertility data available (2).

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (2).

12. Undesirable effects

- None reported (2).
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

13. Overdose

- No case of overdose has been reported (2).
- Large doses of Roman chamomile are stated to act as an emetic (1).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of last revision

1/9/2022.

References

1	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
2	European Union Herbal monograph on *Chamaemelum nobile* L. (2011). EMA/HMPC/424583/2010. Committee on Herbal Medicinal Products (HMPC).
3	Natural Health Product, *Chamaemelum nobile* L. (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=153&lang=eng.
4	ESCOP Monographs (2019). *Chamaemelum nobile* L. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills.
5	Sadiki, F. Z. and El Idrissi, M. (2019). Chemical composition of essential oil of *Anthemis nobilis* L. flowers from Morocco. *Appl. J. Envir. Eng. Sci.,* **5**(4), 342-348.
6	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Cinnamomum verum J. Presl قرفة

1. Names & Synonyms (1)

***Cinnamomum verum* J. Presl.**
Family: Lauraceae.
Syns.: *Camphorina cinnamomum* (L.) Farw., *Cinnamomum zeylanicum* var. *commune* Meisn., *Cinnamomum zeylanicum* var. *vulgare* Hayne, *Laurus cinnamomum* L.
Arabic: Qirfah قرفة
English name: Cinnamon, Ceylon cinnamon, true cinnamon (2,3).

2. Parts used for medicinal purpose

Dried inner bark (decorticated) (2-10).

3. Major chemical constituents

-Essential oil: Cinnamaldehyde, methoxy-cinnamaldehyde**,** linalool, *β*-caryophyllene, eucalyptol, eugenol, copaene, cadina-3,9-diene, cadina-4,9-diene and 17-pentatriacontene (11-15).

-Polyphenols (12)**:**
Procyanidins: Procyanidin (A-type) trimers and tetramers (11).
Phenolic acids*:* Protocatechuic and cinnamic acids.
Flavanols**:** Catechin.

-Fatty acids/esters: Stearic and palmitic acids, glycerol monostearate and 1-monopalmitin (12).

-Organic acids: Quinic and oxalic acids (12).

-Others: sugars (glucose, fructose), diterpenes (cinncassiols A and B, cinnzeylanol and its acetyl derivative cinnzeylanine) (12, 16).

4. Medicinal Uses (Indications)

A. Symptomatic treatment of mild spasmodic gastrointestinal complaints (dyspeptic conditions) including bloating and flatulence (2, 4, 7) and for anorexia (loss of appetite) (2, 7, 8, 10).

B. Symptomatic treatment of mild diarrhoea (2-4, 7, 17) and to treat abdominal pain with diarrhoea (2).

C. Treatment of pain associated with amenorrhoea and dysmenorrhoea (2, 4, 7, 18).

5. Herbal preparations correlated to medicinal use

1. Comminuted herbal substance as an herbal tea in the form of infusion or decoction (3, 5, 17).
2. Powdered drug (2, 4) (or its equivalent as a dry extract).
3. Liquid extract (5, 17) (Ethanol 70%) (4, 6).
4. Tincture (Ethanol 70%, 1:5) (5, 6, 17, 19).
5. Essential oil (2, 4, 6, 20).

Herbal preparations (2-5) are in a pharmaceutical dosage form. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use.

Adults and elderly
Preparation 1

- 0.5 - 1 g, up to 4 times daily (2, 4, 6, 8, 17).
- One teaspoonful/ cup water, 2-3 times daily with meals (4, 21).

Preparation 2
Daily dose, 2–4 g, in divided doses (2, 4, 5).

Preparation 3
Single dose: 0.5 - 1 ml, 3 times daily, up to 4 ml daily (2, 4, 5, 8, 17, 21).

Preparation 4
Daily dose: 2 - 4 ml (2, 4, 8, 10, 17).

Preparation 5
Indication A
50 to 200 mg (0.05-0.2 ml), daily in 2 - 3 divided doses, diluted in carrier oil (vegetable oil) (2, 4, 5, 22, 20).

Duration of use (17):
Indication A: If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.
Indication B: If the symptoms persist longer than two days, a doctor or a pharmacist should be consulted.
Indications C and D: As directed by a physician.

Method of administration: Oral use.

7. Contraindications

- Hypersensitivity to the active substance or to Peru balsam (5, 17, 20).
- The use in children and adolescents under 18 years of age has not been established (5, 17, 20).
- In cases of fever of unknown origin, stomach or duodenal ulcers, major surgery, haemophilia and other bleeding disorders (2, 22).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Rehydration should be the first measure in case of diarrhoea (17).
- If recurrent diarrhoea or bloody stools occur, a doctor should be consulted (17).
- Contact with the skin by undiluted cinnamon oil is frequently irritating, associated with a burning sensation and occasional blistering (22).

9. Interactions with other medicinal products and other forms of interaction

- Diabetes and anticoagulant medications (22).
- May reduce activity of tetracycline (2).

10. Fertility, pregnancy and lactation

- It should not be used during pregnancy and breastfeeding (5, 17, 20).
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.

- Allergic reactions of the skin and local irritation of the oral mucosa (2, 17, 20, 22).

13. Overdose

High doses cause vomiting (4).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of last compilation/last revision

16/07/2023.

References

1	www.science.kew.org
2	WHO monographs on selected medicinal plants (1999). Monographs on selected medicinal plants, **1**, 95-104.
3	Edwards, S. E., Rocha, I. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st ed., John Wiley & Sons, Ltd. ISBN: 978-1-118-54356-6.
4	Duke, J. A. (2002). Handbook of Medicinal Herbs. 2nd ed. CRC Press. ISBN 978084931284.
5	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed. ISBN: 978-0-323-05741-7.
6	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
7	https://www.herbalgram.org/resources/herbalgram/issues/95/table-of contents/herbalgram-95-herb-profile-cinnamon/
8	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
9	https://www.health.belgium.be/nl/cinnamomum-verum.
10	Spiteri, M. (2011). Herbal Monographs including Herbal Medicinal Products and Food Supplements. Department of Pharmacy University of Malta. Set and printed by Print Right Ltd, Qormi.
11	Elgendy, E. M., Ibrahim, H. S., Elmeherry, H. F., Sedki, A. G. and Mekhemer, F. U. (2017). Chemical and biological comparative *in vitro* studies of Cinnamon bark and lemon peel essential oils. *Food and Nutrition Sciences*, **8**, 110 – 125.
12	Farag, M. A., Kabbash, E. M., Mediani, A., Döll, S., Esatbeyoglu, T. and Afifi, S. M. (2022). Comparative metabolite fingerprinting of four different Cinnamon species analyzed via UPLC–MS and GC–MS and chemometric tools. *Molecules,* **27**, 2935. https://doi.org/10.3390/molecules27092935.
13	Behbahani, B. A., Falah, F., Arab, F. L., Vasiee, M. and Yazdi F. T. (2020). Chemical composition and antioxidant, antimicrobial, and antiproliferative activities of *Cinnamomum zeylanicum* bark essential oil. *Evidence-Based Complementary and Alternative Medicine*, Article ID: 5190603. https://doi.org/10.1155/2020/5190603.
14	Singh, G., Maurya, S., deLampasona, M.P. and Catalan, C.A.N.(2007). A comparison of chemical, antioxidant and antimicrobial studies of cinnamon leaf and bark volatile oils, oleoresins and their constituents. *Food and chemical toxicology*, **45**(9), 1650-1661.
15	Sharifi-Rad, J., Dey, A., Koirala, N., Shaheen, S., El Omari, N., Salehi, B., Goloshvili, T., Cirone Silva, N. C., Bouyahya, A., Vitalini, S., Varoni, E. M., Martorell, M., Abdolshahi, A., Docea, A. O., Iriti, M,, Calina, D, Les, F., López, V. and Caruntu, C. (2021). *Cinnamomum* Species: Bridging phytochemistry knowledge, pharmacological properties and toxicological safety for health benefits. *Front. Pharmacol.*, **11**(12), 600139. doi: 10.3389/fphar.2021.600139.
16	Pathak, R. and Sharma, H. (2021). A Review on medicinal uses of *Cinnamomum verum* (Cinnamon). *Journal of Drug Delivery and Therapeutics*, **11**(6-S): 161-166. doi: http://dx.doi.org/10.22270/jddt.v11i6-S.5145.

17	European Union Herbal Monograph on *Cinnamomum verum* J.S. Presl, Cortex (2011). EMA/HMPC/246774/2009. Committee on Herbal Medicinal Products (HMPC).
18	Heinrich, M., Barnes, J., Gibbons, S. and Williamson, E. M. (2012). Fundamentals of Pharmacognosy and Phytotherapy. 2nd edition, Elsevier Churchill Livingstone. ISBN 978-0-7020-3388-9.
19	Fisher, C. and Painter G. (1996). Materia Medica for the Southern Hemisphere. Auckland: Fisher-Painter Publishers.
20	European Union Herbal Monograph on *Cinnamomum verum* J.S. Presl, corticis aetheroleum (2011). EMA/HMPC/706229/2009 Committee on Herbal Medicinal Products (HMPC).
21	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements, An evidence-Based Guide, 3rd ed. ISBN: 978 0 7295 3910 4.
22	Tisserand, R. and Young, R. (2014). Essential Oil Safety. A Guide for Health Care Professionals, 2nd ed. Churchill Livingstone. ISBN 978-0-443-06241-4.

Egyptian Herbal Monograph
Medicinal Plants Used in Egypt

***Coffea arabica* L.** قهوة خضراء

1. Names & Synonyms (1)

***Coffea arabica* L.**

Family: Rubiaceae.

Syns.: *Coffea bourbonica* Pharm. ex Wehmer. *C. corymbulosa* Bertol. *C. laurifolia* Salisb. *C. moka* Heynh. *C. sundana* Miq. *C. vulgaris* Moench.

Arabic: Kahwa khadra قهوة خضراء .

English name: Green coffee.

2. Parts used for medicinal purpose

Unroasted beans (2).

3. Major chemical constituents

- **Phenolic acids and derivatives:** Chlorogenic acids (composed of four isomers where the most common isomer is 5-*O*-caffeoylquinic acid (5-CQA) (3), followed by di-caffeoylquinic (diCQA), feruloylquinic (FQA) and *p*-coumaroylquinic acids (4,5).
- **Alkaloids:** Caffeine and trigonelline (6).
- **Diterpenes:** Coffeol and 16-*O*-methyl-coffeol (7).
- **Lipids**: mainly as linoleic and palmitic acids (8).
- **Others**: Insoluble polysaccharides (8), proteins, fats, tannins, minerals (mainly potassium, calcium, magnesium), sterols (*β*-sitosterol, stigmasterol, campesterol, cholesterol, Δ^5-avenasterol, $^7\Delta$-avenasterol and Δ^7-stigmastenol), anthranone compounds (mangiferin, isomangiferin), coumarin (scopoletin), and carotenoids (7).

4. Medicinal Uses (Indications) (2)

A. Weight management during weight control diet program.

B. Adjunct therapy in hypertension and cardiovascular diseases.

5. Herbal preparations correlated to medicinal use (2)

1. Comminuted herbal substance as decoction or infusion.
2. Liquid extract.
3. Dry extract.
4. Tincture.

Herbal preparations (2-4) are in a pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use (2)

Adults:
Preparations 1–4
Indication A
400 - 1000 mg daily, standardized to 45-50% chlorogenic acids and up to 4% caffeine.

Indication B
115 - 1000 mg daily, standardized to 45-50% chlorogenic acids and up to 4% caffeine.

Method of administration: Oral use.

Duration of use: Up to 12 weeks (9).

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Children and adolescent less than 18 years of age (2).

8. Special warnings and precautions for use

- If symptoms worsen during the use of the medicinal products, a doctor or pharmacist should be consulted.
- Patients with sensitive cardiovascular systems, kidney diseases, hyperthyroidism, higher disposition to convulsions and certain psychic disorders (including panic anxiety states) should consult the physician before use (10).
- Green coffee beans extract (maximum 4% caffeine) cannot be combined with caffeine or other medicinal or non-medicinal ingredients containing caffeine (2, 11).
- Caffeine should be used with caution in patients with type-2 diabetes and the blood sugar should be monitored (9).

- In osteoporosis, limit caffeine consumption to less than 300 mg daily. Caffeine can increase the amount of calcium that is flushed out in the urine; this might weaken the bones (9).
- People with epilepsy should avoid using caffeine in high doses; even low doses of caffeine should be used cautiously (9).
- Caffeine can increase pressure inside the eye, which can make glaucoma worse and might increase blood pressure in people with hypertension (9).

9. Interactions with other medicinal products and other forms of interaction (12)

- Concurrent use with stimulant drugs might cause too much stimulation and sometimes serious side effects and heart problems.
- Taking green coffee along with medications that slow blood clotting might increase the risk of bruising and bleeding.
- Taking caffeine along with nicotine/medications for depression (MAOIs) might increase heart rate and blood pressure.

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data is available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- Green coffee does contain caffeine, which can have numerous side effects as anxiety, jitteriness and rapid heartbeat. (13)
- If adverse reactions occur a doctor or a pharmacist should be consulted.

13. Overdose (10, 13)

- Consuming a high dose of chlorogenic acid might increase homocysteine levels, which might be linked to conditions such as heart diseases.

- Caffeine when taken in large amounts can worsen diarrhoea in some people with irritable bowel syndrome and might make anxiety and bleeding disorders worse.
- Consuming large amounts of green coffee might cause caffeine-related side effects, including hyperacidity, reduced appetite, sleeplessness, anxiety, tremor, nervous restlessness, palpitations and withdrawal headaches.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

Green coffee is considered as a source of antioxidants (2).

16. Date of last revision

08/06/2023.

References

1	www.powo.science.kew.org
2	Natural Health Product. Green Coffee Bean Extract (2018). Health Canada. https://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=greencoffeebean.ext. fevescafevert&lang=eng
3	Rojas-González, A., Figueroa-Hernández, C. Y., González-Rios, O., Suárez-Quiroz, M. L., González-Amaro, R. M., Hernández-Estrada, Z. J . and Rayas-Duarte, P. (2022). Coffee chlorogenic acids incorporation for bioactivity enhancement of foods. *Molecules,* **27**(11), 3400. doi: 10.3390/molecules27113400.
4	Farah, A. and Donangelo, C. M. (2006). Phenolic compounds in Coffee. *Braz. J. Plant Physiol.*, **18**, 23–36.
5	Pimpley, V., Patil, S., Srinivasan, K., Desai, N. and Murthy, P. S. (2020). The chemistry of chlorogenic acid from green coffee and its role in attenuation of obesity and diabetes. *Prep. Biochem. Biotechnol.,* **50**(10), 969-978. doi: 10.1080/10826068.2020.1786699.
6	Sualeh, A., Tolessa, K. and Mohammed, A. (2020). Biochemical composition of green and roasted coffee beans and their association with coffee quality from different districts of southwest Ethiopia. *Heliyon,* **6**(12), e05812. doi: 10.1016/j.heliyon.2020.e05812.
7	Saud, S. and Salamatullah, A. M. (2021). Relationship between the chemical composition and the biological functions of Coffee. *Molecules,* **26**(24), 7 634. doi: 10.3390/molecules26247634.
8	Solange I. Mussatto, S. I., Ercília M. S. Machado, E. M. S., Martins, S. and Teixeira, J. A. (2011). Production, composition, and application of Coffee and its industrial residues. *Food Bioprocess Technol.*, **4**, 661–672. doi 10.1007/s11947-011-0565-z.
9	https://medlineplus.gov/druginfo/natural/1264.html
10	Spiteri, M. (2011). Herbal monographs including herbal medicinal products and food supplements. Department of Pharmacy, University of Malta. Set and printed by Print Right Ltd, Qormi.
11	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
12	GREEN COFFEE: Overview, Uses, Side Effects, Precautions, Interactions, Dosing and Reviews (http://www.webmd.com)
13	https://www.medicalnewstoday.com/articles/318611

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Crataegus* spp.** زعرور

1. Names & Synonyms (1)

***Crataegus* spp.**
(Mainly *C. laevigata* (Poir.) DC., *C. monogyna* Jacq., *C. rhipidophylla* Gand., and their hybrids).

Crataegus laevigata (Poir.) DC.
Syn.: *Crataegus oxyacanthoides* Thuill., *C. oxyacantha* auct.

Crataegus monogyna Jacq.
Syn.: *Crataegus oxyacantha* L., nom. ambig.

Crataegus x *sinaica* Boiss. (2)
Syn.: *C. azarolus* × *C. monogyna*.

Family: Rosaceae
Arabic name: Za'arour زعرور (2)
English name: Hawthorn (3-5).

2. Parts used for medicinal purpose

Fresh and dried leaves with flowers (4-6), and dried fruits (berries) (1,3,4,7).

3. Major chemical constituents

1. Phenolics:
- Flavan-3-ols: (-)-Epicatechin, catechin (5), and procyanidins B2, B5, C-1 and D1 (8,9).
- Flavonols: Isoquercitrin, rutin, hyperoside, and quercetin (5).
- Flavones: Vitexin, vitexin-rhamnoside (8,9), and isovitexin (5).
- Phenolic acids: Chlorogenic, ferulic (10) and caffeic acids (5).

2. Triterpenic acids: Oleanolic, ursolic (8,9,11) and crataegolic acids (5).

3. Pectin (in fruits only) (12).

4. Medicinal Uses (Indications)

A. Adjunct therapy for heart failure stage ll (6,7).
B. Relieve symptoms of temporary nervous cardiac complaints (e.g. palpitations, perceived extra heart beat due to mild anxiety) after serious conditions have been excluded (5).
C. Relief of mild symptoms of mental stress and to aid sleep (5).

5. Herbal preparations correlated to medicinal use (5)

1. **Comminuted herbal substance as herbal tea** in the form of infusion.
2. **Powdered herbal substance**.
3. **Dry extract**
   3.1 Ethanol (45-70%)
   3.2 Water
4. **Liquid extract**
   4.1 Ethanol 45% (DER 1:0.9-1.1)
   4.2 Ethanol 45% (DER 1:2)
   4.3 Ethanol 25% (1: 1)
5. **Expressed juice from the fresh leaves with flowers**
   5.1 (DER 1:0.63-0.9)
   5.2 (DER 1:0.9-1.1)
6. **Tincture** (Ethanol 35%- 45%) (1:5) (13).

Herbal preparations (2-6) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1
Adults and elderly (5)
Indication A

- 1-1.5 g of dried leaves with flowers, 3-4 times daily (3,6).

Indication B

- 1-2 g of dried leaves with flowers, up to 4 times daily (max. 6 g) (3,5).
- 0.3–1 g of dried fruits, 3 times daily, up to 3.5 g (3,4,13).

Preparation 2 (5)
Indication B
Adults and elderly
Single dose: 190 - 350 mg of dried leaves with flowers, daily dose: 570 - 1750 mg.
Indication C
Adolescents, adults and elderly
Single dose: 190 - 350 mg of dried leaves with flowers, daily dose: 570 - 1750 mg.
1– 3 g dry fruits daily (13).

Preparation 3.1
Adults and elderly
Indications A and B

- 160 - 900 mg of dried leaves with flowers daily in divided doses, dry extract of the dried flower and leaf standardized to 18.75% of Oligomeric procyanidins, as epi-catechin, and/or to 2.2% of flavonoids, as hyperoside (3,5,6,13).

Indication B

- 300 - 750 mg of fruit extract daily, standardized to 0.9 - 10% of Oligomeric proanthocyanidins (3).

Preparation 3.2 (5)

Indication C
Adolescents, adults and elderly
Single dose: 250 mg of dried leaves with flowers, daily dose: 750–1000 mg.

Preparation 4.1 (5)

Indication B
Adults and elderly
Single dose: 0.56 - 1.25 g of dried leaves with flowers, daily dose: 1.68 - 3.75 g.

Preparation 4.2 (5)
Indication B
Adults and elderly
Single dose: 1.84 g of dried leaves with flowers, daily dose: 5.52 g.

Preparation 4.3 (4)

Indication B
0.5 – 1.0 ml dried fruit, 3 times daily.

Preparation 5.1 (5)

Indication B
Adults and elderly
Single dose: 7 ml of fresh leaves with flowers, daily dose: 21 ml.

Preparation 5.2 (5)

Indication B
Adults and elderly
Single dose: 2.4 ml of fresh leaves with flowers, daily dose: 7.5 ml.

Preparation 6 (5)
Indication B
Adults and elderly
Dried leaves with flowers

Single dose: 1.68 g, daily dose: 5.1 g.

10 - 20 drops, 3 times daily (14).

1–2 ml, 3 times daily in a little water (14).

Fruits: 1 – 2 ml, 3 times daily (4).

Duration of use:

Indication A (6):

Therapeutic effect may require 4 - 6weeks of continuous therapy.

Indications B and C (5):

If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor.

or a pharmacist should be consulted.

Method of administration: Oral use.

7. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Not suitable for self-medication (13).
- Accurate diagnosis of stage II congestive heart failure should be obtained prior the use (6).
- If the ankles or legs become swollen, when pain occurs in the region of the heart, which may spread out to the arms, upper abdomen or the area around the neck, or in case of respiratory distress (dyspnea), a doctor or a pharmacist should be consulted (4-6).
- In case of taking cardiac glycosides such as digitalis/digoxin, or blood pressure medication, it is considered to be potentially harmful if not used under medical supervision (3).
- The use in children and adolescents under 18 years of age is not recommended for indications A and B (5, 6).
- The use in children under 12 years of age has not been established for indication C (5).

9. Interactions with other medicinal products and other forms of interaction

Drugs

- Cardiac, hypertensive and hypotensive therapies (13), CNS depressants and iron salts (7, 15).

- Drugs that inhibit the inward flow of potassium channels resulting in an increased action
- potential in cardiac ventricular cells (15).

Herbs

- Adonis, lily of the valley, squill and Fenugreek (7).

Lab Test

- Serum digoxin (7).

10. Fertility, pregnancy and lactation (5)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data is available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (5).

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Sedation, dizziness, decreased reaction time, nausea, vomiting, fatigue, anorexia, sweating, hypersensitivity reactions, including dermatitis rash, anaphylaxis and gastrointestinal symptoms (7,13,16).

13. Overdose

High doses may induce hypotension (that can be good in hypertension) and sedation (which can be good in insomnia) (13).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

It should be emphasized that hawthorn preparations are not specific drugs “NOT used as Monotherapy” for acute disease treatment. They are primarily used as a preventive measure for milder forms of myocardial insufficiency (heart failure, hypertension, and arteriosclerosis of the elderly heart) (17,18).

16. Date of last compilation/last revision

05/06/2023.

References

1	Edwards, S. E., Rocha, I. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st Edition, John Wiley & Sons, Ltd. ISBN: 978-1-118-54356-6.
2	Omer, E. A and Fouad, R. (2018). *Crataegus sinaica* Boiss. In: Egyptian Encyclopedia of Wild Medicinal Plants, **6**, 338-349. Academy of Scientific Research and Technology, Cairo, Egypt.
3	Natural Health Product, Hawthorn (2021). Health Canada. https://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=crataegus.monogyna&lang=eng.
4	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
5	European Union Herbal Monograph on *Crataegus* spp., folium cum flore (2016). EMA/HMPC/159075/2014. Committee on Herbal Medicinal Products (HMPC).
6	WHO monographs on selected medicinal plants (2002). Monographs on Selected Medicinal Plants, **2**, 66- 82.
7	Skidmore-Roth (2010). Mosby's Handbook of Herbs and Natural Supplements. St. Louis: Mosby, 4th ed. ISBN: 978-0-323-05741-7.
8	Cui, T., Nakamura, K., Tian, S., Kayahara, H. and Tian, Y. L (2006). Polyphenolic content and physiological activities of Chinese hawthorn extracts. *Bioscience, Biotechnology, and Biochemistry*, **70**(12), 2948–2956. https://doi.org/10.1271/bbb.60361.
9	Cui, T., Jian-Zhong, L., Hiroshi, K., Liang, M., Li-Xia, W. and Kozo, N. (2006). Quantification of the polyphenols and triterpene acids in Chinese hawthorn fruit by high-performance liquid chromatography. *Journal of Agricultural and Food Chemistry,* **54**(13), 4574–4581. doi:10.1021/jf060310m.
10	Du, W., Fan, H-M., Zhang, Y-X., Jiang, X-H. and Li, Y. (2022). Effect of flavonoids in hawthorn and vitamin C prevents hypertension in rats induced by heat exposure. *Molecules,* **27**(3), 866. https://doi.org/10.3390/molecules27030866.
11	Nabavi, S. F., Habtemariam, S., Ahmed, T., Sureda, A., Daglia, M., Sobarzo-Sánchez, E. and Nabavi, S. M. (2015). Polyphenolic composition of *Crataegus monogyna* Jacq.: From chemistry to medical applications. *Nutrients*, **7**(9), 7708-7728. doi: 10.3390/nu7095361.
12	Guo, Q., Du, J., Jiang, Y., Goff, H. D. and Cui, S. W. (2019). Pectic polysaccharides from hawthorn: Physicochemical and partial structural characterization. *Food Hydrocolloids*, **90**, 146-153. 10.1016/j.foodhyd.2018.10.011.
13	Duke, J. A. (2002). Handbook of Medicinal Herbs. 2nd ed. CRC Press. ISBN 978084931284.
14	Kraft, K. and Hobbs, C. (2004). Pocket Guide to Herbal Medicine. Stuttgart; New York: Thieme. ISBN 3-13-126991-X (GTV), ISBN 1-58890-063-0 (TNY).
15	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
16	Spiteri, M. (2011). Herbal Monographs including Herbal Medicinal Products and Food Supplements. Department of Pharmacy University of Malta. Set and printed by Print Right Ltd, Qormi.
17	Assessment Report on *Crataegus* spp., folium cum flore (2016). EMA/HMPC/159076/2014. Committee on Herbal Medicinal Products (HMPC).
18	Hänsel, R., Sticher, O. and Steinegger, E. (1999). Pharmakognosie - Phytopharmazie, Springer-Lehrbuch, Springer Berlin Heidelberg, Berlin, Heidelberg.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Cucurbita pepo* L.** قرع عسل

1. Names & Synonyms (1)

***Cucurbita pepo* L.**

Family: Cucurbitaceae.

Syns: *Cucurbita aurantia* Willd., *C. courgero* Ser., *C. esculenta* Gray, *C. fastuosa* Salisb., *C. melopepo* L., *C. ovifera* L., *C subverrucosus* Willd., *C. verrucosus* L., *Pepo melopepo* Moench., *P. verrucosus* Moench., *P. vulgaris* Moench.

Arabic: kar-e-asal قرع عسل

English: Pumpkin.

2. Parts used for medicinal purposes

Dried seeds (1-3).

3. Major chemical constituents

-Fixed oil: composed mainly of linoleic, oleic, palmitic and stearic acids (4).

-Phytosterols: β-Sitosterol, $\Delta^{5,24}$ - stigmastadienol, Δ^{7}-stigmastenol, Δ^{7}- avenasterol (5).

-Phytoestrogens: including lignans (as secoisolarisiresinol), isoflavones (as genistin, daidzin and formononetin) and quercetin (6).

-Phenolic acids: Protocatechuic, caffeic, syringic, vanillic, *p*-coumaric and ferulic acids (6).

-Protein: composed mainly of the amino acids: arginine, glutamic and aspartic acids (7).

-Others: Vitamin E (Tocopherols), micro-elements such as phosphorus, magnesium, potassium, zinc and iron (7) as well as β-carotene (8).

4. Medicinal uses (Indications)

Relief of lower urinary tract symptoms related to benign prostatic hyperplasia (2, 3, 9-11) or related to an overactive bladder, after serious conditions have been excluded by a medical doctor (2,3).

5. Herbal preparations correlated to medicinal use (2)

1. Comminuted herbal substance.
2. Soft extract, extraction solvent ethanol 92% m/m.
3. Dry extract, extraction solvent ethanol 60% v/v.
4. Pumpkin seed oil.

Herbal preparations (2-4) are in pharmaceutical dosage forms. The pharmaceutical dosage form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use (2)

Adults and elderly:

Preparation 1: Comminuted herbal substance, single dose: 2.5 – 7.5 g, 2 times daily.

Preparation 2: Soft extract, single dose: 500 mg, 2 times daily.

Preparation 3: Dry extract, single dose: 105 mg,3 times daily or 152 mg, 2 times daily.

Preparation 4: Pumpkin seed oil, single dose: 1 – 1.2 g, 3 times daily, daily dose: 3-4 g.

Method of administration: Oral use.

7. Contraindications (2)

Hypersensitivity to active substances and to other plants of the same family.

8. Special warnings and precautions for use (2)

- If complaints worsen or if symptoms such as fever, spasms or blood in the urine, painful urination or urinary retention occur during the use of the medicinal product, a doctor or a pharmacist should be consulted.

- The use in children and adolescents under 18 years of age is not recommended.

9. Interactions with other medicinal products and other forms of interaction

Diuretics: Pumpkin may increase the action of diuretics; use together cautiously (11).

10. Fertility, pregnancy and lactation

- Pumpkin is prohibited in pregnancy (12).

-Safety during lactation has not been established. In the absence of sufficient data, the use during lactation is not recommended (2).

- No fertility data available (2).

11. Effects on ability to drive and use machines (2)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.

- Gastric disorders (Vomiting, nausea, anorexia) (2).

- Pumpkin Seed oil: Hypersensitivity reactions and skin irritation have been observed (2).

- Electrolyte loss (sodium, potassium chloride) (11).

13. Overdose

No case of overdose has been reported (2).

14. Relevant biological properties

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

For benign prostatic hyperplasia (BPH): pumpkin seed oil could be used in combination with saw palmetto and other herbs (10).

16. Date of compilation/last revision

26/04/2022.

References

1	WHO monographs on selected medicinal plants (2007). Monographs on Selected Medicinal Plants, **4**, 83-91.
2	Community Herbal Monograph on *Cucurbita pepo* L., semen (2012). EMA/HMPC/136024/2010. Committee on Herbal Medicinal Products (HMPC).
3	PDR for herbal medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
4	Ardabili, A. G., Farhoosh, R. and Khodaparast, M. H. (2011). Chemical composition and physicochemical properties of pumpkin seeds (*Cucurbita pepo* Subsp. *pepo* var. *Styriaka*) grown in Iran. *J Agr Sci Tech*, **13**, 1053-1063.
5	Rabrenovic, B. B., Dimic E. B., Novakovic M. M., Tesevic, V. V. and Basic, Z. N. (2014). The most important bioactive components of cold pressed oil from different pumpkin (*Cucurbita pepo* L.) seeds. *LWT Food Sci. Technol.,* **55**, 521–527.
6	Richter, D., Abarzua, S., Chrobak, M., Vrekoussis, T., Weissenbacher, T., Kuhn, C., Schulze S., Kupka, M.S., Friese, K., Briese, V., Piechulla, B., Makrigiannakis, A., Jeschke, U. and Dian, D. (2013). Effects of phytoestrogen extracts isolated from pumpkin seeds on estradiol production and er/pr expression in breast cancer and trophoblast tumor cells. *Nutrition and Cancer*, **65**(5), 739-745.
7	Dowidar, M. F., Ahmed, A. I., Hanaa, R. and Mohamed, H. R. (2020). The critical nutraceutical role of pumpkin seeds in human and animal health: An updated review. *Zagazig Vet J*, **48** (2), 199-212.
8	Stevenson, D. G., Eller, F. J., Wang, L., Jane, J. L., Wang, T. and Inglett, G. E. (2007). Oil and tocopherol content and composition of pumpkin seed oil in 12 cultivars. *J. Agric. Food Chem.*, **55**, 4005–4013. doi: 10.1021/jf0706979.
9	https://www.webmd.com/vitamins/ai/ingredientmono-810/pumpkin
10	https://www.rxlist.com/pumpkin/supplements.htm
11	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed. ISBN: 978-0-323-05741-7.
12	Rouhi-Boroujeni, H., Rouhi-Boroujeni, H., Gharipour, M., Mohammadizadeh, S. Ahmadi, F. and Rafieian-kopaei, M. (2015). A systematic review on safety and drug interaction of herbal therapy in hyperlipidemia: a guide for internist. *Acta Biomed,* **86**(2), 130-136.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Curcuma longa* L.** كركم

1. Names & Synonyms (1)

***Curcuma longa* L.**

Family: Zingiberaceae.

Syns. *Curcuma domestica* Valeton.,

Arabic: Kurkum كركم

English: Turmeric.

2. Parts used for medicinal purpose

The dried rhizome (1-3).

3. Major chemical constituents (1)

-Curcuminoids: A mixture of curcumin, monodesmethoxycurcumin and bisdesmethoxycurcumin (1, 4).

-Essential oil: Composed of a number of monoterpenes and sesquiterpenes, including sesquiphellandrene, ar-turmerone, curcuminol, *cis*-β-elemenone, zingiberene, curcumene, α- and β- turmerone (1, 4, 5).

-Others: Acidic polysaccharides (4).

4. Medicinal uses (Indications)

A. Relief of digestive disturbances, such as feelings of fullness, flatulence, acid dyspepsia and aid digestion (1-3).

B. Relieve pain and inflammation due to rheumatoid arthritis and help relieve joint pain (1, 3).

5. Herbal preparations correlated to medicinal use (2)

1. **Comminuted herbal substance as herbal tea for oral use.**
   0.5-1.0g comminuted herbal substance in 150 ml of boiling water as an infusion (1)
2. **Powdered herbal substance** (1).

3. **Tincture** (ratio of herbal substance to extraction solvent 1:10), extraction solvent ethanol 70% (V/V).
4. **Tincture** (ratio of herbal substance to extraction solvent 1:5), extraction solvent ethanol 70% (V/V).
5. **Dry extract**, extraction solvent ethanol 96% (V/V).
6. **Dry extract**, extraction solvent ethanol 50% (V/V).

Herbal preparations (2-6) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Indication A (2)
Adults and elderly:
Preparation 1: 0.5-1.0 g in 150 ml of boiling water as an infusion, 2-3 times daily (1)
Preparation 2: 0.5-1 g, 2-3 times daily, 1.5–3.0g daily (1).
Preparation 3: 0.5-1 ml, 3 times daily (1).
Preparation 4 :10 ml once daily or 5 ml in 60 ml water, 3 times daily.
Preparation 5: 90-162 mg, divided in 2-5 doses daily.
Preparation 6: 100-200 mg, 2 times daily.

Indication B
Adults and elderly:
Preparation 1: 0.5-1.0 g oral infusion 3 times daily.
Preparation 2: 1.5–3.0g daily (1).
Preparation 3: 0.5–1 ml 3 times daily (1).

Duration of use (2)
For indication A, if the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (2).
It should be taken on an empty stomach (6).

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Due to possible stimulation on bile secretion *Curcuma longa* is not recommended in case of obstruction of the bile duct, cholangitis, liver disease, gallstones and any other biliary diseases (1-3).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children and adolescents under 18 years of age is not recommended (1, 2).
- Coagulation studies should be monitored in the case of long-term treatment of turmeric (6).

9. Interactions with other medicinal products and other forms of interaction (6)

- Use of turmeric with anticoagulants, antiplatelets, NSAIDs and anticoagulant/ antiplatelets herbs may result in an increased risk of bleeding; concurrent use should be avoided.
- Turmeric may decrease the effectiveness of immunosuppressants (cyclosporine)؛ concurrent use should be avoided.

10. Fertility, pregnancy and lactation (1, 2)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (2)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Mild symptoms of dry mouth, flatulence, gastric irritation (2).
- Hypersensitivity reactions, including contact dermatitis (6).

13. Overdose

- Gastrointestinal ulceration (6).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

13/10/2022.

References

1	WHO monographs on selected medicinal plants (1999). Monographs on selected medicinal plants, **1**, 115-124.
2	European Union Herbal Monograph on *Curcuma longa* L., rhizome (2018). EMA/HMPC/329755/2017. Committee on Herbal Medicinal Products (HMPC).
3	Natural Health Product Turmeric – Curcuma longa (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=216
4	Niranjan, A. and Prakash, D. (2008). Chemical constituents and biological activities of turmeric (*Curcuma longa* L.) - A review. *J. Food Sci. Technol.*, **45**(2), 109–116.
5	Abdel-Lateef, E., Mahmoud, F., Hammam, O., El-Ahwany, E., El-Wakil, E., Kandil, S., Abu Taleb, H., El-Sayed, M. and Hassenein, H. (2016). Bioactive chemical constituents of *Curcuma longa* L. rhizomes extract inhibit the growth of human hepatoma cell line (HepG2). *Acta Pharm.*, **66**(3), 387-98. doi: 10.1515/acph-2016-0028.
6	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Cynara cardunculus* L.** خرشوف

1. Names & Synonyms (1)

***Cynara cardunculus* L.**

Family: Asteraceae (Compositae).

Syns: *Cynara scolymus* L.

Arabic: Kharshouf خرشوف

English: Artichoke, Globe Artichoke.

2. Parts used for medicinal purposes (1)

Fresh and dried leaves.

3. Major chemical constituents (2)

- Phenolic acids: Caffeic acid, chlorogenic acid (3-*O*-caffeoylquinic acid), cynarin (1,5-di-*O*-caffeoylquinic acid),1-*O*-caffeoylquinic acid, 4-*O*-caffeoylquinic acid, 5-*O*-caffeoylquinic acid.

- Sesquiterpene lactones: Cynaropicrin, dehydrocynaropicrin, grosheimin and their derivatives.

- Flavonoids: Luteolin-7-*O*-rutinoside (scolymoside), luteolin-7-*O*-glucoside, and luteolin-4-*O*-glucoside, cynaroside and cynarotrioside.

- Essential oil: Consisting mainly of *β*-selinene and caryophyllene.

- Phytosterols: Taraxasterol.

4. Medicinal uses (Indications)

A. Symptomatic relief of digestive disorders such as dyspepsia with a sensation of fullness, bloating and flatulence (3).

B. In hyperlipidemia (high levels of fats) (4).

C. As choleretic (increase bile flow) (4, 5).

5. Herbal preparations correlated to medicinal use

1. Comminuted dried leaves for herbal tea as an infusion (3).

Comminuted herbal substance in 150ml of boiling water as a herbal infusion.

2. Powdered dried leaves (3).
3. Dry extract of dried leaves, extraction solvent water (3).
4. Dry extract of fresh leaves, extraction solvent water (3).
5. Soft extract of fresh leaves, extraction solvent water (3).
6. Soft extract of dried leaves, extraction solvent ethanol 20% (V/V) (3).
7. Liquid extract (4, 6).

Herbal preparations (2-7) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1: Comminuted dried leaves for herbal tea (3):

1.1 1.5g of the herbal substance as a herbal infusion 4 times daily.

1.2 3g of the herbal substance as a herbal infusion 1-2 times daily.

Preparation 2: Daily dose: 600-1500g (in divided doses, 2-4 times a day) (3).

Preparation 3: Daily dose: 400-1320mg in divided dose (3).

Preparation 4: Daily dose: 600-2700mg in divided dose (3).

Preparation 5: Daily dose: 600mg-1800 mg in divided dose (3).

Preparation 6: Daily dose: 700 mg three times daily (3).

Preparation 7: Daily dose: 3-8 ml three times daily (4, 6).

Duration of use: It is possibly safe when taken as a medicine for up to 12 weeks (7).

Method of administration: Oral use (3).

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.

- Obstruction of bile duct (1, 3, 8).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

- The use in children under 12 years of age is not recommended (3).

-The use in cholangitis, gallstones and any other biliary disorders require medical supervision and advice (3, 6, 8-10).

- Use cautiously in hepatic or renal diseases (9).

9. Interactions with other medicinal products and other forms of interaction

- Possible interaction with coumarin-type anticoagulants (1).
- Artichoke tea may interfere with the absorption of iron salts (9).

- Artichoke decreases blood glucose, taking artichoke along with diabetes medications might cause blood sugar to drop too low (7, 9).

10. Fertility, pregnancy, and lactation

-Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (1, 3, 9, 10).

- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been Performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.

- Gastrointestinal complaints included mild diarrhea, accompanied by abdominal cramps, upper abdominal pain, nausea, and heartburn (3, 7).

13. Overdose

No case of overdose has been reported (3).

14. Relevant biological properties

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

13/10/2022.

References

1	WHO monographs on selected medicinal plants (2006). Monographs on selected medicinal plants, **4**, 92-107.
2	El-Mesallamy, A. M. D., Abdel-Hamid, N., Srour, L. and Hussein, S. A. M. (2020). Identification of colyphenolic compounds and hepatoprotective activity of Artichoke (*Cynara scolymus* L.) edible part extracts in rats. *Egypt. J. Chem*. **63**, 6, 2273 – 2285.
3	European Union Herbal Monograph on *Cynara cardunculus* L. (syn. *Cynara scolymus* L.), folium (2017). EMA/HMPC/194014/2017. Committee on Herbal Medicinal Products (HMPC).
4	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
5	https://restorativemedicine.org/library/monographs/artichoke
٦	Braun, L. and Cohen, M. (2009). Herbs and natural Supplements: an Evidence-Based Guide. 3rd ed., ISBN 9780729539104.
7	https://www.webmd.com/vitamins/ai/ingredientmono-842/artichoke
8	http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=101&lang=eng
9	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.
10	https://www.rxlist.com/consumer_artichoke_cynara_scolymuscynarin/drugs-condition.htm

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Echinacea purpurea L. Moench. إشنسيا

1. Names and Synonyms (1-2)

***Echinacea purpurea* L. Moench.**

Family: Asteraceae (Compositae).

Syns.: *Echinacea intermedia* Lindl., *E. purpurea* (L.) Moench var. *arkansana Steyerm.*, *E. purpurea* var. *purpurea* f. liggettii., *E. speciosa* Paxt., *Brauneria purpurea* (L.) Britton, *Rudbeckia purpurea* L., *R. hispida* Hoffm., *R. serotina* Sweet.

Arabic: إشنسيا Echinacea

English name: Purple coneflower.

2. Parts used for medicinal purpose

- Fresh or dried herb (aerial parts) (1-2).

- Rhizome/ root (2-3).

3. Major chemical constituents

Root:

-Phenylpropanoids: Caffeic acid esters; cichoric acid, caftaric acid, chlorogenic and isochlorogenic acids and **caffeic acid glycosides**; echinacoside, verbascoside, caffeoylechinacoside (4).

-Alkamides: Isobutylamides of straight-chain fatty acids with olefinic and/or acetylenic bonds contain mainly 2,4-dienoic units (2,4).

-Polysaccharides: Methylglucuronoarabinoxylan, rhamnoarabinogalactan, xyloglucan and glycoproteins; arabinogalactan-protein (protein has high concentrations of serine, alanine and hydroxyproline) (2).

-Others: **Polyacetylene (volatile oil components):** Alkylketones; (2,4) saturated pyrrolizidine-type **alkaloids** (tussilagine and isotussilagine) (2,4); **flavonoids** (quercetin, kaempferol, isorhamnetin and their glycosides; betaine, fatty acids, simple sugars, sterols and vanillin (2).

Herb/aerial parts:

-Phenylpropanoids: Caffeic acid esters; cichoric acid, caftaric acid, chlorogenic and isochlorogenic acids, and **caffeic acid glycosides**; echinacoside, verbascoside, caffeoylechinacoside (4).

-phenolic acids: *p*-coumaric, *p*-hydroxybenzoic and protocatechuic acids; betaine (2).
-Flavonoids: quercetin, kaempferol, isorhamnetin and their glycosides (2,5).

-Alkamides: Isobutylamides of straight-chain fatty acids with olefinic and/or acetylenic bonds contain mainly 2,4-dienoic units (2,4).

-Polysaccharides: Methylglucuronoarabinoxylan, rhamnoarabinogalactan, xyloglucan and glycoproteins; arabinogalactan-protein (protein has high concentrations of serine, alanine and hydroxyproline) (2).

-Others: **volatile oil components;** borneol, bornyl acetate, germacrene D and caryophyllene (2,4), saturated pyrrolizidine-type alkaloids (tussilagine and isotussilagine) (2,4), anthocyanins, fatty acids, simple sugars, sterols and vanillin (2).

4. Medicinal Uses (Indications) (1, 4)

A. Treatment and prevention of recurrent infections of the common cold, influenza and other upper respiratory tract infections as well as lower urinary tract infections through the immunostimulant-effects (2, 4, 6, 7).

B. Treatment and relief of inflammatory skin conditions: as poorly healing small superficial wounds, spots and pimples due to mild acne, bruises, burns, scratches, leg ulcers, persistent recurring episodes of painful nodules in the skin, boils, carbuncles and abscesses (1, 2, 4).

5. Herbal preparations correlated to medicinal use

1. **Comminuted herbal substances as a herbal tea** (3, 8).

   Powdered dried herb/ root or a combination of both are simmered for 15 minutes in 150 ml hot water as infusion or boiled with 150ml water as decoction.

2. **Powdered herbal drug** (3, 8).
3. **Herb Juice** (4)
   - **3.1.** Expressed juice (DER 1.5 - 2.5:1).
   - **3.2.** Dried expressed juice.

4. **Root dry extract** (4)

   4.1. Extraction solvent ethanol, 45% (V/V).

   4.2. Extraction solvent water.

5. **Root tincture** (2,8)

   5.1. Extraction solvent ethanol 55%, extraction ratio:1:5 (2,8).

   5.2. Extraction ratio:1: 2 (8).

6. **Herb/ root fluid extract** (8).

Herbal preparations (2-6) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use (4)

Preparation 1, 2 (3,8)

Indication A

Adults:

2.5- 6 gm (dried herb), 0.9 - 4.5 gm (dried root), 3 - 5.5 gm (dried herb and root), daily.

Adolescents:

15-17 years: 2.5 -6 gm (dried herb), 0.9 - 4.5 gm (dried root), 3 -5.5 gm (dried herb and root) daily.

12-14 years: 1.3 - 3gm (dried herb), 0.45 - 2.3 gm (dried root) ,1.5 - 2.8 gm (dried herb and root) daily.

Children:

10-11 years: 1.3 – 3 gm (dried herb), 0.45 - 2.3 gm (dried root), 3 - 5.5 gm (dried herb and root) daily.

5-9 years: 0.15 - 0.8 gm (dried herb), 0.6 - 1.5 gm (dried root), 0.8 - 1.4 gm (dried herb and root) daily.

2-4 years: 0.4 – 1 gm (dried herb), 0.15 – 8 gm (dried root), 0.5 - 0.9 gm (dried herb and root) daily.

Duration of use: Not more than 10 days (9).

Method of administration: Oral use.

Preparation 3

Indication A

3.1. **Adolescents, adults and elderly:** 1.5 - 4.5 ml, daily dose: 6 - 9 ml (1, 2, 4).
Children: 10 - 11 years: 2 - 5 ml, daily; **5 - 9 years:** 1- 2.5 ml, daily; **2 - 4 years:** 0.7 - 1.7 ml daily (8).

3.2. Corresponds to the posology of the expressed juice (4).

Duration of use (4).

- For treatment, start the therapy at first signs of common cold.
- Do not use the medicinal product for more than 10 days.
- If the symptoms persist for more than 10 days, a doctor or a pharmacist should be consulted.

Method of administration: Oral use.

Indication B

Adolescents, adults and elderly:

10 to 20 g /100 g of expressed juice or equivalent amount of dried expressed juice (4).

- Semisolid preparations containing at least 15% pressed juice (1).

Duration of use: (4)

- Not to be used for more than 1 week.
- If the symptoms persist during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Cutaneous use (4).

Preparation 4

Preparation 4.1

Indication A

Adolescents, adults and elderly: 40 mg of extract every second hour, daily dose: 360 mg (40 mg, 9 times daily) (4).

Children: correspond to the posology of powdered herbal drug (8).

Duration of use (4)

- The therapy should start at the first signs of common cold.
- If the symptoms persist longer than 10 days during the use of the medicinal product, a doctor or a pharmacist should be consulted

Method of administration: Oral and oromucosal use (4).

Preparation 4.2
Indication B
Adults and elderly: 50-100 mg, 3 times daily, daily dose: 150-300 mg
Adolescents: 50 mg, 2 times daily, daily dose: 100 mg

Duration of use
If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use.

Preparation 5
Indication A
Adults:
Preparation 5.1.
2 - 4 ml, 3 times daily (3) (Equivalent to 60 drops, 3 times daily (2).

Preparation 5.2.
Adults: 3 - 9 ml, daily (equivalent to 1.5 - 4.5 gm drug) (8).
Adolescents and children: Correspond to the posology of powdered herbal drug (8).

Preparation 6
Indication A
Adults: 3 -5.5 ml, daily (equivalent to 3 - 5.5 gm drug) (8).
Adolescents and children: correspond to the posology of powdered herbal drug (8).

7. Contraindications

- Hypersensitivity to the active substances and to other plants of the same family (4).

- Echinacea should not be given to children younger than 2 years of age (3).

- Progressive systemic disorders, collagen disease, tuberculosis, immunodeficencies (HIV/AIDS), immunosuppression diseases of white blood cell system, and autoimmune diseases such as lupus erythematosus and multiple sclerosis (3, 4, 8).

8. Special warnings and precautions for use (4, 8)

- If the symptoms worsen during the use of the medicinal product or high fever, a doctor or a pharmacist should be consulted.

- The use in children under 12 years is not recommended (4) without medical supervision due to the risk of rare allergic reactions that may sometimes be sever in this age group (10).

- There is a possible risk of allergic reactions in allergic individuals. Those patients should consult their doctor before using Echinacea.

- There is a possible risk of anaphylactic reactions in atopic patient. Atopic patient should consult their doctor before using Echinacea.

- Echinacea should not be use for longer than 8weeks without a 3-week rest period (3).

- Immunosuppression may occur after extended therapy with this herb (3).

9. Interactions with other medicinal products and other forms of interaction

None reported (4).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (4).

- No fertility data available (11).

11. Effects on ability to drive and use machines (4)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.

- Hypersensitivity reactions (skin reactions) may occur (3, 4).

- Hepatotoxicity, acute asthma attack, anaphylaxis and angioedema may occur (3).

13. Overdose

No case of overdose has been reported (4).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of last revision

13/9/2023.

References

1	WHO monographs on selected medicinal plants (1999). Monographs on selected medicinal plants, **1**, 136-144.
2	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
3	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
4	European Union Herbal Monograph on *Echinacea purpurea* (L.) Moench, (2017). EMA/HMPC/424583/2016. Committee on Herbal Medicinal Products (HMPC).
5	Coelho, J., Barros, L., Dias, M. I., Finimundy, T. C., Amaral, J. S., Alves M. J., Calhelha, R. C., Santos, P. F. and Ferreira, I. C.F.R. (2020). *Echinacea purpurea* (L.) Moench: Chemical characterization and bioactivity of its extracts and fractions. *Pharmaceuticals*, **13**, 125.
6	ESCOP Monographs (2019). *Echinacea purpurea* (L.)-radix-purple-coneflower-root-European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills.
7	Blumenthal, M. (1998). The Complete German Commission E Monographs. Austin, Texas: American Botanical Council.
8	Natural Health Product, *Echinacea purpurea* (L.) (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=echinacea.purpurea&lang=eng
9	https://www.drugs.com/npc/echinacea.html
10	Medicines and Healthcare products Regulatory Agency, MHRA (2018). Press release. *Echinacea* herbal products should not be used in children under 12 years old. https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency.
11	PDR for herbal medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Foeniculum vulgare* Mill.** شمر

1. Names & Synonyms (1)

***Foeniculum vulgare* Mill.**

Family: Apiaceae (Umbelliferae).

Syns: *Anethum foeniculum* Clairv., *A. foeniculum* L., *A. rupestre* Salisb., *Feniculum commune* Bubani., *F. azoricum* Mill., *F. capillaceum* Gilib., *F. dulce* DC., *F. foeniculum* L. H. Karst., *F. officinale* All., *F. panmorium*DC., *F. piperitum* DC., *F. sativum* Bertol., *Ligusticum divaricatum* Hoffmannsegg et Link, L., *Foeniculum* Crantz., *Meum foeniculum* L. Spreng., *Ozodia foeniculacea* Wight et Arn., *Selinum foeniculum* L. E.H.L.Krause.

Arabic: Shamar شمر

English: Fennel.

2. Parts used for medicinal purposes

Dried ripe fruits (2).

3. Major chemical constituents

-**Essential oil**: *trans*-anethole (+)-fenchone, estragole (methylchavicol), limonene, *p*-anisaldehyde, *α*-pinene and *α*-phellandrene.

-**Phenolic acids**: rosmarinic acid and caffeoylquinic acid derivatives.

-**Flavonoids**: eriodictyol-7-rutinoside, quercetin-3-rutinoside.

- **Others**: triterpenes, smaller terpenes (monoterpenoids, sesquiterpenoids and diterpenoids) and reducing sugars (3).

4. Medicinal uses (Indications)

A. Symptomatic treatment of mild, spasmodic gastro-intestinal complaints including bloating and flatulence (2,5).

B. Symptomatic treatment of minor spasm associated with menstrual periods (2,5).

C. Expectorant in cough associated with cold (2,4,5).

5. Herbal preparations correlated to medicinal use (6)

1. Whole or comminuted dried ripe fruits (freshly comminuted fennel fruits) in herbal tea bags with 0.25 L of boiling water (brew for 15 minutes).
2. Fennel powder.
3. Fennel liquid extract, using water as solvent.
4. Fennel dry extract, using mixture of ethanol and water in different concentrations as solvent.
5. Fennel oil.

Herbal preparations (2-5) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration

Generally

Doses in adolescents (12 years and older) are the same as in adults (18 years and older) doses (2, 5,7).

Duration of use: Not to be taken for more than two weeks for adults and adolescents (2,4,7) and one week for children. (7-8)**.**

Children: To be used under medical supervision, for short-term use in mild transitory symptoms only (2,4,7).

Fennel is possibly safe for up to one week when used at appropriate doses (7).

Due to safety concerns regarding estragole, the daily amount of estragole must be adjusted to the body weight of the age group as estragole/day
Acceptable daily intake of estragole/day =10 µg x body weight (kg) (9).

Preparation 1
Indication A, B
i) Adults and adolescents: 1.5 to 2.5 g three times daily as an herbal tea (2,5,7).
ii) Children:

- **Above 4 years of age:** Average daily dose: 3-5 g (2,5,7) in three divided doses (2,7).
- **>1-4 years of age:** Average daily dose 1.5-3 g in three divided doses (2 ,5).
- **0-1 year of age:** Average daily dose 1-2 g in three divided doses (5).

Preparation 2
Indication A, B
Adults: 5-7 g daily (6).

Preparation 3
Indication A, B, C
i) Adults: 3-6 ml daily (6).
ii) Children: An aqueous preparation of average daily dose of equivalent crushed fruits, calculated as follows (5):
Above 4 years of age: 3-5 g.

- **1-4 years of age:** 1.5-3 g.
- **0-1 year of age:** 1-2 g.

Preparation 4
Indication A, B, C
Adults:
- The appropriate dose depends on several factors such as the users age, health, and several conditions.
-Relevant directions on product labels should be followed and physician or pharmacist should be consulted before use**.**

Preparation 5
Indication A, C
Adults: 0.2 ml of essential oil, as a single dose per day or in multiple divided doses (4,7).
Children: Pure essential oil should not be given to infants and young children (1) but it may be used in a pharmaceutical dosage form, under medical supervision and not exceed the appropriate dose

(The acceptable daily intake of estragole/day NMT 10 µg x body weight of the child (kg)) (9).

Method of administration: Oral use (2,4,5,7)**.**

7. Contraindications

-Hypersensitivity to active substances and to other plants of the same family.

-Pharmaceutical preparations containing 0.05gm fennel oil are contraindicated in children under the age of 1 year (10).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted

- In rare cases, allergic reactions such as asthma, contact dermatitis and rhinoconjunctivitis have been reported in sensitive patients (1).

-Patients with known hypersensitivity to Asteraceae (Compositae) should avoid the use of fennel and its preparations because of cross reactivity risk (2).

-The pure essential oil from the fruits may cause inflammation and has an irritant action on the gastrointestinal tract (1).

-Bleeding disorders: Fennel might slow blood clotting, taking fennel might increase the risk of bleeding or bruising in people with bleeding disorders (8).

-Because of its estrogenic activity, excessive doses of fennel oil may affect hormone therapy, oral contraceptive pill and hormone replacement therapy (8).

- For children under 4 years of age fennel oil should be used under medical supervision (2).

- The pure essential oil should not be given to infants and young children without medical supervision owing to the danger of laryngeal spasm, dyspnea and central nervous system excitation (1,11).

9. Interactions with other medicinal products and other forms of interaction

Anticonvulsants: Fennel may increase the risk of seizures; avoid concurrent use (6).

Ciprofloxacin: Fennel affects the absorption, distribution, and elimination of ciprofloxacin. If the two are used concurrently, their dosages should be separated by at least 2 hours (6,8,12).

10. Fertility, pregnancy and lactation

-Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy or lactation is not recommended (2,4).

-Fennel fruit may be used during pregnancy and lactation at the recommended dosage, as infusions only (5).

- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.

-**Allergic reactions to fennel**, affecting the skin or the respiratory system may occur (6).

- Hypersensitivity reactions, contact dermatitis, photosensitivity (6).
- Pulmonary edema, possible hormone-sensitive cancers (6).

-**Allergic reactions to fennel oil**, affecting the skin, the respiratory and gastro-intestinal system, seizures, hallucinations, nausea, vomiting or anorexia may occur (6).

13. Overdose

No case of overdose has been reported (2,4).

14. Relevant biological properties

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-There are two varieties of fennel fruit: bitter fennel (*Foeniculi amari fructus*) and sweet fennel (*Foeniculi dulcis fructus*) (5).

- Bitter fennel is richer in essential oil than sweet fennel (5).

16. Date of compilation/last revision

19/07/2022.

References

1	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, **3**, 136-144.
2	Community Herbal Monograph on *Foeniculum vulgare* Miller Subsp. *vulgare*, Fructus (2007). EMEA/HMPC/137428/2006 Corr. Committee on herbal Medicine Products (HMPC).
3	Faudale, M., Viladomat, F., Bastida, J., Poli, F. and Codina, C. (2008). Antioxidant activity and phenolic composition of wild, edible, and medicinal fennel from different Mediterranean countries. *J. Agric. Food Chem*. **56**, 1912–1920.
4	Community Herbal Monograph on *Foeniculum vulgare* Miller Subsp. *vulgare*, Aetheroleum (2007). EMEA/HMPC/263292/2006. Committee on herbal Medicine Products (HMPC).
5	https://escop.com/wp-content/uploads/edd/2019/03/Foeniculi-fructus-ESCOP-2019.pdf
6	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.
7	http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=50&lang=eng
8	https://www.webmd.com/vitamins/ai/ingredientmono-311/fennel
9	https://www.ema.europa.eu/en/documents/public-statement/public-statement-use-herbal-medicinal-products-containing-estragole_en.pdf.
10	PV Safety Report on Fennel Oil. EPVC-EDA, 12/6/2022.
11	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
12	https://www.rxlist.com/fennel/supplements. htm.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Garcinia gummi-gutta (L.) Roxb. جارسينيا

1. Names & Synonyms

***Garcinia gummi-gutta* (L.) Roxb.**

Family: Clusiaceae /Guttifereae

Syns.: *Cambogia gummi-gutta* L., *Cambogia gutta* L., *Garcinia cambogia* Desr., *Mangostana cambogia* Gaertn., (1, 2).

Arabic: Garcinia جارسينيا

English name: Malabar tamarind (2, 3).

2. Parts used for medicinal purpose

Fruit peel (3) (rind (4), pericarp (5)).

3. Major chemical constituents

-Organic acid: Hydroxycitric acid (HCA) (6).

-Benzophenones: Camboginol (garcinol), cambogin (isogarcinol; xanthochymol), guttiferones - K, I, J, M and N (7).

-Xanthones: Oxy-guttiferones M, K2, I and K, rheediaxanthone-A (7).

-Others: Bioflavonoids (volkensiflavone, fukugetin) (6, 8).

4. Medicinal Uses (Indications)

A. Used for weight reduction during weight control programs (9, 10).

B. Used for suppression of appetite; temporarily increase satiety and feeling of fullness (3).

5. Herbal preparations correlated to medicinal use

Standardized extracts (3, 5, 10).

Herbal preparation is in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adults:

- 1.5 - 2 g as single dose, 2-3 g daily (3).
- 500 mg, 3 - 4 times daily (2, 10, 11).

Method of administration: Oral use, before meals.

7. Contraindications.

Hypersensitivity to active substances and to other plants of the same family.

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Physician should be consulted prior to use in case of kidney problems, liver disorder or develop symptoms of liver trouble (such as abdominal pain, dark urine or jaundice).
- Use in children under 18 years of age is not recommended (3).

9. Interactions with other medicinal products and other forms of interaction

None reported.

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (11).
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

Headache, dizziness, dry mouth, and GI complaints such as nausea and diarrhoea (11).

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of last revision

16/08/2022.

References

1	https://powo.science.kew.org.
2	Duke, J. A. (2002). Handbook of Medicinal Herbs. CRC Press, 2nd edition, ISBN 9780849312847.
3	Natural Health Product, *Garcinia gummi-gutta* (L.) Roxb. (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=2696&lang=eng.
4	Prakash, J., Srivastava, S., Ray, R. S., Singh, N., Rajpali, R. and Singh, G. N. (2017). Current status of herbal drug standards in the Indian Pharmacopoeia. *Phytother. Res*. **31**, 1817–1823.
5	United States Pharmacopeia (2022). Dietary Supplement Monographs, *Garcinia cambogia*. USP-NF. Rockville, MD: United States Pharmacopeia. https://doi.usp.org/USPNF/USPNF_M3536_01_01.html.
6	Santo, B. L. S., Santana, L. F., Junior, W. H. K., de Araújo, F., Bogo, D., Freitas, K., Guimarães, R. A., Hiane, P. A., Pott, A., Filiú, W. F., Asato, M. A., Figueiredo, P. and Bastos, P. R. H. (2020). Medicinal potential of *Garcinia* species and their compounds. *Molecules*, **25**(19), 4513. https://doi.org/10.3390/molecules25194513.
7	Semwal R. B., Semwal D. K., Vermaak I. and Viljoen A. (2015). A comprehensive scientific overview of *Garcinia cambogia*. *Fitoterapia*, **102** 134–148.
8	Botta, B., Mac-Quhae, M. M., Delle-Monache, G., Delle-Monache, F. and De Mello, J. F. (1984). Chemical investigation of the genus *Rheedia*, V. Biflavonoids and xanthochymol. *J. Nat. Prod.*, **47**, 1053. doi: 10.1021/np50036a033.
9	Ferrara, L. (2014). The *Garcinia cambogia* in phytotreatment of obesity: Activities of the hydroxycitric acid. *European Scientific Journal*, **10** (21), 291-301.
10	https://www.rxlist.com/garcinia/supplements. htm.
11	https://www.drugs.com/npc/ garcinia .html.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Glycine max* (L.) Merr.** فول صويا

1. Names & Synonyms (1)

***Glycine max* (L.) Merr.**

Family: Fabaceae.

Syns.: *Phaseolus max* L., *Phaseolus sordidus* Salisb., *Soja max* (L.) Piper.

Arabic: Ful suyah فول صويا (2).

English: Soybean, soy bean, soya bean, soja (3).

2. Pats used for medicinal purpose

Seeds/Beans (4-7).

3. Major chemical constituents

Isoflavones: Daidzin, genistin, glycitin, and their respective aglycones; daidzein, genistein and glycitein; respectively (8, 9).

Oil: Triglycerides of polyunsaturated (linoleic and α-linolenic acids), monounsaturated (oleic acid) and saturated (palmitic acid) fatty acids, as well as phospholipids (lecithins) (8, 10).

Protein: Glycinin, conglycinin, hemagglutinin, trypsin inhibitors, *α*-amylase and lipoxygenases (8).

Others: Non-starch polysaccharides, vitamins, tocopherols, minerals (K, P, Ca, Mg and Fe), oleonane type saponins (8).

4. Medicinal uses (Indications)

A. Treatment of the menopausal symptoms (11, 12).
B. Symptomatic treatment of the premenstrual syndrome (13).
C. Reduce postmenopausal osteoporosis (13).
D. Lower serum cholesterol, hepatic cholesterol and triglycerides (13).
E. Symptomatic relief of dry skin conditions associated with mild recurrent eczema (6).
F. Relief of temporary fatigue and sensation of weakness (5).

5. Herbal preparations correlated to medicinal use (4,5,13)

1. Soya isoflavones.
2. Soya oil.
3. Soya lecithin.

Herbal preparations are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1 (13)

Indications A - D

Adults: 50-100 mg daily.

Duration of use: As directed by the a physician.

Method of administration: Oral use.

Preparation 2 (6)

Indication E

Liquid preparations containing 70–90% of soyabean oil as bath additive, 2–3 times per week.

Adolescents, adults and elderly

- Full bath (approximately 100–150 l): 15–45 ml.
- Partial bath (approximately 25–50 l): 5–15 ml.
- Partial bath (approximately 5 l): 1–2.5 ml.
- Shower bath with direct application on skin: 20 ml.
- In particularly dry skin, 2–3 times the above quantities can be used.

Infants and children

- Children's bath (approximately 50 l): 20 ml.
- Children's bath (approximately 25 l): 2.5–10 ml.
- In particularly dry skin, 2–3 times the above quantities can be used.

Duration of bath:

- **Adolescents, adults and elderly:** Maximum 20 minutes**.**
- **Infants and children:** A few minutes.

If the symptoms persist during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration

Use as bath additive. Bath temperature: Not exceed 36 °C.

Preparation 3 (5)

Indication F

Adults and elderly

- Single dose: 750 – 2700 mg, 2-3 times daily.

Adolescents:

- Single dose: 750 mg, 2 times daily.

Duration of use:

If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use.

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Full baths are contraindicated in cases of open wounds, large skin injuries, acute skin diseases, high fever, severe infections, severe circulatory disturbances and cardiac insufficiency (6).
- Women with breast cancer especially oestrogen positive tumours and men with prostate cancer should avoid soy isoflavone (13).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- In case of baths, eye contact may cause keratitis and should be avoided. In cases of accidental eye contact, the eye should be rinsed immediately with cold water. If eye irritation remains, a doctor or a pharmacist should be consulted (6).
- The use of soya lecithin in children under 12 years of age is not recommended (5).

9. Interactions with other medicinal products and other forms of interaction (13).

- Soy may interfere with the absorption of estrogens, tamoxifen and thyroid agents; concurrent use should be avoided.
- **Lab Test:** Soy may cause increase in HDL cholesterol and decrease in LDL cholesterol, triglycerides and total cholesterol.

10. Fertility, pregnancy and lactation (5,6)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (5)

- Allergic reactions including severe anaphylaxis and angioedema.
- Skin reactions like pruritus, dermatitis, exanthema and urticaria (6).
- Gastrointestinal disorders like stomach discomfort, nausea, bloating, diarrhoea and abdominal pain (13).
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

13. Overdose

No case of overdose has been reported (5).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

---

16. Date of compilation/last revision

11/6/2023.

References

1	www.powo.science.kew.org
2	http://www.stuartxchange.org/Soya.html
3	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements - An evidence-based guide. 3rd edition, Churchill Livingstone. ISBN 978 0 7295 3910 4.
4	http://www.pharmacopeia.cn/v29240/usp29nf24s0_m77720.html
5	European Union Herbal Monograph on *Glycine max* (L.) Merr., lecithinum (2017). EMA/HMPC/220599/2016. Committee on Herbal Medicinal Products (HMPC).
6	European Union Herbal Monograph on *Glycine max* (L.) Merr., oleum raffinatum (2017). EMA/HMPC/338914/2016. Committee on Herbal Medicinal Products (HMPC).
7	Natural Health Product, The Biology of *Glycin max* (L.) Merr. (Soybean) (2021). Health Canada. https://inspection.canada.ca/plant-varieties/plants-with-novel-traits/applicants/directive-94-08/biology-documents/glycine-max-l-merr-/eng/1330975306785/1330975382668
8	Dixit, A. K., Antony, J. I. X., Sharma, N. K. and Tiwari, R. K. (2011). Soybean constituents and their functional benefits. In book: Opportunity, Challenge and Scope of Natural Products in Medicinal Chemistry, pp. 367 - 384. ISBN: 978-81-308-0448-4.
9	Ciabotti, S., Silva, A. C. B. B., Juhasz, A. C. P., Mendonça, C. D., Tavano, O. L., Mandarino, J. M. G. and Gonçalves, C. A. A. (2016). Chemical composition, protein profile, and isoflavones content in soybean genotypes with different seed coat colors. *International Food Research Journal,* **23**(2), 621-629.
10	Assessment Report on *Glycine max* (L.) Merr., Oleum raffinatum (2017). EMA/HMPC/338915/2016. Committee on Herbal Medicinal Products (HMPC).
11	Heinrich, M., Barnes, J., Gibbons, S. and Williamson, E. M. (2012). Fundamentals of Pharmacognosy and Phytotherapy. 2nd edition, Elsevier Churchill Livingstone. ISBN 978-0-7020-3388-9.
12	Duke, J. A. (2002). Handbook of Medicinal Herbs. 2nd ed. CRC Press. ISBN 978084931284.
13	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Glycyrrhiza glabra* L.** عرقسوس

1. Names & Synonyms (1)

***Glycyrrhiza glabra* L. and its varieties or *Glycyrrhiza uralensis* Fisch.**

Syn. *Liquiritae officinalis* Moench.

Family: Fabaceae (Leguminosae).

Arabic: Irksos, Erqsos عرقسوس

English: licorice, licorice root, liquorice, liquorice root, sweet root and sweet wood.

2. Parts used for medicinal purpose

Dried Root (1-4) and rhizome (1, 4).

3. Major chemical constituents (5)

- **Saponins:** Glycyrrhizin and glycyrrhizic acid (glycyrrhizinic acid), as a mixture of potassium and calcium salts.

- **Flavonoids:** glycosides of liquiritigenin and isoliquiritigenin, such as liquiritin, isoliquiritin, liquiritin apioside and licuraside (6).

- **Others:** Essential oil (mainly geraniol and geranyl hexanolate) and sterols (*β*-sitosterol, dihydrostigmasterol) (7).

4. Medicinal uses (Indications)

A. Relief of digestive symptoms including burning sensation and dyspepsia (2), inflammatory conditions, such as gastritis in adults (3).

B. Expectorant in cough associated with cold (2, 3) to help relief chest complaints, such as mucous build up (catarrhs) and bronchitis (3).

C. Relieve minor inflammations of mucous membranes of the mouth (such as canker sores) (demulcent) (3).

5. Herbal preparations correlated to medicinal use (2)

1. **Comminuted herbal substance as herbal tea** for oral use in the form of infusion or decoction.
   1.5 - 2 g of comminuted herbal substance in 150 ml of boiling water as a herbal infusion or decoction.

2. **Soft extract** (1:0.4-0.5), extraction solvent water.
3. **Soft extract** (3:1), extraction solvent water.
4. **Dry extracts** that correspond to preparations mentioned under 2) and 3).
5. **Deglycyrrhizinated (DGL) dry extract** (3)

   5.1. Acceptable dosage forms for the age category listed in this monograph and specified route of administration are limited to chewables.

   5.2. In dosage forms suited to buccal administration which allow for contact between the affected tissue and the medicinal ingredient including but not limited to lozenges, chewables (e.g. gummies, tablets), strips and liquids (such as gargles, rinses).

Herbal preparations (2-5) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use (2)

Preparation 1-4
Indication A
Adults and elderly

1. 2 to 4 times daily. Take one cup after meals.
2. Soft extract (1: 0.4-0.5) 32 mg 2-3 times daily for oral use. Not more than 160 mg (32 mg 5 times) daily.
3. Doses of dry extracts are corresponding to preparation 2.

Not to be used for more than 4 weeks.

If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or pharmacist should be consulted.

Indication B

Adults and elderly

1. 2 times daily. Take one cup after meals.
2. Soft extract (3:1) 1.2-1.5 g 3-4 times daily.
3. Doses of dry extracts corresponding to preparation 3.

Dose: 60mg (minimum) -600mg (maximum) of glycyrrhizin daily.

Adolescents 15-17 years

Dose: 60mg (minimum) - 600mg (maximum) of glycyrrhizin daily.

Children 10-14 years of age

Dose: 30mg (minimum) - 300mg (maximum) of glycyrrhizin daily.

Children 5-9 years of age

Dose: 15mg (minimum) - 150mg (maximum) of glycyrrhizin daily.

Children 4 years of age

Dose: 10mg (minimum) - 100mg (maximum) of glycyrrhizin daily.

Duration of use: If the symptoms persist longer than 1 week during the use of the medicinal product, a doctor or pharmacist should be consulted.

Method of administration: Oral use.

Preparation 5.1

Indication A

Adults and elderly:

380 mg -1520 mg (3 times a day).

Adolescents:

15-17 years: 380 mg - 1520 mg (3 times a day).
12-14 years: 190 mg -760 mg (3 times a day).

Children:
10-11 years: 190 mg -760 mg (3 times a day).
5-9 years: 95 mg - 380 mg (3 times a day).
3-4 years: 63 mg -253 mg (3 times a day).

Chew between meals or 20 minutes before meals, 3 times a day.

Method of administration: Oral use.

Preparation 5.2
Indication C
Adults and elderly:
200 mg -1140 mg (4 times a day).

Adolescents:

15-17 years: 200 mg - 1140 mg (4times a day).
12-14 years: 100 mg -570 mg (4 times a day).

Children:

10-11 years: 100 mg -570 mg (4 times a day).
5-9 years: 50 mg - 285 mg (4 times a day).
3-4 years: 33 mg -190 mg (4 times a day).

Gargle four times daily with 200 mg DGL powder dissolved in 200 ml of warm water, 4times a day.

Method of administration: Buccal use.

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Cholestatic liver disorders, liver cirrhosis, hypertonia, hypokalemia, severe kidney insufficiency and cardiovascular-related disorder, because liquorice ingestion has resulted in symptoms of primary hyperaldosteronism, such as water and sodium retention and hypokalaemia (8).

8. Special warnings and precautions for use (2)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Patients taking licorice medication should not take other licorice containing products as serious adverse effects may occur such as water retention, hypokalemia, hypertension, cardiac rhythm disorders (4).
- Licorice medication is not recommended to be used in patients affected by hypertension, kidney diseases, liver or cardiovascular disorders or hypokalemia, as they are more sensitive to the adverse effects of licorice (4).
- If dyspnoea, fever or purulent sputum occurs, a doctor or pharmacist should be consulted

9. Interactions with other medicinal products and other forms of interaction

- Licorice root may counteract antihypertensive action of prescribed medications (2) and may cause increased hypokalemia (4).
- Not to be used concomitantly with diuretics, cardiac glycosides, corticosteroids, stimulant laxatives or other medications which may aggravate electrolyte imbalance (2, 4, 9, 10).
- Azole antifungals: Licorice may increase the levels of azole antifungals; avoid concurrent use (3).
- Cytochrome P450 3A4, 2B6 substrates: Licorice may decrease the action of these agents (4).

- **Herb** (4)

  Aloe (taken internally), buckthorn, cascara and chinese rhubarb: Licorice may cause hypokalemia when used with stimulant laxative herbs.

- **Food** (4)

  Grapefruit juice: Use of licorice with grapefruit juice may increase corticosteroid action of licorice.

- **Lab Test** (4)

  Anion gap, blood, potassium, serum prolactin, serum or urine sodium: Licorice may decrease anion gap, blood; potassium (greater than 6 weeks); serum prolactin; serum or urine sodium results.

  Serum, urine myoglobin: Licorice may cause a possible positive test for serum, urine myoglobin.

10. Fertility, pregnancy and lactation

- The use during pregnancy and lactation should be avoided (8). Studies in animals have shown reproductive toxicity (2).
- No fertility data available (2).

11. Effects on ability to drive and use machines (2)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- None reported (2).
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

13. Overdose

- Cases of overdose have been reported with prolonged use (more than 4 weeks) and/or intake of high amount of licorice, with symptoms such as water retention, hypokalaemia, hypertension, cardiac rhythm disorders, hypertensive encephalopathy (2, 10) and in rare cases, myoglobinuria (10).
- Individuals consuming 10–45 g licorice/day have exhibited raised blood pressure, together with a block of the aldosterone/renin axis and electrocardiogram changes, which resolved one month after withdrawal of licorice. Individuals consuming vastly differing amounts of licorice have exhibited similar side-effect symptoms, indicating that the mineralocorticoid effect of licorice is not dose dependent and is a saturable process (8).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

A deglycyrrhizinated licorice (DGL) preparation has been developed to provide some of the therapeutic benefits of licorice while reducing risk. It is a form of licorice that people have processed for safer consumption. DGL, which as the name implies, removed its glycyrrhizinate content, making it safer to use this form of licorice than the former. This makes DGL safer for long-term use and has less interactions with medical conditions. DGL contains less than 2% of glycyrrhizin, making it suitable as an alternative long-term treatment against conditions related to gastrointestinal problems such as peptic ulcers, canker sores, and reflux (GERD). DGL or Deglycyrrhizinated Licorice DGL, doesn't seem to have the same side effects.
Some people are so sensitive to glycyrrhizin that even the tiny amounts left in deglycyrrhizinated licorice can pose a problem.
DGL licorice although considered safer it may still pose certain health risks. You should also avoid DGL licorice if you have a history of diabetes, edema, high blood pressure, or heart, kidney or liver disease (11).

16. Date of compilation/last revision

03/08/2023.

References

1	WHO monographs on selected medicinal plants (1999). Monographs on selected medicinal plants, **1**, 183-194.
2	Community Herbal Monograph on *Glycyrrhiza glabra* L. and/or *Glycyrrhiza inflata* Bat. and/or *Glycyrrhiza uralensis* Fisch., radix (2012). EMA/HMPC/571119/2010. Committee on Herbal Medicinal Products (HMPC).
3	Natural Health Product Licorice – *Glycyrrhiza glabra* (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=licorice.reglisse&lang=eng
4	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.
5	Pastorino, G., Cornara, L., Soares, S., Rodrigues, F., and Oliveira, M. (2018). Liquorice (*Glycyrrhiza glabra*): A phytochemical and pharmacological review. *Phytotherapy Research*, **32**(12), 2323–2339. https://doi.org/10.1002/ptr.6178.
6	Rizzato, G., Scalabrin, E., Radaelli, M., Capodaglio, G. and Piccolo, O. (2017). A new exploration of licorice metabolome. *Food Chemistry*, **221**, 959–968.
7	Mamedov, N. A. and Egamberdieva, D. (2019). Phytochemical constituents and pharmacological effects of Licorice: A Review. *Plant and Human Health*, **3**, 1-21. doi:10.1007/978-3-030-04408-4-1.
8	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
9	European Scientific Cooperative on Phytotherapy (ESCOP) (2020). Table of herb-drug interactions based on the monographs of ESCOP. Source: https://escop.com/interactions/ Updated: 4/5/2020.
10	https://www.herbalgram.org/resources/expanded-commission-e/licorice-root/.
11	Ghulam, D., and Muhammad, A. R. REVIEW. *Glycyrrhiza glabra* L. (2016). (Licorice) *Pak. J. Pharm. Sci.*, **29**(5), 1727-1733 https://www.livestrong.com/article/415583-is-black-licorice-a laxative/https://licoriceproducts. com/licorice/deglycyrrhizinated licorice/

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Ginkgo biloba* L.** چنكو

1. Names & Synonyms (1)

***Ginkgo biloba* L.**

Family: Ginkgoaceae.

Syns. *Pterophyllus salisburiensis* Nelson, *Salisburia adiantifolia* Smith, *S. macrophylla* C. Koch

Arabic: Ginkgo چنكو

English: Ginkgo leaf (1-2), Fossil tree; Kew tree; Maidenhair tree (3).

2. Parts used for medicinal purpose

Dried leaf (1, 3, 4).

3. Major chemical constituents (1, 3, 5)

- **Flavonoids**: Biflavonoids (dimeric flavones (3)/ biflavones (6)) (e.g. amentoflavone, bilobetin, ginkgetin, isoginkgetin, sciadopitysin); flavonols (e.g. quercetin, kaempferol) and their glycosides and coumaroyl esters. flavones, including luteolin and tricetin (6).
- **Terpenoids**: Sesquiterpenes (e.g. bilobalide), diterpenes (e.g. ginkgolides A, B, C, J, M) and triterpenes.
- **Tannins**: Proanthocyanidins. Catechins; proanthocyanidins (1, 6).
- **Amino acids:** 6-Hydroxykynurenic acid (2-carboxy-4-one-6- hydroxyquinoline), a metabolite of tryptophan.
- **Acidic polysaccharide** (7).
- **Others**: Benzoic acid, ginkgolic acids, 2-hexenal, polyprenols (e.g. di-trans-poly-cis-octadecaprenol), sugars, waxes, a peptide.

4. Medicinal uses (Indications)

A. Improvement of (age-associated) cognitive impairment and of quality of life in mild dementia (1, 4, 5). Also helps to enhance cognitive function and memory in adults (8).

B. Improvement of peripheral arterial occlusive disease particularly intermittent claudication (poor circulation to the lower legs), and vertigo tinnitus of vascular origin (2, 3, 5).

C. Relief of heaviness of legs and the sensation of cold hands and feet associated with minor circulatory disorders, after serious conditions have been excluded by a medical doctor (4, 8).

5. Herbal preparations correlated to medicinal use (4)

1. Powdered herbal substance.
2. Dry extract, extraction solvent: acetone 60% m/m^3, (extraction ratio 35-67:1) (1).

Herbal preparations are in pharmaceutical dosage forms. The pharmaceutical form should be described by the Pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1
Indication C
Adults and elderly Single dose: 250-360 mg, daily dose: 750 mg (4).
Duration of use
If the symptoms persist for more than 2 weeks, a doctor or a pharmacist should be consulted.

Preparation 2
Indication A
Adults and elderly:
120–240 mg daily in 2 - 3 divided doses (1, 9).

Indication B
120–160 mg daily in 2 - 3 divided doses (3, 9).

Duration of use (4)
Treatment should last for at least 8 weeks. If there is no symptomatic improvement after 3 months, or if pathological symptoms should intensify, the doctor should check whether continuation of treatment is still justified.

Method of administration (4)**:** Oral use.

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- The use is contraindicated in pregnancy (4).
- The use in children and adolescents under 18 years of age has not been established (2, 4, 8).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted (4).
- In patients with a pathologically increased bleeding tendency (haemorrhagic diathesis) and concomitant anticoagulant and antiplatelet treatment, the medicinal product should only be used after consultation with a doctor (2, 4, 8).
- In patients with epilepsy: onset of further seizures may occur (2, 4).
- Use should be stopped prior to surgery due to a potential risk of increased bleeding or interaction with perioperative drug treatment (10).

9. Interactions with other medicinal products and other forms of interaction

- Concomitant use of Ginkgo biloba containing products and efavirenz is not recommended (4).
- Anticoagulants, platelet inhibitor, salicylates and other non-steroidal anti-inflammatory drugs: Because of the increased risk of bleeding, ginkgo should not be taken concurrently with these products (4).
- Anticonvulsants: Ginkgo components may decrease the anticonvulsant effect, concurrent use should be avoided (4).
- Buspirone, fluoxetine: Ginkgo given with these agents may cause hypomania (2).
- Cytochrome P450IA2/P4502D6/P4503A4 substrates: Ginkgo may affect drugs metabolized by these agents (2).
- Selective serotonin reuptake inhibitors (SSRIs): Ginkgo is often used to reverse the sexual side effects of SSRIs (2).
- Trazadone: Ginkgo with trazadone may cause coma (2).
- Anticoagulant/antiplatelet herbs: Ginkgo may increase the risk of bleeding when used with these herbs (2).

- St. John's wort: Ginkgo with St. John's wort can lead to hypomania (2).

Lab Test (2):

- Partial thromboplastin time, ASA tolerance test: Ginkgo may cause increased bleeding.
- Platelet activity: Ginkgo may decrease platelet activity.
- Prothrombin time, blood salicylate: Ginkgo may increase prothrombin time and blood salicylate.

10. Fertility, pregnancy and lactation

- The use during lactation is not recommended (1, 2, 4, 8).
- Use of ginkgo during pregnancy and breastfeeding should be avoided (3).
- No fertility data available (1, 4).
- Should be avoided during pregnancy and lactation (3, 10).

11. Effects on ability to drive and use machines

No adequate studies on the effect on the ability to drive and use machines have been performed (4).

12. Undesirable effects (4)

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Bleeding of individual organs has been reported (eye, nose, cerebral and gastrointestinal haemorrhage).
- Headache and dizziness.
- Mild gastrointestinal complaints: diarrhoea, abdominal pain, nausea and vomiting.
- Hypersensitivity reactions (allergic shock) may occur, skin, subcutaneous tissue disorders and allergic skin reactions (erythema, oedema, itching, rash) may also occur.

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

---

16. Date of compilation/last revision

02/08/2022.

References

1	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, **1**, 154 -167.
2	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
3	Barnes J., Anderson L. A., Phillipson J. D. (2007). Herbal Medicines, 3rd ed., Pharmaceutical Press, London, p. 293-298.
4	European Union Herbal Monograph on *Ginkgo biloba* L., (2015). EMA/HMPC/321097/2012. Committee on Herbal Medicinal Products (HMPC).
5	PDR for herbal medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
6	Blumenthal, M. (1998). The Complete German Commission E Monographs. Austin, Texas: American Botanical Council.
7	Wang, F., Ye, S., Ding, Y., Ma, Z., Zhao, Q., Zang, M. and Li, Y. (2022). Research on structure and antioxidant activity of polysaccharides from *Ginkgo biloba* leaves, *Journal of Molecular Structure*, **1252**, 132185. https://doi.org/10.1016/j.molstruc.2021.132185.
8	Natural Health Product, *Ginkgo biloba* (L.) (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=100&lang=eng.
9	Kraft, K. and Hobbs, C. (2004). Pocket Guide to Herbal Medicine. Stuttgart; New York: Thieme. ISBN 3-13-126991-X (GTV), ISBN 1-58890-063-0 (TNY).
10	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. Wiley-Blackwell. ISBN: 978-1-118-54356-6.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Gymnema sylvestre (Retz.) R.Br. ex Sm. جيمنيما

1. Names & Synonyms (1)

***Gymnema sylvestre* (Retz.) R.Br. ex Sm.**

Family: Asclepiadaceae.

Syns.: *Marsdenia sylvestris* (Retz.) P.I.Forst., *Periploca sylvestris* Retz., *Apocynum alterniflorum* Lour., *Asclepias geminata* Roxb., *Conocalpis umbellata* Bojer ex Decne., *Cynanchum senegalense* Sieber ex Decne., *Cynanchum subvolubile* Schumach. & Thonn., *Periploca tenuifolia* Humb. & Bonpl. ex Schult., *Strophanthus alterniflorus* (Lour.) Spreng.

Arabic: Gymnema جيمنيما

English name: Gymnema (2,3).

2. Parts used for medicinal purpose

Dried leaves (2, 4).

3. Major chemical constituents (5)

- **Saponins:** Gymnemic acids, gymnemasaponins, gymnemoside A,B,C,D,E,F, and gymnemasin A,B,C,D
- **Terpenes**: Gymmestrogenin, gymnemanol, stigmasterol-and lupeol
- **Others**: Gurmarin (polypeptide), flavonol glycoside (Kaempferol 3-glycoside), *d*-quercitol, conduritol A, tannins and paraben.

4. Medicinal Uses (Indications) (2, 4)

A. For sweet-taste suppression and weight loss during weight control diet program.

B. As an adjunct therapy for diabetes (4,6,7).

C. As an adjunct lipid lowering agent in type 2 diabetes.

5. Herbal preparations correlated to medicinal use (2)

1. Dried leaves (as infusion/decoction).
2. Liquid Extract (1:1).
3. Dry extract.

4. Powdered leaves.

Herbal preparations (2-4) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1
Indication B
Adults

6–60 g daily as infusion (2).

14-28 ml daily as decoction (8).

Preparation 2
Indication A

1-2ml dropped onto the tongue and rinsed off, repeat every 2-3 hours as required (2, 8).

Indication B

3.6–11.0 ml daily (25–75 ml weekly) (2, 8).

Preparation 3
Indication A

The appropriate oral dose depends on several factors such as the user's age, health and other several conditions.

Indication B

- 400– 600 mg daily in divided doses (standardised to contain 24% gymnemic acid (2, 6).
- 200-400 mg twice daily (4).

Duration of use: As directed by physician.

Method of administration: Oral use, with meals (2, 6).

Preparation 3
Indication C
Adults

200-300 mg two times daily (2).

Duration of use: As directed by physician.

Method of administration: Oral use.

Preparation 4 (9)
Indication C
Adults
500 mg two times daily (1g daily)

Duration of use: 30 days.

Method of administration: Oral use.

7. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Gymnema might affect blood sugar levels and could interfere with blood sugar control during and after surgery. Gymnema should be stopped at least 2 weeks before a scheduled surgery (2).
- Use cautiously in diabetic patients using hypoglycaemic medications, due to possible potentiation of effects. Serum glucose levels should be monitored, and doses of concomitant hypoglycaemic drugs may require adjustment under the medical supervision. Hypoglycaemia may also occur in nondiabetic patients (10).
- Use cautiously in patients taking weight loss agents because there may be a potential for additive affects (10).
- Use cautiously in patients taking antilipemic agents. Concomitant use of gymnema with other lipid-lowering agents may potentiate their effects (10).

9. Interactions with other medicinal products and other forms of interaction

- Gymnema may potentiate the effects of hypoglycemic drugs in diabetic patients (2, 10).
- Concomitant use of gymnema with other lipid-lowering agents may potentiate their effects (10).
- Concomitant use of gymnema with antiobesity herbs and supplements, appetite suppressants, chromium, may potentiate their effects (10).
- **Lab test:** Gymnema may lead to decrease in blood glucose, glycosylated hemoglobin (HbA1c), LDL and total cholesterol (4).

10. Fertility, pregnancy and lactation (8)

- Contraindicated in pregnancy and lactation.
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect of Gymnema on the ability to drive and use machine.

12. Undesirable effects (4)

- Gastrointestinal symptoms (e.g. nausea, vomiting, inhibition of bitter/sweet taste), hypoglycaemia and hypersensitivity reactions.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

The Indian term for *Gymnema sylvestre* is “gurmar”, which is translated as “sugar destroyer”. This is because gymnema leaves contain a compound called gymnemic acid that suppresses the taste of sugar (11).

16. Date of last compilation/last revision

11/06/2023.

References

1	www.powo.science.kew.org
2	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements - An Evidence-Based Guide. 3rd edition, Churchill Livingstone. ISBN: 978 0 7295 3910 4.
3	Chevallier, A. (1996). The Encyclopedia of Medicinal Plants, Dorling Kindersley, London, UK.
4	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed. ISBN: 978-0-323-05741-7.
5	Tiwari, P., Mishra, B. N. and Sangwan, N. S. (2014). Phytochemical and pharmacological properties of *Gymnema sylvestre*: An important medicinal plant. *Biomed. Res. Int.*, article ID: 830285. doi: 10.1155/2014/830285.
6	Heinrich, M., Barnes, J., Gibbons, S. and Williamson, E. M. (2012). Fundamentals of Pharmacognosy and Phytotherapy, 2nd edition, Elsevier Churchill Livingstone. ISBN 978-0-7020-3388-9.
7	Spiteri, M. (2011). Herbal Monographs including Herbal Medicinal Products and Food Supplements. Department of Pharmacy University of Malta. Set and printed by Print Right Ltd, Qormi.
8	Duke, J. A. (2002). Handbook of Medicinal Herbs. CRC Press, 2nd edition. ISBN9780849312847.
9	Li, Y., Zheng, M., Zhai, X., Huang, Y., Khalid, A., Malik, A., Shah, P., Karim, S., Azhar, S. and Hou, X. (2015). Effect of *Gymnema sylvestre*, *Citrullus colocynthis* and *Artemisia absinthium* on blood glucose and lipid profile in diabetic human. *Acta Pol. Pharm.*, **72**, 981– 985.
10	Ulbricht, C., Abrams, T. R., Basch, E., Davies-Heerema, T., Foppa, I., Hammerness, P., Rusie, E., Tanguay-Colucci, S., Taylor, S., Ulbricht, C., Varghese, M., Weissner, W. and Woods, J. (2011). An evidence-based systematic review of gymnema (*Gymnema sylvestre* R. Br.) by the Natural Standard Research Collaboration. *J. Diet. Suppl.*, **3**, 311-330. doi: 10.3109/19390211.2011.597977.
11	www.verywellhealth.com

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Harpagophytum procumbens* (Burch.) DC. ex. Meisn** مخلب الشيطان

1. Names & Synonyms (1)

***Harpagophytum procumbens* (Burch.) DC. ex. Meisn**

Family: Pedaliaceae

Syns.: *Uncaria procumbens* Burch.

Arabic: Makhlab Elshaytan مخلب الشيطان

English name: Devil's Claw root, grapple plant, wood spider (2-6).

2. Parts used for medicinal purpose

Dried root (tuber) and dried tuberous secondary root (2-8).

3. Major chemical constituents

-Iridoids: Harpagoside, harpagide. (5, 9)

-Phenylpropanoids: Acteoside and isoacteoside, 6-O-acetylacteoside and 2,6-O-diacetylacteoside (5).

-Carbohydrates: Monosaccharides (fructose, galactose, glucose and myo-inositol), raffinose, stachyose and sucrose (5).

-Diterpenes: (+)-8,11,13-Totaratriene-12,13-diol and (+)-8,11,13- abietatrien-12-ol (5).

-Others: Phytosterols, aromatic acids and flavonoids (10-12).

4. Medicinal Uses (Indications)

A. Anti-inflammatory and anti-rheumatic to relief joint pain associated with osteoarthritis (5, 6).

B. Relief of mild digestive disorders such as bloating, flatulence in temporary loss of appetite and dyspeptic complains (7).

5. Herbal preparations correlated to medicinal use (3)

1. **Comminuted herbal substance** is added to the boiling water as herbal infusion (Infusion time: 8 hours) or boiled with water as decoction.
2. **Powdered herbal substance**.
3. **Liquid extract**
   - **3.1.** Ethanol 30% V/V.
   - **3.2.** Ethanol 25%.
4. **Soft extract** (DER 2.5-4.0:1), ethanol 70% V/V.
5. **Dry extract**
   - **5.1.** (DER 1.5-2.5:1), water.
   - **5.2.** (DER 5-10:1), water.
   - **5.3.** Dry extract, ethanol 30% V/V.
   - **5.4.** Dry extract, ethanol 40% V/V.
   - **5.5.** Dry extract, ethanol 60% V/V.
   - **5.6.** Dry extract, ethanol 80% V/V.
   - **5.7.** Dry extract, ethanol 90% V/V.
6. **Tincture** (1:5), ethanol 25% (V/V).

Herbal preparations (2–6) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adults and elderly (3)

Preparation 1
Indication A
Daily dose:

- **a.** 4.5 g in 500 ml boiling water as herbal infusion, in 3 divided doses (3, 5).
- **b.** 2 – 6 g, daily (2).
- **c.** 1.5 – 3 g as a decoction, 3 times daily (2, 5).
- **d.** 0.6 - 7.5 g, daily (6, 13).

Indication B
Daily dose: 1.5 g, in 3 divided doses (3, 5, 6) up to 4.5 g, daily (6, 14).

Preparation 2
Indication A
Single dose:
- 435 mg, 3 times daily. Daily dose: 1.35 g (3).
- 1–3 g of drug 3 times, daily (5).
- 0.6 - 7.5 g, daily (6).

Indication B: 0.6-1.5 g up to 4.5 g, daily (6).

Preparation 3
Indication A
Preparation 3.1: 1.03 g extract, as single dose (3).
Preparation 3.2: 1 – 3 ml, 3 times daily (5).

Preparation 4
Indications A and B: 240 mg extract, as single dose (3).

Preparation 5
Preparation 5.1
Indication A
Single dose: 100 - 1200 mg, 2 - 3 times daily. Daily dose: up to 2.4 g.
Indication B
Single dose: 100 mg, 2 - 3 times daily. Daily dose: up to 300 mg.

Preparation 5.2
Indication A: Single dose: 200 - 400 mg, 2 to 3 times daily. Daily dose: 600 - 800 mg.

Preparation 5.3
Indication A
Single dose: 400 - 800 mg, 2 - 4 times daily. Daily dose: 800 mg up to 1.6 g.
Indication B
Single dose: 140 - 280 mg, 3 times daily. Daily dose: 420 up to 840 mg.

Preparation 5.4
Indication A
Single dose: 300 - 900 mg, 2 - 3 times daily. Daily dose: 600 mg up to 2.7 g.

Preparation 5.5
Indication A: Single dose: 480 mg, 2 times daily. Daily dose: 960 mg.
Indication B: Single dose: 480 mg, 2 times daily.

Preparation 5.6
Indication B: Single dose: 100 mg, 3 times daily. Daily dose: 300 mg.

Preparation 5.7
Indication A: Single dose: 45 mg, 2 times daily. Daily dose: 90 mg.

Preparation 6

Indication A

- Single dose: 0.5 - 1 ml, 3 times daily. Daily dose: up to 3 ml (3, 5).
- 2 – 5 ml, 3 times daily (2, 5, 14).

Duration of use

For relief of joint pain associated with osteoarthritis: Use for a minimum of 2 - 3 months to see beneficial effects (6).

- **Indication A:** If the symptoms persist longer than 4 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted (3).
- **Indication B:** If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted (3).

Method of administration: Oral use (3).

7. Contraindications

- Hypersensitivity to the active substances and to other plants of the same family.
- Patients with gastric or duodenal ulcer and cholecystitis (3, 5, 14).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Articular pain accompanied by swelling of joints, redness or fever should be examined by a doctor (3).
- For patients with gallstones; a physician should be consulted prior to use devil's claw (3, 7).
- The use in children and adolescents under 18 years of age is not recommended (3).
- Use cautiously in patients with gastric and duodenal ulcers, acute diarrhoea or gallstones, as devil's claw may cause gastric irritation (2).

9. Interactions with other medicinal products and other forms of interaction (14)

- **Antacids, H2-blockers, proton pump inhibitors:** Devil's claw may decrease the action of these agents.
- **Antidiabetics:** Devil's claw may cause an additive effect with antidiabetics.
- **Warfarin:** Devil's claw taken with warfarin may cause risk of bleeding.

Lab Test:

-Activated partial thromboplastin time (APTT) and Prothrombin time (PT): Devil's claw may increase these levels.

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Diarrhea, nausea, vomiting, abdominal pain, anorexia (3, 14), headache, vertigo, hypersensitivity reactions (e.g. rash, hives, facial oedema) (3) and hypotension (14).

13. Overdose

No case of overdose has been reported (3).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/ last revision

31/8/2022.

References

1	https://powo.science.kew.org.
2	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements - An Evidence-Based Guide. 3rd edition, Churchill Livingstone is an imprint of Elsevier. ISBN: 978 0 7295 3910 4.
3	European Union Herbal Monograph on *Harpagophytum procumbens* (Burch.) DC. ex. Meisn. (2016). EMA/HMPC/627058/2015. Committee on Herbal Medicinal Products (HMPC).
4	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd.
5	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
6	Natural Health Product, *Harpagophytum procumbens* (Burch.) DC. ex. Meisn. (2022). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=77&lang=eng.
7	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **2**, 317-324.
8	Blumenthal, M. (1998). The Complete German Commission E Monographs. Austin, Texas: American Botanical Council.
9	Gxaba, N. and Manganyi, M. C. (2022). The fight against infection and pain: Devil's Claw (*Harpagophytum procumbens*) a rich source of anti-Inflammatory activity: 2011-2022. *Molecules*, **27**(11), 3637.
10	Raditic, D. M. and Bartges, J. W. (2014). The Role of Chondroprotectants, Nutraceuticals and Nutrition in Rehabilitation. *Canine Rehabilitation and Physical Therapy* (2nd ed), 254-276.
11	Mncwangi, N. P., Chen, W., Vermaak, I., Viljoen, A. M. and Gericke, N. (2012). Devil's claw—A review of the ethnobotany, phytochemistry and biological activity of *Hargagophytum procumbens*. *J. Ethnopharmacol,* **143**, 755–771.
12	De Lima, V. B., Ribeiro, M. F., Carpilovsky, C. K., Carpilovsky, P. K. and Krause, L. M. F. (2020). Devil's claw: Action on the central nervous system. *Discip. Sci*., **21**, 65–72.
13	ESCOP Monographs (2003). Harpagophytum procumbens (Burch.) DC. ex. Meisn. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills.
14	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Hedera helix* L.** لبلاب

1. Names & Synonyms

***Hedera helix* L.**

Family: Araliaceae.

Syns.: *Hedera communis* Gray, *H. poetarum* Bertol., *H. poetica* Salisb (1).

Arabic : Liblab لبلاب

English name: English Ivy, Common Ivy (1-2).

2. Parts used for medicinal purpose (3)

Dried leaves.

3. Major chemical constituents (4-6)

-Triterpenoid saponins: Hederasaponin C (=hederacoside C), hedrasaponins B, D, D E, F, G, H and I, and α-hederin, hederagenin 3-*O*-*β*-glucoside (7).

-Flavonoids: Quercetin, kaempferol including their 3-*O*-rutinosides and 3-*O*-glucosides (= isoquercitrin and astragalin) (8).

-Phenolic acids: Caffeic, chlorogenic, neochlorogenic, 3,5-*O*-dicaffeoyl-quinic, 4,5-*O*-dicaffeoyl-quinic, rosmarinic, dihydroxybenzoic, protocatechuic and *p*-coumaric acids.

-Others: Coumarin glycoside (scopolin), polyacetylenes, anthocyanins**,** volatile oil, phytosterols, amino acids (8).

4. Medicinal Uses (Indications) (8)

Expectorant in case of productive cough.

5. Herbal preparations correlated to medicinal use (8)

1. **Dry extract**
   - **1.1.** Extraction solvent ethanol, 24-30% m/m.
   - **1.2.** Extraction solvent ethanol, 40% m/m.
   - **1.3.** Extraction solvent ethanol, 60% m/m.
2. **Liquid extract:** extraction solvent ethanol, 70% V/V.
3. **Soft extract:** extraction solvent ethanol, 50% V/V: propylene glycol (98:2).

Herbal preparations are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use (8)

Preparation 1
Adolescents, adults and elderly
1.1. Single dose: 15-65 mg, 1-3 times daily, daily dose: 45-105 mg.
1.2. Single dose: 14-18 mg, 3 times daily.
1.3. Single dose: 33 mg, 2 times daily.

Children between 6-11 years of age
1.1. Single dose: 11-35 mg, 2-3 times daily, daily dose: 33-70 mg.
1.2. Single dose: 9-18 mg, 1-3 times daily, daily dose: 15-40 mg.
1.3. Single dose: 25 mg, 2 times daily, daily dose: 50 mg.

Children between 2-5 years of age
1.1. Single dose: 8-18 mg, 2-3 times daily, daily dose: 24-36 mg.
1.2. Single dose: 7-9 mg, 2-3 times daily, daily dose: 17-27 mg.
1.3. Single dose: 17 mg, 2 times daily, daily dose: 34 mg.

Preparation 2
Adolescents, adults and elderly
Single dose: 100 mg, 3 times daily, daily dose: 300 mg.

Children between 6-11 years of age
Single dose: 75 mg, 3 times daily, daily dose: 225 mg.

Preparation 3
Adolescents, adults and elderly
Single dose: 40 mg, 3 times daily, daily dose: 120 mg.

Children between 6-11 years of age
Single dose: 20-26 mg, 3-4 times daily, daily dose: maximum 80 mg.

Children between 2-5 years of age
Single dose: 20 mg, 3 times daily, daily dose: 60 mg.

Duration of use
If the symptoms persist longer than one week during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use.

7. Contraindications (8)

Hypersensitivity to active substances and to other plants of the same family.

8. Special warnings and precautions for use (8)

- If the symptoms worsen or persist longer than 1 week during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Persistent or recurrent cough in children between 2-4 years of age requires medical diagnosis before treatment.
- When dyspnoea, fever or purulent sputum occurs, a doctor or a pharmacist should be consulted.
- Concomitant use with opiate antitussives such as codeine or dextromethorphan is not recommended without medical advice.
- Caution is recommended in patients with gastritis or gastric ulcer.
- Preparation (2) should not be administered to children under 6 years of age because of the alcohol content.
- Use in children under 2 years of age is not recommended because of the general risk of aggravation of respiratory symptoms through secretoytic drugs so medical supervision is needed.

9. Interactions with other medicinal products and other forms of interaction (8)

None reported.

10. Fertility, pregnancy and lactation (8)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

- No fertility data available.

11. Effects on ability to drive and use machines (8)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (8)

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Gastrointestinal reactions (nausea, vomiting, diarrhoea) have been reported.
- Allergic reactions (urticaria, skin rash, dyspnoea) have been reported.

13. Overdose (8)

Overdose can provoke nausea, vomiting, diarrhoea and agitation.

14. Relevant biological activities (8)

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of last revision

28/07/2022.

References

1	https://powo.science.kew.org
2	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
3	Martindale: The Complete Drug Reference (2007). Pharmaceutical Press. Electronic version, London.
4	Lutsenko, Y., Bylka, W., Matławska, I. and Darmohray, R. (2010). *Hedera helix* as a medicinal plant, *Herba Polonica*, **56**(1), 83-96.
5	Yu, M., Shin, Y. J., Kim, N., Yoo, G., Park, S. and Kim, S. H. (2015). Determination of Saponins and Flavonoids in Ivy Leaf Extracts Using HPLC-DAD. *Journal of Chromatographic Science*, **53**(4), 478–483. https://doi.org/10.1093/chromsci/bmu068.
6	Shawky, E. and El Sohafy, S. M. (2020). Untargeted and targeted chemical profiling for efficacy-directed discrimination of *Hedera helix* L. subspecies using HPTLC-image analysis and HPTLC/MS. *Industrial Crops and Products*, **145**, 111980.
7	Heinrich, M., Barnes, J., Gibbons, S. and Williamson, E. M. (2012). Fundamentals of Pharmacognosy and Phytotherapy. 2nd edition, Elsevier Churchill Livingstone. ISBN 978-0-7020-3388-9.
8	European Union Herbal Monograph on *Hedera helix* L., folium (2017). EMA/HMPC/325716/2017. Committee on Herbal Medicinal Products (HMPC).

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Hypericum perforatum L. عشبة القديس يوحنا

1. Names & Synonyms (1)

***Hypericum perforatum* L.**

Family: Hypericaceae (Clusiaceae).

Syns.: *Hypericum officinale* Gaterau, *Hypericum officinarum* Crantz, *Hypericum vulgare* Lam.

Arabic: Oshbet Alkedees Yohanna عشبة القديس يوحنا

English: St. John's wort (2, 3), Perforate St. John's wort (4), Goatweed (5).

2. Part used for medicinal purpose

Fresh and dried flowering tops and/or flowering aerial parts (1).

3. Major chemical constituents

- **Naphthodianthrones**: Hypericin, pseudohypericin, protohypericin, protopseudohypericin and cyclopseudohypericin (3, 6, 7, 8).
- **Phloroglucinol derivates**: Hyperforin, adhyperforin and furanohyperforin (3, 7-9).
- **Flavonoids**: Hyperoside, quercetin, rutin, quercitrin, isoquercitrin, astilbin, apigenin-7-*O*-glucoside and biapigenin (3, 7, 8, 10).
- **Procyanidines**: Procyanidine B2 (3).
- **Others**: Caffeic, chlorogenic, caffeoylquinic, *p*-coumaroylquinic acids and amino acids (3, 8).

4. Medicinal uses (Indications)

A. Treatment of mild to moderate depressive episodes (1, 2).

B. Short term treatment of symptoms in mild depressive disorders (2).

C. Relief of temporary mental exhaustion (3).

D. Restores mood balance and relieves associated sleep disturbances (5).

E. Symptomatic treatment of minor inflammations of the skin (such as sunburn) and as antiseptic and/or antimicrobial to assist in healing of minor wounds, cuts, burns and bruises (1, 3, 11).

F. Symptomatic relief of mild gastrointestinal discomfort (3).

5. Herbal preparations correlated to medicinal use* (2, 3, 5, 6)

1. **Comminuted herbal substance** in 150ml boiling water as an herbal tea as infusion (3, 5).
2. **Powdered herbal substance** (3, 5).
3. **Dry extracts**
   - **3.1.** Extraction solvent ethanol (80% V/V) (2).
   - **3.2.** Extraction solvent ethanol (50 - 68% V/V) (2).
   - **3.3.** Extraction solvent ethanol 38% (m/m) = 45% V/V (3).
4. **Liquid extracts** (3).
   - **4.1.** Extraction solvent vegetable oil (DER 1:4-20).
     Preparation: maceration of the fresh or dried herbal substance with vegetable oil over a period of 2 days to several weeks under sun light exposure
   - **4.2.** Extraction solvent maize oil or other suitable vegetable oil (DER 1:13).
   - **4.3.** Extraction solvent ethanol 50% (V/V) (DER 1:2).
   - **4.4.** Extraction solvent ethanol 50% (V/V) (DER 1:7-5).
5. **Tincture** (3).
   - **5.1.** Extraction solvent ethanol 45-50% (V/V), (1:10).
   - **5.2.** Extraction solvent ethanol 45-50% (V/V), (1:5).
6. **Expressed juice from the fresh herb** (1.1-2.5:1) (3).

***The daily intake of hyperforin has to be below 1 mg** (2).
Herbal preparations (2-6) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use *

Preparation 1
Indications A and B:
Adults: 2 – 4 g, 3 times daily (6).
Indication C
Adults and elderly: Single dose: 1.5-2 g, Daily dose: 3-6 g (3, 12).

Indication D
Adults: 2 - 12.5 g daily. Not to exceed 4.2 g per single dose (5).
Indication F
Adults and elderly: Single dose: 2 g. Daily dose: 4 g (3).

Preparation 2
Indication C
Adults and elderly: Single dose: 300-500 mg. Daily dose: 900-1000 mg (3).
Indication D
Adults: 2 - 12.5 g daily. Not to exceed 4.2 g per single dose (6).

Preparation 3
Preparation 3.1
Indication A
Adults and elderly: Single dose: 900 mg, once daily. Daily dose: 900 mg (2).

Duration of use: The onset of the effect can be expected within 4 weeks of treatment. If the symptoms persist during the use of the medicinal product, a doctor should be consulted.

Method of administration: Oral use.

Preparation 3.2
Indication B
Adults and elderly: 612 mg, once daily (2), or
Single dose: 250 - 650 mg, 2-3 times daily, Daily dose: 500-1200 mg (2).

Duration of use: The onset of the effect can be expected within 4 weeks of treatment. If the symptoms persist during the use of the medicinal product, a doctor should be consulted.

Method of administration: Oral use.

Preparation 3.3
Indication C
Adults and elderly: Single dose: 60-180 mg. Daily dose: 180-360 mg (3).

Preparation 4 (3)
Preparation 4.1 (3)
Indication E: Topical: Apply hypericum preparations to the affected skin area as needed (11).
Preparation 4.2
Indication C: Single dose: 200 mg. Daily dose: 600 mg (3).
Preparation 4.3
Indication C: Single dose: 0.8 - 1.2 ml. Daily dose: 2.4-3.6 ml (3).

Preparation 4.4
Indication C: Single dose: 1.3 ml. Daily dose: 4 ml (3).

Preparation 5
Preparation 5.1
Indication C: Single dose: 2 - 4 ml. Daily dose: 6 - 12 ml (3).
Preparation 5.2
Indication C: Single dose: 1 - 1.5 ml. Daily dose: 3 - 4.5 ml (3).
Indication E (11)
Preparations 5.1 and 5.2
Topical: Apply hypericum preparations to the affected skin area as needed.

Preparation 6
Indication C: Single dose: 10 - 20 ml. Daily dose: 10 - 30 ml.

***The daily intake of hyperforin has to be below 1 mg** (2).

7. Contraindications (2, 3)

Hypersensitivity to active substances and to other plants of the same family.

8. Special warnings and precautions for use (2, 3)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Intense UV-exposure should be avoided during the treatment.
- The oral use in children and adolescents under 18 years of age is not recommended.
- The amount of hyperforin and hypericin should be specified. The daily intake of hyperforin has to be below 1 mg (3).

9. Interactions with other medicinal products and other forms of interaction (2, 3)

- *Hypericum* dry extract induces the activity of CYP3A4, CYP2C9, CYP2C19 and P-glycoprotein.
- The reduction of plasma concentrations of oral contraceptives may lead to increased intermenstrual bleeding and reduced safety in birth control. Women using oral contraceptives should take additional contraceptive measures.

- Prior to elective surgery possible interactions with products used during general and regional anaesthesia should be identified. If necessary the herbal medicinal product should be discontinued. The elevated enzyme activity returns within one week after cessation to normal level.
- *Hypericum* dry extract may contribute to serotonergic effects when combined with antidepressants.
- Patients taking other medicines on prescription should consult a doctor or pharmacist before taking *Hypericum*.

10. Fertility, pregnancy and lactation (2, 3)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (2, 3)

No adequate studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (2, 3)

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Gastrointestinal disorders, allergic skin reactions, fatigue and restlessness may occur.
- Fair-skinned individuals may react with intensified sunburn-like symptoms under intense sunlight.
- If signs of skin infections are observed, a doctor or a pharmacist should be consulted.

13. Overdose (2, 3)

- Seizures and confusion have been reported.
- After ingestion of massive overdoses, the patient should be protected from sunlight and other UV-light sources for 1-2 weeks.

14. Relevant biological activities (2)

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information (2)

Extracts should be quantified with respect to hypericin. The amounts of hyperforin and of flavonoids should be declared.

16. Date of compilation/last revision

6/9/2022.

References

1	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **2**, 149-171.
2	Community Herbal Monograph on *Hypericum perforatum* L., Herba (Well-established medicinal use) (2009). EMA/HMPC/101304/2008. Committee on Herbal Medicinal Products (HMPC).
3	Community Herbal Monograph on *Hypericum perforatum* L**.,** Herba (Traditional use) (2009). EMEA/HMPC/745582/2009. Committee on Herbal Medicinal Products (HMPC).
4	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd.
5	Natural Health Product, St. John's Wort - Oral - *Hypericum perforatum* L. (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=163&lang=eng.
6	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
7	Oliveira, A. I., Pinho, C., Sarmento, B. and Dias, A. C. P. (2016). Neuroprotective activity of *Hypericum perforatum* and its major components. *Front. Plant Sci*., **7**, 1004.
8	Çirak, C., Radušienė, J., Janulis, V., Ivanauskas, L. and Arslan, B. (2007). Chemical constituents of some *Hypericum* species growing in Turkey. *Journal of Plant Biology*, **50**(6), 632-635.
9	Albert, D., Zundorf, I., Dingermann, T., Muller, W. E., Steinhilber, D. and Werz, O. (2002). Hyperforin is a dual inhibitor of cyclooxygenase-1 and 5-lipoxygenase. *Biochem. Pharmacol*., **64**, 1767–1775.
10	Silva, B. A., Malva, J. O. and Dias, A. C. P. (2008). St John's Wort (*Hypericum perforatum*) extracts and isolated phenolic compounds are effective antioxidants in several in vitro models of oxidative stress. *Food Chem*., **110**, 611–619.
11	Natural Health Product, St. John's Wort - Topical - *Hypericum perforatum* L. (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=165.
12	ESCOP Monographs (2019). *Hypericum perforatum* L. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Matricaria chamomilla* L.** بابونج

1. Names & Synonyms

***Matricaria chamomilla* L.** (1,2).

Family: Asteraceae (Compositae) (1).

Syns.: *Chamomilla recutita* (L.) Rausch., *Chamomilla officinalis* K. Koch, *Matricaria recutita* L. and others (1,3).

Arabic: Baboonig بابونج

English name: Matricaria Flower (4), Blue Chamomile, Hungarian Chamomile, Matricaria, Sweet False Chamomile, Wild Chamomile (3), German Chamomile (5).

2. Parts used for medicinal purpose

Flowerheads (4-7).

3. Major chemical constituents

- Essential oil: α and β-Farnesene, α-bisabolol and its oxide, chamazulene, germacrene D, spiroether, proazulenes (matricarin and matricin) (5,8).

- Phenolic compounds: **Phenylpropanoids**: Chlorogenic and caffeic acids; **Flavonoids**: Apigenin, luteolin, quercetin (and their glycosides) and naringenin; **Coumarins**: y - Herniarin and umbelliferone (9).

- Others: Polyacetylenes, polysaccharides, fatty acids, anthemic acid and triterpene hydrocarbons (e.g. triacontane) (5,9).

4. Medicinal Uses (Indications) (4,6)

Internal:

A. Symptomatic treatment of minor digestive ailments such as dyspepsia, epigastric bloating, impaired digestion, and flatulence.

B. Treatment of restlessness and mild cases of insomnia due to nervous disorders.

External:

C. Treatment of minor inflammation of the skin (sunburn), superficial wounds, small boils (furuncles), skin cracks, bruises, frostbite and insect bites.

D. Treatment of minor ulcers and inflammations of the mouth and throat.

E. Irritations of skin and mucosa in the anal and genital, after serious conditions have been excluded by a medical doctor (10).

Inhalation:

F. Symptomatic relief of irritations of the respiratory tract due to the common cold.

5. Herbal preparations correlated to medicinal use

1. **Comminuted herbal substance** (3-6).
2. **Fluid (liquid) extract**

2.1 Ethanol 45% (1:1) (5,6).

2.2 Ethanol 48% V/V (4).

2.3 Ethanol 55% V/V (4).

2.4 Ethanol 96% V/V: water: ammonia solution 10% m/m (50:47.5:2.5) (4).

2.5 Ethanol 45% V/V: ammonia solution 10% m/m (14.7:1) (4).

3. **Dry Extract, extraction solvent**: ethanol 50% m/m (4).
4. **Tincture** (6,7,11).
5. **Oil** (10).

Herbal preparations (2-5) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1

Indication A (as infusion) (4)
Adolescents, adults and elderly: 1.5 - 4 g in 150 ml of boiling water, 3 - 4 times daily.
Children (6 - 12 years): 1.5 - 3.0 g, 2 - 4 times daily.

Children (2 - 6 years): 1.0 - 1.5 g, 2 - 4 times daily.
Children (6 months - 2 years): 0.5 - 1.0 g, 2 - 4 times daily.

Indication B (as infusion)
Adults: 2 – 8 g, 3 times daily (5,6,11)
Adolescents and children from 3 years: 2 g, 3 times daily (6).

Indication C (4,6,12)
Adolescents, adults and elderly: Washings and impregnated dressings: 3 – 10% (30 – 100g/l water), several times daily.

Indication D
Adolescents, adults and elderly: Oromucosal use for rinsing and gargling: 1 – 5% (10 – 50g/l water) (4) or 3 – 10% (30 – 100g/l) (6,13), several times daily (4).

Children (6 - 12 years): 3 – 10% (30 – 100g/l) (13).

Indication E (4)
Adolescents, adults and elderly: 4.5 - 5 g/l water (irrigation), several times daily.

Indication F (4)
Adolescents, adults and elderly: 3 - 10 g in 100 ml hot water, several times daily.
Children (6-12 years): 2 - 5 g in 100 ml hot water, 1-2 times daily.

Preparation 2

Preparation 2.1 (6)
Indications A and B
Adults: 1 – 4ml, 3 times daily (5).
Children from 3 years: Single dose: 0.6 – 2ml.

Preparation 2.2 (4)
Indication A
Adolescents, adults and elderly: 1.5 ml in 150 ml water, 3 - 4 times daily.
Children (6-12 years): 0.7 – 1 ml in 150 ml water, 3 - 4 times daily.

Preparations 2.2 and 2.3
Indications C and E (4)
Adolescents, adults and elderly: 15 ml / l hot water. One to several times daily.

Indication D
Adolescents, adults and elderly: 1-2 ml in 150 ml water, 3 - 4 times daily (4) **or** 1% v/v fluid extract (1 ml of fluid extract per 100 ml of finished liquid formulation) (13).
Children (6-12 years): 0.5 – 1 ml in 150 ml water, 3 - 4 times daily (4).
or 1% v/v fluid extract (1 ml of fluid extract per 100 ml of finished liquid formulation) (13).

Indication F (4)
Adolescents, adults and elderly: 15 ml/l hot water, 1 - 2 times daily.

Preparation 2.3 (4)
Indications C and E
Adolescents, adults and elderly: Single dose: 15 - 30 ml/5l warm water for partial baths. One to several times daily.

Preparation 2.4 (4)
Indication A
Adolescents, adults and elderly: 2 g in 150 ml warm water, 3 - 4 times daily.

Preparation 2.5 (4)
Indication A
Adolescents, adults and elderly: 5 ml in 150 ml water**,** up to 4 times daily.
Children (6-12 years): 2.5 ml in 150 ml water**,** up to 4 times daily.

Indications C and E
Adolescents, adults and elderly: 20 ml/l water for compresses and irrigation **or** 10 ml/l water for partial baths**,** several times daily.

Indication D
Adolescents, adults and elderly: 2.5 ml in 125 ml water for gargling or rinsing**,** 3-4 times daily.

Indication F
Adolescents, adults and elderly: 5 ml in 150 ml hot water for inhalation, several times daily.

Preparation 3 (4)

Indication C
Adolescents, adults and elderly Single dose: in case of sunburns, few drops are applied in a thin layer on affected area, several times daily.

Preparation 4

Indications A and B
Adults: Tincture (1:5): 3 – 10 ml, 3 times daily (11).

Indication D
Children from 6 years of age, adolescents and adults: 5% v/v tincture (5 ml of tincture/100 ml of finished liquid formulation) (13).

Preparation 5

Indications C and E

Adolescents, adults and elderly: 5 drops per 100 ml of oil, or per 100 g of cream or ointment (11).

Indication E (10)
Adolescents, adults and elderly: Single dose: Use as bath additive: 0.5 – 1 mg/l.
Average daily dose
Full bath: One bath per day or every second day.
Partial bath: One or two times per day.
Duration of bath: 10 – 20 minutes.
Use as bath additive. Recommended temperature of bath: 35 – 38 °C.

Indication F
Adolescents, adults and elderly: 5 drops of essential oil in one l hot water (11).

Duration of use (4)
If the symptoms persist more than one week during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration (4)**:**
Indications A and B: Oral use.
Indications C and E: Cutaneous use.
Indications D: Oromucosal (buccal) use.
Indication F: Inhalation use.

7. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

Use as bath additive (4,10)**:**

- Full baths are contraindicated in cases of open wounds, large skin injuries, acute skin diseases, high fever, severe infections, severe circulatory disturbances and cardiac insufficiency.
- Partial baths or hip baths are contraindicated in cases of open wounds, large skin injuries, acute skin diseases, high fever and severe infections

8. Special warnings and precautions for use

If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

- The oral use of the **herbal preparation 1** is neither recommended for indication A in children below 6 months of age nor indication B in children below 3 years of age (4).

- The use of the **herbal preparation 1** as mouth wash or steam inhalation is neither recommended in children below 6 years of age nor in partial bath or local cutaneous use in children below 12 years of age (4).
- The oral use of the **herbal preparation 2.1** is not recommended for in children under 3 years of age (6). Also; the oral use of the **herbal preparations 2.2 and 2.5** is not recommended in children under 6 years of age (4,13).
- As mouth wash or gargling, the **herbal preparations 2.2, 2.3 and 4** is not recommended in children under 6 years of age (4,13). Also, the **herbal preparation 2.5** is not recommended in children under 12 years of age (4).
- The **herbal preparations 2.2, 2.3 and 2.5** are not recommended in children under 12 years of age as partial bath, for local cutaneous use or as steam inhalation (4,13).
- The use of **oil, dry extract and herbal preparation 2.4** in children under 12 years of age is not recommended (4,10,14).

9. Interactions with other medicinal products and other forms of interaction

Oral use:

- For patients after renal transplantation taking high dosages for longer periods (about two months) interactions based on effects on CYP450 have been reported (4).
- Due to the content of hydroxy coumarins in *M. recutita*, there may be an additive effect when taken with warfarin (15).
- **CNS depressants:** Chamomile may increase the effects of other sedatives; concurrent use should be avoided (14,15).

Cutaneous, oromucosal use, inhalation, or as bath additive:

- None reported (4,10).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has been established for **preparation 1**. If applied before nursing the baby, the nipples should be cleaned of Matricaria containing products for cutaneous use to prevent a sensitization of the baby (4).
- **For other preparations**, safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (4,10).
- No fertility data available (4,10).

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (4,10).

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Hypersensitivity reactions (4,6,10,15) including severe allergic reaction (dyspnoea, Quincke's disease, vascular collapse, anaphylactic shock) following mucosal contact with liquid chamomile preparations have been reported (4,10).
- Burning of the face, eyes and mucous membranes (topical) (14).

13. Overdose

No case of overdose has been reported (4,6, 10).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of last revision

23/08/2022.

References

1	https://powo.science.kew.org.
2	https://www.herbalgram.org/resources/commission-e-monographs/approved-herbs/chamomile-flower-german/
3	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd.
4	European Union Herbal Monograph on *Matricaria recutita* L., Flos (2015). EMA/HMPC/55843/2011. Committee on Herbal Medicinal Products (HMPC).
5	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
6	WHO monographs on selected medicinal plants (1999). Monographs on selected medicinal plants **1**, 86-94.
7	Natural Health Product, German Chamomile – *Matricaria chamomilla* (2018). Health Canada. http://webprod.hcsc.gc.ca/nhpidbdipsn/atReq.do?atid=cham.germ.oral.orale&lang=eng
8	Stanojevic, L. P., Marjanovic-Balaban, Z. R., Kalaba, V. D., Stanojevic, J. S. and Cvetkovic, D. J. (2016). Chemical composition, antioxidant and antimicrobial activity of Chamomile flowers essential oil (*Matricaria chamomilla* L.). *Journal of Essential Oil Bearing Plants*, **19**(8), 2017-2028, DOI: 10.1080/0972060X.2016.1224689.
9	Singh, O., Khanam, Z., Misra, N. and Srivastava, M. K. (2011). Chamomile (*Matricaria chamomilla* L.): An overview. *Pharmacogn. Rev*., **5**(9), 82-95. doi: 10.4103/0973-7847.79103.
10	European Union Herbal Monograph on *Matricaria recutita* L., aetheroleum (2015). EMA/HMPC/278814/2010. Committee on Herbal Medicinal Products (HMPC).
11	Braun, L. and Cohen, M. (2014). Herbs and Natural Supplements, an Evidence-Based Guide. 3rd ed. ISBN: 978 0 7295 3910 4.
12	Natural Health Product, German Chamomile – *Matricaria chamomilla* Topical (2018). Health Canada. http://webprod.hcsc.gc.ca/nhpidbdipsn/atReq.do?atid=germ_chamom_allem&lang=eng
13	Natural Health Product, German Chamomile – *Matricaria chamomilla* Buccal (2021). Health Canada. http://webprod.hcsc.gc.ca/nhpidbdipsn/atReq.do?atid=germ_chamom_allem_buccal&lang=eng
14	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
15	PDR for herbal medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Mentha piperita* L.** نعناع

1. Names & Synonyms (1)

***Mentha piperita* L.**

Family: Lamiaceae.

Arabic: Ni'na نعناع

English: Peppermint.

2. Parts used for medicinal purpose

The fresh overground parts and the dried leaves (1-3).

3. Major chemical constituents

- **Essential oils**: Menthol, menthone, menthyl acetate, menthofuran, and 1,8-cineole (eucalyptol) (4).

- **Flavonoids:** Luteolin, luteolin-7-O-glucoside, naringenin-7-O-glucoside, isorhoifolin, eriodictyol, eriocitrin glycoside and apigenin (5).

4. Medicinal uses (Indications)

A. Symptomatic treatment of digestive disorders such as dyspepsia, flatulence, minor spasms of the gastrointestinal tract, abdominal pain and irritable bowel syndrome (1-3, 6,7), gastritis and indigestion (1,2,7).

B. Relief of symptoms in coughs and colds (1,8).

C. Symptomatic relief of mild tension type headache (1,8).

D. Symptomatic relief of localised muscle pain (8).

E. Symptomatic relief of localised pruritic conditions in intact skin (8).

5. Herbal preparations correlated to medicinal use

1. Comminuted herbal substance as herbal tea for oral use in the form of infusion (3, 6).
2. Herbal substance or the comminuted herbal substance is added to 100-150 ml of boiling water as herbal infusion (3, 6).
3. Tincture, (1:5, 45% ethanol (3, 6) or 70% ethanol (6)).
4. Essential oil (1, 2,7,8).

Herbal preparations (2,3) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

- The internal solid dosage form should be in enteric coated form (gastric resistant) (1,7,8).
- Liquid form should be in diluted preparations or suspensions (1).

6. Posology and method of administration correlated to medicinal use

Preparation 1
Indication A
Adults and elderly: 1.5-3 g as oral infusion, 3 times daily (3,6).
Children from 4 years and adolescents: 1-2g, 3 times daily (3,6).

Preparation 2
Indication A
Adults and elderly: 2-3 ml, 3 times daily (3,6).

Duration of use (6)
If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (6).

Preparation 3
Indication A (1,8)
Adolescents, adults and elderly: 0.2–0.4 ml essential oil, 2 or 3 times daily in solid gastro–resistant dosage forms, diluted preparations or suspensions.

Children from 8 to 11 years of age: 0.2 ml in solid gastro–resistant dosage forms 3 times daily.

Duration of use (8)

The gastro-resistant dosage forms should be taken until symptoms resolve, usually within one or two weeks. At times when the symptoms are more persistent, the intake of gastro-resistant dosage forms can be continued for periods of no longer than 3 months per course.

Method of administration (8)**:** Oral use.

The gastro-resistant dosage forms must be taken whole 30 minutes before meals.

Indication B

Oral use in lozenges or oromucosal use in oral spray (8)**:**

Adolescents, adults and elderly: 0.08-0.12 ml essential oil, 3-4 times per day (8).

2–10 mg essential oil per lozenge (1).

Inhalation:

The essential oil is added to hot water and the vapour is inhaled (8).

Adolescents, adults and elderly: 0.08-0.16 ml of essential oil up to 3 times daily (8).

3–4 drops essential oil in hot water (1).

Cutaneous use (8)**:**

Adolescents, adults and elderly: Nasal ointments 1-5%, up to 3 times daily.

Cutaneous and transdermal use (8)**:**

Apply a thin layer on the chest, on the back or around the nostrils.

Adults and elderly:

- Semi-solid and oily preparations 5-20%.
- Hydroethanolic preparations 5-10%.

Up to 3 times daily.

Adolescents:

- Semi-solid preparations 5-15%.
- Hydroethanolic preparations 3-6%.

Up to 3 times daily.

Children from 4 to 11 years of age:

- Semi-solid preparations 2-10%.
- Hydroethanolic preparations 2-4%.

Up to 3 times daily.

Duration of use

If the symptoms persist longer than two weeks during the use of the medicinal product, a doctor or pharmacist should be consulted.

Indication C (8)

Adults and elderly: In liquid or semi-solid preparations 10% in ethanol.
The treatment consists of one application, which can be repeated two times at 15 minutes intervals, once daily.

Method of administration: Cutaneous use.
The preparation should be rubbed on the skin of the forehead and temples.

Indication D, E (8)

Cutaneous and transdermal use: Apply a thin layer on the affected area.

Adults and elderly:
- Semi-solid and oily preparations 5-20%.
- Hydroethanolic preparations 5-10%.

Up to 3 times daily.

Adolescents:
- Semi-solid preparations 5-15%.
- Hydroethanolic preparations 3-6%.

Up to 3 times daily.

Children from 4 to 11 years of age:
- Semi-solid preparations 2-10%.
- Hydroethanolic preparations 2-4%.

Up to 3 times daily.

Duration of use
- It is not recommended to use the medicinal product continuously for more than two weeks.
- If the symptoms persist longer than two weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

7. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

(Oral use of peppermint leaf preparations) (6)**:**
- Patients with gastroesophageal reflux (heartburn) because it can worsen the case.
- The use in children under 4 years of age is not recommended.

(Oral use of oil):
- Patients with liver disease, cholangitis, achlorhydria, gallstones and any other biliary disorders (2,7-9).
- Peppermint oil should not be given internally to children (2, 7).

- Children under 2 years of age, because menthol can induce reflex apnoea and laryngospasm (8).
- Children with history of seizures (febrile or not) (8).

(Topical use of oil):

- Peppermint oil should not be used topically on the face, particularly near the nose, or on infants or small children (7, 9).
- Children under 2 years of age, because menthol can induce reflex apnoea and laryngospasm (8).
- Children with history of seizures (febrile or not) (8).

8. Special warnings and precautions for use

If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Oral use of peppermint leaf preparations (6)**:**
Patients with gallstones and any other biliary disorders should be cautious in using peppermint leaf preparations.

Use of oil (8)**:**
- Other medicinal products containing peppermint oil should be avoided during the use of this medicinal product.
- Eye contact with unwashed hands after the application of peppermint oil may potentially cause irritation.

o **Oral use for the symptomatic relief of digestive disorders** (8)**:**
- The gastro-resistant solid dosage forms should be swallowed whole, *i.e.*, not broken, or chewed, because this would release the peppermint oil prematurely, possibly causing local irritation of the mouth and oesophagus.
- Patients, who already suffer from heartburn or hiatal hernia, have sometimes an exacerbation of this symptom after taking peppermint oil**.** Treatment should be discontinued in these patients.
- The use of peppermint oil in children under 8 years of age is not recommended.

o **Cutaneous use for the symptomatic relief of mild tension type headache** (8)**:**
- The use in children and adolescents under 18 years of age is not recommended.

o **Inhalation, cutaneous (nasal application), oral (as lozenges) and oromucosal use (as oral spray) for relief of symptoms in coughs and colds:**
- Peppermint oil should be used with caution in inflamed and ulcerated conditions of the gastrointestinal tract (8).

- Patients with gallstones and any other biliary disorder should be cautious using peppermint oil (8).
- The use in children between 2 and 11 years of age is not recommended (1,8).

○ **Cutaneous and transdermal use for relief of symptoms in coughs and colds, for the symptomatic relief of localized muscle pain and for the symptomatic relief of localized pruritic conditions in intact skin:**

- Peppermint oil should not be applied on broken or irritated skin (8).
- The use is not recommended in children below 4 years of age (8).

9. Interactions with other medicinal products and other forms of interaction

- Use of food or antacids administered at the same time of oral use of the peppermint oil for the symptomatic relief of digestive disorders could cause early release of the capsule content (8).
- Other medicinal products used to decrease stomach acid, such as histamine-2 blockers and proton pump inhibitors may cause premature dissolution of the enteric coating and should be avoided (8).
- Cytochrome P450 3A4 substrate: Peppermint oil may decrease drugs metabolized by cytochrome P450 3A4 substrates (7).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (2,6,8).
- No fertility data available (6,8).

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (6,8).

12. Undesirable effects

If adverse reactions occur, a doctor or a pharmacist should be consulted.

Peppermint leaves:

- Nausea, anorexia, increased indigestion with hiatal hernia, exacerbation of biliary colic, bronchospasm (7), gastroesophageal reflux may worsen and heartburn may increase (8).

Peppermint oil:

- **Inhalation**
  - Apnoea, broncho- and laryngo-constriction in hypersensitive patients have been reported (8).
- **Oral and oromucosal use**
  - Urine and stools with an odour of menthol were observed; dysuria and inflammation of the glans of the penis have been reported (8).
  - Allergic reactions to menthol were reported, with bradycardia, muscle tremor, ataxia, anaphylactic shock (8), flushing, mucous membrane irritation, urticaria (7) headache and erythematous skin rash (7,8).
  - Heartburn, nausea (7,8), vomiting, perianal burning blurred vision and dry mouth (8).
- **Cutaneous and transdermal use** (8)
  - Hypersensitivity reactions such as skin rash, contact dermatitis, and eye irritation have been reported.
  - Irritation of the skin and mucosa of the nose is possible, after local application.

13. Overdose

Peppermint leaves: No case of overdose has been reported (9).

Peppermint oil (8)**:**

- **Inhalation**

Inhalation of large doses of menthol may lead to dizziness, confusion, muscle weakness, nausea and double vision.

- **Oral and oromucosal use**
  - Overdose may cause severe gastro-intestinal symptoms, diarrhoea, rectal ulceration, epileptic convulsions, loss of consciousness, apnoea, nausea and disturbances in cardiac rhythms, ataxia and other CNS problems, probably due to the presence of menthol.
  - In the event of overdose, the stomach should be emptied by gastric lavage. Observation should be carried out with symptomatic treatment if necessary.
- **Cutaneous and transdermal use**

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

The amount of pulegone and menthofuran has to be specified in the given product. The daily exposure has to be below 37.5 mg per person. For children, the daily exposure has to be below 0.75 mg/kg b.w. per day (10).

16. Date of compilation/last revision

14/06/2022.

References

1	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **2**, 188-198, 199-205.
2	Natural Health Product Peppermint – *Mentha piperita* (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=144
3	ESCOP Monographs (2019). *Mentha piperita* folium- Peppermint Leaf. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills. ISBN 978-1-901964-66-0.
4	Desam, N. R., Al-Rajab, A. J., Sharma, M., Mylabathula, M. M., Gowkanapalli, R. R. and Albratty, M. (2019). Chemical constituents, *in vitro* antibacterial and antifungal activity of *Mentha piperita* L. (peppermint) essential oils. *Journal of King Saud University* - Science, **31**(4), 528-533.
5	Brahmi, F., Khodir, M., Mohamed, C. and Pierre, D. (2017). Chemical composition and biological activities of *Mentha* species. *InTech.* doi: 10.5772/67291 https://doi.org/10.5772/67291.
6	European Union Herbal Monograph on *Mentha x piperita* L., folium (2020). EMA/HMPC/572705/2014. Committee on Herbal Medicinal Products (HMPC).
7	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.
8	European Union Herbal Monograph on *Mentha x piperita* L., aetheroleum. (2020). EMA/HMPC/679997/2013. Committee on Herbal Medicinal Products (HMPC).
9	PDR for herbal medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
10	Committee on Herbal Medicinal Products (HMPC) (2016). Public statement on the use of herbal medicinal products containing pulegone and menthofuran.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Nigella sativa* L.** **حبة البركة - الحبة السوداء**

1. Names & Synonyms (1, 2)

***Nigella sativa* L.**
Family: Ranunculaceae
Syns: *Nigella cretica* Mill., *Nigella indica* Roxb. ex Flem., *Nigella truncata* Viv.
Arabic: al-haba-el-sauda الحبة السوداء, habat-al-baraka حبة البركة
English: Nigella, black seed, black cumin, black caraway.

2. Parts used for medicinal purpose (3, 4)

Dried mature seeds.

3. Major chemical constituents (5-7)

-**Fixed oil**: Unsaturated fatty acids (linoleic, oleic, eicosadienoic and dihomo-gamma-linolenic acid(DGLA)) and saturated fatty acids (palmitic and stearic acids).
-**Essential oil**: Thymoquinone, thymohydroquinone, dithymoquinone (nigellone), *p*-cymene, carvacrol, 4- terpineol, *t*-anethole, sesquiterpene longifolene, *α*-pinene and thymol.
-**Alkaloids**: Isoquinoline alkaloids (e.g. nigellicimine and nigellicimine-N-oxide) and pyrazole alkaloids (e.g.: nigellidine and nigellicine).
-**Others:** Sterols (*β*-sitosterol, stigmasterol), protein, carbohydrates, vitamins and minerals.

4. Medicinal uses (Indications) (3,8-10)

A. Relief symptoms of asthma.
B. Amelioration of Hyperlipidemia (Dyslipidemia).
C. As adjuvant therapy for managing hypertension.
D. As adjuvant therapy for controlling of blood glucose levels in Type 2 diabetes mellitus.
E. Modulate immune system.
F. As adjuvant therapy to improve inflammatory conditions (Anti-inflammatory) (11-15).

5. Herbal preparations correlated to medicinal use (3,8,10)

1. Powdered seeds.
2. Aqueous extract.
3. Oil.

Herbal preparations are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1

Indication A
500 mg - 1.0 g twice daily, for 3 months (16).
Indication B
- 1.0 g daily, for 1-2 months (9).
- 500 mg daily, for 6 months (9), up to 1.0 g, twice daily (2.0 g daily), for 3 months (3, 17).

Indication C
200 - 400 mg daily, for 2 months (9).
Indication D
2.0 – 3.0 g daily, for 3 months (3, 9,17).
Indication F
2 g daily, for 3 months (11).

Method of administration: Oral use.

Preparation 2

Indication A
- 2.0 g extract daily, for 2 weeks (21).
- 700 mg – 1.4 g extract daily, as adjuvant therapy (22).

Indication C
100–200 mg twice daily, for 2 months (3, 17, 10).

Method of administration: Oral use.

Preparation 3

Indication A

- 5 ml 3 times daily (3).
- 500 mg twice daily, for 4 weeks (23).

Indication B

5 ml or 2.0 –3.0 g daily, for 2- 3 months (3, 9).

Indication C

- 5 ml daily, for 2-3 months (3, 9).
- 2.5 ml twice daily, for 2 months (9).

Indication D

5 ml once or 2.5 ml twice daily, for 6 weeks (3, 9,10) up to 3 months (9).

Indication E

500 mg daily (18).

Method of administration: Oral use.

Indication F

- **Orally:** 500 mg, twice daily, for 1-2 months (12,13), up to one g, twice daily, for 3 months (14).
- **Topical application**: twice daily (in the morning and night) for 21 days (15) or 600mg twice daily for 2months (9).

Method of administration: Oral and topical use.

7. Contraindications

Hypersensitivity to the active substances and to other plants of the same family.

8. Special warnings and precautions for use

If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

9. Interactions with other medicinal products and other forms of interaction (3,19,20)

- **Anti-diabetic drugs:** might decrease blood sugar levels. Blood sugar should be monitored closely (24).
- **Antihypertensive drugs:** might decrease blood pressure levels. Blood pressure should be monitored closely.

- **Immunosuppressants:** concurrent use might decrease the effects of these medications.
- **Anticoagulant / antiplatelet drugs:** might increase the risk of bruising and bleeding.
- **CNS depressants:** might cause breathing problems and/or too much sleepiness.
- **Diuretic drugs:** might make potassium levels drop too low.
- **Serotonergic Drugs:** might increase serotonin too much. This might cause serious side effects including heart problems, seizures and vomiting.

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (25).
- The oil is contraindicated in pregnancy and breastfeeding (24).
- No enough data available about fertility.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (19,20)

- If other adverse reactions occur, a doctor or a pharmacist should be consulted.
- Black seed can cause allergic rashes in some people. It can also cause stomach upset, vomiting, or constipation.

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/last revision

19 /7/2022.

References

1	https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:711687-1.
2	Herbal Medicine Compendium (2021). https://hmc.usp.org/monographs/nigella-sativa-seed-0-1.
3	Ahmed, M., editor (2017). Monographs on Research oriented Natural Drugs in Modern Medical Systems. Pakistan Society of Pharmacognosy, University of Karachi. http://www.pspuok.com/books/monograph%20on/33.pdf
4	Isa, T., Ayse, S-Y., Ferda, E., Huseyin, A., Ibrahim, D. and Saban, T. (2014). Comparison of seed oil composition of *Nigella sativa* L. and *N. damascene* L. during seed maturation stages. *Journal of the American Oil Chemists' Society,* **91**(10), 1723-1729. doi:10.1007/s11746-014-2513-3.
5	Forouzanfar, F., Bazzaz, B. S. and Hosseinzadeh, H. (2014). Black cumin (*Nigella sativa*) and its constituent (thymoquinone): A review on antimicrobial effects. *Iran J. Basic Med. Sci.*, **17**(12), 929-938.
6	Majid, A. (2018). The chemical constituents and pharmacological effects of *Nigella sativa* - A Review. *Journal of Bioscience and Applied Research*, **4** (4), 389-400.
7	Srinivasan, K. (2018). Cumin (*Cuminum cyminum*) and black cumin (*Nigella sativa*) seeds: traditional uses, chemical constituents, and nutraceutical effects. *Food Quality and Safety*, **2**(1), 1–16. https://doi.org/10.1093/fqsafe/fyx031.
8	Malhotra, S. K. (2004, 2012). Nigella: Handbook of Herbs and Spices, 2nd ed., Volume 2, 219-242, 391-416. Woodhead Publishing. https://search.yahoo.com/search?fr=mcafee&type=E211US105G91649&p=Nigella+S.+K.+Malhotra. https://www.researchgate.net/publication/323691873_13_Nigella.
9	Tavakkoli, A., Mahdian, V., Razavi, B. M. and Hosseinzadeh, H. (2017). Review on clinical trials of black seed (*Nigella sativa*) and its active constituent, thymoquinone. *Journal of Pharmacopuncture*, **20**(3), 179-193.
10	Salehi, B., Quispe, C., Imran, M., Ul-Haq, I., Zivkovi, J., Abu-Reidah, I. M., Sen, S., Taheri, Y., Acharya, K., Azadi, H., Contreras, M., Segura-Carretero, A., Mnayer, D., Sethi, G., Martorell, M., Abdull Razis, A. F., Sunusi, U., Kamal, R. M., Suleria, H. A. R. and Sharifi-Rad, J. (2021). Nigella Plants – Traditional uses, bioactive phytoconstituents, preclinical and clinical studies. *Front. Pharmacol*., article 625386, https://doi.org/10.3389/fphar.2021.625386.
11	Darand, M., Darabi, Z., Yar,i Z., Saadati, S., Hedayati, M., Khoncheh, A., Hosseini-Ahangar, B., Alavian, S. M. and Hekmatdoost, A. (2019). *Nigella sativa* and inflammatory biomarkers in patients with non-alcoholic fatty liver disease: Results from a randomized, double-blind, placebo-controlled, clinical trial. *Complement. Ther. Med.*, **44**, 204- 209.
12	Gheita, T. A. and Kenawy, S. K. (2012). Effectiveness of *Nigella sativa* oil in the management of rheumatoid arthritis patients: A placebo controlled study. *Phytother. Res*., **26**, 1246–1248.
13	Hadi, V., Kheirouri, S., Alizadeh, M., Khabbazi, A. and Hosseini, H. (2016). Effects of *Nigella sativa* oil extract on inflammatory cytokine response and oxidative stress status in patients with rheumatoid arthritis: a randomized, double-blind, placebo-controlled clinical trial. *Avicenna Journal of Phytomedicine*, **6**(1), 34 – 43.

14	Rahmani, A., Niknafs, B., Naseri, M., Nouri, M. and Tarighat-Esfanjani, A. (2022) .Effect of *Nigella sativa* oil on oxidative stress, inflammatory, and glycemic control indices in diabetic hemodialysis patients: A randomized double-blind, controlled trial. *Evidence-Based Complementary and Alternative Medicine*, 2753294. doi: 10.1155/2022/2753294.
15	Azizi, F., Ghorat, F., Rakhshani, M. H. and Rad, M. (2019). Comparison of the effect of topical use of *Nigella sativa* oil and diclofenac gel on osteoarthritis pain in older people: A randomized, double-blind, clinical trial. *Journal of Herbal Medicine*, **16**, http://dx.doi.org/10.1016/j.hermed.2019.100259.
16	Salem, A. M., Bamosa, A. O., Qutub, H. O., Gupta, R. K., Badar, A., Elnour, A. and Afzal, M. N. (2017). Effect of *Nigella sativa* supplementation on lung function and inflammatory mediators in partly controlled asthma: a randomized controlled trial. *Ann. Saudi Med.* 37, 64-71.
17	Braun, L. and Cohen, M. (2014). Herbs and Natural Supplements, Volume 2, an Evidence-Based Guide. 4th edition. ISBN: 9780729541725.
18	The Therapeutic Goods Administration, Department of Health, Australian Government. https://myhealthbox.eu/en/view/3350321/bfc8fa27c1dc9d8d851be64a80e17a3e/leaflet.
19	https://www.webmd.com/vitamins/ai/ingredientmono-901/black-seed.
20	https://www.rxlist.com/black_seed/supplements.htm.
21	Boskabady, M. H. and Farhadi, J. (2008). The possible prophylactic effect of *Nigella sativa* seed aqueous extract on respiratory symptoms and pulmonary function tests on chemical war victims: A randomized, double-blind, placebo - controlled trial. *J. Altern. Complement. Med*., 14(9), 1137–1144.
22	Boskabady, M. H., Mohsenpoor, N. and Takaloo, L. (2010). Antiasthmatic effect of *Nigella sativa* in airways of asthmatic patients. *Phytomedicine*, **17**(10), 707-713.
23	Koshak, A., Wei, L., Koshak, E., Wali, S., Alamoudi, O., Demerdash, A., Qutub, M., Pushparaj, P. N. and Heinrich, M. (2017). *Nigella sativa* supplementation improves asthma control and biomarkers: A randomized, double-blind, placebo-controlled trial. *Phytother. Res*., **31**, 403–409.
24	Tisserand, R. and Young, R. (2014). Essential Oil Safety. A Guide for Health Care Professionals, 2nd ed. Churchill Livingstone. ISBN 978-0-443-06241-4.
25	*Nigella sativa*: Benefits, Side Effects and Medications. Articles https://www.pharmaonlinerx.com/nigella-sativa-benefits-side-effects-and_medications/
26	Rohman, A., Lukitaningsih, E., Rafi, M., Nurrulhidayah, A. F. and Windarsih, A. (2019). *Nigella sativa* oil: physico-chemical properties, authentication analysis and its antioxidant activity. *Food Research,* **3**(6), 628 - 634.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Oenothera biennis* L.** زهرة الربيع المسائية

1. Names & Synonyms

***Oenothera biennis* L.**

Family: Onagraceae (1).

Syns.: *Oenothera biennis* var. *vulgaris Torr. & A. Gray. Onagra biennes* (L.) *Scop, Pseudo-oenothera virginiana Rupr* (1).

Arabic: Zahrat El-Rabei El-Masaeia زهرة الربيع المسائية

English name: Evening primrose (2), Evening star, King's cure-all, Suncup, Sundrop (3).

2. Parts used for medicinal purpose

Seeds (2, 4).

3. Major chemical constituents

Fixed oil: Mainly linoleic acid and γ- linolenic acid and less amount of other fatty acids (oleic, palmitic and stearic acids) (5), aliphatic alcohols and β-amyrin (6).

4. Medicinal Uses (Indications)

A. For symptomatic treatment of atopic eczema, itching in acute and chronic dry skin conditions (2, 4).

B. Mastalgia; one of the symptoms of Premenstrual Syndrome (PMS) (2).

5. Herbal preparations correlated to medicinal use

Fatty oil obtained from seeds by extraction and/or expression (4).

Herbal preparation is in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Indication A:

Adolescents, adults and elderly:
Single dose: 2 - 3 g, Daily dose: 4 - 6 g (4) or 320 – 480 mg, daily (calculated as ϒ-linolenic acid), in divided doses (2).

Indication B: 240 – 320 mg, daily (calculated as ϒ-linolenic acid), in divided doses (2).

Duration of use:
If the symptoms persist longer than 8 weeks during the use of the medicinal product, a doctor or pharmacist should be consulted.

Method of administration: Oral use (4).

7. Contraindications

Hypersensitivity to the active substances and to other plants of the same family.

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children under 12 years of age is not recommended (4).
- Evening primrose oil is recommended to be used with caution in epileptic patients, especially in those with schizophrenia and/or those taking phenothiazines (2, 5).
- Oral evening primrose oil should be used with caution by patients with bleeding disorders (3).

9. Interactions with other medicinal products and other forms of interaction

- **Anticoagulant drugs:** due to potential additive effect, as it can inhibit platelets aggregation and increase bleeding time (2, 3).
- Seizures have occurred in a few schizophrenic patients taking evening primrose oil with phenothiazine (5).

10. Fertility, pregnancy and lactation (4)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (4)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (4)

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Gastrointestinal effects, indigestion, nausea, softening of stool, rise in temperature, hypersensitive reactions like exanthema and headache have been reported.

13. Overdose (4)

The symptoms of overdosing are mild diarrhoea and abdominal pain. No special treatment is required.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/ last revision

22/08/2022.

References

1	https://powo.science.kew.org.
2	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **2**, 217-230.
3	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd.
4	European Union Herbal Monograph on *Oenothera biennis* L., (2018). EMA/HMPC/424583/2017. Committee on Herbal Medicinal Products (HMPC).
5	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
6	Timoszuk, M., Bielawska, K. and Skrzydlewska, E. (2018). Evening Primrose (*Oenothera biennis*) biological activity dependent on chemical composition. *Antioxidants*, **7**(8), 108.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Olea europaea* L.** زيتون

1. Names & Synonyms (1)

***Olea europaea* L.**
Family: Oleaceae.
Syns: *Olea pallida* Salisb., *Olea sativa* Hoffmanns. & Link .
English: Olive (2).
Arabic: Zaytun زيتون (3).

2. Parts used for medicinal purpose

Fresh or dried leaves (4) and fruits (5-7).

3. Major chemical constituents

Olive leaves:

- **Secoiridoids**: Oleuropein (8), methyloleuropein, oleoside (9), verbascoside and ligstroside (10).
- **Flavonoids**: Apigenin, kaempferol, luteolin, diosmetin and chrysoeriol (9).
- **Triterpenoids**: Oleanolic, ursolic and maslinic acids (11), uvaol and erythrodiol (12).
- **Phenolic compounds**: Tyrosol, hydroxytyrosol (10) and caffeic acid (9).

Olive oil:

- **Triglycerides:** Unsaturated fatty acids mainly as oleic, linoleic and palmitoleic acids and saturated fatty acids as palmitic and stearic acids (13).
- **Phenolic compounds:** Oleuropein, hydroxytyrosol and α-tocopherol (13).
- **Volatiles**: Hexanal, *trans*-2-hexenal, 1-hexanol and 3-methylbutanol (14).
- **Hydrocarbons**: Squalene and β-carotene (14).

4. Medicinal uses (Indications)

A. Diuretic and promote the renal elimination of water in mild cases of water retention after serious conditions have been excluded by a medical doctor (4, 15).
B. Adjunct therapy in hypertension and hyperlipidemia (16).
C. Purgative / laxative (6, 17).
D. For chronic gastritis and protect stomach lining (6, 7).
E. **Externally/Topically:** Emollient: soften crusty lesions, psoriasis, eczema, for skin and mucosal infections, sooth mild and sun burns and protect the skin from sun damage (17, 18).

5. Herbal preparations correlated to medicinal use

1. Comminuted fresh or dried leaves (decoction and infusion) (4, 15).
2. Powdered dried leaves (4, 15)
3. Ethanolic leaves extract (dry and fluid extracts, tincture) (15).

Note: Preparations are standardized to contain 17-20 % oleuropein (19).

4. Olive oil from the fruits (5-7).

Herbal preparations (2-4) are in a pharmaceutical dosage form. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adults and elderly

Preparation 1 (4, 15)
Indications A and B

- 10 g of fresh leaves or 5 g of dried leaves in 150 ml of water as a decoction, allow to simmer to reach 100 ml, 1-2 times daily.
- Single dose: 6–10 g, 1-3 times daily; daily dose: 6–30g as infusion.

Preparation 2 (4, 20)
Indications A and B
- Single dose: 275 mg, 3-5 times daily or 210 – 400 mg, 3 times daily.
- Daily dose: 630–1375 mg.

Preparation 3
Indications A and B
The equivalent of 0.6 - 3.5 g of dried leaves, daily (15).

Indication B

5 ml, 3 times daily with water or juice, if necessary (18, 21).
400 mg, 4 times daily (21, 22).

Preparation 4
Indication B
1½ - 3 tablespoonful (≃ 25 - 50 ml), daily (21, 23).
Indication C
2 - 4 tablespoonful (30 - 60 ml), daily (6).
Indication D
one tablespoonful (15 ml) each morning, slowly sipped (7).
Indication E
The appropriate dose depends on several factors such as the user's condition.

Duration of use:

- For occasional use only (15); 2-4 weeks (4) (**Indication A**).
- If the symptoms persist longer than one week during the use of the medicinal product, a doctor or a pharmacist should be consulted (4).

Method of administration

- Oral use, to be taken with food (4, 15), water or juice (18, 21).
- Topical use (17, 18).

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Decoction and infusion (preparation 1) are contraindicated in conditions where a reduced fluid intake is recommended (e.g. severe cardiac or renal disease) (4).

8. Special warnings and precautions for use (4)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Patients with cardiac disease or renal impairment should seek medical advice before taking olive preparations.
- The use in children and adolescents under 18 years of age has not been established.

9. Interactions with other medicinal products and other forms of interaction

Due to the hypotensive and antiplatelet aggregating properties of olive leaf extract, concomitant use with blood-pressure lowering medications and blood thinners may have a potentiating effect (24).

10. Fertility, pregnancy and lactation (4)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- None known (4).
- If adverse reactions occur, a doctor or pharmacist should be consulted.

13. Overdose

No case of overdose has been reported (4).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

Olive leaf and oil have antioxidants effect. This effect is believed to be responsible for the action of olive to reduce risk of heart disease by protecting cells from oxidative damage. (5,15,17,21)

16. Date of compilation/last revision

01/06/2023.

References

1	www.powo.science.kew.org
2	https://www.gbif.org/species/5415040
3	Provençal, P. (2010). The Arabic Plant Names of Peter Forsskål's Flora Aegyptiaco-Arabica. The Royal Danish Academy of Sciences and Letters.
4	European Union Herbal Monograph on *Olea europaea* L.,Folium (2017). EMA/HMPC/359238/2016. Committee on Herbal Medicinal Products (HMPC).
5	Natural Health Product. Multiple Ingredient fixed oil products (2022). Health Canada, https://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=multiple.oil&lang=eng
6	Duke, J. A. (2002). Handbook of Medicinal Herbs. CRC Press, 2nd edition. ISBN 9780849312847.
7	Kraft, K. and Hobbs, C. (2004). Pocket Guide to Herbal Medicine. George Thieme Verlag, ISBN: 1-58890-063-0.
8	Bilel, H., Yahia, M. and Moustafa, S. M. N. (2023). An overview of chemical composition and fungicidal activity of Olive (*Olea europaea* L.) leaf extract. *Egyptian Journal of Chemistry*, **66**(1), 303-311.
9	Acar-Tek, N. and Ağagündüz, D. (2020). Olive leaf (*Olea europaea* L. folium): Potential effects on glycemia and lipidemia. *Ann. Nutr. Metab.,* **76**(1), 10-15. doi: 10.1159/000505508.
10	Ben-Amor, I., Musarra-Pizzo, M., Smeriglio, A., D'Arrigo, M., Pennisi, R., Attia, H., Gargouri, B., Trombetta, D., Mandalari, G., and Sciortino, M.T. (2021). Phytochemical characterization of *Olea europaea* leaf extracts and assessment of their antimicrobial and anti-HSV-1 activity. *Viruses,* **13**(6), 1085. doi: 10.3390/v13061085.
11	Kabbash, E. M., Abdel-Shakour, Z. T., El-Ahmady, S. H., Wink, M. and Ayoub, I. M. (2023). Comparative metabolic profiling of olive leaf extracts from twelve different cultivars collected in both fruiting and flowering seasons. *Sci. Rep*., **13**(1), 612. doi: 10.1038/s41598-022-27119-5.
12	Suárez Montenegro, Z. J., Álvarez-Rivera, G., Mendiola, J. A., Ibáñez, E. and Cifuentes, A. (2021). Extraction and mass spectrometric characterization of terpenes recovered from olive leaves using a new adsorbent-assisted supercritical CO_2 process. *Foods,* **10**(6), 1301. doi: 10.3390/foods10061301.
13	Jimenez-Lopez, C., Carpena, M., Lourenço-Lopes, C., Gallardo-Gomez, M., Lorenzo, J. M., Barba, F. J., Prieto, M. A. and Simal-Gandara, J. (2020). Bioactive compounds and quality of extra virgin olive oil. *Foods*, **9**(8), 1014. doi: 10.3390/foods9081014.
14	Kiritsakis, A. K. (1998). Flavor components of olive oil—A Review. *JAOCS*, **75**(6), 673-681.
15	Natural Health Product. Olive Leaf - *Olea europaea* (2018). Health Canada, https://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=feuille.olea.europaea.leaf&lang=eng
16	Martindale (1996). The Extra Pharmacopoeia. Reynolds, J. E. F., Ed., 31st edition, Royal Pharmaceutical Society, London.
17	Fischer, C. (2018). Materia Medica of Western Herbs. Aeon Books Ltd, London. ISBN-13: 978-1-91159-751-3.
18	Spiteri, M. (2011). Herbal monographs including herbal medicinal products and food supplements. Department of Pharmacy, University of Malta. Set and printed by Print Right Ltd, Qormi.

19	Williams, L. and Wilkins (2004). Professional's Handbook of Complementary and Alternative Medicines, 3rd edition. ISBN13: 978-1-58255-243-9. ISBN10: 1-58255-243-6. ISSN 1522-0877.
20	Assessment Report on *Olea europaea* L.,Folium, (2017). EMA/HMPC/359236/2016. Committee on Herbal Medicinal Products (HMPC).
21	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements - An Evidence-Based Guide. 3rd edition, Churchill Livingstone. ISBN: 978 0 7295 3910 4.
22	https://www.rxlist.com/olive/supplements.htm
23	https://www.fda.gov/food/cfsan-constituent-updates/fda-completes-review-qualified-health-claim-petition-oleic-acid-and-risk-coronary-heart-disease#:~:text=The%20U.S.%20Food%20and%20Drug, risk %20of%20coronary%20heart%20disease
24	Olive leaf Monograph (2009). *Alternative Medicine Review, A journal of clinical therapeutic*, **14**(1), 62-66.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Panax ginseng C. A. Meyer. چنسنج

1. Names & Synonyms

***Panax ginseng* C. A. Meyer.**

Family: Araliaceae.

Syns.: *Aralia ginseng* (C. A. Mey.) Baill, *Panax verus* Oken (1).

Arabic: Ginseng جنسنج

English: Korean Ginseng, Red Ginseng, White Ginseng (2), Asian Ginseng (3).

2. Parts used for medicinal purpose

Dried root (4- 7).

N.B. White ginseng represents the peeled and sun-dried root whilst red ginseng is unpeeled, steamed and dried (6).

3. Major chemical constituents

- **Triterpenoid saponins (Ginsenosides)**: A complex mixture of compounds including Rb1, Rb2, Rc, Rd, Re, and Rg-1 (6,8).
- **Polysaccharides:** Pectins and glucans (9).
- **Others**: Peptides, polyacetylenic alcohols, fatty acids (6), starch, β-amylase, vitamins (B1 , B2 , B12, pantothenic acid, biotin), choline, minerals (6).

4. Medicinal uses (Indications)

A. Used as a prophylactic and restorative agent for enhancement of mental and physical capacities (5).

B. For symptoms of asthenia such as fatigue and weakness, exhaustion, tiredness, loss of concentration, and during convalescence (5,7, 10).

5. Herbal preparations correlated to medicinal use

1. **Comminuted herbal substance as a herbal tea** (5-7,11,12)
   Powdered dried roots are simmered for 15 minutes in 150 ml hot water as infusion or boiled with 150 ml water as decoction.
2. **Powdered ginseng root** (5,7,11,12)
   2.1. White ginseng.
   2.2. Red ginseng.

3. **Dry extract** (7)
   - **3.1.** White ginseng
     - **3.1.1.** Extraction solvent ethanol 34 - 40% V/ V.
     - **3.1.2.** Extraction solvent ethanol 40% V/ V, containing 4% ginsenosides.
     - **3.1.3.** Extraction solvent ethanol 57.9% V/ V (= 50% m/m) - 60% V/ V.
   - **3.2.** Red ginseng, extraction solvent ethanol 60% V/ V.
4. **Soft extract** of white ginseng, extraction solvent ethanol 60% -70% V/ V (7).
5. **Liquid extract** of white ginseng: extraction solvent ethanol 30.5% V/V (=25% m/m) – 34% V/ V (7).
6. **Tincture** (11).

Herbal preparations (2-6) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adults and elderly

Preparation 1

- 0.5 – 2 g, taken in the morning daily (5) or 1- 2 g, 2-3 times daily as a decoction (7).

- 3 - 10 g, daily as decoction or decoction concentrate (6,12).

- 3 g as infusion, 3 times daily for 3-4 weeks (11).

Preparation 2

0.5 – 4 g, daily (5,11,12).

2.1. Single dose: 250 -1200 mg, daily dose: 600-2000 mg, once daily (1200 mg) or 2-8 times, daily (7).

2.2. Single dose: 600 mg, daily dose: 1800 mg, 3 times daily (7).

Preparation 3 (7)

3.1.1. Single dose: 90-360 mg, daily dose: 200-670 mg, 1-4 times daily.

3.1.2. Single dose: 40-200 mg, daily dose: 40-200 mg (can be increased up to 600 mg in the first 5 days in special situations), 1-2 times daily.

3.1.3. Single dose: 98-220 mg, daily dose: 196-525 mg, 2-4 times daily.

3.2. 180-500 mg, daily dose: 360-500 mg, once daily (475 mg or 500 mg), or 2 times daily.

Preparation 4 (7)

Single dose: 300-440 mg, daily dose: 440-700 mg, once daily (440 mg) or 2 times daily.

Preparation 5 (7)

Single dose: 500- 1250 mg, daily dose: 900– 2500 mg, 1-2 times daily.

Preparation 6 (11)

1-2 ml daily (1:1 dilution).

Duration of use: Up to 3 months (7, 12)
If the symptoms persist for more than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (7, 12).

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- If breast cancer or other estrogen-dependent conditions are present, ginseng should not be used (11).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children and adolescents under 18 years of age has not been established (7, 12).
- General caution should be taken in patients with cardiovascular disease or diabetes (5, 6, 13).

9. Interactions with other medicinal products and other forms of interaction (11)

- Anticoagulants, antiplatelets, salicylates: Ginseng may decrease the action of these products.

- Antidiabetics, **Insulin**: Ginseng is known to decrease blood glucose levels, it may increase the hypoglycemic effect of antidiabetics; avoid concurrent use.

- Immunosuppressants: Ginseng may diminish the effect of immunosuppressants; do not use immediately before, during, or after transplant surgery.

- MAOIs: Concurrent use of MAOIs with ginseng may result in manic-like syndrome.

- **Stimulants**: Use of stimulants (e.g., xanthines) concurrently with ginseng is not recommended; overstimulation may occur.

- Concurrent use with caffeine-containing preparations or drinks should be avoided (14).

- **Ephedra:** Concurrent use of ephedra and ginseng may increase hypertension and central nervous system stimulation; concurrent use should be avoided.

Lab Test

- **Blood glucose**: Ginseng may decrease blood glucose (decoctions, infusions).

- **Plasma partial thromboplastin time, INR**: Ginseng may increase plasma partial thromboplastin time and INR.

- **Serum, urine estrogens**: Ginseng may have an additive effect on serum and 24-hour urine estrogens.

- **Serum digoxin**: Ginseng may falsely increase serum digoxin.

10. Fertility, pregnancy and lactation (6,7)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (7).

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Hypersensitivity reactions (urticaria, itching) (7, 11), insomnia (7, 11-13), anxiety, headache (11,12) and gastrointestinal disorders like stomach discomfort, nausea, vomiting, diarrhoea, and constipation have been reported (7).
- Hypertension, chest pain, palpitations, decreased diastolic blood pressure and increased QTC interval (11).

13. Overdose

- Restlessness (11,12), nausea, vomiting, anorexia and diarrhea (11).
- Ginseng Abuse Syndrome: edema, insomnia and hypertonia (11).
- Hypertension resulting from Ginseng Abuse Syndrome is associated with prolonged high dose Ginseng with concomitant use of caffeine (13).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/last revision

26/07/2022.

References

1	https://powo.science.kew.org
2	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements – An Evidence Based Guide. 3rd edition, Churchill Livingstone, ISBN: 978 0 7295 3910 4.
3	Aronson, J. K. (2009). Meyler's Side Effects of Herbal Medicines. Elsevier, ISBN: 978-044-453269-5.
4	British Pharmacopoeia (2020). Volume IV, www.webofpharma.com.
5	WHO monographs on selected medicinal plants (1999). Monographs on selected medicinal plants, **1**, 168-182.
6	Park, J. D., Rhee, D. K. and Lee, Y. H. Biological activities and chemistry of saponins from *Panax ginseng* C. A. Meyer. *Phytochem., Rev.,* **4**, 159–175 (2005). https://doi.org/10.1007/s11101-005-2835-8.
7	European Union Herbal Monograph on *Panax ginseng* A.C. Mayer, radix. (2014). EMA/HMPC/475726/201٢. Committee on Herbal Medicinal Products (HMPC).
8	Chen, W., Balan, P., Popovich, D. G. (2019). Analysis of ginsenoside content (*Panax ginseng*) from different regions. *Molecules*, **24**(19), 3491. doi: 10.3390/molecules24193491.
9	Kim, D. H. (2012). Chemical diversity of *Panax ginseng*, *Panax quinquifolium*, and *Panax notoginseng*. *J. Ginseng Res.*, **36**(1), 1-15. doi: 10.5142/jgr.2012.36.1.1.
10	https://www.herbalgram.org/resources/expanded-commission-e/ginseng-root.
11	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
12	Natural Health Product, *Panax ginseng* (L.) (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=29&lang=eng.
13	PDR for herbal medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
14	Kraft, K. and Hobbs, C. (2004). Pocket Guide to Herbal Medicine. Georg Thieme Verlag, ISBN: 1-58890-063-0.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Panax quinquefolius* L.** **چنسنج**

1. Names & Synonyms (1)

***Panax quinquefolius* L.**
Family: Araliaceae
Syns.: *Aralia quinquefolia* (L.) Decne. & Planch, *Ginseng quinquefolium* (L.) Alph. Wood (2).
Arabic: Ginseng جنسنج
English: Ginseng, American ginseng, American white ginseng, Canadian ginseng, Canadian white ginseng (3).

2. Parts used for medicinal purpose

Dried root (1, 3-5).

3. Major chemical constituents (1)

- **Triterpenoid saponins (Ginsenosides):** A complex mixture of compounds including Rb1, Re, Rc, and Rd (6).
- **Polysaccharides:** Pectins and glucans.
- **Unsaturated fatty acids:** Linolenic acid (7).
- **Others:** Starch, *β*-amylase, vitamins (B1, B2, B12, pantothenic acid, biotin), choline, fats, minerals.

4. Medicinal uses (Indications)

A. As adaptogen to increase recuperative power of the body (3, 5, 8).

B. Mild sedative to relieve nervousness, nervous dyspepsia and enhance stress resistance (3, 5).

5. Herbal preparations correlated to medicinal use (3-5)

1. Comminuted herbal substances as herbal tea.
The dried roots are added to 150 ml of hot water as infusion or boiled with water as a decoction or concentrated decoction.
2. Powder dried root.
3. Dry extract.
4. Fluid extract.
5. Tincture.

Herbal preparations (2-5) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the Pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1: 2.4 - 9 g, daily (4, 5).

Preparations 2: 0.5 - 12 g, daily (4, 5) or 3 – 9 g, daily in divided doses (3).

Preparations 3 – 5: The equivalent amount of the dried root (0.5- 12 g, daily) (5).

Preparations 5: 1-2 ml, daily (1:1 dilution) (4).

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- If breast cancer or other estrogen-dependent conditions are present, ginseng should not be used (4).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children and adolescents under 18 years of age is not recommended (5).
- Diabetic patients should consult a physician prior to use (5).

9. Interactions with other medicinal products and other forms of interaction

- Blood thinner and Digoxin (5).
- An extract of the root (containing 10% ginsenosides) inhibited the activity of cytochrome P450 isozymes CYP1A1, CYP1A2 and CYP1B1 *in vitro* in human liver microsomes. Thus, there is a potential for interactions with other drugs that are metabolized by these enzymes (3).

Lab Test (4)

- **Blood glucose**: Ginseng may decrease blood glucose.
- **Plasma partial thromboplastin time, INR**: Ginseng may increase plasma partial thromboplastin time and INR.
- **Serum digoxin**: Ginseng may falsely increase serum digoxin.

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (1, 3).
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- None reported (3, 5).
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/last revision

9/8/2022.

References

1	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
2	https://powo.science.kew.org.
3	WHO monographs on selected medicinal plants (2009). Monographs on selected medicinal plants, **4**, 226-243.
4	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
5	Natural Health Product, *Panax quinquefolius* (L.) (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=29&lang=eng
6	Qi, L. W., Wang, C. Z. and Yuan, C. S. (2011). Ginsenosides from American ginseng: chemical and pharmacological diversity. *Phytochemistry*, **72**(8), 689-99. doi: 10.1016/j.phytochem.2011.02.012.
7	Kochan, E. Szymańska, G. Motyl, I. and Blasiak J. (2019). American ginseng (*Panax quinquefolium* L.) as a source of bioactive phytochemicals with pro-health properties. *Nutrients*, **11**(5), 1041.
8	Martindale: The Complete Drug Reference (2007). Pharmaceutical Press. Electronic version, London.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Passiflora incarnata* L.** زهر الآلام

1. Names & Synonyms (1)

***Passiflora incarnata* L.**
Family: Passifloraceae (2-4).
Syns.: *Granadilla incarnata* Medik. (1, 2).
English name: Passionflower (3, 5), Passion vine, Apricot vine, Grenadille, Maypop, Passiflora (3, 6).
Arabic name: Zahr el-alam زهر الآلام (7).

2. Parts used for medicinal purpose

Herb / dried aerial parts (2, 3, 5, 6, 8).

3. Major chemical constituents

- **Flavonoids:** as C-glycosides of apigenin (e.g. vitexin, isovitexin, schaftoside, isoschaftoside) and of luteolin (e.g. orientin, iso-orientin) (3) and their aglycones (apigenin, chrysin (9), luteolin, quercetin, kaempferol) (6, 10, 11).
- **Others:** indole alkaloids (as harmane, harmine and harmaline), cyanogenic glycosides, volatile oil, maltol (6, ١٠, 11), amino acids, fatty acids (e.g. linoleic, linolenic, myristic, palmitic, oleic acids), formic and butyric acids, sterols (e.g. stigmasterol, sitosterol) and sugars (e.g. raffinose, sucrose, glucose, fructose) (3).

4. Medicinal Uses (Indications)

A. Relief of mild symptoms of mental stress, to aid sleep (insomnia) (5, 6) and as a mild sedative for nervous restlessness and anxiety (2, 12).
B. As a calming agent for hemorrhoids, burns, and inflammation (6, 13).

5. Herbal preparations correlated to medicinal use

1. **Comminuted herbal substance in boiling water as an herbal infusion** (5)
2. **Powdered herbal substance** (5).
3. **Liquid extract** (5)
   - **3.1** Ethanol 25% V/V
     - **3.1.1** Ethanol 25% V/V (DER 1:8)
     - **3.1.2** Ethanol 25% V/V (DER 1:1) (15)

3.2 Ethanol 45% V/V

3.3 Ethanol 60% V/V

3.4 Ethanol 70% V/V

3.5 Ethanol (96% V/V) + glycerol (85% m/m) + Water (11.8 + 1 + 7.9)

4. **Dried extracts** (5)

Corresponding to the tea and liquid extracts above.

5. **Tincture**

5.1 Ethanol 25% (1:8) (4).

5.2 Ethanol 45% (1:8) (15).

Herbal preparations (2-5) are in a pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adolescents, adults and elderly

Preparation 1

Indication A: Orally

1-2.5 g in 150 ml of boiling water as an herbal tea, 1-4 times daily (2, 5).

Indication B: Topically

20 g simmered in 200 ml water, strained and cooled before application (13).

Preparation 2

Indication A: Orally

0.5 - 2g, 1-4 times daily (2, 3, 5).

Preparation 3 (5)

Indication A: Orally

3.1.1 2 - 4 ml, up to 4 times daily

3.1.2 0.5 - 2 ml, up to 4 times daily

3.2 2 ml, up to 3 times daily

3.3 1 ml, 3-5 times daily

3.4 2 ml, up to 3 times daily

3.5 Adults: 0.3-0.4 ml, 3-5 times daily

Adolescents: 0.3-0.4 ml 3 times daily

Preparation 4 (5)

Doses of dried extracts corresponding to the posologies of tea and liquid extracts above.

Preparation 5

Indication A: Orally

5.1: 2-4 ml, up to 4 times daily (2-4).
5.2: 0.5-2.0 ml, 3 times daily (6).

Duration of use (5)

If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or pharmacist should be consulted.

Method of administration (5): Oral and topical use.

7. Contraindications

Hypersensitivity to active substances and to other plants of the same family (5).

8. Special warnings and precautions for use (5)

- If the symptoms worsen during the use of the medicinal product, a doctor or pharmacist should be consulted.
- The use in children under 12 years of age is not recommended.
- The use at dosages higher than those recommended and/or for longer periods should be avoided (3).

9. Interactions with other medicinal products and other forms of interaction

- None reported (5). However, potential interactions with other medicines with similar or opposing effects and used concurrently should be considered (3) such as benzodiazepines (additive effects at high doses), barbiturates (additive CNS effects) and anticoagulants (increased risk of bleeding) (4, 13).
- Passionflower may lower blood pressure, caution is advised when using with antihypertensive medications (13).

10. Fertility, pregnancy and lactation (5, 15)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (5)

May impair ability to drive and use machines. Affected patients should not drive or operate machinery.

12. Undesirable effects (5)

- None known.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

13. Overdose (5)

No case of overdose has been reported. However, it is possible that overdoses may cause sedation to a greater extent than intended (3), drowsiness (4) and potentiation of MAOI therapy (15) are also possible.

14. Relevant biological activities (5)

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional data

-

16. Date of last revision

10/05/2023.

References

1	www.powo.science.kew.org
2	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, **3**, 257-267.
3	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
4	Spiteri, M. (2011). Herbal monographs including herbal medicinal products and food supplements. Department of Pharmacy, University of Malta. Set and printed by Print Right Ltd, Qormi.
5	European Union Herbal Monograph on *Passiflora incarnata* L., Hrotherba (2014). EMA/HMPC/715092/2013. Committee on Herbal Medicinal Products (HMPC).
6	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.
7	Bedevian, A. K. (1936). Illustrated Polyglottic Dictionary of Plant Names. Argus and Papazian Presses.
8	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements - An Evidence-Based Guide. 3rd edition, Churchill Livingstone. ISBN: 978 0 7295 3910 4.
9	Seetharaman, P., Gnanasekar, S., Chandrasekaran, R., Chandrakasan, G., Kadarkarai, M. and Sivaperumal, S. (2017). Isolation and characterization of anticancer flavone chrysin (5,7-dihydroxy flavone)-producing endophytic fungi from *Passiflora incarnata* L. leaves. *Annals of Microbiology*, **67**(4), 321- 331.
10	PDR for herbal medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
11	Smruthi, R., Divya, M., Archana, K. and Ravi, M. (2021). The active compounds of Passiflora spp and their potential medicinal uses from both *in vitro* and *in vivo* evidences. *J. Adv. Biomed. & Pharm. Sci.* **4**, 45-55.
12	Natural Health Product, *Passiflora incarnata* (L.) (2018). Health Canada, https://webprod.hc-sc.gc.ca/nhpid bdipsn/atReq.do?atid=passionflower.passiflore& lang=eng
13	Passionflower (2014). In: Natural Medicines [database on the Internet]. Somerville (MA): Therapeutic Research Center. https://naturalmedicines.therapeuticresearch.com
14	Williams, L. and Wilkins (2004). Professional's Handbook of Complementary and Alternative Medicines, 3rd edition. ISBN13: 978-1-58255-243-9. ISBN10: 1-58255-243-6 ISSN 1522-0877.
15	Duke, J. A. (2002). Handbook of Medicinal Herbs. 2nd ed. CRC Press. ISBN 978084931284.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Pelargonium sidoides DC. بيلارجونيوم

1. Names & Synonyms (1)

***Pelargonium sidoides* DC.**
Family: Geraniaceae.
Syns.: *Cortusina sidifolia* (Thunb.) Eckl. & Zeyh., *Geraniospermum sidifolium* (Thunb.) Kuntze, *Geranium sidifolium* Thunb.
Arabic name: Pelargonium بيلارجونيوم.
English name: Pelargonium root (2), Geranium; South African geranium.

2. Parts used for medicinal purpose

Root (2-4).

3. Major chemical constituents

- **Highly oxygenated coumarins:** 7-Hydroxy-5,6-dimethoxycoumarin (umckalin), 5,6,7-trimethoxycoumarin, 5,6,7,8-tetramethoxycoumarin (artelin), 6,8-dihydroxy-5,7-dimethoxycoumarin (and their sulfooxy derivatives), esculin and scopoletin (5-8).
- **Phenolic acids:** Gallic acid and its methyl ester, and hydroxy-cinnamic acids (caffeic acid, *p*-coumaric acid).
- **Flavan-3-ols:** Calechin, oligomeric and polymeric proanthocyanidins (mainly with catechin and gallocatechin units).
- **Amino acids:** Adenosine 3′,5′-cyclic monophosphate, guanosine-3',5'-cyclomonophosphate, and 1-methyl guanosine-3',5'-cyclomonophosphate (7).

4. Medicinal Uses (Indications) (2,4)

Symptoms of upper respiratory tract infections including common cold, such as blocked or runny nose, sore throat and cough.

5. Herbal preparations correlated to medicinal use.

1. Liquid herbal extract ethanol 11-12% (2,4).
2. Dry herbal extract ethanol 11% (2).

Herbal preparations are in a pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use (4)

Preparation 1

Adults, elderly and children over 12 years: 2.5-7.5 mL daily in divided doses.
Children aged 6-12 years: 1.25–2.5 mL daily in divided doses.
Children aged 2-6 years: 0.6-1.25 mL daily in divided doses.

Preparation 2

Adults, elderly and children above 12 years: Single dose 20 mg, 3 times daily.
Children aged 6-12 years: Single dose 20 mg, 2 times daily.

Duration of use

If the symptoms persist longer than one week, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (2,4).

7. Contraindications

Hypersensitivity to the active substance and to other plants of the same family (2).

8. Special warnings and precautions for use (2)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children should be under medical supervision.
- In case signs of hepatotoxicity occur, the administration of the medicinal product should be stopped immediately and a medical doctor should be consulted.
- In case of liver disorders, a medical doctor should be consulted prior to use.

9. Interactions with other medicinal products and other forms of interaction (2)

None reported.

10. Fertility, pregnancy and lactation (2)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (2)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (2,4)

- Mild gastrointestinal complaints (diarrhea, epigastric discomfort, nausea or vomiting, dysphagia), mild nasal, gingival bleeding and allergic reactions have been reported.
- If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.

13. Overdose (2)

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional data

-

16. Date of last revision

01/05/2023.

References

1	https://powo.science.kew.org.
2	European Union Herbal Monograph on *Pelargonium sidoides* DC and/or *Pelargonium reniforme* Curt., Radix. EMA/HMPC/444244/2015. Committee on Herbal Medicinal Products (HMPC).
3	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd.
4	ESCOP Monographs (2015). *Pelargonium* Root. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills.
5	Alossaimi, M. A., Alzeer, M. A., Abdel Bar, F. M. and ElNaggar, M. H. (2022). *Pelargonium sidoides* root extract: Simultaneous HPLC separation, determination, and validation of selected biomolecules and evaluation of SARS-CoV-2 inhibitory activity. *Pharmaceuticals*, **15**, 1184. https://doi.org/ 10.3390/ph15101184.
6	Kayser, O. and Kolodziej, H. (1995). Highly oxygenated coumarins from *Pelargonium sidoides*. *Phytochemistry*, **39**(5), 1181–1185. doi:10.1016/0031-9422(95)00166-5.
7	Mofokeng, M, M., Prinsloo, G., Araya, H. T., du Plooy, C. P., Sathekge, N. R., Amoo, S. O. and Steyn, J. M. (2020). Yield and metabolite production of *Pelargonium sidoides* DC. in response to irrigation and nitrogen management. *Metabolites*, **10**(6), 219. doi: 10.3390/metabo10060219.
8	Yu, S. M., Kim, S. J., Yoon, Y. C. and Kim, J. H. (2021). Development and application of a chemical profiling method for the assessment of the quality and consistency of the *Pelargonium sidoides* extract. *J. Anal. Sci. Technol*. **12**, 46. https://doi.org/10.1186/s40543-021-00297-z.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Pimpinella anisum* L.** **ينسون**

1. Names & Synonyms (1)

***Pimpinella anisum* L.**

Family: Apiaceae (Umbelliferae).

Syns: *Anisum officinarum* Moench., *A. vulgare* Gaertn., *Apium anisum* L. Crantz., *Carum anisum* L. Baill., *Pimpinella anisum* cultum Alef., *P. aromatica* Bieb., *Selinum anisum* L. E.H.L. Krause., *Sison anisum* Spreng., *Tragium anisum* Link.

Arabic: Yansoon ينسون

English: Anise, Aniseed.

2. Parts used for medicinal purposes

Dried ripe fruits (1).

3. Major chemical constituents

Essential oil: contains mainly trans-anethole, estragole (methylchavicol, isoanethole), *β*-anisaldehyde, *α*-terpenol, *cis*-anethole (1).

4. Medicinal uses

A. Symptomatic treatment of mild, spasmodic gastrointestinal complaints including dyspepsia, bloating and flatulence (2, 3).

B. Expectorant in cough associated with cold and inflammation of respiratory tract (2-4).

5. Herbal preparations correlated to medicinal use (3)

1. **Comminuted herbal substance as herbal tea for oral use as an infusion.**

Whole or comminuted dried ripe fruits (freshly comminuted) with 0.25L. of boiling water (brew for 15 minutes).

2. **Anise powder**.
3. **Anise dry extract**, using mixture of ethanol and water in different concentrations as solvent.
4. **The essential oil.**

Herbal preparations (2-4) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration (2)

Generally

Doses in adolescents (12 years and older) are the same as in adults (18 years and older) doses (2,5).
Duration of use: Not to be taken for more than two weeks for adults and adolescents (2).
Due to safety concerns regarding estragole, the daily amount of estragole must be adjusted to the body weight of the age group as acceptable daily intake of estragole/day =10 µg x body weight (kg) (6).

Preparation 1

Adults and adolescents: 1 to 3.5 g of the whole or (freshly comminuted or crushed) aniseed in 150 ml of boiling water as a herbal infusion 3 times daily (2).

Children (5)**:**

- **0-1 year of age**: average daily dose of 0.5 g of crushed fruits as an infusion.
- > **1-4 years of age**: average daily dose of 1 g of crushed fruits as an infusion.
- **4-10 years of age**: average daily dose of 2 g of crushed fruits as an infusion.

Preparation 2

Adults: 3 g powder taken after each meal three times daily for 4 weeks for treatment of dypepsia (7,8).

- For a long-term disorder of the large intestines that causes stomach pain (irritable bowel syndrome or (IBS)): 200 mg of anise oil in a special coated capsule, to be taken three times daily for 4 weeks (7).

- Menopausal symptoms 330 gm to be taken 3 times daily for 4 weeks (8).

Preparation 3

Adults:
-The appropriate dose depends on several factors such as the user's age, health, and several conditions.

-Relevant directions on product labels should be followed and physician or pharmacist should be consulted before use (9)**.**

Preparation 4

Adults: 0.05-0.2 ml of anise oil, three times daily (10).

Children: Pure essential oil should not be given to infants and young children (1) but it may be used in a pharmaceutical dosage form, under medical supervision and not exceed the appropriate dose (**Estragole/day NMT 10µg/kg/day x body weight of the child kg)** (6).

Method of administration: Oral use (2).

7. Contraindications

Hypersensitivity to active substances and to other plants of the same family (2,9).

8. Special warnings and precautions for use

-If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted

-Anise might lower blood sugar, so blood sugar levels should be monitored carefully if diabetic patients use anise (7).

- The use in children under the age of 12 years is not recommended without medical supervision (1,2).

-Anise oil should not be given to children and adolescents under age of 18 years due to the presence of estragole and physician advice should be sought (1-3).

9. Interactions with other medicinal products and other forms of interaction

- **Estrogens, hormonal contraceptives**: large quantities of anise may interfere with estrogen replacement therapy or hormonal contraceptives (theoretical). Some types of cancer are affected by hormones in the body. Estrogen-sensitive cancers are cancers that are affected by estrogen levels in the body (3,7,9).

- **Iron**: Anise may increase the action of iron (3).

- **Warfarin**: Anise may increase the action of warfarin (3).

- **Lab Test:** Increased Prothrombin time (PT/INR) (3).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy or lactation is not recommended (2).

- Aniseed may be used during pregnancy and lactation at the recommended dosage, as aqueous infusions only (5).

-Owing to the traditional use of the oil as an emmenagogue and to induce labour, its experimental estrogenic and potential mutagenic effects, and reports of anethole toxicity in infants (2).

-No fertility data available but there are a mild oestrogenic activity and antifertility effects of the essential oil and anethole (the major constituent of the essential oil) (5).

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Allergic reactions to aniseed affecting the skin or the respiratory system may occur (1-3).
- Occasional allergic reactions to the oil affecting the skin, respiratory system and gastrointestinal tract are reported e.g. nausea and vomiting (1,3).
- Hypermineralocorticism (3).

13. Overdose

- Ingestion of 1.0–5.0 ml of the oil can result in nausea, vomiting, seizures and pulmonary edema (1,3).
- Anethole toxicity in infants has been reported, and presents clinically with symptoms of hypertonia, continued crying, atypical ocular movements, twitching, cyanosis, vomiting and lack of appetite (1).
- In cases of overdose (> 50 mg/kg), the ingestion of milk and alcohol is contraindicated owing to increased resorption (1).

14. Relevant biological properties

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

20/8/2023.

References

1	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, **3**, 42-63.
2	Community Herbal Monograph on *Pimpinella anisum* L., Fructus (2013). EMA/HMPC/321184/2012. Committee on Herbal Medicine Products (HMPC).
3	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.
4	PDR for herbal medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
5	https://escop.com/wp-content/uploads/edd/2015/09/Anisi.pdf
6	https://www.ema.europa.eu/en/documents/public-statement/public-statement-use-herbal-medicinal-products-containing-estragole_en.pdf
7	https://www.webmd.com/vitamins/ai/ingredientmono-582/anise
8	https://www.drugs.com/npc/anise.html
9	https://www.rxlist.com/anise/supplements.html
10	Community Herbal Monograph on *Pimpinella anisum* L., Aetheroleum (2013). EMA/HMPC/321185/2012. Committee on herbal Medicine Products (HMPC).

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Pinus pinaster* Aiton** صنوبر بحري

1. Names & Synonyms (1)

***Pinus pinaster* Aiton**
Family: Pinaceae.
Syns.: *Pinus maritima* L., *Pinus glomerata* Salisb., *Pinus pinaster* subsp. *atlantica* Villar.
Arabic: Senouber Bahri صنوبر بحري (2).
English name: French maritime pine (3), Maritime pine, Cluster pine (4,5).

2. Parts used for medicinal purpose

Bark (3,5,6) fresh needles and branch tips (7).

3. Major chemical constituents

- **Bark:**

Flavonoids: Taxifolin (dihydroquercetin), catechin, and procyanidins (oligomers of catechin/and or epicatechin) (8,9).

Acids: Quinic and phenolic acids (caffeic, ferulic, protocatechuic, gallic, and ellagic acids) (10).

Essential oil: α-Terpineol, β-caryophyllene, β-pinene, cyclofenchene, valencene, α-humulene, α-pinene, 3-carene, and junipene (8,11).

Others: Abietic acid and derivatives (12), resveratrol, cellulose, hemicellulose and lignin (13).

- **Needles and branch tips:**

Essential oil: β-Caryophyllene (14), abietane, Δ-cadinene, β-cadinene sclarene, α-amorphene (15), and (Z,E)-farnesyl propionate (16).

Others: monoterpenes, neutral diterpenes, fatty acids and resin acids (16).

4. Medicinal Uses (Indications) (3, 5-7)

A- Improvement of chronic venous insufficiency.

B- Reduction of cardiovascular risks such as hypertension, thrombosis and impaired blood circulation.

C- Improvement of the endothelial function in coronary artery disease.

D- Enhancement of retinal blood circulation in vascular retinopathyy in early stages of diabetic retinopathy and in slowing its progression.

E- Relief menopausal symptoms.

F- Symptomatic relief of asthma.

G- Alleviate symptoms of Attention Deficit–Hyperactivity Disorder (ADHD) (17).

H- Symptomatic relief of osteoarthritis.

I- Symptomatic treatment of the respiratory tract infections and inflammations (coughs, acute bronchitis, laryngitis, pharyngitis, tracheitis rhinopharyngitis, tonsillitis), as well as those of the mouth.

J- Symptomatic relief of rheumatism, acute rheumatic fever and arthropathies.

K- Symptomatic relief of neuralgia and neuritis.

5. Herbal preparations correlated to medicinal use

1. Pine bark extract (3,6,13).
2. Essential oil from needles and branch tips (7).

Herbal preparations are in a pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1
Adults
Indication A
45-360 mg daily or 100 mg, 3 times daily (3, 6).
Duration of use: 4 weeks (3).
Method of administration: Oral use.

Indication B
25 mg daily (preventative dose) (3).
100 – 150 mg daily (3).

Duration of use: As directed by a physician.
Method of administration: Oral use.

Indication C
150 mg, 3 times daily (6).
Duration of use: As directed by a physician.
Method of administration: Oral use.

Indication D
50 mg, 3 times daily (6,17).
Duration of use: As directed by a physician.
Method of administration: Oral use.

Indication E
30 – 60 mg daily (3,6).
Duration of use: As directed by a physician.
Method of administration: Oral use.

Indications F, G, H
100 mg daily (3).
Duration of use: As directed by a physician.
Method of administration: Oral use.

Indications J, K
Bath additive: 100 g ethanolic extract to a full tub of bath water (7).
Duration of use: As directed by a physician.
Method of administration: Topical use.

Preparation 2 (7)
Adults
Indication I
2 g (9 to 10 drops) of pine oil to 2 cups of hot water and inhale the vapours. Repeat several times a day.
Duration of use: As directed by a physician.
Method of administration: Inhalation use.

Indications J, K
Bath additive: One drop of the oil per litre of water bath for 10 to 20 minutes at a water temperature of 35–38°C.
Oil: Apply a few drops of the oil to the affected areas of the skin and rub in thoroughly.
Ointment: Apply a 10–50 % ointment several times a day, rub onto the affected area.
Cream: Apply up to 4 times daily.

Duration of use: As directed by a physician.

Method of administration: Topical use.

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- The use of oil or ethanolic extract as a bath additive is contraindicated in bronchial asthma, whooping cough. Individuals with extensive wounds, acute skin diseases (acute dermatitis), febrile and infectious diseases, heart failure and/or hypertension (cardiac insufficiency) (7).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children should be under medical supervision (7).

9. Interactions with other medicinal products and other forms of interaction

Lab test: Pine bark extract may reduce blood platelet aggregation (7).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur a doctor or a pharmacist should be consulted.
- Mild side effects such as gastrointestinal problems, nausea, headache, dizziness and skin sensitisation are rare and transient in most cases (6).
- The oil can irritate the skin and mucous membranes or worsen bronchospasms (7).

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

As an antioxidant pine bark extract may be effective at any dose. However, in order to have measurable physiological effects related to prevention of oxidative tissue damage, the daily intake should be at least 20 mg (3).

16. Date of last compilation/last revision

08/06/2023.

References

1	www.powo.science.kew.org
2	https://algerianativeplants.net/html-ang/plante-algerieinventaire.php?char=P &page=2
3	Oliff, H. (2019). Scientific and Clinical Monograph of Pycnogenol (French maritime pine bark extract) *Pinus pinaster* Aiton subsp. atlantica [Fam. Pinaceae]. American Botanical Council (ABC). www.herbalgram.org.
4	https://www.conifers.org/pi/Pinus_pinaster.php
5	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. Wiley-Blackwell, ISBN: 978-1-118-54356-6.
6	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.
7	Kraft, K. and Hobbs, C. (2004). Pocket Guide to Herbal Medicine. Stuttgart; New York: Thieme.ISBN 3-13-126991-X (GTV), ISBN 1-58890-063-0 (TNY).
8	Alonso-Esteban, J. I., Carocho, M., Barros, D., Velho, M. V., Heleno, S. and Barros, L. (2022). Chemical composition and industrial applications of Maritime pine (*Pinus pinaster* Ait.) bark and other non-wood parts. *Rev. Environ. Sci. Biotechnol.*, **21**, 583- 633. https://doi.org/10.1007/s11157-022-09624-1.
9	Iravani, S. and Zolfaghari, B. (2014). Phytochemical analysis of *Pinus eldarica* bark. *Res. Pharm. Sci.*, **9**(4), 243-250.
10	Ramos, P. A. B., Pereira, C., Gomes, A. P., Neto, R. T., Almeida, A., Santos, S. A. O., Silva, A. M. S. and Silvestre, A. J. D. (2022). Chemical characterisation, antioxidant and antibacterial activities of *Pinus pinaster* Ait. and *Pinus pinea* L. bark polar extracts: Prospecting forestry by-products as renewable sources of bioactive compounds. *Appl. Sci.*, **12**, 784. https://doi.org/10.3390/app12020784.
11	Zolfaghari, B. and Iravani, S. (2012). Essential oil constituents of the bark of *Pinus pinaster* from Iran. *Journal of Essential Oil-Bearing Plants,* **15**(3), 348-351.
12	Sousa, J. L. C., Ramos, P. A. B., Freire, C. S. R., Silva, A. M. S. and Silvestre, A. J. D. (2018). Chemical composition of lipophilic bark extracts from *Pinus pinaster* and *Pinus pinea* cultivated in Portugal. *Appl. Sci.*, **8**, 2575. https://doi.org/10.3390/app8122575.
13	Fradinho, D.M., Pascoal, C. N., D. Evtuguin, F. C., Jorge, M. A., Irle, M. H., Gil, J. and Pedrosa d. J. (2002). Chemical characterisation of bark and of alkaline bark extracts from maritime pine grown in Portugal. *Industrial Crops and Products*, **16** (1), 23-32. ISSN 0926-6690, https://doi.org/10.1016/S0926-6690(02)00004-3.
14	Dob, T., Berramdane, T. and Chelghoum, C. (2005). Analysis of essential oil from the needles of *Pinus pinaster* growing in Algeria. *Chem. Nat. Compd.*, **41**, 545–548. https://doi.org/10.1007/s10600-005-0202-z.
15	Fkiri, S., Ghazghazi, H., Rigane, G., Salem, B. E. N., Mezni, F., Khaldi, A., Khouja, M. L. and Nasr, Z. (2019). Chemical compositions and biological activities essential oil from the needles of North African *Pinus pinaster* Var. *Rev. Roum. Chim.*, **64**(6), 511-517.
16	Arrabal, C., García-Vallejo, M. C., Cadahia, E., Cortijo, M. and Fernández de Simón, B. (2012). Characterization of two chemotypes of *Pinus pinaster* by their terpene and acid patterns in needles. *Plant Syst. Evol.*, **298**, 511–522. https://doi.org/10.1007/s00606-011-0562-8.
17	https://www.rxlist.com.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Primula veris* L.** زَهْرة الرَبيعِ

1. Names & Synonyms (1)

***Primula veris* L.**

Family: Primulaceae

Syns.: *Primula officinalis* L. Hill.

Arabic: Zahr El-hakl زهر الحقل , Zahrat El-rabee' زهرة الربيع

English name: Cowslip (2-4), Primula (4).

2. Parts used for medicinal purpose

Dried Flowers and Roots (2-4).

3. Major chemical constituents

Flowers:

- Phenolic compounds: including flavonoids as rutin and isorhamnetin 3-*O*-rutinoside (5), hyperoside catechin, astragalin and catechin (6).

Leaves:

- Kaempferol 3-*O*-rutinoside-7-*O*-rhamnoside, rutin, vitamin C (5).

Roots:

- Triterpene saponins (6): Primula saponins I and II, priverosaponin B22-acetate (4, 5).
- Phenolic glycosides: primverin and primulaverin (4, 6).

4. Medicinal Uses (Indications)

Expectorant in cough associated with cold (4).

5. Herbal preparations correlated to medicinal use (4)

1. **Comminuted herbal substance as herbal tea for oral use**
   - **1.1** Roots.
   - **1.2** Flowers.
2. **Dry extract** (DER 3-9:1), extraction solvent ethanol 40-50 % v/v (Roots).
3. **Liquid extract**
   - **3.1** Extraction solvent ethanol, 70 % v/v (Roots), (DER 1:1).
   - **3.2** Extraction solvent ethanol 70% v/v (Roots), (DER 1:2.0-2.5).
   - **3.3** Extraction solvent ethanol 25% v/v (flowers), (DER 1:1).
4. **Tincture** (1:5), extraction solvent ethanol 70 % v/v (Roots).
5. **Soft extract** (Roots)
   - **1.1** Extraction solvent water (DER 5-10:1).
   - **5.2** Extraction solvent ethanol 20-55% v/v, (DER 1-4:1).

Herbal preparations (2-5) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use (4)

Preparation 1

Preparations 1.1

Adolescents, adults, elderly: 0.2 – 0.5 g in 150 ml of boiling water as an herbal infusion, 3 times daily.

Preparation 1.2

Adolescents, adults, elderly: 1 g in 150 ml of boiling water as an herbal infusion, 3 times daily.

Preparation 2

Adolescents, adults, elderly:

- Single dose: 0.1 – 0.2 g, 3 times daily.
- Single dose equivalent to 0.2 – 0.5 g herbal substance, 3 times daily.

Preparation 3

Preparations 3.1

Adolescents, adults, elderly: Single dose: 0.5 g, 3 times daily.

Preparations 3.2

Adolescents, adults, elderly: Single dose: 0.6 g, 4 times daily.

Children between4-12 years of age: Single dose 0.33 g, 3 times daily.

Preparations 3.3

Single dose: 1 - 3 ml, up to 3 times daily, Maximum daily dose 6 ml (2, 3).

Preparation 4
Adolescents, adults, elderly: Single dose: 0.5 – 1 g, 3 times daily.
Children between 4-12 years of age: Single dose 0.3 – 0.5 ml, 3 times daily.

Preparation 5
Preparations 5.1 and 5.2
Adolescents, adults, elderly: Single dose equivalent to 0.2 – 0.5 g herbal substance,3 times daily.
Preparation 5.2
Children between 6 - 12 years of age: Single dose 0.12 g, 3-4 times daily.
Children between 4 - 6 years of age: Single dose 0.12 g, 3 times daily.

Duration of use

If the symptoms persist longer than 1 week, a doctor or a pharmacist should be consulted.

Method of administration: Oral use.

7. Contraindications

Hypersensitivity to the active substance or to other Primula species (4).

8. Special warnings and precautions for use (4)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Preparations **1, 2, 3.1, 3.3 and 5.2**: The use in children under 12 years of age is not recommended.
- Preparations **3.2, 4 and 5.2:** The use in children under 4 years of age is not recommended.
- Caution is recommended in patients with gastritis or gastric ulcer.
- If dyspnoea, fever or purulent sputum occurs, a doctor or a pharmacist should be consulted.

9. Interactions with other medicinal products and other forms of interaction (2)

- **Antihypertensives, diuretics:** Cowslip may increase the effect of antihypertensives, diuretics.
- **CNS depressants:** Cowslip may increase the effect of antianxiety agents and sedatives/hypnotics; concurrent use should be avoided.

- **Lab Test: AST, ALT, alkaline phosphatase:** Cowslip may increase these levels.

10. Fertility, pregnancy and lactation (4)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (4)

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Allergic reactions may occur.

13. Overdose (4)

Overdose may lead to stomach upset, vomiting or diarrhoea.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of last revision

06/09/2022.

References

1	http://www.theplantlist.org.
2	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.
3	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
4	European Union Herbal Monograph on *Primula veris* L. and/or *Primula elatior* L. Hill, Radix (2012). EMA/HMPC/104095/2012. Committee on Herbal Medicinal Products (HMPC).
5	Tarapatskyy, M., Gumienna, A., Sowa, P., Kapusta, I. and Puchalski, C. (2021). Bioactive phenolic compounds from *Primula veris* L.: Influence of the extraction conditions and purification. *Molecules*, **26**(4), 997.
6	Katarzyna, B., Jarosław, L. P., Małgorzata, M., Olga, K., Izabela, S. S. and Zenon, W. (2017). Phenolics in *Primula veris* L. and *P. elatior* (L.) Hill raw materials. *International Journal of Analytical Chemistry,* Article ID 2871579. https://doi.org/10.1155/2017/2871579.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Prunus africana (Hook.f.) Kalkman خوخ أفريقى - برقوق أفريقي

1. Names & Synonyms (1)

***Prunus africana* (Hook.f.) Kalkman.**

Family: Rosaceae.

Syns.: *Lauro-cerasus africana* (Hook.f.) Browicz, *Pygeum africanum* Hook.f.

Arabic: Barkouk Afriki برقوق أفريقي - Khoukh Afriki خوخ أفريقي

English: African stinkwood, African prune, African cherry, bitter almond, iron wood, pygeum, red stinkwood (2).

2. Parts used for medicinal purpose

Dried bark (stem /trunk) (3,4).

3. Major chemical constituents

- **Phytosterols**: *β*-Sitosterol and its glucoside (5) and *β*-sitostenone (6, 7).
- **Triterpenes**: Ursolic (5) and oleanolic acids (8).
- **Phenolic acids**: Ferulic acid and its esters of docosanol and tetracosanol (8).
- **Fatty acids**: Lauric and myristic acids (7).
- **Others:** *N*-Butylbenzene-sulfonamide and atraric, benzoic and *p*-hydroxybenzoic acids (5, 8).

4. Medicinal uses (Indications)

Relief of lower urinary tract symptoms related to benign prostatic hyperplasia stages I and II such as nocturia, polyuria and urinary retention after serious conditions have been excluded by a medical doctor (3, 4, 9-12).

5. Herbal preparations correlated to medicinal use

1. Comminuted herbal substances are added to water as herbal tea in the form of decoction or infusion (4).
2. Lipophilic extract (4, 9, 10).

Herbal preparation (2) is in a pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adults and elderly

Preparation 1

Not to exceed 4 g, daily (4).

Preparation 2

50–200 mg in divided doses, standardized to 12-14% of phytosterols (3, 4, 9-13).

Duration of use: Long-term use is possible (3).

Method of administration: Oral use (3).

- There is no relevant use in women, adolescents and children (3)
- To be taken with food or milk to minimize gastrointestinal disturbances. (9).

7. Contraindications

- Hypersensitivity to the active substances and to other plants of the same family (3).
- The use in children and adolescents under 18 years of age is contraindicated because of its effects on androgen and oestrogen metabolism (9,10) and the lower urinary tract symptoms in these populations requires medical supervision (3).

8. Special warnings and precautions for use

- If complaints worsen or if symptoms such as fever, spasms or blood in the urine, painful urination or urinary retention occur during the use of the medicinal product, a doctor should be consulted (3, 4, 9).
- Diagnosis of prostate cancer should be excluded before use (4).

9. Interactions with other medicinal products and other forms of interaction.

None reported (3, 4).

10. Fertility, pregnancy and lactation

- Pregnancy and lactation: Not relevant (3, 9).
- No fertility data available (3).

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (3).

12. Undesirable effects (3, 9, 10)

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Mild gastrointestinal discomfort (such as nausea, vomiting, anorexia, diarrhoea, gastric pain), dizziness, visual disturbance and hypersensitivity reactions.

13. Overdose

No case of overdose has been reported (3).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of last revision

18/06/2023.

References

1	https://www.powo.science.kew.org.
2	Maurice, M. Iwu, M. M. (2014). Pharmacognostical Profile of Selected Medicinal Plants from: Handbook of African Medicinal Plants. CRC Press. Print ISBN: 9781466571976, eBook ISBN: 9781466571983, Adobe ISBN:10.1201/b16292-4.
3	European Union Herbal Monograph on *Prunus africana* (Hook f.) Kalkm., Cortex (2016). EMA/HMPC/680626/2013. Committee on Herbal Medicinal Products (HMPC).
4	Natura Health Product, Pygeum – *Prunus africana* (2019). Health Canada. https://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=pygeum&lang=eng.
5	Deresa, D. A., Abdissa, Z., Gurmessa, G. T. and Abdissa, N. (2022). Chemical constituents of the stem bark of *Prunus africana* and evaluation of their antibacterial activity. *JOTCSA,* **9**(2), 395-414. doi: https://doi.org/10.18596/jotcsa.1001676.
6	Rubegeta, E., Makolo, F., Kamatou, G., Enslin, G., Chaudhary, S., Sandasi, M., Cunningham, A. B. and Viljoen, A. (2023). The African cherry: A review of the botany, traditional uses, phytochemistry, and biological activities of *Prunus africana* (Hook.f.) Kalkman. *Journal of Ethnopharmacology*, **305**, 116004. ISSN 0378-8741. https://doi.org/10.1016/j.jep.2022.116004.
7	Nyamai, D. W., Mawia, A. M., Wambua, F. K., Njoroge, A., Matheri, F., Lagat, R., Kiambi, J., Ogola, P., Arika, W., Cheseto, X., King'ori, E., Ramni, J., Ngugi, M. P., Muchugi, A., Ng'ang'a, M. and Burugu, M. W. (2015). Phytochemical profile of *Prunus africana* stem bark from Kenya. *Journal of Pharmacognosy and Natural Products,* **1**, 110-118. 10.4172/jpnp.1000110.
8	Komakech, R., Kang, Y., Lee, J. H. and Omujal, F. (2017). A Review of the potential of phytochemicals from *Prunus africana* (Hook f.) Kalkman stem bark for chemoprevention and chemotherapy of prostate cancer. *Evid. Based Complement. Alternat. Med.,* ID 3014019. doi: 10.1155/2017/3014019.
9	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **2**, 246 – 258.
10	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.
11	Duke, J. A. (2002). Handbook of Medicinal Herbs. CRC Press, 2nd edition, ISBN 9780849312847.
12	Spiteri, M. (2011). Herbal monographs including herbal medicinal products and food supplements. Department of Pharmacy, University of Malta. Set and printed by Print Right Ltd, Qormi.
13	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements - An Evidence-Based Guide. 3rd edition, Churchill Livingstone. ISBN: 978 0 7295 3910 4.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Psidium guajava* L.** جوافة

1. Names & Synonyms (1)

***Psidium guajava* L.**

Family: Myrtaceae.

Syns.: *Psidium aromaticum*, *P. cujavillus* Burm, *P. pomiferum*, *P. pyriferum*, *P. pumilum*.

Arabic: Gawafa جوافة

English name: Guava.

2. Parts used for medicinal purpose

Dried leaves (1).

3. Major chemical constituents

Phenolic Compounds (2)

- Flavonoids: Quercetin and its glycosides, avicularin, apigenin, guaijaverin, kaempferol, kaempferol-3-arabofuranoside, hyperin, myricetin, rutin, catechin, epicatechin, epigallocatechin gallate and proanthocyanidins.
- Phenolic acids: Gallic acid and caffeic acid.

Essential Oil (3,4)

- *β*-Caryophyllene, 4*α*-selin-7 (11)-enol, *β*-caryophyllene oxide, *α*-selinene, *β*-selinene, *δ*-cadinene, daucol, cubenol, 1,8-cineole (eucalyptol) and aromadendrene.

Others (2)

- Sugars: Sulphated and unsulphated polysaccharides (uronic acid), minerals (calcium, potassium, sulfur, sodium, iron, boron, magnesium, manganese and zinc), vitamins (C and B) and macronutrients (protein and fat).

4. Medicinal Uses (Indications)

A. Cough sedative (1-3, 5, 6).

B. Antidiarrheal agent (1, 2, 7-9).

C. For gingivitis and bleeding gum (1).

It is also reported to be used in certain gastrointestinal disorders as antispasmodic (2, 7-9) and in viral and infectious gastroenteritis (1, 10).

5. Herbal preparations correlated to medicinal use

1. Decoction (1,10).
2. Powdered drug (1).
3. Aqueous liquid extract (1).
4. Dry extract (10).

Herbal preparations (3 and 4) are in liquid and solid dosage forms, respectively. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1
Indication A: The appropriate oral dose depends on several factors such as the user's age, health and other several conditions.
Indication B: Three times daily (10).

Preparation 2
Indication B: 500 mg of the powdered leaves to be taken orally 3-4 times daily (1).

Preparation 3
Indication A: The appropriate oral dose depends on several factors such as the user's age, health and other several conditions.
Indication C: 15 ml to be used externally as mouthwash 3 times daily for at least one minute per session (1).
Preparation 4
Indication B: 500 mg oral capsule containing powder dry extract every 8 hours for 3 days (10).

Method of administration: Oral and external use.

7. Contraindications

Hypersensitivity to the active substances and to other plants of the same family.

8. Special warnings and precautions for use

If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

9. Interactions with other medicinal products and other forms of interaction

None reported.

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- None reported.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

24/05/2022.

References

1	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, **4**, 127-139.
2	Kumar, M., Tomar, M., Amarowicz, R., Saurabh, V., Nair, M. S., Maheshwari, C., Sasi, M., Prajapati, U., Hasan, M., Singh, S., Changan, S., Prajapat, R. K, Berwal, M. K. and Satankar, V. (2021). Guava (*Psidium guajava* L.) leaves: Nutritional composition, phytochemical profile, and health-promoting bioactivities. *Foods*, **10**, 752.
3	Karawya, M. S., Abdel Wahab, S. M., Hifnawy M. S., Azzam S. M. and EL- Gohary H. M. (1999). Essential oil of Egyptian Guajava leaves. Egypt. *J. Pharm. Sci.,* **40**(2), 209-217.
4	El-Ahmady, S. H, Ashour, M. L. and Wink, M. (2013). Chemical composition and anti-inflammatory activity of the essential oils of *Psidium guajava* fruits and leaves. *The Journal of Essential Oil Research*, **25**(6), 475–481. http://dx.doi.org/10.1080/10412905.2013.796498.
5	Abou Zid, S. F. and Mohamed, A. A. (2011). Survey on medicinal plants and spices used in Beni-Sueif, Upper Egypt. *Journal of Ethnobiology and Ethnomedicine*, 7-18.
6	Jaiarj, P., Khoohaswan, P., Wongkrajang, Y., Peungvicha, P., Suriyawong, P., Saraya, M. L. and Ruangsomboon, O. (1999). Anticough and antimicrobial activities of *Psidium guajava* Linn. leaf extract. *Journal of Ethnopharmacology*, **67**, 203–212.
7	Metwally, A. M., Omar, A. A., Ghazy, N. M., Harraz, F. M. and El Sohafy, S. M. (2011). Monograph of *Psidium guajava* L. leaves. *Pharmacognosy Journal*, **3**(21), 89-104.
8	Mazumdar, S., Akter, R. and Talukder, D. (2015). Antidiabetic and antidiarrhoeal effects on ethanolic extract of *Psidium guajava* (L.) Bat. leaves in Wister rats. *Asian Pac. J. Trop. Biomed.*, **5**, 10–14.
9	Ojewole, J. A. O., Awe, E. O. and Chiwororo, W. D. H. (2008). Antidiarrhoeal activity of *Psidium guajava* Linn. (Myrtaceae) leaf aqueous extract in rodents. *J. Smooth Muscle Res.*, **44**, 195–207.
10	https://www.drugs.com/npp/guava.html.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Rhodiola rosea* L.** روديا ريزا

1. Names & Synonyms (1)

***Rhodiola rosea* L.**
Family: Crassulaceae.
Syns.: *Sedum rosea* (L.) Scop.
Arabic: Rudiyariza روديا ريزا (2).
English: Arctic root (3), Golden root, Rhodiola, Rodiola, Rose root (4,5).

2. Parts used for medicinal purpose

Rhizome and root (3-5).

3. Major chemical constituents

- **Flavonoids:** Rhodiosin, herbacetin, rhodionin, rhodionidin, kaempferol (6, 7) and their glycosides (4).
- **Phenylethanoids**: Salidroside and its aglycone tyrosol (6, 7).
- **Phenylpropanoids:** Rosarin, rosin, rosavin and cinnamyl alcohol (4,6, 7).
- **Phenolic acids**: Gallic, chlorogenic, and hydroxycinnamic acids (8).
- **Volatile oil**: Monoterpene alcohols (geraniol, myrtenol, 1,4-*p*-menthadien-7-ol) and aliphatic alcohols (octanol) (9,10).
- **Others**: Sterols (*β*-sitosterol, daucosterol), tannins and gallic acid esters (6, 7).

4. Medicinal uses (Indications)

A. Symptomatic relief of stress, such as fatigue and sensation of weakness (as an adaptogen) (3-5).

B. Supports cognitive functions (such as mental focus and mental stamina) (5).

5. Herbal preparations correlated to medicinal use (3)

- **Dry extract**, extraction solvent: ethanol 67-70% v/v.

Herbal preparation is in a pharmaceutical dosage forms. The pharmaceutical form should be described by the Pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adults and elderly
Single dose: 144 - 200 mg (3,4).
Daily dose: 144 – 400 mg (3,4).
Not to exceed 200 mg per single dose and 680 mg daily (5).

Duration of use (3)**:**
If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration (3)**:** Oral use.

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family (3).
- Bipolar disorder or bipolar spectrum disorder (5).

8. Special warnings and precautions for use (3,4).

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children and adolescents under 18 years of age has not been recommended.
- In case of persons taking antidepressant medication, hormone replacement therapy or birth control medication, a doctor or a pharmacist should be consulted.
- The use at dosages higher than those recommended and/or for longer periods should be avoided (4).
- Use should be stopped if a person experience irritability or insomnia (5).

9. Interactions with other medicinal products and other forms of interaction

No interactions have been documented. However, potential interactions with other medicines with similar or opposing effects should be considered (5).

10. Fertility, pregnancy and lactation (3)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

- No fertility data available.

11. Effects on ability to drive and use machines

No adequate studies on the effect on the ability to drive and use machines have been performed (3).

12. Undesirable effects

- Rhodiola might cause dizziness, dry mouth, or excessive saliva (11,12).
- If other adverse reactions occur, a doctor or a pharmacist should be consulted.

13. Overdose

No case of overdose has been reported (3). However, irritability and insomnia may occur (5,13).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/last revision

11/05/2023.

References

1	powo.science.kew.org.
2	Bedevian, A. K. (1936). Illustrated Polyglottic Dictionary of Plant Names. Argus and Papazian Presses.
3	European Union Herbal Monograph on *Rhodiola rosea* L., Rhizoma et Radix (2012). EMA/HMPC/232091/2011. Committee on Herbal Medicinal Products (HMPC).
4	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0. p. 293-298.
5	Natural Health Product, *Rhodiola rosea* (L.) (2023). Health Canada, https://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=2697&lang=eng
6	Zomborszki, Z. P., Kúsz, N., Csupor, D. and Peschel, W. (2019). Rhodiosin and herbacetin in *Rhodiola rosea* preparations: additional markers for quality control? *Pharm. Biol.,* **57**(1), 295-305. doi: 10.1080/13880209.2019.1577460.
7	Alperth, F., Turek, I, Weiss, S., Vogt, D. and Bucar, F. (2019). Qualitative and quantitative analysis of different *Rhodiola rosea* rhizome extracts by UHPLC-DAD-ESI-MSn. *Scientia Pharmaceutica*, **87**(2), 8. https://doi.org/10.3390/scipharm87020008.
8	Nabavi, S. F., Braidy, N., Orhan, I. E., Badiee, A., Daglia, M., and Nabavi, S. M. (2016). *Rhodiola rosea* L. and Alzheimer's disease: From farm to pharmacy. *Phytother. Res.*, **30**, 532– 539. doi: 10.1002/ptr.5569.
9	Shatar, S., Adams, R. P. and Koenig, W. (2007). Comparative study of the essential oil of *Rhodiola* rosea L. from Mongolia. *Journal of Essential Oil Research,* **19**(3), 215–217. doi:10.1080/10412905.2007.9699264.
10	Evstatieva, L., Todorova, M., Antonova, D. and Staneva, J. (2010). Chemical composition of the essential oils of *Rhodiola rosea* L. of three different origins. *Pharmacogn. Mag.*, **6**(24), 256-258. doi: 10.4103/0973-1296.71782.
11	https://www.nccih.nih.gov/health/rhodiola
12	https://www.webmd.com/vitamins/ai/ingredientmono-883/rhodiola
13	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Salvia rosmarinus* Spenn.** حصى البان- إكليل الجبل

1. Names & Synonyms (1)

***Salvia rosmarinus* Spenn.**

Family: Lamiaceae (Labiateae).

Syn.: *Rosmarinus officinalis* L. (2, 3).

Arabic: Iklyl aljabal إكليل الجبل (4), Ḥaṣa l-ban حصى البان (5), Ruzmari روزْماري (5, 6).

English: Rosemary.

2. Parts used for medicinal purpose

- Fresh and dried leaves (7, 8).
- Flowering aerial parts (2, 9-12).

3. Major chemical constituents

- **Essential oil**: 1,8-Cineole, α-pinene, camphor (13,14), limonene, camphene and linalool (15).
- **Phenolic acids**: Rosmarinic, caffeic and chlorogenic acids (2).
- **Diterpenes**: Carnosic acid, carnosol, epirosmanol and hinokiol (16).
- **Triterpenes**: Ursolic, oleanolic and betulinic acids (16).

4. Medicinal uses (Indications)

A. Relief of dyspepsia and mild spasmodic disorders of the gastrointestinal tract (2,7, 8).

B. An adjuvant in the relief of minor muscular and articular pain, muscle and joint pain associated with rheumatism, sciatica, neuralgia and in minor peripheral circulatory disorders (2, 7, 8, 17).

C. As a mild antiseptic (8).

5. Herbal preparations correlated to medicinal use

1. Comminuted dried leaves in the form of decoction or infusion (2, 7).
2. Liquid extract of dried leaves (45% ethanol) (2, 7).
3. Dry extract of dried leaves (4.5–5.5:1, ethanol) (2, 8).
4. Tincture of dried leaves (1:5, 70% ethanol) (2).
5. Expressed juice from fresh leaves (7).
6. Essential oil from flowering aerial parts (2, 9, 10).

Herbal preparations (2-6) are in a pharmaceutical dosage form. The pharmaceutical form should be described by the Pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adolescents, adults and elderly (2, 7, 8)

Preparation 1

Indication A

Single dose: 1-2 g, 2-3 times daily are added to 150 - 250 ml of boiling water in the form of decoction or infusion as herbal tea.

Daily dose: 2-6 g (2, 7, 8, 11).

Duration of use (7)

If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use.

Indication B and C

Boil 50 g of herb in one L of water (decoction 1:20), add to one full bath (once daily or twice weekly) (2, 7, 8).

Duration of use (7):

If the symptoms persist longer than 4 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Direction(s) for use: As bath additive, place dried leaves in one L of cold water. Bring to a boil and simmer for 5-10 minutes. Let stand covered for 15 to 30 minutes and strain.

Recommended bath temperature is 35 – 38°C for 10 to 20 minutes.

Method of administration: External use (7, 8).

Preparation 2

Indication A

- 1.5 - 4 ml daily (2, 7).
- Equivalent to 0.6 - 12 g of dried leaves, daily (8).

Duration of use (7):

If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (7).

Preparation 3

Indication A

- 360 - 440mg, 3 times daily (2).
- Equivalent to 0.6 - 12 g of dried leaves, daily (8).

Method of administration: Oral use.

Preparation 4

Indication A

- 3 – 8.5 ml, daily (2).
- Equivalent to 0.6 - 12 g of dried leaves, daily (8).

Method of administration: Oral use.

Preparation 5 (7)

Indication A

- 5 ml (100% expressed juice), 2-3 times daily.
- Equivalent to 0.6 - 12 g of dried leaves daily (8).

Duration of use (7):

If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (7).

Preparation 6

Indication A

Two drops daily (9).

Duration of use (9)**:**

If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (2, 9).

Indication B

10-27 mg per liter, use as bath additive. One bath every 2 to 3 days (9).

Direction(s) for use (9)**:**

As bath additive, recommended bath temperature is 35 – 38°C, for 10 to 20 minutes.

Duration of use (9)**:**

If the symptoms persist longer than 4 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: External use (2, 9).

Indication B, C

- 6 –10 % essential oil in semi-solid and liquid preparations (2).
- 4 – 6 % essential oil diluted with almond oil or in semi-solid preparations for application to joints and muscles (18).

Duration of use (9)**:**

If the symptoms persist longer than 4 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: External use (2, 9).

7. Contraindications

- Hypersensitivity to the active substances and to other plants of the same family.
- Oral use: obstruction of bile duct, cholangitis, liver disease, gallstones and any other biliary disorders that require medical supervision and advice (7).
- Use as bath additive: full baths are contraindicated in cases of large skin injuries and open wounds, acute skin diseases, high fever, severe infections, severe circulatory disturbances and cardiac failure (7).
- In case of epileptic patients, oral use of rosemary oil may trigger seizures (18, 19).
- The oil is contraindicated in patients suffering from bronchial asthma or bronchitis or on damaged skin, such as in cases of burns, lesions or skin rashes (2).

8. Special warnings and precautions for use

- If symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children under 12 years of age is not recommended without medical supervision.
- The use of oil in children and adolescents under 18 years of age is not recommended.
- In cases of hypertension, a full hot bath should be used with caution (8).
- Articular pain accompanied by swelling of joints, redness or fever should be examined by a doctor (7).
- The essential oil should not be used on the face or mucosa and contact with the eyes should be avoided. After application of the essential oil, hands should be washed to avoid accidental contact with the face and eyes (2).
- The essential oil should be diluted before topical application to minimise irritation. (2, 19).

9. Interactions with other medicinal products and other forms of interaction

Iron, anticoagulants and drugs dependent on P-glycoprotein transport (18).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (7).
- Rosemary oil has an abortifacient effect (12).
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (7).

12. Undesirable effects

- Hypersensitivity (contact dermatitis and occupational asthma) has been reported (7).
- Photosensitivity has been associated with rosemary oil (12).
- If adverse reactions occur, a doctor or a pharmacist should be consulted

13. Overdose

Stomach, intestinal irritation, seizures and allergic contact dermatitis have been reported with large doses of rosemary oil (18).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

The popular evergreen shrub and herb rosemary recently underwent a name change as genetic science more accurately identifies its relationships. In 2019, members of the Royal Horticultural Society (RHS) Nomenclature and Taxonomy Advisory Group accepted the move to absorb Rosmarinus into the genus Salvia (20,21).

16. Date of compilation/last revision

25/06/2023.

References

1	www.powo.science.kew.org.
2	WHO monographs on selected medicinal plants (2009). Monographs on selected medicinal plants, **4**, 284-293.
3	WHO monographs on selected medicinal plants (2009). Monographs on selected medicinal plants, **4**, 294 -308.
4	http://greekmedicine.net/A_Greek_and_Unani_Herbal/herb.
5	https://en.bab.la/dictionary/english-arabic/rosemary.
6	https://dictionary.cambridge.org/dictionary/englisharabic/rosemary.
7	European Union Herbal Monograph on *Rosmarinus officinalis* L., Folium (2010). EMA/HMPC/13633/2009. Committee on Herbal Medicinal Products (HMPC).
8	Natural Health Product, Rosemary – *Rosemarinus officinalis* – Oral (2018). Health Canada. https://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=155.
9	European Union Herbal Monograph on *Rosmarinus officinalis* L., Aetheroleum (2010). EMA/HMPC/235453/2009. Committee on Herbal Medicinal Products (HMPC).
10	Natural Health Product, Rosemary – *Rosemarinus officinalis,* Topical (2018). Health Canada. https://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=rosemary.romarin.topical&lang=eng
11	Duke, J. A. (2002). Handbook of Medicinal Herbs. CRC Press, 2nd edition. ISBN 9780849312847.
12	Edwards, S. E., Rocha, I. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st Edition, John Wiley & Sons, Ltd. ISBN: 978-1-118-54356-6.
13	Elyemni, M., El Ouadrhiri, F., Lahkimi, A., Elkamli, T., Bouia, A. and Eloutassi, N. (2022). Chemical composition and antimicrobial activity of essential oil of wild and cultivated *Rosmarinus officinalis* from two Moroccan localities. *Journal of Ecological Engineering,* **23**(3), 214-222. https://doi.org/10.12911/22998993/145458
14	Al-Maharik, N., Jaradat, N., Hawash, M., Al-Lahham, S., Qadi, M., Shoman, I., Jaber, S., Rahem, R. A., Hussein, F. and Issa, L. (2022). Chemical composition, antioxidant, antimicrobial and anti-proliferative activities of essential oils of *Rosmarinus officinalis* from five different sites in Palestine. *Separations*, **9**, 339. https://doi.org/10.3390/separations9110339.
15	Hussain, A. I., Anwar, F., Chatha, S. A., Jabbar, A., Mahboob, S. and Nigam, P. S. (2010). *Rosmarinus officinalis* essential oil: antiproliferative, antioxidant and antibacterial activities. *Braz. J. Microbiol.*, **4**, 1070-8. doi: 10.1590/S1517-838220100004000027.
16	Andrade, J. M., Faustino, C., Garcia, C., Ladeiras, D., Reis, C. P. and Rijo P. (2018). *Rosmarinus officinalis* L.: an update review of its phytochemistry and biological activity. *Future Sci. OA,* **4**(4), FSO283. doi: 10.4155/fsoa-2017-0124.
17	Fisher, C. and Painter G. (1996). Materia Medica for the Southern Hemisphere. Auckland: Fisher-Painter Publishers.

18	Spiteri, M. (2011). Herbal Monographs including Herbal Medicinal Products and Food Supplements. Department of Pharmacy University of Malta. Set and printed by Print Right Ltd, Qormi.
19	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
20	https://www.rhs.org.uk
21	https: //www.uniprot.org/taxonomy/39367

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Serenoa repens (W.Bartram) Small بلميط منشاري

1. Names & Synonyms

***Serenoa repens* (W.Bartram) Small** (1,2).

Family: Arecaceae (1,2).

Syns: *Corypha repens* W.Bartram, *Corypha obliqua* W.Bartram, *Diglossophyllum serrulatum* (Michx.) H. Wendl. ex Salomon, *Sabal serrulata* (Michx.) Schult.f., *Chamaerops serrulata* Michx., *Brahea serrulata* (Michx.) H. Wendl. (1,2).

Arabic: Balmit minshary بلميط منشاري

English: Serenoa , Saw palmetto (3) and Saw palmetto berry (4).

2. Parts used for medicinal purpose

Dried ripe fruit (5).

3. Major chemical constituents (6)

-Fatty acids and their glycerides: Monoacylglycerides (1-monolaurin, 1-monomyristicin). Oleic acid (unsaturated) and capric acid, caproic acid, caprylic acid, lauric acid, myristic acid, palmitic acid and stearic acid (saturated).

-Steroids: β-Sitosterol, campesterol and stigmasterol.

-Carbohydrates: Invert sugar, mannitol, high molecular weight polysaccharides with galactose, arabinose and uronic acid identified as main sugar components.

-Other constituents: Flavonoids (e.g. rutin, isoquercitrin, kaempferol), pigment (carotene), resin, tannin and volatile oil.

4. Medicinal Uses (Indications)

Symptomatic treatment of benign prostatic hyperplasia; relief of lower urinary tract symptoms (7, 8).

5. Herbal preparations correlated to medicinal use (7)

1. Soft extract, extraction solvent: hexane.
2. Soft extract, extraction solvent: ethanol 90% to 96% m/m.

Herbal preparations are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adults and elderly
320 mg, once daily or 160 mg, 2 times daily (7).

Duration of use

Long-term use, up to 6 months, is possible (7,9).
Typically, symptom reduction is experienced within 1–2 months' treatment (3).

If the symptoms persist during the use of the medicinal product, a doctor or a pharmacist should be consulted (7).

Method of administration: Oral use (7).

7. Contraindications

Hypersensitivity to the active substances and to other plants of the same family (7).

8. Special warnings and precautions for use

If complaints worsen or if symptoms such as fever, spasms or blood in the urine, painful urination, or urinary retention occur during the use of the medicinal product, a doctor or a pharmacist should be consulted (7).

9. Interactions with other medicinal products and other forms of interaction (7)

A few cases of suspected interactions with warfarin have been reported. Increased INR- values have been described.

10. Fertility, pregnancy and lactation (7)

- Pregnancy and lactation: not relevant.
- No fertility data available.

11. Effects on ability to drive and use machines (7)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (7)

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Abdominal pain, nausea, vomiting, diarrhea, abdominal pain (especially when taken on an empty stomach), allergic or hypersensitivity reactions may occur such as skin rash, headache, increase of transaminases or gamma-glutamyl transferases and reversible gynecomastia.

13. Overdose (7)

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

21/06/2022.

References

1	https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:941782-1#synonyms
2	http://www.theplantlist.org/tpl/record/kew-190787
3	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements, An Evidence-Based Guide, 3rd ed. ISBN: 978 0 7295 3910 4.
4	https://www.herbalgram.org/resources/expanded-commission-e/saw-palmetto-berry/.
5	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **2**, 285-299.
6	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
7	European Union Herbal Monograph on *Serenoa repens* (W. Bartram) Small, Fructus (2013). EMA/HMPC/280079/2013. Committee on Herbal Medicinal Products (HMPC).
8	Natural Health Product Saw Palmetto – Liposterolic Extract (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=157&lang=eng.
9	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Tanacetum parthenium (L.) Sch. Bip. منيات

1. Names & Synonyms (1)

***Tanacetum parthenium* (L.) Sch. Bip.**

Family: Asteraceae (Compositae)

Syns.: *Chamaemelum parthenium* (L.), J.W. Sturm, *Chrysanthemum parthenium* (L.) Bernh., *Dendranthema parthenium* (L.) Des Moul., *Matricaria parthenium* L., *Parthenium matricaria* Gesn. ex Rupr., *Pyrethrum parthenium* (L.) Sm.

Arabic: Moniat, Monyat منيات (2).

English name: Feverfew, Altamisa, featherfew and featherfoil (3-6).

2. Parts used for medicinal purpose

Dried leaves; dried aerial parts (3, 5-8).

3. Major chemical constituents

- **Sesquiterpene lactones:** Parthenolide (6, 9).
- **Volatile oil**: Camphor, camphene, *p*-cymene and bornyl acetate (9).
- **Others**: Flavonoids, coumarins (9), pyrethrin, tannins and melatonin (6).

4. Medicinal Uses (Indications)

A. Headache relief, migraine prevention, reduce the severity and /or frequency and symptoms of migraine such as nausea and vomiting when taken as prophylactic (5, 6, 8).

B. Aid digestion (stomachic) (8).

5. Herbal preparations correlated to medicinal use

1. **Comminuted herbal substances as herbal tea** for oral use as decoction (3).
2. **Powdered herbal substances** (5, 7, 8).
   - **2.1** Leaves
   - **2.2** Herb

3. **Dry extract** (3, 8)
   1. Leaves
   3.2 Herb

4. **Tincture** (3, 8)
   4.1 Leaves
   4.2 Herb

Herbal preparations (2-4) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1.
Indications A and B
Drug equivalent to 0.2–0.6 mg parthenolide daily (3).

Preparation 2
Preparation 2.1
Adults:
- 300 - 400 mg ,3 - 4 times daily (10).
- 50 mg, daily (6)

Preparation 2.2
Adults and elderly:
Single dose: 100 mg once daily or 200 mg, 3 times daily. Daily dose: 100 mg–600 mg. The daily dosage of 100 mg may be gradually increased until obtaining an effect, not exceeding 600 mg (5).

Adults:
- 50 – 200 mg, daily (6).
- 50 – 120 mg, daily (7).

Preparations 2.1 and 2.2
Adults:
- 50 – 120 mg, daily (7).
- 50 - 250 mg, daily (0.2-2 % parthenolide) (8).
- Drug equivalent to 0.2–0.6 mg parthenolide daily (3).

Preparation 3
Preparation 3.1
Adults:
- 25 mg daily (10).
- 50-100 mg (10).
- 275 mg/day Standardized extract (10).

Preparation 3.2

Adults: 18.75 mg of a supercritical CO_2 extract corresponding to 3 g fresh feverfew (7).

Preparations 3.1 and 3.2:

1. Equivalent to 50 - 250 mg, daily (0.2 - 2 % parthenolide) (8).
2. Drug equivalent to 0.2–0.6 mg parthenolide daily (3).

Preparation 4

Preparation 4.1

Adults: 15-30 drops daily (10)

Preparation 4.1 and 4.2:

Adults:

- Equivalent to 50 - 250 mg, daily (0.2-2 % parthenolide) (8).
- Drug equivalent to 0.2–0.6 mg parthenolide daily (3).
- 15-30 drops, daily (10).

Duration of use: (5)

If migraine headaches recur after using the medicinal product for 2 months (usual period of treatment to obtain an effect), a doctor or a pharmacist should be consulted.

Method of administration: Oral use.

7. Contraindications

- Hypersensitivity to the active substances and to other plants of the same family.
- Feverfew should not be given to children (10).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children and adolescents under 18 years of age is not recommended (5).
- Abrupt ending of a long-term treatment can provoke withdrawal symptoms, including a rebound of migraine symptoms, anxiety, insomnia as well as muscle and joint stiffness (7).

9. Interactions with other medicinal products and other forms of interaction (10)

- **Iron supplements***:* Feverfew may decrease the absorption of iron, separate by ≥2 hours

- **Lab Test:**
    - **Platelet aggregation:** Feverfew may decrease platelet aggregation.
    - **Prothrombin time, plasma partial prothrombin time:** It may increase prothrombin time and plasma partial prothrombin time in patients taking warfarin concurrently.

10. Fertility, pregnancy and lactation (3)

- The use during pregnancy and lactation is avoided. It is reputed to be an abortifacient and to affect the menstrual cycle (3, 6).
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Gastrointestinal disturbances have been reported (5).
- In rare cases, allergic contact dermatitis, mouth ulceration or tongue irritation and inflammation may occur (7).

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of last revision

31/08/2022.

References

1	https://powo.science.kew.org.
2	Khare, C. P (2004). Indian Herbal Remedies. Springer – Verlag Berlin Heidelberg New York. ISBN 3-540-01026-2.
3	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **2**, 317-324.
4	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd.
5	European Union Herbal Monograph on *Tanacetum parthenium* (L.) Sch. Bip. (2010). EMA/HMPC/587578/2009. Committee on Herbal Medicinal Products (HMPC).
6	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
7	ESCOP Monographs (2014). *Tanacetum parthenium* (L.) Sch. Bip. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills.
8	Natural Health Product, *Tanacetum parthenium* (L.) Sch. Bip. (2022). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=86.
9	Pareek, A., Suthar, M., Rathore, G. S. and Bansal, V. (2011). Feverfew (*Tanacetum parthenium* L.): A systematic review. *Pharmacogn.*, **5**(9), 103-110.
10	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
11	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements - An Evidence-Based Guide. 3rd edition, Churchill Livingstone. ISBN: 978 0 7295 3910 4.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Taraxacum officinale Weber هندباء

1. Names & Synonyms

***Taraxacum officinale* Weber**

Family: Asteraceae/Compositae (3 - 7).

Syns.: *Leontodon taraxacum* L., *Taraxacum vulgare* (Lam.) Schrank, *T. campylodes* G. E. Haglund. (1-2).

Arabic: Handebaa, Hindbeh, Hindiba هندباء

English name: Lion's Tooth (6, 8 -10), Common Dandelion (8, 9), Dandelion (1).

2. Parts used for medicinal purpose

Leaves, roots and root with herb (whole plant) (3 - 7).

3. Major chemical constituents

Generally, dandelion plant is rich in polysaccharides, phenolic acids, flavonoids, terpenoids, minerals (particularly potassium), amino acids, and vitamins (9, 11).

Roots:

- Polysaccharides: Inulin (9, 11).

- Phenolic acids: Chicoric, chlorogenic, caffeic, monocaffeoyltartaric, hydroxycinnamic, synergic, vanillic and *p*-hydroxyphenyl acetic acids (9, 11).

- Sesquiterpene lactones: 4,11*β*, 13, 15''-Tetrahydroridentin B and taraxacolide-O-glucopyranoside (7, 12), 11,13-dihydrolactucin and ixerin D (13), and taraxinic acid D-glucopyranoside, its 11,13-dihydro-derivative (7) and ainslioside (12 - 14).

- Minerals: Mainly potassium (15).

- Others: Sterols/Triterpenes: Taraxasterol, *β*-taraxasterol, their acetates and their 16-hydroxy derivatives arnidol and faradiol, *β*-sitosterol, *β*-sitosterol-D-glucopyranoside and stigmasterol, and *β*-amyrin (12, 16, 17). A Triterpenoid: 3*β*-hydroxylup-18(19)-ene-21-one in fresh roots (13).

Leaves:

- Phenolic acids: Chicoric, caffeic and chlorogenic acids (9).

- Flavonoids: Luteolin, quercetin, apigenin, and their glycosides (9).

- Sesquiterpene lactones: Taraxinic acid β-D-glucopyranoside and 11β, 13-dihydrotaraxinic acid (18).

- Coumarins: Cichoriin and aesculin (9).

- Minerals: Mainly potassium (15).

- Others: Polysaccharides and ascorbic acid (9).

4. Medicinal Uses (Indications) (3- 5)

A. For the relief of symptoms related to mild digestive disorders (such as feeling of abdominal fullness, flatulence, and slow digestion) and temporary loss of appetite.

B. To increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints.

5. Herbal preparations correlated to medicinal use

1. **Comminuted herbal substances as herbal tea**.

   The dried drug is added to 150 ml of hot water as an infusion or boiled with water as a decoction.

   1.1 Root with herb (3, 7, 10).
   1.2 Leaf (4, 6, 10).
   1.3 Root (5, 6, 10).

2. **Dry extract of dried root with herb**, extraction solvent ethanol 60% (V/V) (3, 7).

3. **Liquid extract**

   3.1 Dried root with herb, extraction solvent ethanol 30% (V/V) or (m/m) (3, 7).
   3.2 Dried leaf, extraction solvent ethanol 25% (4, 6, 10).
   3.3 Dried root, extraction solvent ethanol 30% V/V (5).

4. **Expressed juice.**

   4.1 Fresh root with herb (3).
   4.2 Fresh leaf (4, 6).
   4.3 Fresh root (5).

5. **Tincture** (1:5 in 45% alcohol).

   5.1 Dried root with herb (3).
   5.2 Dried leaf (6).
   5.3 Dried root (5, 6).

6. Posology and method of administration correlated to medicinal use

Preparation 1
Indications A and B
Adolescents, adults and elderly:
Preparation 1.1: 3 - 4 g as a decoction, or 4-10 g as an infusion up to 3 times daily (3, 7).
Preparation 1.2: 4-10 g as an infusion, up to 3 times daily (5, 6, 10).
Preparation 1.3: 1 - 5 g as a decoction, 2-3 times daily (5).

Preparation 2
Indication A
Adolescents, adults and elderly:
300 mg, twice daily (4).
150 mg, 3 times daily (4).

Indication A & B
Adults: 0.75 – 1.0 g (750-1000 mg), daily (6).

Preparation 3
Indications A and B
Adolescents, adults and elderly:
Preparation 3.1: 3.15 ml, 3 times daily (3.15 ml equivalent to 3.31 g), or 1 ml, 3 times daily (1 ml equivalent to 1 g), respectively (3).
Preparation 3.2: 4-10 ml, 3 times daily (4).
Preparation 3.3: 2-8 ml, 3 times daily (5).

Preparation 4
Indications A and B
Adolescents, adults and elderly:
Preparation 4.1: 10 ml, 3 times daily (3).
Preparation 4.2: 5-10ml, once or twice daily (4, 6).
Preparation 4.3: 4-8 ml, 3 times daily (5).

Preparation 5
Indications A and B
Adolescents, adults and elderly:
Preparation 5.3: 5-10ml, 3 times daily (5).

Adults:
Preparation 5.1, 5.3: 5–10 ml, 3 times daily (6).
Preparation 5.2: 2-5 ml, daily (6).

Duration of use

If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted (3 – 5).

Method of administration: Oral use (3 – 5).

For indication B: to ensure an increase of the amount of urine, adequate fluid intake is required during treatment.

7. Contraindications

- Hypersensitivity to the active substance or to plants of the same family (3 - 5).
- Obstructions of bile ducts, cholangitis, liver diseases, gallstones, active peptic ulcer and any other biliary diseases (4, 6, 7).
- The use in patients with renal failure, diabetes and/or heart failure should be avoided because of possible risks due to hyperkalemia (3, 4).

8. Special warnings and precautions for use (3 - 5)

- If complaints or symptoms such as fever, dysuria, spasms or blood in urine occur during the use of the medicinal product, a doctor or a pharmacist should be consulted
- The use in children under 12 years of age is not recommended.
- Patients with conditions where reduced fluid intake is advised by a medical doctor, dandelion root is not recommended (5).

9. Interactions with other medicinal products and other forms of interaction (10)

- **Antacids, H2-blockers, proton pump inhibitors**: Dandelion may decrease their action.
- **Anticoagulants, antiplatelets, NSAIDs, salicylates**: Dandelion may increase bleeding when used with these products.
- **Antihypertensives, insulin, antidiabetics and hypoglycemic herbs**: Dandelion may increase their effects; concurrent use should be avoided.
- **Diuretics and diuretic herbs:** Dandelion may increase diuresis when used concurrently with diuretics, leading to fluid loss and electrolyte imbalances; concurrent use should be avoided.
- **Lithium:** Toxicity may occur as a result of sodium excretion if dandelion is used concurrently with lithium.

Lab test:

- **AST, ALT, alkaline phosphatase, APTT, INR, PT:** Dandelion may increase these levels.
- **Blood glucose**: Dandelion may decrease blood glucose levels.

10. Fertility, pregnancy and lactation (3 - 5)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (3 - 5)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted (3 - 5).
- Allergic reactions (3 - 5) including anaphylaxis and pseudoallergic contact dermatitis may occur (7). Cross-reactivity has been reported in individuals with an allergy to the pollen of other members of Asteraceae family (7).

13. Overdose

No case of overdose has been reported (3- 5).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of last revision

02/08/2022.

References

1	https://powo.science.kew.org.
2	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd.
3	European Union Herbal Monograph on *Taraxacum officinale* Weber ex Wigg., Radix cum Herba. (2019). EMA/HMPC/212895/2008 Corr 1. Committee on Herbal Medicinal Products (HMPC).
4	European Union Herbal Monograph on *Taraxacum officinale* Weber ex Wigg., Folium. (2009). EMA/HMPC/579636/2008. Committee on Herbal Medicinal Products (HMPC).
5	European Union Herbal Monograph on *Taraxacum officinale* F.H. Wigg., Radix. (2021). EMA/HMPC/475726/2020. Committee on Herbal Medicinal Products (HMPC).
6	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
7	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, **3**, 328-337.
8	Natural Health Product, *Taraxacum officinale* (L.) (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=dandelion.pissenlit &lang=eng
9	Mahboubi, M. and Mahboubi, M. (2020). Hepatoprotection by dandelion (*Taraxacum officinale*) and mechanisms. *Asian Pacific Journal of Tropical Biomedicine*, **10**(1), 1-10. doi: 10.4103/2221-1691.273081.
10	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
11	Jalili C., Taghadosi M., Pazhouhi M., Bahrehmand F., Miraghaee S. S., Pourmand D. and Rashidi I. (2020). An overview of therapeutic potentials of *Taraxacum officinale* (dandelion): a traditionally valuable herb with a reach historical background. *World Cancer Res. Journal,* **7**, 1679.
12	Hansel, R., Kartarahardja, M., Huang, J. T. and Bohlmann, F. (1980). Sesquiterpene lactone-beta-D-glucopyranosidee sowie ein neues Eudesmanolid aus *Taraxacum officinale*. *Phytochemistry*, **19**, 857-861.
13	Kisiel, W. and Barszcz, B. (2000). Further sesquiterpenoids and phenolics from *Taraxacum officinale*. *Fitoterapia*, **71**(3), 269-273. doi: 10.1016/s0367-326x(99)00158-6.
14	Kuusi, T., Pyysalo, H., and Autio, K. (1985). Bitterness properties of dandelion: II. Chemical investigations. *Lebensmittel-Wissenschaft und Technologie*, **18**(6), 339-346.
15	Hook, I., McGee, A., and Henman, M. (1993). Evaluation of Dandelion for diuretic activity and variation in potassium content. *International Journal of Pharmacognosy,* **31**(1), 29 – 34. doi:10.3109/13880209309082914.
16	Burrows, S. and Simpson, J. C. E. (1938). The triterpene group. Part IV. The triterpene alcohols of Taraxacum root. *Journal of Chemical Society*, **141**, 2042 - 2047.

17	Akashi, T., Furuno, T., Takahashi, T. and Ayabe, S. I. (1994). Biosynthesis of triterpenoids in cultured cells, and regenerated and wild plant organs of *Taraxacum officinale*. *Phytochemistry*, **36**, 303– 308.
18	Esatbeyoglu, T., Obermair, B., Dorn, T., Siems, K., Rimbach, G. and Birringer, M. (2017). Sesquiterpene lactone composition and cellular Nrf2 induction of *Taraxacum officinale* leaves and roots and taraxinic acid β-d-glucopyranosyl ester. *Journal of Medicinal Food*, **20**(1), 71–78. doi:10.1089/jmf.2016.0105.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Thymus vulgaris* L.** زعتر

1. Names & Synonyms

***Thymus vulgaris* L.** (1)
Syns.: *Origanum thymus* Kuntze, *Thymus collinus* Salisb.
Family: Lamiaceae (Labiatae).
Arabic: Za'ater زعتر
English name: English Thyme, Garden Thyme.

***Thymus zygis* L.** (2)
Syns.: *Origanum zygis* (L.) Kuntze, *Thymus angustifolius* Salisb.
Family: Lamiaceae (Labiatae).
Arabic: Za'ater زعتر
English name: Spanish Thyme.

2. Parts used for medicinal purpose

Dried and fresh herb (3, 4).

3. Major chemical constituents

- Essential oil: the main components are thymol, carvacrol, *p*-cymene**,** α and β-terpinene, linalool, terpinen-4-ol, borneol, 1,8- cineole**,** α-thujene, α-pinene, and caryophyllene (4).

- Flavonoids: apigenin, narigenin, kaempferol, and luteolin (and its glycosides) (5).

- Phenolic acids: salvianolic, rosmarinic, cinnamic, ferulic, caffeic and gallic acids (5).

- Others: monoterpene glycosides.

4. Medicinal Uses (Indications)

A. Cough associated with cold (4,10).
B. Symptoms of bronchitis, whooping cough and catarrh of the upper respiratory tract (6-8,10).
C. Indigestion, flatulence, dyspepsia and colic (carminative) (9).
D. Acne (11,12).
E. Topically for warts and inflamed swellings (13).

5. Herbal preparations correlated to medicinal use

1. **Comminuted herbal substance as infusion**

1.1 Comminuted herbal substance (1-2 g) in a cup of 150 ml of boiling water (4). One teaspoonful of the comminuted herbal substance is equivalent to 1.4 g drug (8).

1.2 Topical compresses: using a 5% infusion (8).

2. **Extracts** (4)**:**

2.1 Liquid extract

a) Extraction solvent: ammonia solution 10% (m/m), glycerol 85% (m/m), ethanol 90% (V/V) , water (1:20:70:109).

b) Extraction solvent: water (of fresh herb and often referred as expressed juice).

c) Extraction solvent: ethanol 24% (V/V).

2.2 Dry extract

d) Extraction solvent: ethanol 70%.

e) Extraction solvent: ethanol 96%.

f) Extraction solvent: water.

2.3 Soft extract

g) Extraction solvent: ethanol 25% - 30% (V/V).

2.4 Tincture

h) Tincture (1:10), extraction solvent: ethanol 70% (V/V).

i) Tincture (1:5), extraction solvent: ethanol 70% (V/V).

3. **Thyme oil**

Herbal preparations (2-3) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

General Daily Dosage (8)

The recommended daily dose is 10 g drug (with 0.03% phenols, calculated as thymol).

Preparation 1
Indications A, B, C and E
Preparation 1.1. Oral Herbal tea: 1-2 g, 3-4 times daily (4).
Preparation 1.2. Topical: 5% infusion, 3 times daily (8).

Method of administration: Oral and topical use.

Preparation 2 (4)

Indications A, B, C and E

Preparation 2.1.

- Adolescents, adults and elderly

a) Single dose 1-4 g, 1-7 times daily, maximum daily dose 14 g.

b) Single dose 10 ml, 3-4 times daily.

c) Single dose: 1-2 ml, 3-4 times daily.

- Children between 4 and 12 years of age

a) Single dose 0.5-0.9 ml, 3-5 times daily

b) Single dose 7-10 ml, 2-3 times daily

Preparation 2.2.

- Adolescents, adults and elderly

d) Single dose 75-200 mg, 3 times daily.

e) Single dose 135 mg, 1-3 times daily.

f) Single dose 100 – 200 mg, 3-4 times daily.

Preparation 2.3.

- Adolescents, adults and elderly

g) Single dose 50 mg, 6 times daily

Preparation 2.4.

- Adolescents, adults and elderly

h) Single dose 40 drops, 3 times daily.

i) Single dose 2-6 ml, 3 times daily.

Method of administration: Oral use.

Preparation 3 (8,10)

Indication A

1. **Oral**

Adults and elderly:

Single dose: 0.2-0.25 ml, 3-5 times daily

Daily dose: 0.6-1.25 ml

2. **Topical use**

2.1 Cutaneous use: **Adults and elderly**: in liquid and semi-solid dosage forms in concentrations up to 10%; apply up to 3 times daily.

2.2 Bath additive:

Adolescents, Adults and elderly:0.007-0.025 g per litre.

Children 6-12 years: 0.0035-0.017 g per litre.

Children 3-6 years: 0.0017-0.0082 g per litre.
One bath every day or every second day (10).

Indication D
Topical use (11-12): 5% Diluted oil is applied to the inflamed area.

Method of administration: Oral and topical use.

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- **Thyme oil** as bath additive full hot baths is contraindicated in case of open wounds, large skin injuries, acute skin diseases, high fever, severe infections, severe circulatory disturbances and cardiac insufficiency (10).

8. Special warnings and precautions for use

- If the symptoms worsen or persist longer than 1 week during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- If dyspnea, fever or purulent sputum occurs, a doctor or a pharmacist should be consulted (4-10).
- **Herbal preparations (a & b):**

  The use in children under 4 years of age is not recommended without medical supervision (4).
- **Herbal preparations (c, d, e, f, g, h and i)**:

  The use in children under 12 years of age has not been established (4).
- Although thyme oil has cytotoxic properties in high concentrations and may cause intestinal cell damage when administered orally, no toxicity has been reported at commonly used doses, and it can be considered as a safe drug (14).
- Like other essential oils, thyme oil should not be applied to the face particularly in the nasal area of babies and infants under the age of two years because of the risk of a laryngospasm (10).
- The use of thyme oil in children and adolescents under 18 years of age is not recommended without medical supervision (10).
- The use of thyme oil as bath additive in children under 3 years of age is not recommended without medical supervision (10).
- In cases of hypertension, a full bath should be used with caution (10).

9. Interactions with other medicinal products and other forms of interaction

None reported (4).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (4,9,15).
- Thyme oil is not recommended in pregnancy (16).
- No fertility data available (4).

11. Effects on ability to drive and use machines (4)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- **Internally**: Gastric disorders may occur (4).
- The thyme oil can cause nausea and vomiting, headache, dizziness, convulsions, cardiac or respiratory arrest if taken internally (Newell et al 1996). As such, the crude herb is considered far safer (16).
- **Topically:** Thyme oil is possibly safe when applied to the skin, but in some people can cause skin irritation (7).
- Contact dermatitis reactions have been reported with topical use (16).

13. Overdose

No case of overdose has been reported (4).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

–

16. Date of compilation/last revision

13/08/2023.

References

1	https://www.gbif.org/species/5341442
2	https://www.gbif.org/species/7793938
3	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, **3**, 259-266
4	Community Herbal Monograph on Thymus vulgaris L. and *Thymus zygis* L., Herba. EMA/HMPC/342332/2013. Committee on Herbal Medicinal Products (HMPC).
5	Sarfaraz, D., Rahimmalek, M. and Saeidi, G. (2021). Polyphenolic and molecular variation in *Thymus* species using HPLC and SRAP analyses. *Sci. Rep.,* **11**, 5019.
6	Blumenthal, M. (1998). The Complete German Commission E Monographs. Austin, Texas: American Botanical Council.
7	https://www.rxlist.com/thyme/supplements.htm
8	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
9	http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=172
10	European Union Herbal Monograph on *Thymus vulgaris* L., *Thymus zygis* L., *Aetheroleum.* EMA/HMPC/59032/2017. Committee on Herbal Medicinal Products (HMPC).
11	https://www.healthline.com/health/thyme-oil#benefits-uses
12	Chevallier, A. (1996). The Encyclopedia of Medicinal Plants. DK Pub., ISBN: 0789410672, 9780789410672.
13	Fisher, C. and Painter G. (1996). Materia Medica for the Southern Hemisphere. Auckland: Fisher-Painter Publishers.
14	Kowalczyk, A., Przychodna, M., Sopata, S., Bodalska, A. and Fecka, I. (2020). Thymol and thyme essential oil- New insights into selected therapeutic applications. *Molecules,* **9**, 25(18), 4125. doi: 10.3390/molecules25184125.
15	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
16	Braun, L. and Cohen, M. (2014). Herbs and Natural Supplements, an Evidence-Based Guide. 3rd ed. ISBN: 978 0 7295 3910 4.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Tilia cordata* Mill.** تيليو

1. Names & Synonyms (1, 2)

***Tilia cordata* Mill.**
Family: Tiliaceae (Malvaceae).
Arabic: Tilio تيليو
English: Lime flower (3), Linden, Tilia and small leaf linden, small leaf lime (4).

***Tilia platyphyllos* Scop.**
Family: Tiliaceae (Malvaceae)
Arabic: Tilio تيليو
English: Lime flower (3), Linden, Tilia and large-leaf Linden

***Tilia x vulgaris* Heyne**
Naturally-occurring hybrid of *T. cordata* and *T. platyphyllos* Scop.
Family: Tiliaceae (Malvaceae)
Syn: *T. europaea* auct. non L.
Arabic: Tilio تيليو
English: European linden, European lime tree, Linden and Tilia (4).

2. Parts used for medicinal purpose

Flower (2-4).

3. Major chemical constituents (2)

- **Flavonoids:** Kaempferol, quercetin, myricetin and their glycosides (mainly Kaempferol-3-*O*-*β*-D-(6″-E-*p*-coumaroyl)-glucopyranoside "tiliroside") and proanthocyanidins (3, 5).
- **Phenolic acids:** Caffeic, chlorogenic and p-coumaric acids (3, 5).
- **Essential oil:** Alkanes (mainly tricosane) (6), phenolic alcohols and esters, and terpenes including citral, citronellal, citronellol, eugenol, limonene, nerol, *α*-pinene and terpineol (monoterpenes), and farnesol (sesquiterpene) (3).
- **Others:** Mucilage, tocopherol (phytosterol) and amino acids (3).

4. Medicinal uses (Indications)

A. Relief cough and irritation of the throat in colds and catarrh of the respiratory tract (3, 4).

B. Relief of mild symptoms of mental stress (3, 4).

5. Herbal preparations correlated to medicinal use (3)

1. **Comminuted herbal substance as herbal tea for oral use**.
   1.5 g of the comminuted herbal substance in 150 ml of boiling water as a herbal infusion
2. **Liquid extract,** extraction solvent ethanol 25% v/v.
3. **Tincture**, extraction solvent ethanol 45% v/v.
4. **Aqueous extract**

Herbal preparations (2-4) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use (3)

Preparation 1
Indication A
Adolescents, adults and elderly: 1.5 g as herbal tea, 2–4 times daily. Daily dose: 3-6g.
Children between 4 and 12 years of age: 1 g as herbal tea, 2–4 times daily. Daily dose: 2-4 g.

Indication B
Adolescents, adults and elderly: 1.5 g as herbal tea 2–4 times daily. Daily dose: 3-6 g.

Preparations 2 and 3
Indications A, B
Adolescents, adults and elderly
Preparation 2: 2 ml, 1-2 times daily. Daily dose: 2-4 ml.
Preparation 3: 1 ml, 1-2 times daily**.** Daily dose: 1-2 ml.

Preparation 4
Indication A
Adolescents, adults and elderly: extract Eq. to3-6 gm, 2–4 times daily.
Children between 4 and 12 years of age: extract eq. to 2-4 gm, 2–4 times daily.

Duration of use:

Indication A

The therapy should start at first signs of common cold. If the symptoms persist longer than one week during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Indication B

If the symptoms persist during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use.

7. Contraindications (2-4)

Hypersensitivity to active substances and to other plants of the same family.

8. Special warnings and precautions for use (3)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children under 12 years of age is not recommended.
- In case of infusion; the use in children under 4 years of age for the relief of symptoms of common cold is not established.

9. Interactions with other medicinal products and other forms of interaction (2, 3)

None reported.

10. Fertility, pregnancy and lactation (2, 3)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (3)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (3)

- None known.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

13. Overdose

No case of overdose has been reported (3).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

06/08/2023.

References

1	Assessment Report on *Tilia cordata* Miller, *Tilia platyphyllos* Scop., *Tilia x vulgaris* Heyne or Their Mixtures, Flos (2012). EMA/HMPC/337067/2011. Committee on Herbal Medicinal Products (HMPC)
2	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
3	Community Herbal Monograph on *Tilia cordata* Miller, *Tilia platyphyllos* Scop., *Tilia x vulgaris* Heyne or Their Mixtures, Flos (2012). EMA/HMPC/337066/2011. Committee on Herbal Medicinal Products (HMPC).
4	Natural Health Product, Linden, Small Leaf – *Tilia cordata* (2017). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=linden.tilleul.smallleaf.Petitesfeuilles &lang=eng.
5	Evans, W. C., Evans, D., & Trease, G. E. (2009). Trease and Evans Pharmacognosy (16th ed.). Edinburgh; New York: Saunders/Elsevier. ISBN 9780702029332.
6	Fitsiou, I., Tzakou, O., Hancianu, M. and Poiata, A. (2007). Volatile constituents and antimicrobial activity of *Tilia tomentosa* Moench and *Tilia cordata* Miller oils. *Journal of Essential Oil Research*, **19**, 2, 183-185, DOI: 10.1080/10412905.2007.9699255.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Trigonella foenum-graecum L. الحلبة

1. Names & Synonyms (1)

***Trigonella foenum-graecum* L.**

Syns.: *Buceras foenum-graecum* (L.) All., *Foenum-graecum officinale* Moench, *Folliculigera graveolens* Pasq., *Telis foenum-graecum* (L.) Kuntze, *Xiphostylis erectus* Gasp.

Family: Fabaceae (Leguminosae)

Arabic: Hulbah, Helba حلبة (2,3).

English name: Fenugreek, Greek hay, Greek clover and Greek hay seed (4-6).

2. Parts used for medicinal purpose

Dried seeds (4,5,7,8).

3. Major chemical constituents

- **Polysaccharides**: Mucilage (mainly galactomannan) (9).
- **Steroidal saponins**: Diosgenin (as main sapogenin) (10).
- **Alkaloids:** Trigonelline (11), carpaine and choline (12,13).
- **Others**: Protein (13), fats, fibres, minerals (zinc and iron), flavonoids (apigenin, orientin, luteolin, quercetrin, vitexin, and isovitexin) and volatile oil (10).

4. Medicinal Uses (Indications)

A. Loss of appetite (anorexia) (4,5).

B. Digestive disorders include constipation (laxative), dyspepsia, gastritis, gastric ulcers and convalescence (5,7,8,14,15).

C. As an adjunct for the management of hypercholesterolaemia (5,8,16) and hyperglycaemia in cases of non-insulin diabetes mellitus (8,15,16).

D. Galactagogue/lactogogue (help promote milk production/secretion) (5,14,15).

E. Ttopically for symptomatic treatment of local inflammation of the skin (4,8), wounds, leg ulcers, eczema, burns, boils (15) and as an emollient (8). Also, for furunculosis, myalgia, lymphadenitis and gout (7).

5. Herbal preparations correlated to medicinal use (4)

1. Comminuted herbal substance.
2. Powdered herbal substance.
3. Dry extract, ethanol 20% V/V.
4. Soft extract, ethanol 60% V/V.
5. Tincture 1:5 (8).

Herbal preparations (2-5) are in a pharmaceutical dosage form. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use (4)

Adults and elderly

Preparation 1

Indication A

1-2 g in 250 ml of boiling water, 3 times daily, before meals (4).

Indications A, B, C and D

- 0.5 g macerated in 150 ml cold water for 3 hours; strain. Drink 3 times daily (4, 8).
- 6 g of cut or crushed seed (8 ,14,15) daily (8).

Indication E

- 1 tbsp mashed seed in about 240 ml water, up to 3 times daily as a gargle (16).
- Infusion for cutaneous use: 50 g in 250 ml of water, 2-3 times daily. The still warm infusion is used in cataplasm over the affected areas (4).

Preparation2

Indication A

Single dose: 380-1100 mg, 3 times daily.

Daily dose: 1140-3300 mg (4).

Indications A, B, C and D

Dose equivalent to 6 g of cut or crushed seeds daily. (8 14,15).

Indication E

- 50 g of powdered seed mixed with 250 ml water, added to a hot bath 2-3 times daily. (8,14-16).

- 50 g of powdered seed per enough hot water to make a semi-solid paste, apply locally as poultice as needed. (5,8).
- 50 g in 250 ml of water, the still warm infusion is used in cataplasm over the affected areas, 2-3 times daily (4).

Preparation3

Indication A

Single dose: 295 mg, 2 times daily.

Daily dose: 590 mg (4).

Indications A, B, C and D

Dose equivalent to 6 g of cut or crushed seed daily. (8,14,15).

Preparation 4

Indication A

Single dose: 500 mg, 2 times daily.

Daily dose: 1 g (4).

Indications A, B, C and D

Dose equivalent to 6 g of cut or crushed seed daily. (8,14,15).

Preparation 5 (8)

30 ml daily.

Duration of use: (4)

If the symptoms persist more than two weeks for **indication A** or one week for **indication D** during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration (4)

- Oral use.
- Cutaneous /topical use.

7. Contraindications (4)

- Hypersensitivity to the active substances and to other plants of the same family.

8. Special warnings and precautions for use (4)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children and adolescents under 18 years of age has not been established.
- Due to a possible hypoglycaemic effect of Fenugreek, close monitoring of glycaemic control should be considered in patients treated for diabetes mellitus.

9. Interactions with other medicinal products and other forms of interaction (14)

There is a possible increased risk of bleeding when Fenugreek is used concurrently with anticoagulants, antiplatelet and NSAIDs.

10. Fertility, pregnancy and lactation (4)

- Owing to its stimulatory effects on the uterus, the seeds should not be used during pregnancy (8).
- Promote lactation (5,14,15).
- No fertility data available.

11. Effects on ability to drive and use machines (4)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (4)

- Flatulence, diarrhea and dizziness may occur.
- Allergic reactions have been reported after local application, ingestion or inhalation. These reactions range from facial angioedema, rhinorrhoea, wheezing, asthma and allergic rhinitis (4,8).
- After its ingestion, a bitter taste and bad odour appear in human sweat and urine due to volatile oils and alkaloids content (12,17).
- If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.

13. Overdose

- High doses (25-100 g of Fenugreek seeds powder divided into two equal daily doses) have been reported to cause minor gastrointestinal symptoms such as diarrhea and flatulence (4).
- High doses of Fenugreek are not recommended in patients with low thyroid activity (18).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of last revision

25/05/2023.

References

1	www.powo.science.kew.org
2	Sultana, A. and Mushtaq, S. (2016). Therapeutic profile of Fenugreek (*Trigonella foenum graecum* Linn): A culinary regime. *Ijppr. Human*, **6**(3), 374-389.
3	Iwu, M. M. (2014). Handbook of African Medicinal Plants. CRC Press, Taylor & Francis Group, LLC. ISBN 13: 978-1-4665-7198-3.
4	European Union Herbal Monograph on *Trigonella foenum graecum* L., Semen (2020). EMA/HMPC/179591/2018. Committee on Herbal Medicinal Products (HMPC).
5	Natural Health Product Health Canada. Fenugreek - *Trigonella foenum graecum* (2018). Health Canada, https://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=84.
6	Herbal Medicine Compendium (2020). *Trigonella foenum graecum* seed. Final authorized version 1.0. https://hmc.usp.org/monographs/trigonella-foenum-graecum-seed-1-0.
7	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
8	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, **3**, 338-348.
9	Yasothai R. (2021). Chemical composition of Fenugreek (*Trigonella foenum graecum* L.) seed and galactomannan depleted Fenugreek residue. *The Pharma Innovation Journal,* **10**(7), 944-947.
10	Wani S. A. and Kumar P. (2018). Fenugreek: A review on its nutraceutical properties and utilization in various food products. *Journal of the Saudi Society of Agricultural Sciences*, **17**(2), 97-106.
11	Zameer S., Najmi A. K., Vohora D., Akhtar M. (2018). A review on therapeutic potentials of *Trigonella foenum graecum* (Fenugreek) and its chemical constituents in neurological disorders: Complementary roles to its hypolipidemic, hypoglycemic, and antioxidant potential. *Nutritional Neuroscience*, **21**(8), 539-545. DOI: 10.1080/1028415X.2017.1327200.
12	Ahmad, A., Alghamdi, S. S., Mahmood, K. and Afzal, M. (2016). Fenugreek a multipurpose crop: Potentialities and improvements. *Saudi J. Biol. Sci.*, **23**(2), 300-10. DOI: 10.1016/j.sjbs.2015.09.015.
13	Visuvanathan, T., Than, L.T.L., Stanslas, J., Chew, S. Y. and Vellasamy, S. (2022). Revisiting *Trigonella foenum graecum* L.: Pharmacology and therapeutic potentialities. *Plants*, **11**, 1450. https://doi.org/ 10.3390/plants11111450.
14	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed. ISBN: 978-0-323-05741-7.
15	Spiteri, M. (2011). Herbal Monographs including Herbal Medicinal Products and Food Supplements. Department of Pharmacy University of Malta. Set and printed by Print Right Ltd, Qormi.
16	Duke, J. A. (2002). Handbook of Medicinal Herbs. CRC Press, 2nd edition. ISBN 9780849312847.

17	Mebazaa, R., Mahmoudi, A., Rega, B., Ben Cheikh, R. and Camel, B. (2010). Analysis of human male armpit sweat after Fenugreek ingestion: Instrumental and sensory optimisation of the extraction method. *Food Chemistry*, **120**, 771–782.
18	Bone, K. (2003). A Clinical Guide to Blending Liquid Herbs, Herbal Formulations for the Individual Patient. Churchill Livingstone, an imprit of Elsevier. 1st edition. Hardcover ISBN: 9780443066320. eBook ISBN: 9781455726196.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Urtica dioica* L.** حريق - قريص

1. Names & Synonyms (1)

***Urtica dioica* L.**

Family: Urticaceae.

Syns. : *Urtica tibetica* W.T. Wang, *U. galeopsifolia* Wierzb. ex Opiz.

Arabic: hhurray حريق - Qurrays قريص

English name: Stinging nettle (2-4), Nettle (3, 4).

2. Parts used for medicinal purpose

Dried roots /rhizomes (2-5) or leaves/ herb (3-7).

3. Major chemical constituents

Herb/ leaves:
-Amines: Acetylcholine, betaine, choline, lecithin, histamine, serotonin and a glycoprotein (8).
-Flavonoids: Flavonol glycosides (e.g. isorhamnetin, kaempferol, quercetin), isoquercitrin, astragalin and rutin (7-9).
-Inorganics: Up to 20% minerals, including calcium, potassium and silicon (8,9).
-Lignans: Several lignans, including (-)-secoisolariciresinol (8).
-Other constituents: Choline acetyltransferase, scopoletin, *β* sitosterol and tannin (8).

Rhizomes (8)**:**
-Lectin (agglutinin) composed of six isolectins, Coumarin (scopoletin).
-Triterpenes: *β*-sitosterol its glucoside, and six stearyl derivatives; two phenylpropane derivatives and six lignans.

Roots (10-12):
Polysaccharides: Glycans, glucogalacturonans, arabinogalactan acid, fatty acid: (10*E*, 12*Z*)-9-hydroxy-10, 12-octadecadienoic acid, lectins, ceramides, terpenes diols, and terpenes diols glucosides.

4. Medicinal Uses (Indications)

A. Relief of lower urinary tract symptoms related to benign prostatic hyperplasia after serious conditions have been excluded by a medical doctor (2-5).

B. As a diuretic (2-4, 6, 7). To increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints (6), as irrigation therapy for inflammatory diseases of the lower urinary tract and for prevention and treatment of kidney stones (12).

C. Relief of minor articular pain. Supportive therapy to help relieve rheumatic complaints (2-4, 7) and for the symptomatic treatment of arthritis and rheumatic conditions (6,7).

5. Herbal preparations correlated to medicinal use

1. **Comminuted herbal substance as herbal tea** for oral use as a decoction or an infusion (5, 6):
   - **1.1** 1.5 g of the root as a decoction (5).
   - **1.2** 2-4 g of the comminuted herb or leaves as an infusion (6).
2. **Dry root extract**, extraction solvent ethanol 20% V/V (5).
3. **Dry root extract**, extraction solvent ethanol 70% V/V (5).
4. **Liquid root extract**, extraction solvent ethanol 30% V/V (5).
5. **Liquid leaves extract**, extraction solvent ethanol 96% (V/V) (6).
6. **Dry leaves extract** (4.7-6:1), extraction solvent water (6).
7. **Dry leaves extract** (5-10:1), extraction solvent water (6).
8. **Dry leaves extract**, extraction solvent ethanol 50% (V/V) (6).
9. **Leaves tincture** 1:5 (25% (7) - 45% (8) ethanol).

Herbal preparations (2-9) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Indication A
Adults and elderly (5)
Preparation 1.1.: 1.5 g as herbal tea 3-4 times daily.
Preparation 2: 240 mg, 3 times daily.
Preparation 3: 150-190 mg, twice a day.

Preparation 4: Maximum 5 ml daily, divided into 3 or 4 single doses.
There is no relevant use in children and adolescents under 18 years of age.

Duration of use: Long-term use, no longer than 6 months (5,13), is possible.

Method of administration: Oral use (5).

Indications B, C (6)
Adults and elderly
Preparation 1.2.: 2-4 g as herbal tea 3-6 times daily (the daily dose 8-12 g) (8,12).
Preparation 5: 30-40 oral drops as a single dose, 3-4 times daily.
Preparation 6: 750 mg as a single dose, 2-3 times daily.
Preparation 7: 450 mg as a single dose, 3 times daily.
Preparation 8: 540 mg as a single dose, 2 times daily.
Preparation 9: 2-6 ml, 3 times daily (7,8).

Duration of use (6)
Indication B: Not to be used for more than 2- 4 weeks.
Indication C: Not to be used for more than 4 weeks.
If the symptoms persist during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (6).

7. Contraindications

- Hypersensitivity to the active substances and to other plants of the same family (5,6).
- Nettle leaves are contraindicated in condition where a reduced fluid intake is recommended (e.g. severe cardiac or renal disease) (6).

8. Special warnings and precautions for use

- If complaints worsen or if symptoms such as fever, spasms or blood in the urine, painful urination, or urinary retention occur during the use of the medicinal product, a doctor or a pharmacist should be consulted (2,5,6).
- When articular pain is accompanied by swelling of joint, redness or fever a doctor should be consulted (6).
- Use of nettle leaves in children under the age of 12 years is not recommended (6).

9. Interactions with other medicinal products and other forms of interaction (4)

- **Anticoagulants (heparin, warfarin) and anticoagulant herbs:** Nettle may decrease the effect of anticoagulants.
- **CNS depressants (alcohol, barbiturates, sedative/hypnotics ,antipsychotics, opiates) and sedative herbs:** Nettle may lead to increased central nervous system depression.
- **Diuretics:** Use of nettle may increase the effects of diuretics, resulting in dehydration and hypokalemia.
- **Iron salts:** Nettle tea may interfere with the absorption of iron salts.
- **Lithium:** Nettle combined with lithium may result in dehydration, lithium toxicity .

10. Fertility, pregnancy and lactation

The use during pregnancy and lactation is contraindicated (2-4) owing to its effects on androgen and estrogen metabolism (2).

11. Effects on ability to drive and use machines (5,6)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Gastro-intestinal complaints such as nausea, heartburn, feeling of fullness, flatulence, diarrhoea may occur (2, 4, 5-8).
- Allergic reactions *i.e.,* pruritus, rash, urticaria may occur (2,4, 5-7).

13. Overdose (5,6)

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

21/06/2022.

References

1	Belwal, T., Nabavi, S. M., Nabavi, S. F., Dehpour, A. R. and Shirooie, S. (2020). Naturally Occurring Chemicals against Alzheimer's Disease. Academic Press. ISBN: 0128192135, 9780128192139.
2	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **2**, 329-341.
3	Natural Health Product Stinging Nettle – *Urtica dioca* (2019). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=166&lang=eng
4	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed. ISBN: 978-0-323-05741-7.
5	European Union Herbal Monograph on *Urtica dioica* L., *Urtica urens* L., Their Hybrids or Their Mixtures, Radix (2012). EMA/HMPC/461160/2008. Committee on Herbal Medicinal Products (HMPC).
6	European Union Herbal Monograph on *Urtica dioica* L.; *Urtica urens* L., Folium (2010). EMA/HMPC/508015/2007. Committee on Herbal Medicinal Products (HMPC).
7	https://escop.com/wp-content/uploads/edd/2018/11/Urticae-folium-herba ESCOP-2018.pdf
8	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
9	Joshi, B. C., Mukhija, M. and Kalia, A. N. (2014). Pharmacognostical review of *Urtica dioica* L. *International Journal of Green Pharmacy*, **8**(4), 201-209.
10	Dhouibi, R., Affes, H., Ben Salem, M., Hammami, S., Sahnoun, S., Zeghal, K. M. and Ksouda, K. (2020). Screening of pharmacological uses of *Urtica dioica* and others benefits. *Progress in Biophysics and Molecular Biology*, **150**, 67–77.
11	Taheri, Y., Quispe, C., Herrera-Bravo, J., Sharifi-Rad, J., Ezzat, S. M., Merghany, R. M., Shaheen, S., Azmi, L., Mishra, A. P., Sener, B., Kılıç, M., Sen, S., Acharya, K., Nasiri, A., Cruz-Martins, N., Fokou, P. V. T., Ydyrys, A., Bassygarayev, Z., Daştan, S. D., Alshehri, M. M., Calina, D. and Cho, W. C. (2022). *Urtica dioica* - derived phytochemicals for pharmacological and therapeutic applications. *Evidence-Based Complementary and Alternative Medicine,* Article ID: 4024331, 30 pages. (https://doi.org/10.1155/2022/4024331).
12	https://www.herbalgram.org/resources/expanded-commission-e/stinging-nettleherb-and-leaf/.
13	www.drugs.com.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Vaccinium macrocarpon* Aiton** توت بري أحمر

1. Names & Synonyms (1)

***Vaccinium macrocarpon* Aiton**

Family: Ericaceae

Syns.: *Oxycoca macrocarpa* (Aiton) Raf., *Oxycoccus macrocarpos* (Aiton) Pursh, *Oxycoccus palustris* var. *macrocarpos* (Aiton) Pers., *Vaccinium propinquum Salisb*.

Arabic name: Toot barry التوت البري – Toot barry ahmar توت بري أحمر .

English name: Cranberry, American cranberry, Large American cranberry, Large cranberry (2-4).

2. Parts used for medicinal purpose

Fresh or dried ripe fruits (2-4).

3. Major chemical constituents

- **Flavonoids**:

  Flavonols: Myricetin and quercitin glycosides (2, 5).

- **Anthocyanins**: 3-*O*-glucosides, galactosides and arabinosides of both cyanidin and peonidin (2, 5).
- **Proanthocyanidins:** Condensed tannins of epicatechin and epigallocatechin (2, 5).
- **Phenolic acids and esters**: *p*-Coumaric, caffeic, ferulic and chlorogenic acids (5, 6), caffeoyl hexoside and caffeoyl dihexoside (5).
- **Organic acids:** Citric, quinic, malic and benzoic acids (2, 5).
- **Carbohydrates**: Glucose, fructose and oligosaccharides (2, 5).
- **Others**: Ursolic acid, vitamins (C, E and K) (5, 7, 8) and minerals (Potassium and Nitrogen) (3, 5, 7, 9).

4. Medicinal Uses (Indications)

Prevention of recurrent urinary tract infections in adults (especially in women) (2-4, 10, 11).

5. Herbal preparations correlated to medicinal use

Dry extract refined from the juice of cranberry fruit.

Herbal preparation is in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Female adults and elderly: 400-500 mg cranberry extract daily in divided doses equivalent to 90 ml cranberry juice (2).

Duration of use
The recommended duration of use for indication A is at least 4 weeks. If the symptoms persist for more than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted (10).

Method of administration: Oral use.

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- The use of cranberry for the treatment of diseases of the urinary tract in pediatric populations is ineffective and is not recommended (2).
- Cranberry should not be used by persons with oliguria and anuria (11).

8. Special warnings and precautions for use (2)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Patients with kidney stones or impaired kidney function should use products containing the fruit only after consulting their health care provider (10).
- The use in children and adolescents under 18 years of age is not recommended.
- People with diabetes should be aware of the high content of sugar in the juice and use sugar-free preparations (13).

- Consult the physician prior to treatment to rule out serious conditions such as pyelonephritis.
- A physician or a pharmacist should be consulted prior to use in patients taking blood thinners (10).

9. Interactions with other medicinal products and other forms of interaction (11)

- **Cytochrome P45 2C9 substrates:** Cranberry may inhibit cytochrome P452C9 enzymes.
- **Warfarin:** Cranberry, when given with warfarin, may increase the international normalized ratio and increase the risk for bleeding.
- **Lab Test: Urine pH:** Cranberry decreases urine pH.

10. Fertility, pregnancy and lactation

- The use of cranberry during pregnancy is not recommended without medical supervision.
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- At high doses (3 L or greater), gastrointestinal discomfort and diarrhea can occur (13).

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of last revision

14/9/2022.

References

1	https://powo.science.kew.org.
2	WHO monographs on selected medicinal plants (2009). Monographs on selected medicinal plants, **4**, 149-166.
3	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
4	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd.
5	Nemzer, B. V., Al-Taher, F., Yashin, A., Revelsky, I. and Yashin, Y. (2022). Cranberry: chemical composition, antioxidant activity and impact on human health: Overview. *Molecules*, **27**(5), 1503. https://doi.org/ 10.3390/molecules27051503.
6	Abeywickrama, G., Debnath, S. C., Ambigaipalan, P. and Shahidi F. (2016). Phenolics of selected cranberry genotypes (*Vaccinium macrocarpon* Ait) and their antioxidant efficacy. *J. Agric. Food Chem*., **64**, 9342–9351.
7	United States Department of Agriculture Food Data Central. (2021). Cranberries, Raw. Available online: https://fdc.nal.usda.gov/falc-app.html#/food-details/171722/nutrients
8	Česonienė, L. and Daubaras, R. (2016). Phytochemical composition of the large cranberry (*Vaccinium macrocarpon*) and the small cranberry (*Vaccinium oxycoccos*). In: Nutritional Composition of Fruit Cultivar. Simmonds M. S. J. and Preedy V. R. (Eds.). Academic Press, 173–194. ISBN: 9780124081178.
9	Karlsons, A., Osvalde, A., Čekstere, G. and Pormale J. (2018). Research on the mineral composition of cultivated and wild blueberries and cranberries. *Agron. Res*., **16**, 454–463.
10	Natural Health Product, cranberry- *Vaccinium macrocarpon* (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=71&lang=eng.
11	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
12	https://www.rxlist.com/ cranberry /supplements.htm.
13	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements – An Evidence Based Guide. 3rd edition, Churchill Livingstone, ISBN: 978 0 7295 3910 4.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Vaccinium myrtillus* L.** التوت الازرق

1. Names & Synonyms (1)

***Vaccinium myrtillus* L.**

Family: Ericaceae

Syns.: *Vitis-idaea myrtillus* (L.) Moench

Arabic: التوت الأزرقToot azrak.

English name: Bilberry, European blueberry, Bogberry (2-4).

2. Parts used for medicinal purpose

Fresh and dried fruits (3, 5).

3. Major chemical constituents

- **Flavonoids:**
  - **Flavan-3-ols:** Procyanidins B1, B2, B3 and B4, and anthocyanins (3-*O*-arabinosides, 3-*O*-glucosides and 3-*O*-galactosides of cyanidin, delphinidin, malvidin, peonidin and petunidin).
  - **Flavonol-*O*-glycosides**: Quercitrin, isoquercitrin, hyperoside and astragalin (6, 7). **Flavonols**: Kaempferol, quercetin and myricetin (7).
- **Organic acids**: Malic, citric and quinic acids (7).
- **Phenolic acids:** Hydroxycinnamic and hydroxybenzoic acids (8, 9, 10).
- **Tannins**: Gallocatechin (7).
- **Stilbenes**: *Trans*-resveratrol (7).

4. Medicinal Uses (Indications)

A. Mild diarrhoea (3-5).

B. Problems related to varicose veins such as painful and heavy legs and peripheral vascular insufficiency (3-6).

C. Microcirculatory disorders of the eye (3-6).

D. Slow the progression of disorders of the eye such as diabetic and hypertensive retinopathy and macular degeneration (4).

E. Minor inflammations of the oral mucosa (3, 5, 6).

5. Herbal preparations correlated to medicinal use

1. **Herbal substance or comminuted herbal substance** of the dried ripe fruits as herbal tea for decoction or macerate (3).

- Decoction**:** Herbal substances boiled for 10 minutes in 150-250 ml water and drunk cold.

- Cold macerate**:** Dried fruit soaked in 150 ml water for 2 hours and drunk.

2. **Dry extract of the fresh fruit,** extraction solvent ethanol (96% V/V) (5).

Herbal preparation (2) is in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adolescents, adults, and elderly
Preparation 1
Indication A

- 5-10 g, several times daily as a decoction/cold macerate (5) or
  15-60 g, in divided doses of 5-15 g in 250 ml of water, 3-4 times daily as a decoction (3).

Duration of use:
If the symptoms persist longer than 3 days during the use of the medicinal product, a doctor or a pharmacist should be consulted (3).

Method of administration: Oral use.

Indication E

- A 10% decoction or equivalent preparations as a gargle or mouthwash (3, 5, 6), rinse the mouth several times daily (3).

Duration of use:

- If the symptoms persist longer than one week during the use of the medicinal product, a doctor or pharmacist should be consulted (3).

Method of administration: Oromucosal use

Preparation 2 (5)
Indications B, C and D
Adults

- 60 to 160 mg, 3 times daily. Not to exceed 160 mg per single dose (equivalent to 65 - 173 mg anthocyanins, daily) (4, 5).

Duration of use: At least 4-8 weeks (5).

Method of administration: Oral use.

7. Contraindications

Hypersensitivity to active substances and to other plants of the same family. (3).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- For oromucosal preparations, the use in children under 12 years of age is not recommended.

9. Interactions with other medicinal products and other forms of interaction (5)

- Bilberry may increase the action of **anticoagulants**; caution should be taken if used concurrently.
- Bilberry may increase the action of **NSAIDs**, caution should be taken if used concurrently.
- **Antidiabetics and hypoglycemic herbs:** Bilberry may increase hypoglycemia; caution should be taken if used concurrently.
- **Antiplatelet agents:** Bilberry may cause antiplatelet aggregation, caution should be taken if used concurrently.
- **Iron:** Bilberry interferes with iron absorption, concurrent use should be avoided.
- **Lab Test**: **Blood glucose***:* Bilberry may decrease blood glucose.

10. Fertility, pregnancy and lactation

- Dried fruit has been used safely during pregnancy and lactation (3, 5).
- No fertility data available (3).

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (3).

12. Undesirable effects

- None known.
- If adverse reactions occur, a doctor or a pharmacist should be consulted (3, 5).

13. Overdose

No case of overdose has been reported (3).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of last revision

14/9/2022.

References

1	https://powo.science.kew.org.
2	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
3	European Union Herbal Monograph on *Vaccinium myrtillus* L., Fructus recens (2015). EMA/HMPC/375808/2014. Committee on Herbal Medicinal Products (HMPC).
4	Natural Health Product, Bilberry - *Vaccinium myrtillus* L. oral (2018). Health Canada http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=39&lang=eng.
5	ESCOP Monographs (2014). *Vaccinium myrtillus* L. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills.
6	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **4**, 210- 243.
7	Pires, T. C. S. P., Caleja, C., Santos-Buelga, C., Barros, L and Ferreira, I. C. F. R. (2020). *Vaccinium myrtillus* L. fruits as a novel source of phenolic compounds with health benefits and industrial applications - A review. *Curr. Pharm. Des.*, **26**(16), 1917-1928.
8	Može, Š., Polak, T., Gašperlin, L., Koron, D., Vanzo, A., Ulrih, N. P. and Abram, V. (2011). Phenolics in Slovenian bilberries (*Vaccinium myrtillus* L.) and blueberries (*Vaccinium corymbosum* L.). *J. Agric. Food Chem.*, **59**, 6998–7004.
9	Michalska, A. and Łysiak, G. (2015). Bioactive compounds of blueberries: Post-harvest factors influencing the nutritional value of products. *Int. J. Mol. Sci.*, **16**, 18642–18663.
10	Ehala, S., Vaher, M. and Kaljurand, M. (2005). Characterization of phenolic profiles of Northern European berries by capillary electrophoresis and determination of their antioxidant activity. *J. Agric. Food Chem.*, **53**(16), 6484–6490.
11	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Valeriana officinalis* L.** فاليريانا

1. Names & Synonyms

***Valeriana officinalis* L.**
Family: Caprifoliaceae/Valerianaceae (1).
Arabic: Valeriana فاليريانا
English name: All-Heal, Belgian Valerian, Common Valerian, Fragrant Valerian, Garden Valerian, Valerian root (2,3).

2. Parts used for medicinal purpose

Roots, rhizomes and stolons (2,3,4).

3. Major chemical constituents

- **Essential oil:** Chief components are bornyl acetate, valerianol, valeranone, intermedeol, camphene, myrtenyl acetate, agarospirol, γ-eudesmol, nootkatone and 6-isopropyl-1-methyl bicycles [3,1,0] hexane (5,6).
- **Sesquiterpenic acids:** Valerenic acid, 2-hydroxyvalerenic acid, 2-acetoxy-valerenic acid (6).
- **Iridoids**: Didrovaltrate and valepotriates derivatives, including valepotriate, isovalepotriate, acetoxyvalepotriate and isovalemxy-hydroxy-dihydrovatrate (5).
- **Others:** Lignanoids, alkaloids, flavonoids and amino acids (5).

4. Medicinal Uses (Indications) (3,4)

A. Relief of mild nervous tension.

B. Mild sedative and relief of sleep disorders.

C. Relief of mild symptoms of mental stress.

5. Herbal preparations correlated to medicinal use (3)

1. **Comminuted herbal substance as herbal** tea for oral use and as bath additive.

(0.3-3 g of the comminuted herbal substance is added to 150ml of boiling water as herbal infusion).

2. **Powdered herbal substance.**

3. **Expressed juice from fresh root**.

4. **Dry extract:**
   4.1 Dry extract, extraction solvent: ethanol 40-70%.
   4.2 Extraction solvent: water.
   4.3 Extraction solvent: ethanol 85%.

5. **Liquid extract:**
   5.1 Extraction solvent: water.
   5.2 Extraction solvent: ethanol 60%.

6. **Tincture:**
   6.1 Extraction solvent: ethanol 60%.
   6.2 Extraction solvent: ethanol 56%.
   6.3 Extraction solvent: ethanol 70%.
   6.4 Extraction solvent: ethanol 60-80%.

Herbal preparations (2-6) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use (3)

Adolescents, adults and elderly
Preparation 1
Indication B
Single dose: 0.3-3 g half to one hour before bedtime with an earlier dose during the evening, if necessary.

Indication C
Single dose: 0.3-3 g, up to 3 times daily.

Use as bath additive:
Indications B, C
Single dose: 100 g for a full bath, one bath daily.
The use in children under 12 years of age is not recommended.

Preparation 2

Indication B

Single dose: 0.3-2 g, half to one hour before bedtime with an earlier dose during the evening, if necessary.

Indication C

Single dose: 0.3-2 g, up to 3 times daily.

Preparation 3

Indication B

Single dose: 10 ml half to one hour before bedtime with an earlier dose during the evening, if necessary.

Indication C

Single dose: 10 ml, up to 3 times daily.

Preparation 4

Preparation 4 .1

Indication A

Single dose: 400-600 mg, up to 3 times daily.

Indication B

Single dose: 400-600 mg half to one hour before bedtime with an earlier dose during the evening, if necessary.

Maximum daily dose: 4 single doses.

Preparation 4.2

Indication B

Single dose: 420 mg half to one hour before bedtime with an earlier dose during the evening, if necessary.

Indication C

Single dose: 420 mg, up to 3 times daily.

Preparation 4.3

Indication C

Single dose: 322 mg, up to 3 times daily.

Preparation 5

Preparation 5.1

Indication B

Single dose: 20 ml, half to one hour before bedtime.

Indication C

Single dose: 20 ml, up to 3 times daily.

Preparation 6
Preparation 6.1
Indications C
Single dose: 4-8 ml, up to 3 times daily.

Preparation 6.2
Indications B
Single dose: 0.84 ml half an hour before bedtime.

Indications C
Single dose: 0.84 ml, 3-5 times daily.

Preparation 6.3
Indication B
Single dose: 1.5 ml half an hour before bedtime.

Indication C
Single dose: 1.5 ml up to 3 times daily.

Preparation 6.4
Indication C
Single dose: 10 ml, up to 3 times daily

Duration of use: If the symptoms persist or worsen after two weeks of continued use, a doctor or a pharmacist should be consulted.

Method of administration: Oral use

Use as bath additive.
Preparation 1
Indications B, C
Single dose: 100 g for a full bath, one bath daily
The use in children under 12 years of age is not recommended.

7. Contraindications (3)

- Hypersensitivity to active substances and to other plants of the same family.
- Use as bath additive:
  Full baths are contraindicated in cases of open wounds, large skin injuries, acute skin diseases, high fever, severe infections, and severe circulatory disturbances.

8. Special warnings and precautions for use (3)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use is not recommended in children under 12 years of age.

9. Interactions with other medicinal products and other forms of interaction (3)

None reported.

10. Fertility, pregnancy and lactation (3)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (3)

May impair ability to drive and use machines. Affected patients should not drive or operate machinery.

12. Undesirable effects (3)

- Gastrointestinal symptoms (e.g. nausea, abdominal cramps) may occur after ingestion of valerian root preparations.
- In case of bath additive: None known
- If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.

13. Overdose (3)

- Valerian root at a dose of approximately 20 g cause symptoms such as fatigue, abdominal cramp, chest tightness, light-headedness, hand tremor and mydriasis, which disappear within 24 hours. If symptoms arise, a medical doctor should be consulted for supportive treatment.
- In case of bath additive: No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of last compilation/last revision

01/05/2023.

References

1	https://powo.science.kew.org.
2	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
3	European Union Herbal Monograph on *Valeriana officinalis* L., Radix (2016). EMA/HMPC/150848/2015. Committee on Herbal Medicinal Products (HMPC).
4	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons,
5	Chen, H. W., Wei, B. J., He, X. H., Liu, Y. and Wang, J. (2015). Chemical components and cardiovascular activities of *Valeriana* spp. *Evid. Based Complement. Alternat. Med*., Article ID 947619, https://doi.org/10.1155/2015/947619.
6	Nakurte, C. I., Mežaka, I., Taškova, I., Primavera, A., Vecvanags, A. and Kronberga, A. (2021). Seasonal changes in chemical composition of *Valeriana officinalis* L. roots in natural conditions and organic production system in Latvia. *Plant Biol. Crop Res.*, **4**(1), 1031.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Vitis vinifera* L.** العِنَب

1. Names & Synonyms

***Vitis vinifera* L**

Family: Vitaceae

Syn.: *Cissus vinifera* (L.) Kuntze (1)

Arabic: Al Inab العِنَب

English: Grapevine (2, 3), Grape (4, 5).

2. Parts used for medicinal purpose

Leaves and seeds (2, 6).

3. Major chemical constituents

Seeds:

- **Phenolics:** Catechin, epicatechin, procyanidins (7, 8); **phenolic acids:** gallic, caffeic, coumaric, coutaric, ferulic and fertaric acids and **flavonoids:** rutin, quercetin-3-*β*-D-glucoside, quercitrin and myricetin (9, 10).
- **Fatty acids:** Linoleic acid (9).
- **Others:** Proanthocyanidins, stilbenes (10), carbohydrates, proteins and vitamin C (9).

Leaves:

- **Phenolics: Condensed tannin**: gallocatechins, catechins, procyanidins, procyanidin B1, procyanidin A1 and epicatechins (10, 12); **phenolic acids:** gallic, vanillic, syringic (10), caftaric, caffeic, and fertaric acids; **flavonoids:** quercetin, quercetin-3-*O*-glucoside, kaempferol, and myricetin (10), apigenin-7-*O*-glucoside, luteolin-7-*O*-glucoside(10), taxifolin, naringenin, hesperetin (10) and anthocyanins (10); **coumarins:** aesculin, fraxin, aesculutin and umbelliferone (10,11); **stilbenes:** monomeric, dimeric, trimeric and tetrameric derivatives (10).
- **Others**: Quinic acid (10).

4. Medicinal uses (Indications)

A. Treatment of chronic venous insufficiency, which is characterised by swollen legs, varicose veins, feeling of heaviness, pain, tiredness, itching, tension and cramps in the calves (2, 6, 13).

B. For symptomatic relief of itching and burning associated with haemorrhoids after serious conditions have been excluded by a medical doctor (2).

5. Herbal preparations correlated to medicinal use

1. **Comminuted herbal substance as decoction or infusion** (2).
2. **Powdered herbal substance** (2).
3. **Dry extract**, extraction solvent water.
   3.1 Leaves (2).
   3.2 Seeds (6).
4. **Soft extract of leaves**, extraction solvent water (2).

Herbal preparations (2-4) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Preparation 1
Indications A and B
Adults and elderly: 5 - 10 g of dried leaves in 250 ml of boiling water as an infusion, 2 times daily (2).

Duration of use: (2)
The recommended duration of use for indication A is 4 weeks and for indication B is one week. If the symptoms persist for more than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (2).

Preparation 2
Indications A and B
Adults and elderly: 270 - 350 mg, 3-5 times daily (2).

Duration of use (2)
The recommended duration of use for indication A is 4 weeks and for indication B is one week. If the symptoms persist for more than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (2).

Preparation 3
Indication A
3.1. Adults and elderly: Single dose: 360 - 720 mg, daily dose: 360 - 720 mg (2).

3.2. Adults and elderly: 150 - 475 mg, daily (6).

75 – 600 mg seed extract (or pycnogenol) daily, up to 3 weeks (4).

Duration of use
The recommended duration of use is 12 weeks. 2-3 weeks of treatment may be required before beneficial effects are observed for leaves (2) and 4 weeks for seeds (4). Long term use is possible in consultation with a doctor (2, 6).

Method of administration: Oral use (2).

Preparation 4
Indication A
Adults and elderly: Soft extract in a cream base (10 g contain 282 mg soft extract). Apply a thin layer on the affected area, 1 - 3 times daily (2).

Duration of use (2)
The recommended duration of use is 4 weeks. If the symptoms persist for more than 2 weeks during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Cutaneous use (2).

7. Contraindications

Hypersensitivity to active substances and to other plants of the same family.

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children and adolescents below 18 years of age is not recommended (2, 6, 13).
- If there is inflammation of the skin, thrombophlebitis or subcutaneous induration, severe pain, ulcers, sudden swelling of one or both legs, cardiac or renal insufficiency, a doctor should be consulted (2, 13).
- In case of inadequate or unsatisfactory symptomatic response to the treatment of chronic venous insufficiency within 2 weeks a doctor should be consulted as oedema may have alternative causes (2).
- In case of inadequate or unsatisfactory symptomatic response within 1 week or if rectal bleeding occurs during the treatment of haemorrhoids, a doctor should be consulted (2).
- Cutaneous use: The product should not be used on broken skin, around the eyes or on mucous membranes (2).

9. Interactions with other medicinal products and other forms of interaction

Not known.

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (2, 13).
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- **Grape seed:** Dizziness, nausea, anorexia and Rash (13).
- **Grape leaves:** Hypersensitivity reactions of the skin (itching and erythema, urticaria), nausea, gastrointestinal complaints and headache may occur (2).

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

23/8/2022.

References

1	https://powo.science.kew.org.
2	European Union Herbal Monograph on *Vitis vinifera* (L.) Kuntze. (2017). EMA/HMPC/424583/2016. Committee on Herbal Medicinal Products (HMPC).
3	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd.
4	Duke, J. A. (2002). Handbook of Medicinal Herbs. CRC Press, 2nd edition, ISBN 9780849312847.
5	www.herbalgram.org
6	Natural Health Product, *Vitis vinifera* (L.) Kuntze. (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=110&lang=eng
7	Spranger, I., Sun, B., Mateus, A. M., Freitas, V. and Ricardo-da-Silva, J. M. (2008). Chemical characterization and antioxidant activities of oligomeric and polymeric procyanidin fractions from grape seeds. *Food Chem.*, **108**, 519–532.
8	Furiga, A., Lonvaud-Funel, A. and Badet, C. (2009). *In vitro* study of antioxidant capacity and antibacterial activity on oral anaerobes of a grape seed extract. *Food Chem.*, **113**, 1037–1040.
9	Yalcin, H., Kavuncouglu, H., Ekici, L. and Sagdic, O. (2017). Determination of fatty acid composition, volatile components, physico-chemical and bioactive properties of grape (*Vitis vinifera*) seed and seed oil. *Journal of Food Processing and Preservation*, **41**, e 12854.
10	Insanu, M., Karimah, H., Pramastya, H. and Fidrianny, I. (2021). Phytochemical compounds and pharmacological activities of *Vitis vinifera* L.: An updated review. *Biointerface Research in Applied Chemistry*, **11**(5), 13829 – 13849.
11	Goufo, P., Singh, R. K. and Cortez, I. (2020). A Reference list of phenolic compounds (including stilbenes) in Grapevine (*Vitis vinifera* L.) roots, woods, canes, stems, and leaves. *Antioxidants*, **9**(5), 398. doi: 10.3390/antiox9050398.
12	Aouey, B., Samet, A. M., Fetoui, H., Simmonds, M. S. J. and Bouaziz, M. (2016). Anti-oxidant, anti-inflammatory, analgesic and antipyretic activities of grapevine leaf extract (*Vitis vinifera*) in mice and identification of its active constituents by LC–MS/MS analyses. *Biomedicine & Pharmacotherapy*, **84**, 1088-1098. https://doi.org/10.1016/j.biopha.2016.10.033.
13	Skidmore-Roth, L. Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

***Vitex agnus-castus* L.** فايتكس

1. Names and Synonyms

Vitex agnus-castus **L.**

Family: Lamiaceae (Labiatae).

Arabic: فايتكسvitex

English name: Agnus castus fruit (1), Chaste tree, Chasteberry, Monk's Pepper (2), Vitex (3).

2. Parts used for medicinal purpose

Fruits (1-4).

3. Major chemical constituents

- **Iridoid glycosides**: Agnuside, aucubin, agnucastosides A-C (1, 5).
- **Flavonoids**: Casticin, penduletin, chrysosplenol D, vitexin, isovitexin, eupatorine, orientin and luteolin glycosides (1, 5).
- **Essential oil**: 1,8-Cineole, *β*-caryophyllene, sabinene (1) and bicyclogermacrene (5, 6).
- **Diterpenoids**: Rotundifuran, vitexilactone and vitetrifolines B and C (1, 5).
- **Fatty acids**: Linoleic, oleic (6), palmitic, stearic and linolenic acids (1).
- **Others**: Fiber and sitosterol (6).

4. Medicinal Uses (Indications)

A. For menstrual cycle irregularities and premenstrual syndrome (1, 3).
B. Menopause symptoms such as hot flushes (3).

5. Herbal preparations correlated to medicinal use

1. **Powdered herbal substance** (1).
2. **Dry extract**
   - **2.1.** (DER 7-13:1), extraction solvent ethanol 60% m/m (1).
   - **2.2.** Extraction solvent ethanol 50-52% m/m
   - **2.3.** (DER 6-12:1), extraction solvent ethanol 60% m/m (1).
3. **Fluid extract** extraction solvent 70% alcohol (v/v) (3).
4. **Tincture**
   - **4.1**. Extraction solvent ethanol 68-70% V/V (1:5) (1).
   - **4.2.** Extraction solvent ethanol 50-70% (1:5) (2).
   - **4.3.** Extraction solvent ethanol 62% (1:10) (7).

6. Posology and method of administration correlated to medicinal use

Preparation 1
Indication A:
Female adults: Single dose: 400 mg, 2 times daily. Daily dose: 800 mg (1, 8).

Indications A and B
Female adults:
30 – 2000 mg dried fruit, daily (3).
0.5 – 1.0 g, 3 times daily (2).

Preparation 2
Indication A (1)**:**
Preparation 2.1: Single dose: 4 mg once daily. Daily dose: 4 mg.
Preparation 2.2: Single dose: 2-3 mg once daily. Daily dose: 2-3 mg.
Preparation 2.3: 20 mg, once daily.

Duration of use:
To achieve an optimal treatment effect, continued use over three months is recommended. If the symptoms persist after a continued use over three months, a doctor should be consulted.

Method of administration: Oral use.

Preparation 3 (7)
Indications A: 0.5–1.0 ml, daily.

Preparation 4
Indication A
Preparation 4.1: Single dose: 165 mg, once daily (1).
Preparation 4.3 162 mg, twice daily (7).

Indications A, B:
Preparation 4.2 (2)
0.15–0.2 ml, daily (2).
40 drops once daily, corresponding to approximately 33 mg herbal substance (7, 8).

7. Contraindications

Hypersensitivity to the active substances and to other plants of the same family.

8. Special warnings and precautions for use (1)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in pubertal children and adolescents under 18 years of age is not recommended.
- Patients under hormonal therapy or have hormone sensitive condition should consult their doctor before using agnus castus fruits.
- Agnus castus fruit is thought to act on the pituitary-hypothalamic axis and therefore patients with a history of a pituitary disorder should consult a doctor before use.
- In cases of prolactin secreting tumors of the pituitary gland the intake of agnus castus fruit can mask symptoms of the tumor.

9. Interactions with other medicinal products and other forms of interaction

- *Agnus castus* has dopamine agonist properties and therefore may interact with drugs with dopamine agonist or dopamine antagonist action.
- Active constituents of Agnus castus may also have additive effects with opioids due to similar pharmacological activity.
- Presence of oestrogenic compounds in *Agnus castus* may result in additive or opposing effects with oestrogens or oestrogen antagonists (8).

10. Fertility, pregnancy and lactation

- The use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Immune system disorders (severe allergic reactions with face swelling, dyspnoea and swallowing difficulties), skin and subcutaneous tissue disorders (allergic skin reactions such as rash and urticaria, acne), nervous system disorders (headache, dizziness), gastrointestinal disorders (nausea, abdominal pain) and reproductive system disorders (menstrual disorders) have been reported (1, 8).

13. Overdose

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of last revision

14/9/2022.

References

1	Community Herbal Monograph on *Vitex agnus-castus* L., Fructus (2018). EMA/HMPC/606742/2017. Committee on Herbal Medicinal Products (HMPC).
2	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
3	Natural Health Product, Chaste tree - *Vitex agnus*-castus L. (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=chaste.tree.vitex&lang=eng.
4	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements - An Evidence-Based Guide. 3rd edition, Churchill Livingstone. ISBN: 978 0 7295 3910 4.
5	Chen, S. N, Friesen, J. B, Webster, D., Nikolic, D., van Breemen, R. B., Wang, Z. J, Fong, H. H, Farnsworth, N. R. and Pauli, G. F. (2011). Phytoconstituents from *Vitex agnus-castus* fruits. *Fitoterapia*, **82**(4), 528-833.
6	Zhelev, I., Petkova, Z., Kostova, I., Damyanova, S., Stoyanova, A., Dimitrova-Dyulgerova, I., Antova, G., Ercisli, S., Assouguem, A., Kara, M., Almeer, R. and Sayed, A. A. (2022). Chemical composition and antimicrobial activity of essential oil of fruits from *Vitex agnus-castus* L., growing in two regions in Bulgaria. *Plants (Basel)*, **11**(7), 896. doi: 10.3390/plants11070896.
7	WHO monographs on selected medicinal plants (2009). Monographs on selected medicinal plants, **4**, 9-29.
8	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. 1st edition. John Wiley & Sons, Ltd.

Egyptian Herbal Monograph

Medicinal Plants Used in Egypt

Zingiber officinale Roscoe چنزبيل

1. Names & Synonyms (1)

***Zingiber officinale* Roscoe.**

Family: Zingiberaceae.

Syns. *Amomum zingiber* L., *Zingiber blancoi* Massk.

Arabic: Janzabeil چنزبيل - Zanjabeel زنچبيل - Zingibil زنجبيل

English: Ginger.

2. Parts used for medicinal purpose

The dried rhizome (1-4).

3. Major chemical constituents (4, 5)

- Oleo-resin: Gingerols, shogaols, paradols, zingerone, gingerenone-A, and 6-dehydrogingerdione.

- Essential oil: *β*-Bisabolene and zingiberene, zingiberol, zingiberenol, *ar*-curcumene, *β*-sesquiphellandrene, *β*-sesquiphellandrol (*cis* and *trans*), phellandrene, camphene, geraniol, neral, linalool, *d*-nerol).

- Others: Starch, lipids, proteins and amino acids.

4. Medicinal uses (Indications)

A. Prevention of nausea and vomiting in motion sickness (1-3, 6), postoperative nausea and seasickness (1).

B. Symptomatic treatment of mild, spasmodic gastrointestinal complaints including bloating and flatulence (1-4), lack of appetite, indigestion, dyspepsia (1, 3, 4, 6).

C. Expectorant (3, 6) and cough suppressant (antitussive), to help relieve bronchitis (3) as well as colds (1, 3, 6).

D. Adjunctive treatment for inflammatory conditions, such as osteoarthritis and rheumatoid arthritis (1, 4, 7).

5. Herbal preparations correlated to medicinal use

1. Comminuted herbal substance as herbal tea for oral use as decoction.
   1.5 teaspoonful of the comminuted herbal substance in 1 cup of boiling water (7).
2. Powdered herbal substance (1-3).
3. Ethanolic extracts (dry extract, fluid extract, tincture) (3, 7).
4. Aqueous dry extracts (3, 7).

Herbal preparations (2-4) are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Indication A

Preparation 1
Adults: 0.7-3g as infusion (3) or decoction (3, 7).
Adolescents and children more than 6 years: 0.7-3g as infusion or decoction (3).
Take a single dose 30 minutes before travel or every 4 hours as needed (optional) (3).

Preparation 2
Adults: 1-2 g, 30 minutes to one hour before traveling or upon arising (2, 4, 7) or 0.5 g, 2-4 times daily as needed (1, 4) without exceeding the maximum daily dose of 3g (3).
Adolescents: 750 mg, 30 minutes before travelling (2) or 0.5 g, 2-4 times daily as needed (1) without exceeding the maximum daily dose of 3g (3).
Children between 6 and 12 years of age: 250 or 500 mg, 30 minutes before travelling (2) or 0.5 g, 2-4 times daily as needed (1) without exceeding the maximum daily dose of 3g (3).

Preparation 3
Adults: 100-200 mg extract, standardized to 20% gingerol and shogaol (7) or extracts equivalent to 0.5g, 2–4 times daily (1) without exceeding the maximum daily dose of 3g of dried rhizome equivalent (3).
Adolescents and children more than 6 years: extracts equivalent to 0.5g, 2–4 times daily (1) without exceeding the maximum daily dose of 3g of dried rhizome equivalent (3).

Preparation 4
Adults: 100-200 mg extract, standardized to 20% gingerol and shogaol (7) or extracts equivalent to 0.5 g, 2–4 times daily (1) without exceeding the maximum daily dose of 3g of dried rhizome equivalent (3).
Adolescents and children more than 6 years: extracts equivalent to 0.5-0.7 g, 2–4 times daily (1, 3) with maximum daily dose of 3g of dried rhizome equivalent (3).

Indication B

Preparation 1
Adults, adolescents and Children more than 6 years: 0.7-3 g as infusion or decoction (3).

Preparation 2
Adults: 180 mg, 3 times daily (2) or 0.5 g, 2-4 times daily (1) without exceeding the maximum daily dose of 3g of dried rhizome (3).
Adolescents and children more than 6 years: 0.3–3g of dried rhizome daily (3).

Preparation 3
Adults: extracts equivalent to 0.3-0.5 g, 2–4 times daily (1, 3) without exceeding the maximum daily dose of 3g of dried rhizome equivalent (3).
Adolescents and children more than 6 years: extracts equivalent to 0.3- 3g of dried rhizome, daily (3).

Preparation 4
Adults: extracts equivalent to 0.5-0.7g, 2–4 times, daily (1, 3) without exceeding the maximum daily dose of 3g of dried rhizome equivalent (3).
Adolescents and children more than 6 years: extracts equivalent to 0.7- 3g of dried rhizome, daily (3).

Indication C (3)

Adults, adolescents, and children more than 6 years:
Preparation 1: 0.7g-3g of dried rhizome as infusion or decoction.
Preparation 2: powdered herbal substances equivalent to 0.3–3 g of dried rhizome daily.
Preparation 3: ethanolic extract equivalent to 0.3- 3 g of dried rhizome daily.
Preparation 4: aqueous extract equivalent to 0.7- 3 g of dried rhizome daily.

Indication D (7)

Preparation 3, 4
Adults: 100-200 mg extract, standardized to 20% gingerol and shogaol.

Duration of use (2)

If the symptoms persist longer than 5 days (for indication A) or longer than 2 weeks (for indication B) during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (2).

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Ginger should not be used by persons with cholelithiasis (6, 7).
- It should not be used during childhood fevers or in children with gallstones (7).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children and adolescents under 6 years of age is not recommended (1-3).

9. Interactions with other medicinal products and other forms of interaction

Ginger may increase plasma partial prothrombin time in clients taking warfarin concurrently and may increase prothrombin time (6, 7).

10. Fertility, pregnancy and lactation

- Ginger use in pregnancy is avoided (2). Ginger is reputed to be an abortifacient and utero-activity has been documented for a related species (4).
- Safety during lactation has not been established. In the absence of sufficient data, the use during lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (2)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Minor gastrointestinal complaints, particularly stomach upset, eructation, dyspepsia and nausea have been reported (2).

13. Overdose

No case of overdose has been reported (2).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

22/06/2022.

References

1	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, **1**, 277-287.
2	Community Herbal Monograph on *Zingiber officinale* Roscoe, Rhizome (2012). EMA/HMPC/749154/2010. Committee on Herbal Medicinal Products (HMPC).
3	Natural Health Product, Ginger – *Zingiber officinale* (2022). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=99&lang=eng
4	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
5	Mao, Q-Q., Xu, X-Y., Cao, S-Y., Gan, R-Y., Corke, H., Beta, T. and Li, H-B. (2019). Bioactive Compounds and Bioactivities of Ginger (*Zingiber officinale* Roscoe). *Foods*, **8**, 185; doi:10.3390/foods8060185.
6	PDR for herbal medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
7	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.

Egyptian Herbal Monograph

Volume 4

Herbal Formulations used in Egypt

Egyptian Drug Authority (EDA)

2023

Preface

For herbal formulations, a clear and logical rationale is required to support the claim being made for the herbal combination, the dosage of each individual active ingredient found in the multiple ingredients product and its safety and efficacy in combination with the other active ingredient(s) under the recommended conditions of use. The control tests for the finished product must be such as to allow the qualitative and quantitative determination of the active ingredients. If quantitative determination of each active ingredient is not feasible, the combined content of several active ingredients may be determined. Therefore, to complete this volume, the earlier work from the Egyptian Herbal Monograph in addition to the scientific files presented on the Specialized Scientific Committee of Herbal Medicines were employed.

Egyptian Herbal Monograph

Herbal Formulations Used in Egypt

Anise oil / Peppermint oil — زيت ينسون/ زيت نعناع

1. Names & Synonyms

Anise (1)
***Pimpinella anisum* L.**
Family: Apiaceae (Umbelliferae).
Syns*: Anisum officinarum* Moench., *A. vulgare* Gaertn., *Apium anisum* L. Crantz., *Carum anisum* L. Baill., *Pimpinella anisum* cultum Alef., *P. aromatica* Bieb., *Selinum anisum* L. E.H.L. Krause., *Sison anisum* Spreng., *Tragium anisum* Link.
Arabic*:* Yansoon ينسون
English*:* Anise, Aniseed.

Peppermint (2)
***Mentha piperita* L.**
Family: Lamiaceae.
Arabic: Ni'na نعناع
English: Peppermint.

2. Parts used for medicinal purpose

Anise oil: Dried ripe fruits (1).
Peppermint oil: Fresh overground parts and the dried leaves (2-4).

3. Major chemical constituents

Anise oil:
Trans-anethole, estragole (methylchavicol, isoanethole), *β*-anisaldehyde, *α*-terpenol and *cis*-anethole (1).

Peppermint oil:
Menthol, menthone, menthyl acetate, menthofuran and 1,8- cineole (eucalyptol) (5).

4. Medicinal uses (Indications)

Symptomatic treatment of digestive disorders such as dyspepsia (indigestion) flatulence, bloating, minor spasms of the gastrointestinal tract and abdominal pain especially in irritable bowel syndrome (2-4, 6,7).

5. Herbal preparations correlated to medicinal use

Combination of Anise oil and Peppermint oil.

Herbal preparation is in solid pharmaceutical gastro-resistant dosage form. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adults and elderly:

- 20 mg of Anise oil and 50 mg of Peppermint oil, 3 times daily.
- 100 mg of Anise oil and 56 mg of Peppermint oil, once daily.
- 150 mg of Anise oil and 30 mg of Peppermint oil 1-3 times daily.

Duration of Use:

- Not to be taken for more than 2 weeks.
- If symptoms persist longer than one week during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use.

Should be taken 30-60 minutes before meals and to be swallowed whole, not broken or chewed (7).

7. Contraindications

- Hypersensitivity to the active substances and to other plants of the same family.

- Patients with liver disease, cholangitis, achlorhydria, gallstones and any other biliary disorders (3,6-8).

8. Special warnings and precautions for use (7)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

- The use in children and adolescents under 18 years of age is not recommended.

- Patients who already suffer from heartburn or hiatal hernia, have sometimes an exacerbation of this symptom after taking peppermint oil. Treatment should be discontinued in these patients.

- The product should be used with caution in inflamed and ulcerated conditions of the gastrointestinal tract.

- Other medicinal products containing peppermint oil should be avoided during the use of this product.

- The gastro-resistant solid dosage forms should be swallowed whole, i.e., not broken, or chewed, because this would release the peppermint oil prematurely, possibly causing local irritation of the mouth and oesophagus.

9. Interactions with other medicinal products and other forms of interaction

- Concomitent use of food or antacids could cause early release of the content the medicinal product (7).

- Other medicinal products used to decrease stomach acid, such as histamine-2 blockers and proton pump inhibitors may cause premature dissolution of the gastro-resistant solid dosage form and should be avoided (7).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy or lactation is not recommended (3, 7, 9).

- No fertility data available (7).

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.

- Urine and stools with an odour of menthol, dysuria and inflammation of the glans of the penis (7).

- Occasional allergic reactions to the skin, respiratory system and gastrointestinal tract are reported e.g. nausea and vomiting (2,4,7).

- Allergic reactions to menthol (bradycardia, muscle tremor, ataxia, anaphylactic shock, headache and erythematous skin rash may occur (7).

- Heartburn, perianal burning, blurred vision and dry mouth (7).

13. Overdose

- Overdose may cause severe gastrointestinal symptoms: diarrhoea, rectal ulceration; epileptic convulsions, loss of consciousness, apnoea, nausea, vomiting, pulmonary edema and disturbances in cardiac rhythms, ataxia and other CNS problems (1,6-7).

- In the case of overdose, the ingestion of milk and alcohol is contraindicated owing to increased resorption (1). The stomach should be emptied by gastric lavage. Observation should be carried out with symptomatic treatment, if necessary (7).

14. Relevant biological properties

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/last revision

20/08/2023.

References

1	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, 3, 42-63
2	WHO monographs on selected medicinal plants (2002). Monographs on selected medicinal plants, 2, 188-198.
3	Natural Health Product Peppermint – *Mentha piperita* (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=144
4	ESCOP Monographs (2019). *Mentha piperita* folium- Peppermint Leaf. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills. ISBN 978-1- 901964-66-0.
5	Desam, N. R., Al-Rajab, A. J., Sharma, M., Mylabathula, M. M., Gowkanapalli, R. R. and Albratty, M. (2019). Chemical constituents, *in vitro* antibacterial and antifungal activity of *Mentha piperita* L. (peppermint) essential oils. Journal of King Saud University - Science, **31**(4), 528- 533.
6	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417
7	European Union Herbal Monograph on *Mentha x piperita* L., aetheroleum (2020). EMA/HMPC/679997/2013 Committee on Herbal Medicinal Products (HMPC).
8	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd 56363-361-2.
9	Community Herbal Monograph on *Pimpinella anisum* L., aetheroleum (2013). EMA/HMPC/321185/2012 Committee on Herbal Medicinal Products (HMPC).

Egyptian Herbal Monograph

Herbal Formulations Used in Egypt

Camel grass weed/ Toothpick حلفابر و خلة بلدي

1. Names & Synonyms

Camel grass weed
***Cymbopogon proximus* (Hochst. ex A. Rich.)** (1, 2)**:**
Family: Gramineae (Poaceae) (2, 3).
Synonyms (3)**:**
Andropogon proximus (Hochst.), *Andropogon sennarensis* (Hochst.), *Andropogon jwarancusa* Jones var. *proximus* (Hochst. ex A. Rich.), *Andropogon jwarancusa* Jones var. *sennarensis* (Hochst.) and *Cymbopogon sennarensis* (Hochst.).
Arabic Names: Halfa bar حلفابر, Mahareb محاريب(1, 4).
English Names: Camel grass, Camel's hay, Geranium grass, Scenanth (1, 2).

Toothpick
***Ammi visnaga* L.** (1, 2, 5)**:**
Family: Umbelliferae (Apiaceae).
Synonyms: *Daucus visnaga* L.
Arabic Names: Khella baladi خلة بلدى, Khella خلة, Gazar sheitani جزر شيطاني, Kammon habashi كمون حبشي.
English Names: Pick-tooth, Toothpick, Bishop's weed.

2. Parts used for medicinal purpose

Camel grass weed: Aerial parts (1).
Toothpick: Fruits and leaves (1, 2, 5).

3. Major chemical constituents

Camel grass weed:

-Essential Oil (4, 6): Piperitone, *β*-elemol, *α*-eudesmol, *β*-eudesmol, *β*-elemene, eudesm-7(11)-en-4-ol, D-limonene,2-, *α*-terpineol, *τ*-cadinol, terpinolene, *β*-selinenol, 3-cyclohexen-1-one,2-isopropyl-5-methy, 4-carene, shyobunol, cadina-1(10),4-diene, (−)-guaia-6,9-diene and *β*-caryophyllaneare.

-Sesquiterpenoids: Proximadiol (biocyclic sesquiterpene diol) in addition to 5*α*-hydroxy-*β*-eudesmol, 1*β*-hydroxy-*β*-eudesmol, 1*β*-hydroxy-*α*-eudesmol, 5*α*-hydroperoxy-*β*-eudesmol and 7α, 11-dihydroxycadin- 10(14)-ene (1, 7).
-Others: Saponins, tannins, triterpenes, flavonoids, alkaloids, phenolic glycosides, cardiac glycosides and steroids (8).

Toothpick:
-Furanochromone derivatives (*γ*-Pyrones): Khellin, visnagin, khellinol, ammiol, visammiol, khellol, khellinin, khellinone, visnaginone (9) and visamminol.
-Pyranocoumarins/visnagans: Samidin, dihydrosamidin and visnadin (9).
-Furanocoumarins: Xanthotoxin, ammoidin, bergapten, and psoralen (10-17).
-Flavonoids: Quercetin, kaempferol, rhamnocitrin, rhamnetin and rhamnazin. Flavonoidal glycosides include quercetin-3-O-glucoside, kaempferol-3-O-glucoside and isorhamnetin 3-O-glucoside, rhamnetin-3-O-glucoside, isorhamnetin-3-O-glucoside, rhamnazin-3-O-glucoside, isorhamnetin-7-O-glucoside, quercetin-7, 3, 3'-O-triglucoside, quercetin-3-O-rutinoside, kaempferol-3-rutinoside and isorhamnetin-3-O-rutinoside.
-Flavonoidal sulfates: Quercetin 3-sulfate, rhamnocitrin 3-sulfate, and isorhamnetin-3-sulfate (18).
-Essential Oil: Oxygenated monoterpenes (linalool and thymol), monoterpene hydrocarbons (*α*-thujene, *α*-pinene, *β*-pinene, and *β*-myrcene) (18), and nonterpene derivatives (isoamyl 2-methylbutyrate, isoamyl isobutyrate, isobutyl 2-methylbutyrate, 2-methylbutyl 2-methylbutyrate, 2-methylbutyl isobutyrate, and isoamyl isovalerate) (19, 20).
-Sterols and Fatty acids: *β*-Sitosterol and *β*-sitosterol-glucoside (21), in addition to palmitic, palmitoleic, stearic, petroselinic, linoleic, linolinic, arachidic and tetracosanoic acids (18).

4. Medicinal uses (Indications)

Urinary tract disorders (22, 23, 24)**:**

A. Diuretic (6, 7), renal colic pain killer (25, 26).

B. Break up and removal of small renal stones from urinary tract (Lithotriptic agent) (25).

5. Herbal preparations correlated to medicinal use

Combination of *C. proximus* herb (Extraction solvent 70% ethanol) dry extract and *A. visnaga* fruits (Extraction solvent 30% ethanol) dry extract.

Herbal preparation is in pharmaceutical dosage forms for oral use. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Single dose: Combination of 72mg *C. proximus* dry extract and 180mg *A. visnaga* dry extract.

Daily dose: 3 times daily.

Method of administration: Oral use.

7. Contraindications

Hypersensitivity to the active substances and to other plants of the same family.

8. Special warnings and precautions for use

-If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

-The exposure to sun or other sources of ultraviolet light should be avoided during treatment, in order to minimize photosensitivity due to *A. visnaga* content (27).

-Patients should be monitored for ophthamologic changes, as *A. visnaga* has been associated with the development of severe ophthalmologic changes, particularly pigmentary retinopathy (28, 30).

-Blood glucose level should be monitored regularly.

-To be used under medical supervision.

9. Interactions with other medicinal products and other forms of interaction

Concurrent use with blood thinners, calcium channel blockers or blood pressure lowering drugs is avoided due to *A. visnaga* content (23).

10. Fertility, pregnancy and lactation

- The use during pregnancy should be avoided (24).

- Safety during lactation has not been established. In the absence of sufficient data, the use during lactation is not recommended.

- No fertility data available.

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Pseudoallergic reactions and reversible cholestatic jaundice and elevated activities of liver transaminases and γ-glutamyltransferase have been observed. These symptoms are typically reversible when the use is discontinued (27).

13. Overdose

Long term use or overdose of the drug can lead to queasiness, dizziness, loss of appetite, headache, sleep disorders and with very high dosage (corresponding to over 100 mg khellin), it caused reversible elevation in the levels of liver enzymes (27, 29).

14. Relevant biological properties

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/last revision

20/8/2023.

References

1	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (With contribution: E. Aboutabl, M. Shabana & F. Soliman). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
2	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
3	Ibrahim A. Saleh and Mohamed Elamir F. Hegazy (2018). *Cymbopogon proximus*. In: Egyptian Encyclopedia of Wild Medicinal Plants, 6, 390-399. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Malin, M. A., Ali, M. M. and Ramadhani, A. M. (2018). GC-MS analysis and antimicrobial activities of *Cymbopogon proximus* essential oil and phytochemical screening of its crude extracts. *Journal of Medicinal Plants Studies*, 6(4), 117-122.
5	Nahed, M. H. and Mona, M. A. (2017). *Ammi visnaga* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, 2, 121-136. Academy of Scientific Research and Technology, Cairo, Egypt.
6	El-Tahir K. E. H. and Abdel Kader M. S. (2008). Chemical and pharmacological study of *Cymbopogon proximus* volatile oil. *Research journal of medicinal plant*, 2, 53-60.
7	El-Askary, H. I., Meselhy, M. R., Galal, A. M., (2003). Sesquiterpenes from *Cymbopogon proximus*. *Molecules*, 8, 670-677.
8	Ali, M. R. (2012). Antibacterial and phytochemical screening *Lepidium sativum* and *Cymbopogon schoenanthus*. BSc thesis, Faculty of Science, Khartoum University.
9	Hashim, S., Jan, A., Marwat, K. B. and Khan, M. A. (2014). Phytochemistry and medicinal properties of *Ammi visnaga* (Apiacae). *Pak. J. Bot.*, 46(3): 861-867.
10	Abou-Mustafa, E. A., Saleh, N. A. M., Elgamal, M. H. A., Shalaby, N. M. M. and Duddeck, H. (1990). A further contribution to the γ-pyrone constituents of *Ammi visnaga* fruits. *Planta Medica*, 56, 134.
11	Martelli, P., Bovalini, L., Ferri, S. and Franchi, G. G. (1984). Rapid separation and quantitative determination of Khellin and Visnagin in *Ammi visnaga* (L.) Lam Fruits by High Performance Liquid-Chromatography. *J. Chromato.*, 301:297-302.
12	Eldomiaty, M. M. (1992). Improved high-performance liquid-chromatographic determination of khellin and visnagin in *Ammi visnaga* fruits and Pharmaceutical formulations. *J. Pharm. Sci.*, 81: 475-478.
13	Zgorka, G., Dragan, T., Głowniak, K. and Basiura, E. (1998). Determination of furanochromones and pyranocoumarins in drugs and *Ammi visnaga* fruits by combined solid-phase extraction, high-performance liquid chromatography and thin layer chromatography. *J. Chromato. A,* 797(1-2):305-309.
14	Balbaa, S. I., Hilal, S. H. and Zaki, A. Y. (1976). Medicinal Plant Constituents. Second Edition, Central Agency for University and School Books, Cairo, Egypt.

15	El-Gamal, M. H., Shalaby, N. M., El-Hagrassy, A. M., Toth, G., Simon, A. and Duddeck, H. (1998). A further contribution to some gamma-pyrone constituents of *Ammi visnaga*. *Fitoterapia*, 69(6):549-550.
16	Sonnenberg, H., Kaloga, M., Eisenbach, N. and Frömming, K. K. (1995). Isolation and characterization of an angular-type dihydro-pyrano-coumarin-glycoside from the fruits of *Ammi visnaga* (L.) LAM. (Apiaceae). *J. Naturforsch*, 50(9-10): 729-731.
17	Razzaghi-Abyaneh, M., Shams-Ghahfarokhi, M., Rezaee, M.B. and Sakuda, S. (2010). Natural Aflatoxin Inhibitors from Medicinal Plants. In Mycotoxins in Food, Feed and Bioweapons; Rai, M., Varma, A., eds.; Springer: Berlin/Heidelberg, Germany, 329–352.
18	Khalil, N., Bishr, M., Desouky, S. and Salama, O. (2020). *Ammi visnaga* L., a Potential Medicinal Plant: A Review. Molecules, 25: 301.
19	Zrira, S., Elamrani, A., Pellerin, P., Bessiere, J. M., Menut, C. and Benjilali, B. (2008). Isolation of Moroccan *Ammi visnaga* oil: comparison between hydrodistillation, steam distillation and supercritical fluid extraction. *J. Essent. Oil Bear. Plants*, 11: 30–35.
20	Abdul-Jalil, T.Z., Saour, K. and Nasser, A. A. (2010). Phytochemical study of some flavonoids present in the fruits of two *Ammi* L. species wildly grown in Iraq. *Iraqi J. Pharma. Sci*., 19: 48–57.
21	Keddad, A., Baaliouamer, A. and Hazzit, M. (2016). Chemical composition and antioxidant activity of essential oils from umbels of Algerian *Ammi visnaga* (L.). *J. Essent. Oil Bear. Plants*, 19: 1243–1250.
22	Egyptian Pharmacopoeia (1984). General Organization for Government Printing, Cairo, 3th ed.
23	Alam, S., Anjum, N., Akhtar, J. and Bashir, F. (2018). Pharmacological investigations on khella- (*Ammi visnaga* L.). *World Journal of Pharmaceutical Research*, 7(13):212-224.
24	WHO monographs on selected medicinal plants (2007). Fructus *Ammi Visnagae*, Volume 3, 23-32.
25	Selim, S. A. (2011). Chemical composition, antioxidant and antimicrobial activity of the essential oil and methanol extract of the Egyptian lemongrass *Cymbopogon proximus* Stapf. Grasasy Aceites, 62(1), 55-61.
26	Conservation and sustainable use of medicinal plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, vol (1-5).
27	Blumenthal, M., Busse, W. R., Goldberg, A., Gruenwald, J., Hall, T., Riggins, C.W. and Rister, R. S. (eds.) Klein, S. and Rister, R.S. (1998). The complete German Commission E monographs, Austin, TX, American Botanical Council.
28	Shlosberg, A., Egyed, M. N. and Eilat, A. (1974). The comparative photosensitizing properties of *Ammi majus* and *Ammi visnaga* in goslings. *Avian Dis*., 18(4):544–550.
29	PDR for Herbal Medicines (1998). Medical Economic Co. Montvale, New Jersey, 639. ISBN 1563633612, 9781563633614.
30	Vanachayangkul, P., Chow, N., Khan, S.R. and Butterweck, V. (2011). Prevention of renal crystal deposition by an extract of *Ammi visnaga* L. and its constituents khellin and visnagin in hyperoxaluric rats. *Urol. Res*., 39(3): 189–195.

Egyptian Herbal Monograph

Herbal Formulations Used in Egypt

Caraway oil/ Dill oil زيت كراوية / زيت شبت

1. Names & Synonyms

Caraway (1)
***Carum carvi* L.**
Family: Apiaceae (Umbelliferae)
Syns.: *Carum velenovskyi* Rohlena
Arabic: Karawya كراوية
English: Caraway

Dill (2)
***Anethum graveolens* L.**
Family: Apiaceae (Umbelliferae)
Syns: *Pastinaca anethum* Spreng., *Peucedanum graveolens* Benth. & Hook., *Selinum anethum* Roth.
Arabic: Shabat شبت
English: Dill

2. Parts used for medicinal purpose

Caraway oil: Dried ripe fruits (3, 4).
Dill oil: Dried ripe fruits (2).

3. Major chemical constituents

Caraway oil: Carvone and limonene (5).

Dill oil: Carvone, limonene, α-phellandrene, dihydrocarvone, dillapiole (6), 1,8 cineole, α-pinene and α-terpene (2).

4. Medicinal uses (Indications)

A. For the symptomatic relief of digestive disorders such as bloating, flatulence, dyspepsia and digestive spasms (3,7).
B. Stimulate appetite (stomachic) (8).
C. Carminative and spasmolytic in infantile colic (9).

5. Herbal preparations correlated to medicinal use

Combination of Caraway oil and Dill oil.

Herbal preparation is in liquid pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Infants and children

Infants up to 6 months:
0.00915 mg Caraway oil and 1.15 mg Dill oil, 2-3 times daily.

Infants 6 -12 months:
0.0183mg Caraway oil and 2.3mg Dill oil, 3 times daily.
2.5mg Caraway oil and 2.25mg Dill oil, 2-3 times daily.
5mg Caraway oil and 0.25mg Dill oil, 2 times daily.

Children above one year:
0.0366 mg Caraway oil and 4.6 mg Dill oil, 3 times daily.

Children above four years:
0.0549 mg Caraway oil and 6.9 mg Dill oil, 3 times daily.

Duration of use:
If the symptoms persist longer than one week a doctor or pharmacist should be consulted.

Method of administration: Oral use (3,4,8).

To be used under medical supervision.

7. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Gastroesophageal reflux disease (10).
- The use in patients with liver disease, cholangitis, achlorhydria, gallstones and any other biliary disorders is not recommended (7).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted (3,7).
- To be used under medical supervision.

9. Interactions with other medicinal products and other forms of interaction

None reported (3,7).

10. Fertility, pregnancy and lactation

Not relevant

11. Effects on ability to drive and use machines

Not relevant

12. Undesirable effects

-If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Anorexia, diarrhea, skin redness and irritation may occur (10).
- May alter sodium balance and cause allergic reaction (10, 11).

13. Overdose

An intake of over dose of the medicinal product for extended periods may lead to kidney and liver damage (10-12).

14. Relevant biological properties

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/last revision

20/8/2023.

References

1	Duke, J. A. (2002). Handbook of Medicinal Herbs. 2nd ed. CRC Press. ISBN 978084931284.
2	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, 3, 33-41.
3	European Union Herbal Monograph on *Carum carvi* L., Fructus (2015). EMA/HMPC/715092/2013. Committee on Herbal Medicinal Products (HMPC).
4	ESCOP Monographs (2019). *Carvi* aetheroleum, Caraway Oil. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills. ISBN 978-1-901964-65-3.
5	Mahboubi, M. (2019). Caraway as important medicinal plants in management of diseases. *Natural Products and Bioprospecting*, 9, 1–11. https://link.springer.com/content/pdf/10.1007/s13659-018-0190-x.pdf
6	Said-Al Ahl, H., Gendy, A. G. and Omer, E. A. (2016). Humic acid and indole acetic acid affect yield and essential oil of dill grown under two different locations in Egypt. *International Journal of Pharmacy and Pharmaceutical Sciences*, **8**, 146-157.
7	European Union Herbal Monograph on *Carum carvi* L., aetheroleum (2015). EMA/HMPC/715094/2013. Committee on Herbal Medicinal Products (HMPC)
8	Natural Health Product, Caraway – *Carum carvi* (2019). Health Canada, http://webprod.hcsc.gc.ca/nhpidbdipsn/atReq.do?atid=caraway.carvi&lang=eng.
9	Wren, R. C. (1988). Potter's New Cyclopaedia of Botanical Drugs and Preparations. Completely revised by Elizabeth M. Williamson and Fred J. Evans. C. W. Daniel Company, Ltd, Saffron Walden.
10	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs and Natural Supplements 4th ed., ISBN: 978-0-323-05741-7.
11	Kraft, K. and Hobbs, C. (2004). Pocket Guide to Herbal Medicine. Stuttgart; New York: Thieme. ISBN 3-13-126991-X (GTV), ISBN 1-58890-063-0.
12	PDR for Herbal Medicines (2002). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-

Egyptian Herbal Monograph

Herbal Formulations Used in Egypt

Guava/ Tilia جوافة / تيليو

1. Names & Synonyms (1)

Guava
***Psidium guajava* L.**
Family: Myrtaceae.
Syns: *Guajava pyrifera* Kuntze, *Myrtus guajava* (L.) Kuntze, *Myrtus guajava* var. *pyrifera* Kuntze, *Psidium pyriferum* L.
Arabic: Gawafa جوافة
English name: Guava (2).

Tilia
***Tilia cordata* Mill.**
Family: Tiliaceae (Malvaceae).
Arabic: Tilio تيليو.
English: Lime flower (3), Linden, Tilia and small leaf linden, small leaf lime (4).

***Tilia platyphyllos* Scop.**
Family: Tiliaceae (Malvaceae).
Arabic: Tilio تيليو.
English: Lime flower (3), Linden, Tilia and large-leaf Linden.

***Tilia x vulgaris* Heyne**
Naturally occurring hybrid of *T. cordata* and *T. platyphyllos* Scop.
Family: Tiliaceae (Malvaceae).
Syns: *T. europaea* auct. non L.
Arabic: Tilio تيليو.
English: European linden (3), European lime tree, Linden and Tilia (4).

2. Parts used for medicinal purpose

Guava: Dried leaves (2).

Tilia: Flowers (7-9).

3. Major chemical constituents

Guava:

Phenolic compounds (7)

-Flavonoids: Quercetin and its glycosides, avicularin, apigenin, guaijaverin, kaempferol, kaempferol-3-arabofuranoside, hyperin, myricetin, rutin, catechin, epicatechin, epigallocatechin gallate and proanthocyanidins.

-Phenolic acids: Gallic acid and caffeic acid.

Essential oil (8,9)

β-Caryophyllene, 4*α*-selin-7 (11)-enol, *β*-caryophyllene oxide, *α*-selinene, *β*-selinene, *δ*-cadinene, daucol, cubenol, 1,8-cineole (eucalyptol) and aromadendrene.

Others (7)

Sugars: Sulphated and unsulphated polysaccharides (uronic acid), minerals (calcium, potassium, sulfur, sodium, iron, boron, magnesium, manganese and zinc), vitamins (C and B) and macronutrients (protein and fat).

Tilia:

Phenolic compounds (3, 5)

Flavonoids: Kaempferol, quercetin, myricetin and their glycosides (mainly Kaempferol-3-*O*-*β*-D-(6″-E-*p*-coumaroyl)-glucopyranoside "tiliroside") and proanthocyanidins.

Phenolic acids: Caffeic, chlorogenic and *p*-coumaric acids.

Essential oil: Alkanes (mainly tricosane) (6), phenolic alcohols and esters, and terpenes including citral, citronellal, citronellol, eugenol, limonene, nerol, *α*-pinene and terpineol (monoterpenes), and farnesol (sesquiterpene) (3).

Others: Mucilage, tocopherol (phytosterol) and amino acids (3).

4. Medicinal Uses (Indications)

Cough sedative, relief irritation of the throat in colds and catarrh of the respiratory tract (2,3,4,8,10,11).

5. Herbal preparations correlated to medicinal use

1. Combination of aqueous liquid extracts of Guava (2:1) and Tilia (1:1).
2. Combination of aqueous liquid extracts of Guava (1:1) and Tilia (1:1).
3. Combination of aqueous liquid extracts of Guava (2:1) and Tilia (15:1).
4. Combination of Guava aqueous liquid extract (4:1) and Tilia dry extract (ethanol 95%) (8:1).
5. Combination of aqueous dry extracts of Guava (2:1) and Tilia (1.5:1).

Herbal preparations are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use.

Preparation 1
Adolescents and Adults

- 333.375 mg Guava extract and 52.5 mg Tilia extract, 3 times daily.

Children above 4 years

- 111.125 - 222.250 mg Guava extract and 17.5 – 35 mg Tilia extract, 3 times daily.

Preparation 2
Adolescents and Adults

- 0.75 -1.5 ml of Guava extract and 0.75 -1.5 ml of Tilia extract, 3-4 times daily.

Children above 4 years

- 111.125 - 222.250 mg Guava extract and 17.5 - 35mg Tilia extract, 3 times daily.
- 0.125 - 0.250 ml Guava extract and 0.125 -0.25 ml Tilia extract, 3-4 times daily.

Preparation 3
Adolescents and Adults

- 140 - 280 mg Guava extract and 31.2- 62.4 mg Tilia extract, 3-4 times daily.

Children above 4 years

- 15.6 - 31.2 mg Guava extract and 15.6 – 31.2 mg Tilia extract, 3-4 times daily.

Preparation 4
Adolescents and Adults

- 125 - 250 mg Guava extract and 15-30 mg Tilia extract, 3-4 times daily.

Children above 4 years

- 62.5 - 125 mg Guava extract and 7.5-15 mg Tilia extract, 3-4 times daily.

Preparation 5
Adolescents and Adults

- 140 mg Guava extract and 31.2 mg Tilia extract, 3-4 times daily.

Children above 4 years

- 70 mg Guava extract and 15.6 mg Tilia extract, 3-4 times daily.

Duration of use (3):

- If the symptoms persist longer than one week during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use (6).

7. Contraindications (3, 4)

Hypersensitivity to active substances and to other plants of the same family.

8. Special warnings and precautions for use (3, 4)

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- The use in children under 4 years of age is not recommended.

9. Interactions with other medicinal products and other forms of interaction (3, 4)

None reported.

10. Fertility, pregnancy and lactation (4,7)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (7)

No studies on the effect on the ability to drive and use machines have beenperformed.

12. Undesirable effects (7)

- None reported.
- If adverse reactions occur, a doctor or a pharmacist should be consulted.

13. Overdose (7)

No case of overdose has been reported.

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

13/09/2023.

References

1	www,powo.science.kew.org.
2	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, 4, 127-139.
3	Community Herbal Monograph on *Tilia cordata* Miller, *Tilia platyphyllos* Scop., *Tilia* x *vulgaris* Heyne or their mixtures, flos (2012). EMA/HMPC/337066/2011. Committee on Herbal Medicinal Products (HMPC).
4	Natural Health Product, Linden, Small Leaf – *Tilia cordata* (2017). Health Canada, http://webprod.hc-sc.gc.ca/nhpid- bdipsn/atReq.do?atid=linden.tilleul.smallleaf.petitesfeuilles&lang=engEvans, W. C.
5	Evans, D. and Trease, G. E. (2009). Trease and Evans Pharmacognosy.16th ed., Edinburgh; New York: Saunders/Elsevier. ISBN 9780702029332.
6	Fitsiou, I., Tzakou, O., Hancianu, M. and Poiata, A. (2007). Volatile constituents and antimicrobial activity of *Tilia tomentosa* Moench and *Tilia cordata* Miller oils. *Journal of Essential Oil Research*, 19:2, 183-185, DOI: 10.1080/10412905.2007.9699255.
7	Kumar, M., Tomar, M., Amarowicz, R., Saurabh, V., Nair, M. S., Maheshwari, C., Sasi, M., Prajapati, U., Hasan, M., Singh, S., Changan, S., Prajapat, R. K, Berwal, M. K. and Satankar, V. (2021). Guava (*Psidium guajava* L.) leaves: Nutritional composition, phytochemical profile, and health-promoting bioactivities. *Foods*, 10, 752.
8	Karawya, M. S., Abdel Wahab, S. M., Hifnawy M. S., Azzam S. M. and EL- Gohary H. M. (1999). Essential oil of Egyptian Guajava leaves. Egypt. *J. Pharm. Sci.,* 40, (2), 209-217.
9	El-Ahmady, S. H, Ashour, M. L. and Wink, M. (2013). Chemical composition and anti-inflammatory activity of the essential oils of *Psidium guajava* fruits and leaves. *The Journal of Essential Oil Research*, 25, 6, 475 – 481. http://dx.doi.org/10.1080/10412905.2013.796498 .
10	Abou Zid, S. F. and Mohamed, A. A. (2011). Survey on medicinal plants and spices used in Beni-Sueif, Upper Egypt. *Journal of Ethnobiology and Ethnomedicine*, 7-18.
11	Jaiarj, P., Khoohaswan, P., Wongkrajang, Y., Peungvicha, P., Suriyawong, P.,Saraya, M. L. and Ruangsomboon, O. (1999). Anticough and antimicrobial activities of *Psidium guajava* Linn. leaf extract. *Journal of Ethnopharmacology*, 67:203–212.

Egyptian Herbal Monograph

Herbal Formulations Used in Egypt

Peppermint oil / Thyme oil زيت نعناع / زيت زعتر

1. Names & Synonyms

Peppermint (1)

***Mentha piperita* L.**
Family: Lamiaceae.
Arabic: Ni'na نعناع .
English: Peppermint.

Thyme (2)

***Thymus vulgaris* L.**
Syns.: *Origanum thymus* Kuntze, *Thymus collinus* Salisb.
Family: Lamiaceae (Labiatae).
Arabic: Za'ater زعتر .
English: English Thyme, Garden Thyme.

***Thymus zygis* L.**
Syns.: Origanum zygis (L.) Kuntze, *Thymus angustifolius* Salisb.
Family: Lamiaceae (Labiatae).
Arabic: Za'aterزعتر .
English: Spanish Thyme.

2. Parts used for medicinal purpose

Peppermint oil: Fresh overground parts and the dried leaves (1,3,4).
Thyme oil: Dried and fresh herb (5,6).

3. Major chemical constituents

Peppermint oil: Menthol, menthone, menthyl acetate, menthofuran, and 1,8-cineole (eucalyptol) (7).

Thyme oil: Thymol, carvacrol, *p*-cymene, γ-terpinene, linalool, terpinen-4-ol, borneol, 1,8- cineole, α-pinene and caryophyllene (6).

4. Medicinal uses (Indications)

Symptomatic treatment of digestive disorders such as dyspepsia (indigestion), flatulence, minor spasms of the gastrointestinal tract and for irritable bowel syndrome (1,3,4,8,9).

5. Herbal preparations correlated to medicinal use

Combination of Peppermint oil and Thyme oil.

Herbal preparation is in solid gastro-resistant pharmaceutical dosage forms. The pharmaceutical form should be described by the Pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

Adults and elderly
20 mg Peppermint oil and 20 mg Thyme oil, 3 times daily.

Duration of use:
The treatment should be taken until symptoms resolve, usually within 2 to 4 weeks.

Method of administration: Oral use.
The gastro-resistant dosage forms must be taken whole 30 minutes before meals (8).

7. Contraindications

- Hypersensitivity to the active substances and to other plants of the same family.

- Patients with liver disease, cholangitis, achlorhydria, gallstones and any other biliary disorders (3, 8-10).

8. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

- The use in children and adolescents under 18 years of age is not recommended (11).

- Other medicinal products containing peppermint oil should be avoided during the use of this medicinal product (8).

- The gastro-resistant solid dosage forms should be swallowed whole, i.e. not broken or chewed, because this would release the peppermint oil prematurely, possibly causing local irritation of the mouth and oesophagus (8).

- Patients who already suffer from heartburn or hiatal hernia, have sometimes an exacerbation of this symptom after taking peppermint oil. Treatment should be discontinued in these patients (8).

- The product should be used with caution in inflamed and ulcerated conditions of the gastrointestinal tract (8).

9. Interactions with other medicinal products and other forms of interaction

- Concomitent use of food or antacids could cause early release of the content the medicinal product (8).

- Other medicinal products used to decrease stomach acid, such as histamine-2 blockers and proton pump inhibitors may cause premature dissolution of the gastro-resistant solid dosage forms and should be avoided (8).

10. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy or lactation is not recommended (3,8,9, 12).

- No fertility data available (8, 4).

11. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed (6,8).

12. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.

- Urine and stools with an odour of menthol, dysuria and inflammation of the glans of the penis (8).

- Allergic reactions to menthol (bradycardia, muscle tremor, ataxia, anaphylactic shock (8), flushing, mucous membrane irritation, urticaria (9), headache and erythematous skin rash) may occur (8,9).

- Heartburn, nausea (8,9), vomiting, perianal burning blurred vision and dry mouth (8).

13. Overdose (8)

Overdose may cause:

- Severe gastro-intestinal symptoms such as diarrhea and rectal ulceration.

- Epileptic convulsions, loss of consciousness, apnoea, nausea, disturbances in cardiac rhythms, ataxia and other CNS problems, probably due to the presence of menthol.

- In the event of overdose, the stomach should be emptied by gastric lavage. Observation should be carried out with symptomatic treatment, if necessary.

14. Relevant biological properties

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/last revision

13/08/2023.

References

1	World Health Organization (2002). Monographs on selected medicinal plants, 2, 188-198.
2	https://www.gbif.org/species/5341442
3	Natural Health Product Peppermint – *Mentha piperita* (2018). Health Canada. http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=144.
4	ESCOP Monographs (2019). *Mentha piperita* folium- Peppermint Leaf. European Scientific Cooperative on Phytotherapy. Edited by Roberta Hutchins and Simon Mills. ISBN 978-1- 901964-66-0.
5	WHO monographs on selected medicinal plants (2007). Monographs selected medicinal plants, 3, 259-266.
6	Galovičová, L., Borotová, P., Valková, V., Vukovic, N. L., Vukic, M., Štefániková, J., Ďúranová, H., Kowalczewski, P. Ł., Čmiková, N. and Kačániová, M. (2021). *Thymus vulgaris* essential oil and its biological activity. *Plants*, 10, 1959. https://doi.org/10.3390/plants10091959.
7	Desam, N. R., Al-Rajab, A. J., Sharma, M., Mylabathula, M. M., Gowkanapalli, R. R. and Albratty, M. (2019). Chemical constituents, in vitro antibacterial and antifungal activity of *Mentha piperita* L. (peppermint) essential oils. *Journal of King Saud University - Science*, 31(4), 528- 533.
8	Committee on Herbal Medicinal Products (HMPC) (2020). European Union herbal monograph on *Mentha x piperita* L., aetheroleum. EMA/HMPC/522410/2013. Committee on Herbal Medicinal Products (HMPC).
9	Skidmore-Roth, L. (2010). Mosby's Handbook of Herbs & Natural Supplements. 4th ed. ISBN 9780323057417.
10	PDR for Herbal Medicines (2000). Montvale, NJ: Medical Economics Company, 2nd ed., ISBN 1-56363-361-2.
11	European Union herbal monograph on *Thymus vulgaris* L., *Thymus zygis* L., aetheroleum. EMA/HMPC/59032/2017. Committee on Herbal Medicinal Products (HMPC).
12	http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=172.

Egyptian Herbal Monograph

Herbal Formulations Used in Egypt

Saw palmetto / Nettle بلميط منشاري/ قريص - حريق

1. Names & Synonyms

Saw palmetto (1,2).

***Serenoa repens* (W.Bartram) Small.**
Family: Arecaceae (1,2).
Syns: *Corypha repens* W.Bartram, *Corypha obliqua* W.Bartram, *Diglossophyllum serrulatum* (Michx.) H. Wendl. ex Salomon، *Sabal serrulata* (Michx.) Schult.f., *Chamaerops serrulata* Michx., *Brahea serrulata* (Michx.) H. Wendl. (1,2).
Arabic: Balmit minshary بلميط منشاري
English: Serenoa , Saw palmetto (3) and Saw palmetto berry (4).

Nettle (5)
***Urtica dioica* L.**
Family: Urticaceae.
Syns.: *Urtica tibetica* W.T. Wang, *U. galeopsifolia* Wierzb. ex Opiz.
Arabic: hhurray حريق - Qurrays قريص
English name: Stinging nettle (6-8), Nettle (7,8).

2. Parts used for medicinal purpose

Saw palmetto: Dried ripe fruit (9).

Nettle: Dried roots (6-8, 10).

3. Major chemical constituents

Saw palmetto (11):

-Fatty acids and their glycerides: Monoacylglycerides (1-monolaurin, 1-monomyristicin). Oleic acid (unsaturated) and capric acid, caproic acid, caprylic acid, lauric acid, myristic acid, palmitic acid and stearic acid (saturated).

-Steroids: β-Sitosterol, campesterol and stigmasterol.

-Carbohydrates: Invert sugar, mannitol, high molecular weight polysaccharides with galactose, arabinose and uronic acid identified as main sugar components.

-Other constituents: Flavonoids (e.g. rutin, isoquercitrin, kaempferol), pigment (carotene), resin, tannin and volatile oil.

Nettle roots (10, 12, 13):

Polysaccharides: Glycans, glucogalacturonans, arabinogalactan acid, fatty acid: (10*E*, 12*Z*)-9-hydroxy-10, 12-octadecadienoic acid, lectins, ceramides, terpenes diols, and terpenes diols glucosides.

4. Medicinal uses (Indications) (14)

Symptomatic treatment of benign prostatic hyperplasia and related lower urinary tract symptoms after serious conditions have been excluded by a medical doctor.

5. Herbal preparations correlated to medicinal use

Combination of saw palmetto liquid extract, extraction solvent: Ethanol 96% and nettle powder extract, extraction solvent: Ethanol 60% - 70%.

Herbal preparation is in pharmaceutical dosage forms for oral use. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

160 mg saw palmetto extract and 120 mg nettle extract, twice daily.

Duration of use:

- Long-term use, up to 6 months, is possible.
- Typically, symptom reduction is experienced within 1–2 months' treatment.
- If the symptoms persist during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- There is no relevant use in children and adolescents under 18 years of age.

Method of administration: Oral use.

7. Contraindications (14)

Hypersensitivity to the active substances and to other plants of the same family.

8. Special warnings and precautions for use (14)

-If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

-If complaints worsen or if symptoms such as fever, spasms or blood in the urine, painful urination, or urinary retention occur during the use of the medicinal product, a doctor or a pharmacist should be consulted.

9. Interactions with other medicinal products and other forms of interaction (14)

- A few cases of suspected interactions with warfarin have been reported. Increased INR- values have been described.
- Anticoagulants (heparin, warfarin) and anticoagulant herbs: Nettle may decrease the effect of anticoagulants.
- CNS depressants (alcohol, barbiturates, sedative/hypnotics, antipsychotics, opiates) and sedative herbs: Nettle may lead to increased central nervous system depression.
- Diuretics: Use of nettle may increase the effects of diuretics, resulting in dehydration and hypokalemia.
- Iron salts: Nettle tea may interfere with the absorption of iron salts.
- Lithium: Nettle combined with lithium may result in dehydration, lithium toxicity.

10. Fertility, pregnancy and lactation (14)

- The use during pregnancy and lactation is contraindicated owing to its effects on androgen and estrogen metabolism.
- No fertility data available.

11. Effects on ability to drive and use machines (14)

No studies on the effect on the ability to drive and use machines have been performed.

12. Undesirable effects (14)

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Abdominal pain, nausea, vomiting, diarrhea, abdominal pain (especially when taken on an empty stomach).
- Allergic or hypersensitivity reactions may occur such as skin rash, headache, increase of transaminases or gamma-glutamyl transferases, reversible gynecomastia, pruritus, rash and urticaria may occur.
- Gastro-intestinal complaints such as nausea, heartburn, feeling of fullness, flatulence, and diarrhea may occur.

13. Overdose (14)

No case of overdose has been reported.

14. Relevant biological properties

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional information

-

16. Date of compilation/last revision

13/09/2023.

References

1	https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:941782-1#synonyms.
2	http://www.theplantlist.org/tpl/record/kew-190787
3	Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements, An evidence-based guide, 3rd ed. ISBN: 978 0 7295 3910 4.
4	https://www.herbalgram.org/resources/expanded-commission-e/saw-palmetto-berry/.
5	Belwal, T., Nabavi, S. M., Nabavi, S. F., Dehpour, A. R. and Shirooie, S. (2020). Naturally Occurring Chemicals against Alzheimer's Disease. Academic Press. ISBN: 0128192135, 9780128192139.
6	World Health Organization (2002). Monographs on selected medicinal plants, 2, 329-341.
7	Natural Health Product Stinging Nettle – *Urtica dioca* (2019). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=166&lang=eng.
8	Mosby's Handbook of Herbs and Natural Supplements (2010). 4th ed., ISBN: 978-0-323-05741-7.
9	World Health Organization (2002). Monographs on selected medicinal plants, 2, 285-299.
10	European Union herbal monograph on *Urtica dioica* L., *Urtica urens* L., their hybrids or their mixtures, radix (2012). EMA/HMPC/461160/2008. Committee on Herbal Medicinal Products (HMPC).
11	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
12	Dhouibi, R., Affes, H., Ben Salem, M., Hammami, S., Sahnoun, S., Zeghal, K. M. and Ksouda, K. (2020). Screening of pharmacological uses of *Urtica dioica* and others benefits. *Progress in Biophysics and Molecular Biology*, 150: 67–77.
13	Taheri, Y., Quispe, C., Herrera-Bravo, J., Sharifi-Rad, J., Ezzat, S. M., Merghany, R. M., Shaheen, S., Azmi, L., Mishra, A. P., Sener, B., Kılıç, M., Sen, S., Acharya, K., Nasiri, A., Cruz-Martins, N., Fokou, P. V. T., Ydyrys, A., Bassygarayev, Z., Daştan, S. D., Alshehri, M. M., Calina, D. and Cho, W. C. (2022). *Urtica dioica* - Derived Phytochemicals for Pharmacological and Therapeutic Applications. *Evidence-Based Complementary and Alternative Medicine,* Volume 2022, Article ID: 4024331, 30 pages https://doi.org/10.1155/2022/4024331).
14	Egyptian Herbal Monograph/volume 3/2022, P. 360-362, P. 388-391.

Egyptian Herbal Monograph

Herbal Formulations Used in Egypt

St. John's wort / Valerian عشبة القديس يوحنا / فاليريانا

1. Names & Synonyms (1)

St. John's wort.
***Hypericum perforatum* L.**
Family: Hypericaceae (Clusiaceae).
Syns: *Hypericum officinale* Gaterau, *Hypericum officinarum* Crantz, *Hypericum vulgare* Lam.
Arabic: Oshbet Alkedees Yohanna عشبة القديس يوحنا.
English: St. John's wort, Perforate St. John's wort, Goatweed (2-5).

Valerian
***Valeriana officinalis* L.**
Family: Caprifoliaceae/Valerianaceae (6).
Arabic: Valeriana فاليريانا
English name: All-Heal, Belgian Valerian, Common Valerian, Fragrant Valerian, Garden Valerian, Valerian root (7, 8).

2. Part used for medicinal purpose

St. John's wort: Fresh and dried flowering tops and/or flowering aerial parts (6).

Valerian: Root, rhizomes and stolons (2-4).

3. Major chemical constituents

St. John's wort.

Naphthodianthrones: Hypericin, pseudohypericin, protohypericin, protopseudo -hypericin and cyclopseudohypericin (3, 7, 9, 10).
Phloroglucinol derivates: Hyperforin, adhyperforin and furanohyperforin (3, 9-11).
Flavonoids: Hyperoside, quercetin, rutin, quercitrin, isoquercitrin, astilbin, apigenin-7-*O*-glucoside and biapigenin (3, 9, 10, 12).
Procyanidines: Procyanidine B2 (3).
Others: Caffeic, chlorogenic, caffeoylquinic, *p*-coumaroylquinic acids and amino acids (3, 10).

Valerian

Essential oil: Chief components are bornyl acetate, valerianol, valeranone, intermedeol, camphene, myrtenyl acetate, agarospirol, γ-eudesmol, nootkatone and 6-isopropyl-1-methyl bicycles [3,1,0] hexane (8,13).
Sesquiterpenic acids: Valerenic acid, 2-hydroxyvalerenic acid, 2-acetoxy-valerenic acid (13).
Iridoids: Didrovaltrate and valepotriates derivatives including valepotriate, isovalepotriate, acetoxyvalepotriate and isovalemxy-hydroxy-dihydrovatrate (8).
Others: Lignanoids, alkaloids, flavonoids and amino acids (8).

4. Medicinal uses (Indications)

Relief of mild nervous tension, temporary mental exhaustion and sleep disorders (3).

5. Herbal preparations correlated to medicinal use (2, 3, 5, 7)

Combination of St. John's wort dry extract (Extraction solvent: Ethanol 60%) and Valerian dry extract (Extraction solvent: Ethanol 70%).

Herbal preparation is in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

6. Posology and method of administration correlated to medicinal use

- 320 mg of Valerian extract and 200 mg St. John's wort extract daily before bedtime.

Duration of use: If the symptoms persist or worsen after two weeks of continued use, a doctor should be consulted.

Method of administration: Oral use.

7. Contraindications (2, 3)

Hypersensitivity to active substances and to other plants of the same family.

8. Special warnings and precautions for use (2, 3)

- If the symptoms worsen during the use of the medicinal product, a doctor or apharmacist should be consulted.
- Intense UV-exposure should be avoided during the treatment.

- Oral use in children and adolescents under 18 years of age is notrecommended.
- The amount of hyperforin and hypericin should be specified. The daily intake of hyperforin has to be below one mg (3).

9. Interactions with other medicinal products and other forms of interaction (2, 3)

- The medicinal product may induce the activity of CYP3A4, CYP2C9, CYP2C19 and P- glycoprotein.
- The medicinal product may reduce plasma concentration of oral contraceptives. Intracyclic menstrual bleeding and reduced safety in birth control may also occur. Accordingly, women taking hormonal contraceptive pills should use additional contraceptive measures.
- Possible interactions with drugs used during general and regional anaesthesia may occur. Accordingly, the herbal medicinal product should be discontinued 10 days prior to elective surgery. The elevated enzyme activity can be expected to return to normal within one week after stopping use of this product.
- Concomitant use of the medicinal product with antidepressants may increase risk of undesirable serotonergic effects.
- Patients taking other medicines on prescription should consult a doctor or pharmacist before use.

10. Fertility, Fertility, pregnancy and lactation (2, 3)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

11. Effects on ability to drive and use machines (2, 3)

May impair ability to drive and use machines.

12. Undesirable effects (2, 3)

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Gastrointestinal disorders, allergic skin reactions, fatigue and restlessness may occur.
- Fair-skinned individuals may react with intensified sunburn-like symptoms under intense sunlight.

13. Overdose

- Seizures and confusion have been reported (2, 3).
- After ingestion of massive overdoses, the patient should be protected from sunlight and other UV-light sources for 1-2 weeks (2,3).

14. Relevant biological activities

Not required as per Egyptian guidelines for registration of herbal medicines.

15. Additional Information

-

16. Date of compilation/last revision

06/08/2023.

References

1	https://powo.science.kew.org
2	Community herbal monograph on *Hypericum perforatum* L., Herba (Well-established medicinal use) (2009). EMA/HMPC/101304/2008. Committee on Herbal Medicinal Products (HMPC).
3	Community herbal monograph on *Hypericum perforatum* L., Herba (Traditional use) (2009). EMEA/HMPC/745582/2009. Committee on Herbal Medicinal Products (HMPC).
4	Edwards, S. E., Rocha, I. D. C., Williamson, E. M. and Heinrich, M. (2015). Phytopharmacy: An evidence-based guide to herbal medicinal products. 1st edition. John Wiley & Sons, Ltd.
5	Natural Health Product, St. John's Wort - Oral - *Hypericum perforatum* L. (2018). Health Canada, http://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id= 163& lang= eng.
6	World Health Organization (2002). Monographs on selected medicinal plants, 2:149-171.
7	Barnes, J., Anderson, L. A. and Phillipson, J. D. (2007). Herbal Medicines, 3rd edition. Published by the Pharmaceutical Press. ISBN 978 0 85369 623 0.
8	Chen, H. W., Wei, B. J., He, X. H., Liu, Y. and Wang, J. (2015). Chemical components and cardiovascular activities of Valeriana spp. *Evid. Based Complement. Alternat. Med.*, Article ID 947619, https://doi.org/10.1155/2015/947619.
9	Oliveira, A. I., Pinho, C., Sarmento, B. and Dias, A. C. P. (2016). Neuroprotective activity of *Hypericum perforatum* and its major components. *Front. Plant Sci.*, 7,1004.
10	Çirak, C., Radušienė, J., Janulis, V., Ivanauskas, L. and Arslan, B. (2007). Chemical constituents of some *Hypericum* species growing in Turkey. *Journal of Plant Biology*, 50(6), 632-635.
11	Albert, D., Zundorf, I., Dingermann, T., Muller, W. E., Steinhilber, D. and Werz, O. (2002). Hyperforin is a dual inhibitor of cyclooxygenase-1 and 5-lipoxygenase. *Biochem. Pharmacol.*, 64, 1767–1775.
12	Silva, B. A., Malva, J. O. and Dias, A. C. P. (2008). St John's Wort (*Hypericumperforatum*) extracts and isolated phenolic compounds are effective antioxidants in several in vitro models of oxidative stress. *Food Chem.*, 110, 611–619.
13	Nakurte, C. I., Mežaka, I., Taškova, I., Primavera, A., Vecvanags, A. and Kronberga, A. (2021). Seasonal changes in chemical composition of Valeriana officinalis L. roots in natural conditions and organic production system in Latvia. *Plant Biol. Crop Res.*, 4(1): 1031.

Egyptian Herbal Monograph

Herbal Formulations Used in Egypt

Thyme/ Primula زعتر/ زهرة الربيع

1. Names & Synonyms

Thyme

***Thymus vulgaris* L.** (1)
Syns: *Origanum thymus* Kuntze, *Thymus collinus* Salisb.
Family: Lamiaceae (Labiatae).
Arabic: Za'ater زعتر.
English name: English Thyme, Garden Thyme.

***Thymus zygis* L.** (2)
Syns.: *Origanum zygis* (L.) Kuntze, *Thymus angustifolius* Salisb.
Family: Lamiaceae (Labiatae).
Arabic: Za'ater زعتر.
English name: Spanish Thyme.

Primula (3)

***Primula veris* L.**
Family: Primulaceae.
Syns.: *Primula officinalis* (L.) Hill.
Arabic: Zahr El-hakl زهر الحقل , Zahrat El-rabee' زهرة الربيع
English name: Cowslip, Primula (2-4).

2. Parts used for medicinal purpose

Thyme: Dried and fresh herb (1, 2, 5).
Primula: Root (6-11).

3. Major chemical constituents

Thyme:

- **Essential oil:** Thymol, carvacrol, *p*-cymene, α and β-terpinene, linalool, terpinen-4-ol, borneol, 1,8-cineole, α-thujene, α-pinene andcaryophyllene (4).
- **Flavonoids:** Apigenin, narigenin, kaempferol and luteolin (and its glycosides) (12).

- **Phenolic acids**: Salvianolic, rosmarinic, cinnamic, ferulic, caffeic and gallic acids (12).
- **Others**: Monoterpene glycosides (13).

Primula:

- **Triterpene saponins**: Primula saponins I and II, priverosaponin B22-acetate (6, 14, 15).
- **Phenolic glycosides**: Primverin and Primulaverin (6, 14).

4. Medicinal uses (Indications)

A. Expectorant in case of productive cough (16).

B. Treat symptoms of acute bronchitis and respiratory infections with thick phlegm following exposure to cold (17).

2. Herbal preparations correlated to medicinal use (16)

1. Thyme liquid extract (Extraction solvent: Ammonia solution 10%, glycerol 85%, ethanol 90%, water (1:20:70:109)) and Primula liquid extract (Extraction solvent: Ethanol 70%).
2. Thyme liquid extract (Extraction solvent: Ammonia solution 10%, glycerol 85%, ethanol 90%, water (1:20:70:109)) and Primula liquid extract (Extraction solvent: Ethanol 55%).
3. Thyme liquid extract (Extraction solvent: Ammonia solution 10%, glycerol 85%, ethanol 90%, water (1:20:70:109)) and Primula tincture (1:5) (Extraction solvent: Ethanol 50%).
4. Thyme liquid extract (Extraction solvent: Ammonia solution 10%, glycerol 85%, ethanol 90%, water) (1:20:70:109)) and Primula soft extract (Extraction solvent: Ethanol 55%).
5. Thyme liquid extract (Extraction solvent: Ethanol 20%) and Primula liquid extract (Extraction solvent: Ethanol 15%).
6. Liquid extract from mixture of Thyme and Primula (Extraction solvent: Water).
7. Dry extract from Thyme (Extraction solvent: Ethanol 70%) and dry extract from Primula, (Extraction solvent: Ethanol 47.4%).
8. Dry extract from Thyme (Extraction solvent: Ethanol 70%) and dry extract from Primula (Extraction solvent: Water).

Herbal preparations are in pharmaceutical dosage forms. The pharmaceutical form should be described by the pharmacopoeia full standard term.

3. Posology and method of administration correlated to medicinal use (16)

Preparation 1
Indication A
Adolescents, adults and elderly: Single dose: 500 mg Thyme extract and 250 mg Primula extract, 6 times daily.
Children 4-11 years: Single dose: 330 mg Thyme extract and 170 mg Primula extract, 3-5 times daily.

Indication B
Infants 6-12 months: 65 mg Thyme extract and 32.4 mg Primula extract, 6 times daily. Total daily dose: 390 mg Thyme extract and 194.4 mg Primula extract.
Children 1-4 years: 162.5 mg Thyme extract and 81 mg Primula extract, 6 times daily. Total daily dose: 975 mg Thyme extract and 486 mg Primula extract.
Children above 5 years, adolescents and adults: 487.5 mg Thyme extract and 243 mg Primula extract, 4 times daily. Total daily dose: 1950 mg Thyme extract and 972 mg Primula extract.

Preparation 2
Indication B
Adults: 500 mg Thyme extract and 250 mg Primula extract, 3 times daily.
Children above 4 years: 250 mg Thyme extract and 125 mg Primula extract, 3 times daily.

Preparation 3
Indication A
Adolescents, adults and elderly: 430 mg Thyme extract and 210 mg Primula tincture, 5 times daily.
Children 4-11 years: 360 mg Thyme extract and 180 mg Primula extract, 3-5 times daily.

Preparation 4
Indication A
Adolescents, adults and elderly: 1160 mg Thyme extract and 170 mg Primula extract, 4 times daily.
Children 4 -11 years: 770 mg Thyme extract and 120 mg Primula extract, 3-4 times daily.

Preparation 5
Indication A
Adolescents, adults and elderly: 1240 mg Thyme and 410 mg Primula, 3-5 times daily.

Preparation 6
Indication A
Adolescents, adults and elderly: 3080 mg equivalent to: 620 mg Thyme extract and 220–510 mg of Primula extract, 4 times daily.

Preparation 7
Indication A
Adults and elderly: 160 mg Thyme extract and 60 mg Primula extract, 3 times daily.

Preparation 8
Indication A
Adolescents, adults and elderly: 75 mg dry Thyme extract and 37.5 mg dry Primula extract, 3 times daily.

Duration of use: If the symptoms persist longer than one week during the use of the medicinal product, a doctor or a pharmacist should be consulted.

Method of administration: Oral use.

4. Contraindications

Hypersensitivity to the active substances and to other plants of the same family.

5. Special warnings and precautions for use

- If the symptoms worsen or persist longer than one week during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- If dyspnea, fever or purulent sputum occurs, a doctor or a pharmacist should be consulted (4-6, 16).
- The use in children under 4 years (Herbal preparations 2, 3 and 4), under 12 years (Herbal preparations 5, 6 and 8) and under 18 years (Herbal preparation 7) is not recommended without medical supervision (5, 16).
- Insufficient data are available concerning administration in infants under 6 months (Herbal preparation 1). Therefore, it should not be given to infants under 6 months.
- Caution is recommended in patients with gastritis or gastric ulcer (16).

6. Interactions with other medicinal products and other forms of interaction

None reported (16).

7. Fertility, pregnancy, and lactation (16)

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No fertility data available.

8. Effects on ability to drive and use machines (16)

No studies on the effect on the ability to drive and use machines have been performed.

9. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Gastric disorders, nausea and allergic reactions may occur (6, 16).

10. Overdose

No case of overdose has been reported (16).

11. Relevant biological properties

Not required as per Egyptian guidelines for registration of herbal medicines.

12. Additional information

-

13. Date of compilation/last revision

06/08/2023.

References

1	https://www.gbif.org/species/5341442
2	https://www.gbif.org/species/7793938
3	http://www.theplantlist.org.
4	Community herbal monograph on *Thymus vulgaris* L. and *Thymus zygis* L., herba. EMA/HMPC/342332/2013. Committee on Herbal Medicinal Products(HMPC).
5	WHO monographs on selected medicinal plants (2007). Monographs on selected medicinal plants, 3, 259-266.
6	Community herbal monograph on *Primula veris* L. and/or *Primula elatior* (L.) Hill, radix. EMA/HMPC/104095/2012. Committee on Herbal Medicinal Products(HMPC).
7	https://www.healthline.com/health/Thyme-oil#benefits-uses
8	Chevallier, A. (1996). The Encyclopedia of Medicinal Plants. *DK Pub*., ISBN: 0789410672, 9780789410672.
9	Fisher, C. and Painter G. (1996). Materia Medica for the Southern Hemisphere. Auckland: Fisher-Painter Publishers.
10	Kowalczyk, A., Przychodna, M., Sopata, S., Bodalska, A. and Fecka, I. (2020).Thymol and Thyme essential oil—New insights into selected therapeutic applications. *Molecules,* **9**, 25(18), 4125. doi: 10.3390/molecules25184125.
11	Mosby's Handbook of Herbs and Natural Supplements. 4th ed., ISBN: 978-0-323-05741-7.
12	Sarfaraz, D., Rahimmalek, M. and Saeidi, G. (2021). Polyphenolic and molecular variation in *Thymus* species using HPLC and SRAP analyses. *Sci. Rep.* **11**, 5019.
13	Kitajima, J., Ishikawa, T., Urabe, A. (2004). A new hydroxyjasmone glucoside and its related compounds from the leaf of Thyme. *Chem. Pharm. Bull*., 52(8) 1013—1014.
14	Katarzyna, B., Jarosław, L. P., Małgorzata, M., Olga, K., Izabela, S. S. and Zenon, W. (2017). Phenolics in *Primula veris* L. and *P. elatior* (L.) Hill raw materials. *International Journal of Analytical Chemistry,* Article ID 2871579. https://doi.org/10.1155/2017/2871579.
15	Tarapatskyy, M., Gumienna, A., Sowa, P., Kapusta, I. and Puchalski, C. (2021). Bioactive phenolic compounds from *Primula veris* L.: Influence of the extraction conditions and purification. *Molecules*, 26(4), 997.
16	European Union herbal monograph on *Thymus vulgaris* L. or *Thymus zygis* L., herba and *Primula veris* L. or *Primula elatior* (L.) Hill, radix. EMA/HMPC/84990/2015 Corr. 1 Committee on Herbal Medicinal Products (HMPC).
17	Egyptian Herbal Monograph (2022). *Thymus vulgaris* L., **3**, 377-382.