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Herbal Monograph on Wild Medicinal Plants in Egypt

(Traditional Plants)

Version 1

Herbal Monograph on Wild Medicinal Plants in Egypt

Egyptian Drug Authority (EDA)

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Contents

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Foreword

With the expansion in the use of traditional medicine worldwide, safety and efficacy as well as quality control of traditional 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 traditional herbal medicine is used properly and to determine how research and evaluation of traditional 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 traditional medicinal use is a must. The Herbal Monograph on Wild Medicinal Plants in Egypt will be considered as the first step to achieve the purpose of improving the quality and value of research in traditional herbal medicine. It promotes the use of traditional herbal medicines and to serve as a model for the development of national formularies.

Egyptian Drug Authority (EDA)

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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. Ancient Egyptians put the bases for natural healings. Most of complementary medicine modalities originated from ancient Egyptian; one of these modalities 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. 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 medicinal plant species in the wild is indispensable. So, Herbal monograph on wild medicinal plants in Egypt is of a great importance, as it is hopefully the one for our country that would help in the rational utilization of our valuable biodiversity resources in the pharmaceutical industries for conservation of wild plants for medicinal uses. The wild medicinal plants growing in the desert region of Egypt can be a good source for cultivating vast areas in the desert with the least ecological consequences in addition to the conservation of such resource.

The 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 pharmacopeial 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
- Biodiversity conservation

4- Sustainable development

- Cultivation of wild plants does not 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.

Trade in the drugs obtained from wild plants is very common everywhere. However, there is no proper attention paid to its socio-economic aspects. The safety and quality of phytopharmaceuticals must be guaranteed, even if efficacy is already recognized and traditionally accepted. World-wide interest in the use of medicinal and aromatic plants is increasing but their development is hindered by lack of technical and economic data. So, there is a great need to provide a framework for the

conservation and sustainable use of plants in medicine. Herbal Monograph on Wild Medicinal Plants in Egypt represents one of steps to help implementing use of Egyptian wild plants in the pharmaceutical industry.

Purpose and content of the monograph

The purpose of the monograph is to:

- Provide scientific information on the safety, efficacy and quality of wild medicinal plants
- Facilitate their appropriate use
- Facilitate information exchange and registration procedures.

This monograph is consisting of monographs complied by a working group of Egyptian Drug Authority (EDA) members and members of Specialized Scientific Committee of Herbal Medicines. It is a compilation or report about Wild Medicinal Plants used traditionally in Egypt providing detailed information which is organized in a logical structure, including botanical and pharmaceutical information. It is intending to promote the responsible use of herbal medicines with the possible degree of efficacy and safety through the review of traditional and scientific data regarding them. 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, geographical distribution, parts used for medicinal purposes, major chemical constituents, traditional medicinal uses, herbal preparations correlated to medicinal use, posology and method of administration correlated to medicinal use, contraindications, special warnings, precautions for use, interactions with other medicinal products, other forms of interaction, effects on fertility, pregnancy, lactation, effects on ability to drive, use machines, undesirable effects, overdose, relevant biological properties and if any additional information. It is anticipated that this monograph will be revised again in the near future, in response to developments in research in traditional herbal medicine. We therefore welcome all comments and views at any time.

Herbal Monograph on Wild Medicinal Plants in Egypt

Acacia nilotica (L.) Delile السنط / القرض

1. Names & Synonyms

Acacia nilotica (L.) Delile.
Syn. *Mimosa nilotica* L. (1,2)
Family: Fabaceae (Leguminosae) (3)
Arabic: *Sant* سنط - *Aschawkah Al misriyah* الشوكة المصرية - Fruit: Qarad الثمرة: قرض
English: Egyptian Acacia, Egyptian Thorn (2)
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: It contains high percentage of phenolic constituents consisting of 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. Fruits contain also coumarins, alkaloids, 17% mucilage (arabinose, xylose, galactose, 8.2%) and saponins (0.069%) (4, 5).

The bark: It is mainly rich in phenolics consisting of condensed tannin and phlobatannin, gallic acid, protocatechuic acid pyrocatechol, (+) - catechin, (-) epigallocatechin-7-gallate, and (-) epigallocatechin-5, 7-digallate (2).

The leaves: The leaves of *A. nilotica* contain organic matter, 94%; crude protein, 17.2%; neutral detergent fiber, 31.2%; total phenolics, 16.2% and tannins, 10.9% (6). Also, 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 were reported (8).

Gum: Gum is composed of galactoaraban which gives on hydrolysis L-arabinose, D-galactose, L-rhamnose, D-glucuronic acid and 4-O-methyl- D-glucuronic acid (9).

5. Traditional medicinal uses (3)

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

Bark: The bark is useful in cough, bronchitis, diarrhea, dysentery, burning sensation, piles. The bark decoction can be used as a nerve stimulant and aid for digestion.

Leaves: The leaves are useful in bronchitis, piles and as liver tonic. The leaflets are chewed for nausea. The leaves are antipyretic, cures leucoderma, gonorrhea and used in urethral discharges.

Gum: The gum found to be useful in diarrhea, liver tonic, urinary discharges, vaginal and uterine discharges, healing of fractures and sore throat. It is also useful in diabetes mellitus.

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

6. Herbal preparations correlated to medicinal use (10)

a) Orally:

***Infusion:**

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.

*** Decoction:**

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

b) Externally:

Place some herb in a warm water bath; sit and relax in the water basin for half an hour, as often as required.

7. Posology and method of administration correlated to medicinal use

a) Oral:

***Infusion:** Average daily dose: 3 cups/ day
***Decoction:** Average daily dose: 3 cups/ day (10)

b) External:
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 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 data were found about the plant effect on fertility

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

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 properties

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

16. Additional information:

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17. Date of compilation/last revision

07/09/2020

Reference

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	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).
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.
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 indomethasene 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. & 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, 3, 88-89.
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

Herbal Monograph on Wild Medicinal Plants in Egypt

Achillea fragrantissima (Forssk.) القيصوم

1. Names & Synonyms (1, 2, 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:
The aerial parts of *Achillea fragrantissima*, wildly grown in Egypt, yielded 0.8 and 1.5% (v/w) of essential oils prepared by hydrodistillation (HD), or by conventional volatile solvent extraction method respectively (4).

Twenty eight compounds were identified in the hydrodistilled oil from the plant growing in Egypt, the main components were: Caryophyllene oxide, 1-terpinen-4-ol viridiflorol and guaienol (4), also limonene, menthol, azulene, and thujone are found in moderate amount, while santolina alcohol, lanceol, cedrene, and granny geraniol are found in a minor amounts (5).
Also, the oil of *A. fragrantissima,* collected from Egypt, was reported rich with sesquisabinene hydrate, bisabolene epoxide, camphor, and caryophyllene oxide;

There are several reports on the constituents of the essential oil (6, 7, 8, 9).

- **Monoterpenes and Triterpenes:** Two highly oxygenated santoline derivatives (irregular oxygenated monoterpenes) (10), chondrillasterol (11) a monoterpene derivative, 2, 7 -dimethylocta-3,7-diene-2,5-diol, traxasterol acetate and pseudo-taraxasterol acetate (12).

- Sesquiterpene Lactones: More than 10 compounds were isolated, from the plant 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).

- **Other Constituents:** A saturated hydrocarbon, a bitter substance (keissosid) which yielded galactose and aglycone, tannins (4-5%) of the catechol type, 2-acetylmethyl-4-hydroxy-6-methyltetrahydropyran (12).

5. Traditional medicinal uses (17)

***oral:**

a) Treatments of gastrointestinal disturbances (anti-spasmodic, astringent, carminative, stomachic).
b) Treatment of respiratory diseases (expectorant, cough).
c) Anthelmintic.
d) For scorpion and snake bites.

***Topical:**

a) Skin diseases (skin inflammations, wound healing, abscess, purulent sore and as insect repellent).
b) As antipyretic and in case of fever.

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

6. Herbal Preparations correlated to medicinal use

***oral:** (17)

As infusion or decoction

Infusion:

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

Decoction:
Add 2teaspoonful 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

***Topical:** (17, 18)

- **Decoction:** prepared by boiling the grind leaves with water .
- **Oil**

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

***Oral:**

Dosage: 3 cups/day.

***Topical:**

a) Apply the extract of the boiled leaves in water after cooling the extract
b) Wash the Body with the decoction

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 when used for diabetics as *A. fragrantissima* has been used in traditional medicine for diabetes.

- If the symptoms worsen during the use of medicinal product, a doctor or 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.

Studies in animals have shown that the plant extract did not affect fertility (19). <<see section 15. Relevant biological properties >>

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.

14. Overdose

No case of overdose has been reported.

15. Relevant biological properties

- 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 weights, heart rates, 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 evidences 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 were tested using the animal model of carrageenan-induced paw edema, it was comparable to that of diclofenac (20, 21). The substance responsible for the anti-inflammatory effects of the plant could be a sesquiterpenic lactone called 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, which is 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 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

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Reference

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	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).
3	Faiza, M., Hammouda 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. & 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", vol. 5. (Rizk, A. M., editor), Misr University for Science & Technology (in press).

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, vol (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, IUCN (International Union for Conservation of Nature), 17-18.
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., 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):277-80.
21	Abdel-Rahman, R. F., Alqasoumi, S, I., El-Desoky, A. H., Soliman, G. A., Paré, P. W., Hegazy, M. E. (2015). Evaluation of the anti-inflammatory, analgesic and anti-ulcerogenic potentials of *Achillea fragrantissima* (Forssk). South African J Botan. 98:122-7.
22	Elmann, A., Mordechay, S., Erlank, H., Telerman, A., Rindner, M., Ofir, R. (2011a). Anti-neuroinflammatory effects of the extract of *Achillea fragrantissima*. BMC Complement Altern Med. 11:98.
23	Elmann, A., Telerman, A., Mordechay, S., Erlank, H., Rindner, M., Kashman, Y., et al (2015). Downregulation of microglial activation by achillolide A. Planta Med. 81(3):215-21.
24	Kharma, A., Hassawi, D. (2006). The antimicrobial activity and the genetic relationship of *Achillea* species. Biotechnology. 5(4):501-7.

25	Almadiy, A. A., Nenaah, G. E., Al Assiuty, B. A., Moussa, E. A., 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. 69:529-37.
26	Soltan, M. M., Zaki, A. K. (2009). Antiviral screening of forty-two Egyptian medicinal plants. *J Ethnopharmacol*. 126(1):102-7.
27	Mohamed, A. A., Ali, S. I., El-Baz, F. K., 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):708-22.
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):139-45.
29	Ezzat, S. M., Salama, M. M. (2014). A new a-glucosidase inhibitor from *Achillea fragrantissima* (Forssk) Sch. Bip. growing in Egypt. Nat Prod Res. 28(11):812-8.
30	El-Fattah, A. B. I., Ali, S. A., Aly, H. F., Abd-Alla, H. I., Shalaby, N. M., 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):115-30.
31	Mustafa, E. H., Abu Zarga, M., Abdalla, S. (1992). Effects of cirsiliol, a flavone isolated from *Achillea fragrantissima*, on rat isolated ileum. Gen Pharmacol Vasc S. 23(3):555-60.
32	Marder, M., Viola, H., Wasowski, C., Wolfman, C., Waterman, P. G., Medina, H., et al (1996). Cirsiliol and caffeic acid ethyl ester, isolated from Salvia guaranitica are competitive ligands for the central benzodiazepine receptors. Phytomedicine. 3(1):29-32.
33	Abbas, M. A., Yasmeen, A. H., Yahiya, I. Y., Hayder, A. A. (2020). The Protective Effects of *Achillea fragrantissima* on Immune Response in Mice Model: A Pilot Study. Sys Rev Pharm; 11(4): 243 246

Herbal Monograph on Wild Medicinal Plants in Egypt

Adiantum capillus-veneris (L.) كزبرة البئر، شعر البنات

1. Names & Synonyms (1, 2, 3)

Adiantum capillus-veneris L., Sp. Pl., ed.
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, 2, 3)

Distributed in all the phytogeographical regions of the country

3. Parts used for medicinal purpose

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

4. Major chemical constituents

- **Triterpenes:** Several triterpenoids (more than 30), most of which belong to the hopane and migrated hopane ones, together with some others including lupenane and oleanane compounds, were isolated from the fronds e.g. adiantone, isoadiantone, adiantoxide, 21-hydroxy adiantone, triterpenoid epoxide (adiantoxide), isoglaucanone, hdoxyhopane, isoadiantol, hydroxyadiantone,4-α-hydroxyfilican-3-one,fernadiene,7-fernene (diploptene), hydroxyhopane (hopanol), neohop-12-ene (neohopene), trisnorhopane isoglaucanone (5, 6, 7, 8, 9, 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-*p*-coumaroyl glucose, 1-*p*-coumaroylglucose 2-sulphate, 1-*p*-coumaroylglucose 6-sulphate, 1-*p*-

coumaroyl galactose 6-sulphate], 1-caffeoylglucose, 1- caffeoylgalactose 3-sulphate, and 1- caffeoylgalactose 6- sulphate were present in high amounts (11, 12).

- Essential Oil:
The major constituents were carvone, carvacrol hexadecanoic acid, thymol, hexahydrofarnesyl acetone and n-nonanal *(13).*

- Others:
Mucilage *(10, 14)* and the betaine lipid, diacylglycerol-O-4'-(*N,N,N*-trimethyl)-homoserine (containing palmitic, linoleic, linolenic and arachidonic acids) *(10),* Other constituents are *β*-sitosterol, stigmasterol, campesterol, (*E*)-2-decanal, a saponin (yielding on hydrolysis a hydroxyhopanone aglycone, galactose, xylose and rhamnose) *(10, 15),* alicyclic acids; quinic acid and shikimic acid.
O**xygenated hydrocarbons;** dodecanoic acid ethyl ester; 3,7,11,15-tetramethyl-2-hexadecen-1-ol; phthalic acid, butyloctyl ester; hexadecanoic acid, 9-octadecenoic acid, octadecenoic acid ethyl ester, di-n-octylphthalate, and others were detected (16).
Carotenoids and chlorophylls pigments; lutein, chlorophyll b′, chlorophyll a, 9′-*Z*-neoxanthin and all-*E*-violaxanthin were present in higher amounts (12).
-Tannins *(10, 11, 15).*
phlobatannins, alkaloids and cardiac glycosides (18).

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
1. Menstrual problems and emmenagogue
2. Hair loss
3. Treatment of snake and spider bites

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

6. Herbal preparations correlated to medicinal use

Herbal tea:

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

Infusion: (19)
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)

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

***Oral**

- It is taken internally as a tea prepared from 1.5g of the drug to 1 cup of liquid **(19)**
- Concentrated decoction of the fronds is used as emmenagogue (2)
- Dose: 3cups/day (4)

***Topical** **(20)**

For hair loss: Apply *A. capillus-veneris* directly to the scalp

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 (20, 21)

- Its use should be avoided during pregnancy
- Safety during lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.
- No sufficient data were found about the plant effect on fertility.

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

14. Overdose (20, 21)

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

15. Relevant biological activities

- The anti-inflammatory and anti-ulcerative effects of *A. capillus-veneris* aqueous extract and hydroalcoholic extract on acetic acid-induced colitis in a rat model were explored. The results showed that both extracts had dose-related beneficial effects on acetic acid-induced colitis and these effects could be attributed to anti-inflammatory, ulcer healing and antioxidant activities of these extracts (22).

- The anti-inflammatory activity of the plant ethanolic extract was 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. The ethyl acetate fraction of the ethanolic extract displayed significant anti-inflammatory activity mediated through inhibition of nitric oxide release and reduction of the TNF-α level (23, 24).

- 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 (25).

  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 (26).

- 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 (27).

- 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 (28).

- 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) (29).

- 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 127.6mg/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 (30). 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 (31).

- 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 conclude that the *A. capillus-veneris*, as antioxidant, can reduce the bisphenol-induced toxicity (32).

- 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 (33). Similar investigation confirmed powerful analgesic effect of the fraction through hot plate and tail immersion tests in mice (34). In addition, 4-α- hydroxyfilican-3-on, isolated from ethanolic extract of the plant, showed significant anti nociceptive activity in writhing test (24).

- 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* (35).

- 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 (36).

- 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 (37).

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%) (38).

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 (39).

17. Date of compilation/last revision

02/11/2020

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: E. Aboutabl, M. Shabana & F. Soliman). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Fahem, A. A., Khaled, A. S., and Ibrahim, A. E. (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, vol (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., 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, 1H/13C, 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, 1, 73-94.
11	Imperato, F. (1982a). Sulphate esters of hydroxycinnamic acid-sugar derivatives from *Adiantum capillus-veneris*. *Phytochemistry*, 21(11), 2717-2718.
12	Alam, Z. and Fareed, U. (2017). Reversed Phase HPLC-DAD Profiling of Carotenoids, Chlorophylls and Phenolic Compounds in *Adiantum capillus-veneris* Leaves Front. *Chem.*, 27 April.

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	El-Tantawy, M., El- Sakhawy, F., El- Deeb, K., Fathi, M. and Hassan, A. K. (1994). A phytochemical and pharmacological study of *Adiantum capillus-veneris* L. growing in Egypt. *Zagazig J. Pharm. Sci*., 3(3A), 97-103.
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	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.
17	Imperato, F. (1982b). Kaempferol 3-sulphate in the fern *Adiantum capillus-veneris*. *Phytochemistry*, 21(8), 2158-2159.
18	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
19	https://www.webmd.com/vitamins/ai/ingredientmono-559/maidenhair-fern
20	https://www.rxlist.com/maidenhair_fern/supplements.htm
21	Montvale, NJ .Thomson (2007). PDR For Herbal Medicines, 4, 491-492.
22	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. AJP, 10 (5), 492-503.
23	Yuan, Q., Z. X., Liu, Z., et al (2013). Ethanol extract of *Adiantum capillus-veneris* L. suppresses the production of inflammatory mediators by inhibiting NF-κB activation. *J Ethnopharmacol*, 147(3), 603-11 .
24	Haider, S., Kharbanda, C., Alam, M.S., et al (2013). Anti-inflammatory and anti-nociceptive activities of two new triterpenoids from *Adiantum capillus-veneris* Linn. Nat Prod Res, 27(24), 2304-2310.
25	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), 222-29.
26	Swaroop, K.K., S.L.V.V.S.N., ANBU, J., Ashwini, 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.
27	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*, 55, 401.

28	Kanchan, G., Swati, D., Joshi, Y.M., Vilasrao, K. (2013). Protective Effect of *Adiantum Capillus* against Chemically Induced Oxidative Stress by Cisplatin. *Journal of Applied*.
29	Yuan, Q.Y., Ruan, J.L., Cai, Y.L. (2010). Effect of water extracts of *Adiantum capillus-veneris* L. on urinary tract infections. *Chin Pharm J,* 45(18), 1389-1392.
30	Ahmed, A., Wadud, A., Jahan, N., et al. (2013a). Efficacy of *Adiantum capillus veneris* Linn in chemically induced urolithiasis in rats. *J Ethnopharmacol*, 146(1), 411-416.
31	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. *IJGP*, 7(2), 106-110.
32	Qudsia, K., Abdul Qadir., Amina., Asmatullah., Hafiza, H.I. & 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.
33	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.
34	Jain SK, Singh T, Pande M, Nema N (2014). Neuropharmacological screening of fronds of *Adiantum capillus veneris* linn. *Pharm Lett*, 6(3), 167-175.
35	Meenakshi, S., Neha, S., Khare P.B., 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.
36	Noubarani, M., Rostamkhani, H., Erfan, M., et al. (2014). Effect of *Adiantum capillus veneris* linn on an animal model of testosterone-induced hair loss. *Iran J Pharm Res*, 13, 113-118.
37	Murthy, R. S. R., et al. (1984). "Anti-implantation activity of isoadiantone." Indian Drugs. 21(4), 141-44.
38	Ahmed, A., Nasreen, J., Abdul Wadud, H.I. and Syeda H.A.B. (2012). Phytochemical and biological properties of *Adiantum capillus –veneris* Linn: An important drug of Unani system of medicine. *IJCRR*, 4(21), 71-75.
39	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.

Herbal Monograph on Wild Medicinal Plants in Egypt

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 &fruiting herb (2)
The whole plant, leaves and stems (3)

4. Major chemical constituents (3)

- **Sesquiterpene Lactones**: mainly ambrosin, neoambrosin, damsin, farnserin, hymenin, parthenin, and neombrasin, and others were isolated from the leaves.
- **Sesquiterpenes**: damsinic acids were isolated from the aerial parts of *Ambrosia maritima*
- **Polyphenols and Flavonoids**: mainly 6-methoxy luteolin-4'-O-lactate, apigenin-4'-O-α-L-rhamnopyranoside (4)
- **Volatile Oils**: Twenty one constituents including carvone, camphor, caryophyllene and cineole were identified (5, 6)
- **Others**: Sterols, coumarins, tannins

5. Traditional medicinal uses

a) **Indication 1**: Gastrointestinal disturbance and abdominal pain. It acts also as anti-spasmodic (7, 8)
b) **Indication 2**: Kidney problems (kidney inflammation, kidney stones, renal colic, spasms and frequent urination) and as diuretic (7, 8)
c) **Indication 3**: Externally for rheumatic pains (9, 10, 11)

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

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

a) Decoction of the aerial parts for oral use (One teaspoonful of aerial parts is boiled and left till cold, then sweeten with honey)
b) Decoction or infusion of aerial parts for oral use
c) The dried powdered plant could be mixed with small amount of oil and used externally

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

a) **Oral:** Dosage: 3 cups/day
b) **Oral:** Dosage: 3 cups/day
c) **External:** Dosage: 4 times/ day

8. Contraindications

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

9. Special warnings and precautions for use

- May exert estrogen like effect (3)
- 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 data were found about the plant effect on fertility

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 properties

- 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 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 adminstration 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

07/09/2020

Reference

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	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, vol (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. & 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 Ibtehal, M. A. (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.

Herbal Monograph on Wild Medicinal Plants in Egypt

Anastatica hierochuntica (L.) كف مريم

1. Names & Synonyms (1, 2, 3)

Anastatica hierochuntica L.

Family: Cruciferae (Brassicaceae)
Arabic: Kaff Mariam كف مريم
English: St. Mary's flower, Rose of Jericho, Jericho resurrection plant.

2. Geographical distribution (1, 2, 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.

4. Parts used for medicinal purposes (2)

Dry whole plant.

3. 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 (4, 5, 6, 7, 8, 9).

-Benzofurano-Flavanones: Anastatin A and anastatin B (10).

-Flavonolignans: Silybin A, silybin B, isosilybin A, isosilybin B, (+)-silychristin and (-)- silychristin (7).

-Lignans: Evofolin B (7).

-Neolignans: Hierochin A, hierochin B and hierochin C, (+)-balanophonin, (+)-dehydrodiconiferyl alcohol and (+)-lariciresinol (10).

-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 (7), 5-O-caffeoylquinic acid, 3,4-O- dicaffeoylquinic acid and 4,5-O-dicaffeoylquinic acid (9)

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

5. Traditional medicinal uses (12)

* 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 herbal medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (12)

***Oral:** Decoction or infusion of the whole plant

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

a) the whole plant: Infusion of dried plant
b) The dried plant crushed with sugar is taken as violent purge, followed by milk as diet.
C) Infusion of dry plant

***External:**

Gynecology: Decoction the whole plant

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

***Oral:**

a) The dried plant is soaked in water and the solution drunk by women at childbirth (2).
b) The dried plant crushed with sugar is taken as violent purge, followed by milk as diet.

***External:** boiled in water and used as pelvic bath.

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

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

- Avoided during pregnancy.

-No data were found about the plant effect on fertility.

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

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 (13).

- In silico study of *A. hierochuntica* L. estrogenic activities and its potential as phytoestrogens was conducted using computer simulation methods (14). 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 (15).

- 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 (16).

- 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 (17).

- 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 (18).

- 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 (9).

- 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 (20).

- 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 (21).

- 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 (22).

- 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 (23).

16. Additional Information

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16. Date of compilation/last revision

04/11/2020

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: E. Aboutabl, M. Shabana & F. Soliman). 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	Khalifa, T. I. and Ahmed, M. A. (1980). A pharmacognostic study of certain species of *Anastatica*. Ph. D. Thesis, Fac. Pharm., Cairo Univ.
5	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.
6	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.
7	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.
8	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.
9	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.
10	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.
11	Amira, S., Abd El-Gaber., Abdel Nasser G. E., Ahmed, E., Ibrahim A. S. and Hesham R. E.(2018). Microwave Extraction of Essential Oil from *Anastatica hierochuntica* (L): Comparison with Conventional Hydro-Distillation and Steam Distillation. *TEOP,* 21(4), 1003–1010.
12	Conservation and sustainable use of medicinal plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, vol (1-5).

13	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.
14	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).
15	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.
16	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*.
17	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.
18	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).
19	Rasheed, R. A., Bashir, A. K., and Ali, B. H. (1997). Fetal toxicity of *Anastatica hierochuntica* L. in mice. *FASEB Journal*, 11(3).
20	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.
21	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 Experimental Models. *Biology and Medicine*, 6(1).
22	Asal, A. T. (2016). Histological Effects of *Anastatica hierochuntica* Aqueous Extract in Female Mice Livers. *The Pharmaceutical and Chemical Journal*, 3(3), 31-37.
23	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.

Herbal Monograph on Wild Medicinal Plants in Egypt

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)

a) 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)

b) 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).

c) 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 herbal medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use

a) 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)

b) Inhaled leaves (1, 3)

7. Posology and method of administration correlated to medicinal use

a) Oral use:

Infusion: Average daily dose: 3 cups/ day (12)

b) Inhalation: Inhaled leaves

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 data were found about the plant effect on fertility

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

14. Overdose

No case of overdose has been reported

15. Relevant Biological properties

- Toxicological and pharmacological studies were carried out on the water and alcoholic extracts of *A. judaica* (13):

  - **Toxicological Studies**:

    Results obtained revealed that no mortalities in mice following oral administration of aqueous extract of *A. judaica* (up to 5g/kg), while in the alcoholic extract the LD_{50} was 9.17g/kg.

- **Pharmacological studies**: using the single and multiple doses of both of *A. judaica* water (0.25g/kg bw, 0.5g/kg bw) and alcoholic extracts (0.5g/kg bw, 1g/kg bw)**:**
    - **Effect on Blood Glucose Level in Diabetic Rats:** significantly reduced the blood glucose level in experimentally diabetic rats while no significant effect was shown on normal rats.
    - **Effect on Liver Functions:** Prolonged oral administration of plant extracts for 2 months showed significant increase in the serum activity of transaminases and ALP.
    - **Effect on serum cholesterol and triglycerides levels in diabetic rats:** The alcoholic extract produced insignificant effect on serum cholesterol levels but there was significant decrease in serum triglycerides levels
    - **Effect on Body Weight Gain:** The body weight gain throughout the 2 months was decreased in the plant extracts groups when compared to the control. This finding may be due to unpalatability of the tested extracts, which may inhibit their appetite.
    - **Effect on organs weight**: there was no significant effect on the relative weights of liver, kidneys, lung, heart and spleen in all groups.

- Volatile oil prepared from flowering branches has insecticidal, anthelmintic, antiinflammatory, analgesic, anti-pyretic and stimulant effects (14, 15). Piperitone and trans-ethyl cinnamate showed pronounced insecticidal and antifeedant activity against the third instar larvae of *Spodoptera littoralis* (Boisd)(16).

- Cirsimaritin, isolated from the plant caused a concentration-dependent inhibition of the amplitude of the phasic contractions of the guinea pig ileum and reduced its tone, which supports the use of the plant in folk medicine for certain gastrointestinal disorders (10).

- *A. judaica* has promising anti-*Blastocystis* potential. 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 protective effect of oral administration of *A. judaica* extract (70% alcoholic ectract) (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 revealed that STZ-injected rats

showed marked hyperglycemia and hypoinsulinemia in addition to high levels of cholesterol, triglycerides, and low- and high-density lipoproteins compared to control rats. Significant elevations in hepatic (AST and ALT) and renal (urea, uric acid, and creatinine) function markers were observed in the serum of diabetic rats. Additionally, STZ injection caused remarkable elevations in lipid peroxidation and nitric oxide levels as well as suppression of antioxidant markers (superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and glutathione). Marked elevations in TNF-α and Bax levels with a decline in Bcl-2 levels were detected after STZ injection. Furthermore, TGF-β1 expression levels were significantly up-regulated in the liver and kidney tissues. Rats that received *Artemisia judaica* extract or metformin showed significant improvement in most of the aforementioned parameters, and the protective efficacy was higher for *Artemisia judaica* extract than for metformin. Histopathological screening confirmed the biochemical findings. The results illustrated the antihyperglycemic, antihyperlipidemic, antioxidant, anti-inflammatory, and antiapoptotic activities of the plant extract against hepatorenal injury in HFD/STZ-induced diabetes (11).

16. Additional information:

-

17. Date of compilation/last revision

28/09/2020

Reference

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	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 volatile oil *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*. *Phytochem.*, 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. Environmental Science and Pollution Research. https://doi.org/10.1007/s11356-020-09997-2.
12	Conservation and sustainable use of medicinal plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, vol (1-5).
13	Nofal S. M., Mahmoud S. S., Ramadan A., Soliman G. A., 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	Abdelgaleil, A. M., Abbassy, M. A., Belal, A. H. and Abdel Rasoul, M. A. (2008). Bioactivity of two major constituents isolated from the essential oil of *Artemisia judaica* L. *Biores. Technol.*, 99, 5947–5950.
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.* Public Health, 16(9), 1555.

Herbal Monograph on Wild Medicinal Plants in Egypt

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 herbal medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use

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

7. Posology and method of administration correlated to medicinal use

Method of administration: Oral

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

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). <<see section 15. Relevant biological properties >>

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

14. Overdose

No case of overdose has been reported

15. Relevant biological properties

- The aqueous extract of *B. aegypticea* fruit demonstrated hypoglycemic properties in diabetic experimental rats (13). It was also reported that whole and extracted pulp of *B. aegyptiaca* fruits exhibited a hypocholesterolemic effect when tested on adult albino rats (14). Moreover, methanol extract of the pulp was also found to exhibit anti-dermatophytic activity on *Microsporum gypseum* and *Trichophyton rubrum* (15).

- Administration of the *B. aegypticea* (BE) capsules to T2D resulted in significant improvements in the glycaemic markers and the lipid profile, without adverse effects or hypoglycaemia. Hard gelatin capsules (400 mg/day) and 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 impacts 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 a 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 make *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, reduced

glutathione levels, catalase and superoxide dismutase activities 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).

- 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).

- 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).

- 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).

- Due to diosgenin content which is used as a raw material for industrial production of contraceptives and other sexual hormones, *B. aegyptiaca* affects different aspects of the activity of the female reproductive tract (interact with steroid sex hormone metabolism). 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 new born (12).

16. Additional information:

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17. Date of compilation/last revision

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Reference

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Mohamed A, ElShanawany (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: E. Aboutabl, M. Shabana & F. Soliman). 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, IUCN (International Union for Conservation of Nature), 51.
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, vol (3).
11	Abdelmuti, O. M. S. (1991). Biochemical and nutritional evaluation of famine foods of the Sudan. Doctoral dissertation in Biochemistry and Nutrition. 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.

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*, 2016, 10.
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.

Herbal Monograph on Wild Medicinal Plants in Egypt

Capparis spinosa (L.) كبار - لصف

1. Names & Synonyms (1, 2, 3)

Capparis spinosa L.

Family: Capparaceae

Arabic: Kabbar كبار, Lasaf لصف , Laisouf ليصوف

English: Common caper-bush.

2. Geographical distribution (1, 2, 3)

Deserts, Oases, and Sinai (Saint Cathreine).

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), leaves, roots and seeds.

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 aglycon, 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, thevetia) (12, 14, 15, 16, 17, 18).

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

Seeds Oil
Seeds yield 27-38 % of oil (21). The major constituents are linoleic (25-51%) and oleic (15-37%) 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 yielded range from 0.02 to 0.9%. 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:**

a) Rheumatism

b) Ulcers, ganglions and scrofula

c) Spleen troubles

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

6. Herbal preparations correlated to medicinal use (31)

***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

***External:**

a) Paste of root bark
b) Crushed flower buds
c) **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)

***Oral:**

- Drinking the decoction or infusion 3 cups/day
- For snake bites: Leaves added to water and taken once

***External:**

a) Apply the paste of root bark on the area of the affected area 4 times/ day
b) Flower buds are crushed and applied externally on the affected area
c) Apply the cataplasm every 4 hours.

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 (32)

-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

- 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

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

14. Overdose

- No case of overdose has been reported

15. Relative 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 *Capparis 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 *Capparis 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 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 *Capparis 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 *Capparis spinosa* regulates inflammation induced *in vivo* in mice 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 soxhlet 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 *Capparis spinosa* on the liver, kidney, and serum enzymes were done. The doses of 200, 400 and 800mg/kg of hydro-alcoholic extract of *Capparis spinosa* were administrated by oral gavages for 28 consecutive days in mice. The results have shown that *Capparis spinosa* can cause nephrotoxicity and hepatotoxicity especially during sub-chronic consumption, dose-dependently. The extracts of *Capparis 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 *Capparis spinosa* extract ameliorates biochemical indices and oxidative stress parameters against Cyclophosphamide -induced nephrotoxicity (45).

- The antioxidant, nephroprotective and hepatoprotective effects of methanolic extract of *Capparis 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).

16. Additional Information

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17. Date of compilation/last revision

14/10/2020

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: E. Aboutabl, M. Shabana & F. Soliman). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Khaled, A., Shams, Nahla, S., Abdel-Azim and Ahmed, R. H. (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, L. X., Aisia, A. H., et al. (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 deciduas*: 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	Hongxia Zhang and Zheng Feei Ma (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	Stephanie Chedraoui, Alain Abi-Rizk, Marc El-Beyrouthy, Lamis Chalak, Naim Ouaini and Loïc Rajjou (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.*.
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, vol (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., 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., *et al*. (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., 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 CCl4 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), JOJUN.MS.ID.5555640.
45	Kalantar , M.,Goudarzi , M.,Khodayar , M.J., Babaei, J., Foruozandeh, H., Bakhtiari, N., 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., Khaldi, A. (2017). *Capparis spinosa* leaves extract: Source of bioantioxidants with nephroprotective and hepatoprotective effects. *Biomedicine & Pharmacotherapy*, 87, 171–179.

Herbal Monograph on Wild Medicinal Plants in Egypt

Cleome droserifolia (Forssk.) Delile سموة

1. Names & Synonyms

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

Family: Capparaceae (3)

Synonyms: *Roridula droserifolia* Forssk. (1, 2, 3)

Arabic Names: Samwa سموة (3)

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

The herb (3)

4. Major chemical constituents

Flavonoids: (quercetin, kaempferol, and isorhamnetin..), flavonol glycosides, Flavones (methoxylated flavones and flavone glycosides) (4, 5, 6, 7, 8, 9, 10)

Terpenes (sesquiterpenes, diterpenes and triterpenes) (11, 12, 13, 14)

Essential oil: Hydrodistillation of the aerial parts of *C. droserifolia* yielded 0.43% .The principal constituents of *C. droserifolia* oil were (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 docosanioc acid (1, 3, 17, 18)

5. Traditional medicinal uses (19)

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 herbal medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparations correlated to medicinal use (19)

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 And Red Sea Coast Area, North Sinai)

2. Powder (Halaib Triangle Area)

b) 1. Paste, Infusion or powder of Leaves and Shoot

2. The leaves powder are 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 (19)

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

- The plant is very toxic if given intraperitoneally (1, 3)
- 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

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 data were found about the plant effect on fertility.

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

14. Overdose

No case of overdose has been reported

15. Relevant biological properties

- The antidiabetic activities of the aqueous and ethanolic extracts of *Cleome droserifolia* (Forssk.) Del., were tested in cultured C2C12 skeletal muscle cells and 3T3-L1 adipocytes. The chloroform and ethyl acetate fractions of *Cleome 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 (20).

- The evaluation of the possible protective effects of Cleome 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 Cleome 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 (17, 21).

- Investigation of the antidiabetic as well as the effect on lipid peroxidation of three different doses (50, 100, and 200 mg/kg) of *Cleome droserifolia* aerial parts methanolic extract in comparison with glibenclamide in alloxan-induced diabetic rats was done. Oral administration of 100 and 200 mg/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 50 mg/kg was not significant (22).

- The antibacterial activities of essential oil from *Cleome droserifolia* was 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).

16. Additional information:

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17. Date of compilation/last revision

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Reference

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	Faiza M. Hammouda and Rasmia A. Hassan (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., & 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& 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., & 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., 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., & Helmy, M. (1984). Flavonoids of *Cleome droserifolia*. Fitoterapia, 55, 231–232.
9	Sharaf, M., Mansour, R.M.A., & Saleh, N.A.M. (1992). Exudate flavonoids from aerial parts of four *Cleome* species. *Biochemical Systematics and Ecology*, 20, 443–448.
10	Eman G.E. Helal*, Nouran Abou Aouf**, Inas Z.A. Abdallah***, ALsayeda Mohammed Khattab*(2015). Hypoglycemic and antioxidant effects of *Cleom 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., & 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., & 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 AN, et al(1999). Flavonoids from *Cleome droserifolia* suppress NO production in activated macrophages in vitro. *Planta Med*. 65:404–7.
15	Riyadh Muhaidat, Mahmoud A. Al-Qudah, Omar Samir, Jacob H. Jacob, Emad Hussein, Ibrahim N. Al Tarawneh, Emad Bsoul, Sultan T. Abu Orabi. (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* (Impact Factor: 1.427). 99: 21–28.
16	Abd EI-Kawy, M.A., EI-Deib, S., Hanna, R.A., EI-Khyat, Z., Mikhail, Y.A., 2000. Chemical and biological studies of *Cleome droserifolia (Forssk.)* Del. Part—II. *Egyptian Journal of Biomedical Sciences* 6, 219–232
17	Helal, E.G.E., Abou Aouf, N., Inas Z.A. 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.

18	Singh H, Mishra A, Mishra AK (2018). The chemistry and pharmacology of *Cleome* genus: a review. *Biomed Pharmacother*, 101:37–48.
19	Conservation and sustainable use of medicinal plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, vol (1-5).
20	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.
21	Nagy, M. A. and Mohamed, S. A. (2014). Antidiabetic Effect of *Cleome droserifolia* (Cleomaceae). *American Journal of Biochemistry*, 4(4), 68-75.
22	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.

Herbal Monograph on Wild Medicinal Plants in Egypt

Cymbopogon proximus (Hochst. ex A. Rich.) حلفابر

1. Names & Synonyms

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.)
- *Cymbopogon sennarensis* (Hochst.)

Arabic Names:
Halfa bar حلفابر , Mahareb محاريب (1, 4)

English Name:
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 (4.6-5.44%)(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: Mainly poroximadiol in addition to 5α-hydroxy-β-eudesmol, 1β-hydroxy-β-eudesmol, 1β-hydroxy-α-eudesmol, 5α-hydroperoxy-β-eudesmol and 7α,

11-dihydroxycadin- 10(14)-ene. Bicyclic sesquiterpene diol (proximadiol) is the main bioactive metabolite (6, 1)

Others: Saponins, tannins, triterpenes, flavonoids, alkaloids, phenolic glycosides, cardiac glycosides and steroids (7)

5. Traditional medicinal uses

- Diuretic (5, 6)
- Antispasmodic (5, 6)
- Renal colic pain killer (8, 9)
- Removal of small stones from the urinary tract (8)
- Antipyretic in fevers (8)

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

6. Herbal preparations correlated to medicinal use

a) Weak infusion in the form of "teas"(1, 9)
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

b) 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, 9)

c) 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

Oral use

d) Dosage: 3 cups/day (9)
e) Dosage: 3 cups/day (9)
f) *C. proximus* herbal extract equivalent to 0.4mg proximadiol in the single dose to be taken 3 times daily

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

Cymbopogon proximus is not recommended during pregnancy <<see section 15. Relevant biological properties >>

No data were found for plant use during lactation

No data were found about the plant effect on fertility

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

14. Overdose

No case of overdose has been reported

15. Relevant biological properties

- The aqueous extract (5%) of *Cymbopogon 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 (10).
- New herbal beverages from *Foeniculum vulgare* and *Cymbopogon 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 (11).

- The prophylactic effect of *Cymbopogon proximus* on Sulfadimidine (200mg/kg) induced urolithiasis in rabbits was investigated. *Cymbopogon 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 *Cymbopogon proximus* groups compared to sulfadimidine treated group. It was conclude that *Cymbopogon proximus* have a nephroprotective and antiurolithiatic effects against sulfadimidine induced crystalluria (12).
- 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 (0.05 mg/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 (13).
- During admistration of proximol (*Cymbopogen proximus*) (0.05 mg/ kg) as herbal drug to the pregnant albino rats during the gestation period, the drug will pass to embryos through placenta causing several implications (14).
- The 70% ethanolic extract and its fractions (pet ether, chloroform and ethyl acetate) were evaluated for their antispasmodic effect. The most potent fraction is pet 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 (15).

16. Additional information:

Moisture (11.5%), Ash (6.5%), Crude fiber (32.0%), Crude protein (11.0%), Crude lipid (8.5%) and Total carbohydrates (42.0%) (11)

17. Date of compilation/last revision

28/09/2020

Reference

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	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.
6	El-Askary, H. I., Meselhy, M. R., Galal, A. M., (2003). Sesquiterpenes from *Cymbopogon proximus*. *Molecules*, 8, 670-677.
7	Ali, M. R. (2012). Antibacterial and phytochemical screening *Lepidium sativum* and *Cymbopogon schoenanthus*. BSc thesis, Faculty of Science, Khartoum University.
8	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.
9	Conservation and sustainable use of medicinal plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, vol (1-5).
10	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.
11	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.
12	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.*
13	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.
14	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.
15	Khalafalla, E. B., Sami, Z. A. and Khalid, A. (2015). Chromatographic Profiling Of *Cymbopogon Proximus* Antispasmodic Fraction(S). Conference: 16th NAPRECA Symposium At: Arusha, Tanzania.

Herbal Monograph on Wild Medicinal Plants in Egypt

Cyperus rotundus (L.) السعد

1. Names & Synonyms (1, 2):

Cyperus rotundus L.

Family: Cyperaceae

Arabic: Se'ed سعد

English: Nut- grass

Two varieties occur in Egypt:

a. var. ***rotundus***

Syns. *Cyperus tuberosus* Rottb.

Cyperus hexastachyos Rottb.

Cyperus comosus Sibth. & Sm.

Cyperus subcapitatus C. B. Clarke.

b. var. ***fenzelianus***

Syns. *Cyperus fenzelianus* Steud.

Cyperus ochreoides Steud.

Cyperus 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 (2,3,4)

4. Major chemical constituents

Volatile oil:

The chemical constituents of the volatile oil obtained from *C. rotundus* 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, l*α*,7*α*,10*α* gaia-4,11(13)-dien-3-one, *β*-pinene, *α*- pinene, *trans*-(-) pinocarveol, and oxo-*α*-ylangene (5).

Volatile oil of *C. rotundus* 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 oils of *C. rotundus* 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 of *α*-pinene, *β*-pinene, limonene and 1,8-cineole were the minor components. The chemical composition of the *C. rotundus* oil changes considerably according to its geographical origin (7, 8, 9, 10, 11).

Flavonoids:

Apigenin, luteolin, tricin, 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) (12, 13, 14, 15, 16).

Nitrogenous constituents

The main compounds are: rotundine A, rotundine 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 and *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 of non-reducing sugars (9, 17).

5. Traditional medicinal uses

a) Stops body hair growth (3)

b) It is used as aphrodisiac, anthelmintic, diuretic, carminative, tonic and stimulant. Also, as a remedy for renal colic and dysentery (18)

c) Aromatic, stomachic, sedative and analgesic (3)

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

6. Herbal preparations correlated to traditional medicinal uses

a) The herb is boiled with water till it becomes thick, then rub the hairy areas (3)

b) - ***Anthelmintic* (4):**

1. **Tablet:** Grind the leaves of *C. rotundus* (or the herb of *C. rotundus*) into a paste and make it in tablets.
2. **Paste:** The rhizome is made into a paste

c) Rhizome, in the form of ellipsoid tubers (3)

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

***Topical**

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

***Oral**

b) *Anthelmintic* (4):

1. Take one tablet orally thrice a day for one or two days.
2. 10-20g of the paste is eaten 3 times a day for 2-3 days. In case of children, the dose is usually halved.

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 closely.
- **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. (Interaction Rating: Moderate)

- **Drying medications (Anticholinergic drugs):** include atropine, scopolamine, some medications used for allergies (antihistamines), and for depression (antidepressants). *C. roduntus* might decrease the effects of drying medications. (Interaction Rating: Moderate).

- **Medications for Alzheimer's disease:** *C. rotundus* might increase effects and side effects of medications used for Alzheimer's disease, e.g. Acetylcholinesterase (AChE) inhibitors. (Interaction Rating: Moderate).

- **Antidiabetic medications:** *C. rotundus* might decrease blood sugar; monitor your blood sugar closely. The dose of your diabetes medication might need to be changed. (Interaction Rating: Moderate).

- **Anticoagulant/ Antiplatelet drugs:** e.g. warfarin and aspirin: taking *C. rotundus* along with medications that also slow clotting might increase the chances of bruising and bleeding. (Interaction Rating: Moderate).

11. Fertility, pregnancy and lactation

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

No data were found about the plant effect on fertility

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

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 (27).

- 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 (28).

- The petroleum ether extract of *C. rotundus* was reported to possess analgesic activity (29).

- 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. (30).

- 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) (31).

- 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 (32).

- 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 (33).

- 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 (34).

- 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* (35).

- 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 (36).

- 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 (37).
- 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 (38).

- 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) (39).

- 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 (40).

- 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 (41).

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.* (42).

- 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* (43).

17. Date of compilation/last revision

18/11/2020

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, vol (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. 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,* 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.
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. ana 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 Antioxidant 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., 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. p. 58.
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 Pharm Lettre, 4, 522-524.
27	Ju, Y. and Xiao, B. (2016). Chemical constituents of *Cyperus rotundus* L. and their inhibitory effects on uterine fibroids. *Afri Health Sci*, 16(4), 1000-1006.
28	Biradar, S., Kangralkar, V.A., Mandavkar, Y., Thakur, M., Chougule, N. (2010). Anti-inflammatory, anti-arthritic, analgesic and anticonvulsant activity of *Cyperus* essential oils. *Int J Pharm Pharm Sci*, 2,112–115.
29	Gupta, M.B., Palit, T.K., Singh, N., 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.
30	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.
31	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.
32	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.
33	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.

34	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.
35	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.
36	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.
37	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*., Conference Issue, 27(6), 2241-2246.
38	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.
39	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.
40	Jahan, N., Bano, H., Makbul, S.A., Kumar, B.N., 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.
41	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.
42	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.
43	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.

Herbal Monograph on Wild Medicinal Plants in Egypt

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) (البذور) حب اليسار (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 acid, stearic acid, behenic acid, palmitoleic acid, arachidic acid, eicosenoic acid, lingnoceric acid, linoleic acid, margaric acid, myristic acid, margaroleic acid and linolenic acid were also detected (Elbatran *et al*., 2005). Furthermore, sterol composition analysis of both the oils showed that β-sitosterol was the major one followed by stigmasterol, campesterol and Δ-5-avenasterol (5).

- **Phenolic Compounds:** Gallic acid, protocatechuic acid, catechin ,4-hydroxybenzoic acid, caffeic acid, syringic acid, trans p-coumaric acid, chlorogenic acid, trans ferulic acid (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-Lrhamnosyloxy) 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 (10)

Ancient Egyptians were using *M. peregrina* for thousands of years to maintain their skin health and mental fitness (9)

a) For slimness: The plant is used to increase appetite and to treat slimness
b) Constipation
c) Headache, fever, abdominal pain, burns, back and muscle pains and during labor in childbirth
d) Soothe rash

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

6. Herbal preparations correlated to medicinal use (10)

a) Jam of several constituents cooked in black honey

b) - Decoction: add 2teaspoonful of seeds in a pot, pour cold water, boil and simmer for 10 minutes then pour into a cup and drink it
- The seed oil

c) The seed oil

d) The leaf extract

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

- **Oral:** *M. peregrina* hot decoction is taken in the morning before breakfast
- **Topical:** The leaf extract is rubbed over the skin

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

No data were found for plant use during lactation

No data were found about the plant effect on fertility

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

14. Overdose

No case of overdose has been reported

15. Relevant biological properties

- 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, 18, 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

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Reference

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	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, vol(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 sp. *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 Antioxid. 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.

Herbal Monograph on Wild Medicinal Plants in Egypt

Origanum syriacum (L.) زعتر ، بردقوش

1. Names & Synonyms (1, 2, 3)

Family: Labiatae (Lamiaceae)

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

Arabic: Bardaqoush بردقوش ، Za'atar زعتر

2. Geographical distribution (1, 2, 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. (4, 5, 6, 7, 8, 9)

Only in one case the bicyclic *cis*-sabinene hydrate was described as a major compound in this species (6).

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 (10, 11).

Phenolics: The major phenolics were catechol, catechinic acid and pyrogallol. Other polyphenol components were chrysin, syringic, gallic, vanillic, coumaric, hydroxybenzoic, chlorogenic, caffeic, and rosmarinic acids (11).

Carotenoid: as *β*-carotene (11)

5. Traditional medicinal uses

Stomach troubles:

- Stomach and digestive disorders **(12)**

Origanum is also used as a stimulant, analgesic, antitussive, expectorant, sedative, antiparasitic and antihelminthic, but mostly for gastrointestinal complaints (6).

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

6. Herbal preparations correlated to medicinal use (12)

*** 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 3cups/day

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 (12, 13)

-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 lactation is not recommended

No data were found about the plant effect on fertility

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

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 (14, 15, 16, 17, 18). The essential oil showed *in vitro* anti-oxidant and anti-microbial properties (19, 20). In addition, the aqueous extract showed anti-oxidant properties (21).
- Ethanol crude extract of the plant showed anti-proliferative activity. The hydrodistilled essential oil and aqueous extract did not show any cytotoxic activity (22).
- 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 (23).
- 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 (24) 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 (23).

- 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 (25).

- 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 (26).

- 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 (27).

- 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 (28).

- 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 (29).

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 (30, 31, 32, 33, 34).

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 (35).

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 (18).

17. Date of compilation/last revision

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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: E. Aboutabl, M. Shabana & F. Soliman). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Faiza, M. H., Nahla, S. A. and Khaled, A. S. (2018). *Origanum syriacum* L. In: Egyptian Encyclopedia of Wild Medicinal Plants, 8, 474-489. Academy of Scientific Research and Technology, Cairo, Egypt.
4	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
5	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.
6	Baser, K. H. C., Ku¨rkcu¨oglu, M., Demirci, B. and O¨zek, T. (2003). The essential oil of *Origanum syriacum* L. var. sinaicum (Boiss.) *Ietswaart. Flavour Fragrance J.,* 18, 98-99.
7	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.
8	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.
9	Loubna Shamseddine and Jose Johann Chidiac (2020) Composition's effect of *Origanum Syriacum* essential oils in the antimicrobial activities for the treatment of denture stomatitis Odontology.
10	Samy K. El-Desoukya et al (2009) Phytochemical Constituents and Biological Activities of *Origanum syriacum* Z. Naturforsch., 64b, 447 – 451.
11	Abd EL-Moneim M.R Afify et al. (2014) ANTIOXIDANT CONTENT ANDCYTOTOXICITY OF *Origanum syriacum* L. Advances in Food Sciences, Volume 36 – No 2.
12	Conservation and sustainable use of medicinal plants in Egypt, National Surveys. (2016). UNDP, GEF, ASRT and NRC, vol (1-5).
13	https://www.drugs.com/npp/capers.html.
14	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), 1147-9.

15	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.
16	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 Egyptain folk medicine. *Veterinary Medical Journal*, 42(1B), 263-270
17	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
18	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.
19	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.
20	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.
21	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.
22	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.
23	Loizzo, M. R., Menichini, F., Conforti, F., Tundis, R., Bonesi, M., Saab, A. M., Statti, G. A., Cindio, B., Houghton, P. J., Menichini, F., 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.
24	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.
25	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.
26	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.

27	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.
28	Assaf, A. M., Amro, B. I., Mashallah, S., Haddadin, R. N. (2016). Antimicrobial and anti-inflammatory potential therapy for opportunistic microorganisms. *J Infect Dev Ctries*; 10(5): 494-505.
29	Ben-Arye, E., Dudai, N., Eini, A., Torem, M., Schiff, E., Rakover, Y. (2011). Treatment of Upper Respiratory Tract Infections in Primary Care; A Randomized Study Using Aromatic Herbs Evid. Based Complement. *Alternat. Med*., 7.
30	Shehadeh, M., Silvio, S., Ghadeer, A., Darwish, R. M., Giangaspero, A., Vassallo, A., Lepore, L., Oran, S. A., Hammad, H., Tubaro, A. (2014). Topical anti-inflammatory potential of six Salvia species grown in Jordan. *Jordan J. Pharm. Sci*., 7 (2), 153–161.
31	Shehadeh, M., Suaifan, G., 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.
32	Aburjai, T., Hudaib, M., Tayyem, R., Yousef, M., Qishawi, M. (2007). Ethnopharmacological survey of medicinal herbs in Jordan, the Ajloun Heights region. *J. Ethnopharmacol.,* 110(2), 294–304.
33	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.
34	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.
35	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*. Vol. 58. No. 10, 1147-1149.

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