CHAPTER ONE

1.1 Introduction

Chamomile [*Chamomilla recutita* L. (Rausch.)] is a well-known medicinal plant species from the Asteraceae family often referred to as the "star among medicinal species." Nowadays it is a highly favored and much used medicinal plant in folk and traditional medicine. It is multitherapeutic, cosmetic, and nutritional values have been established through years of traditional and scientific use and research. *Chamomilla recutita* is known as German chamomile. German chamomile has a very important role in phytotherapy. Chamomile is widely used throughout the world. The plant is indigenous to northern Europe and grows wild in central European countries; it is especially abundant in Eastern Europe. Also found in western Asia, the Mediterranean region of northern Africa, and United States of America. It is cultivated in many countries. It is primary uses are as a sedative, anxiolytic and antispasmodics as a treatment for mild skin irritation and inflammation (Singh et al., 2011; Viapiana et al., 2016).

The part used of the plant is the flowers (Chamomile flos). The drug contains an essential oil (3-15 ml/kg). The essential oil owes its blue color to chamazulene which is often found at a high concentration (1-15%), and arises from the decomposition of the sesquiterpenoid lactones matricin and matricarin.

Chamazulene is the most important compound of the drug because it is strong anti-inflammatory properties (Malik et al., 2015; Sharafzadeh and Alizadeh, 2011).

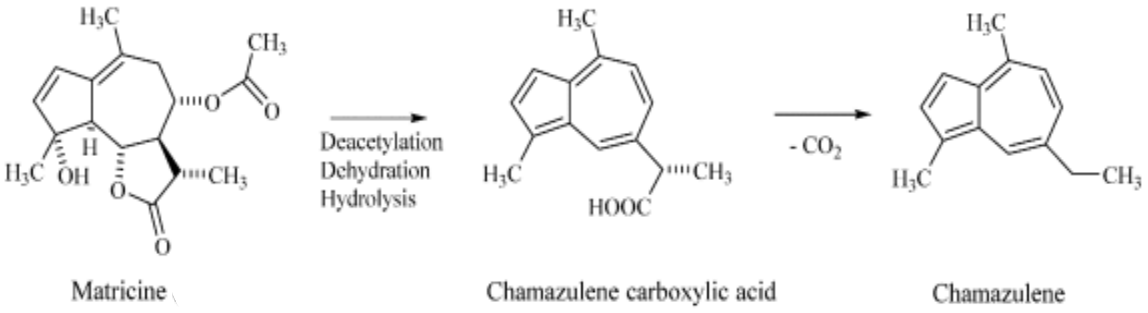


Figure 1: Conversion of matricin to chamazulene.

In Libya, there are three species represented by the genus *Chamomilla*: *C. recutita, C. aurea, and C. pubescens*. However people in Libya that live in the west and east are more familiar to *C. recutita*. Whereas *C. aurea* is mainly known and used by the southern Libyan population. *C. pubescens* is not well known in Libya.

The colors of the essential oils from some *Chamomilla* species are not blue because of the lack of chamazulene. It is a chemical race and especially *Chamomilla* species growing in Mediterranean countries belong to this race. For this reason, we decided to compare *Chamomilla recutita* and *Chamomilla aurea* samples collected from Libya for the presence of chamazulene in their essential oils.

CHAPTER TWO

2.0 Theoretical part

2.1 Botanical part

2.1.1 Asteraceae family

A very large family comprising of c. 1100 genera and over 25,000 species, distributed throughout the world; 97 genera and c. 240 species are reported from Libya.

Herbs or shrubs, lactiferous or not. Leaves alternate, opposite or rosulate, exstipulate, entire, toothed or variously lobed or dissected. Florets small, unisexual or hermaphrodite, sessile, epigynous, usually arranged in globose or radiate heads or capitula on flat conical or ± concave receptacles surrounded by 1-few rows of bracts (the involucral bracts). Capitula solitary or variously arranged on a common stalk, homogamous, heterogamous, radiate or discoid. Receptacles smooth, alveolate or pitted, paleaceous or epaleaceous, glabrous or hairy. Calyx limb absent or represent-ted as pappus; scaly coronate, auriculate, awn-like or setaceous-hairy, setae scabrid, barbellate or plumose. Corolla gamopetalous, tubular (infundibuliform, narrowly cylindrical and campanulate above or filiform throughout), (3-) 4-5-lobed above, actinomorphic or weakly zygomorphic; peripheral florets sometimes tubular with 2-lipped limb or ligulate with a short basal tube and limb prolonged on one side into a (2-) 3-5- toothed ligule; sometimes corolla absent. Stamens (4)-5, epipetalous; filaments free; anthers laterally united into a tube around the style (i.e. syngenesious) or free, often caudate or sagittate at the base and mostly with apical appendages. Ovary inferior, 1-locular; ovule solitary, basal; style usually divided above into 2 branches, bearing stigmatic surface. Cypsela (fruit) sometimes beaked above (Jafri and El-gadi, 1983).

2.1.2 *Chamomilla* genus

Annuals. Stems erect or ascending, usually very leafy. Leaves alternate, 2-3-pinnatisect, with numerous, linear segments. Capitula solitary, terminal or in corymbs, heterogamous or homogamous, radiate or discoid. Involucral bracts 2-3-rowed, with scarious margins. Receptacle conical, hollow, epaleaceous. Ligules when present white. Tubular florets 4-5-lobed, yellow. Cypsela ±terete, obliquely truncate above, with an oblique lateral attachment scar at the base; dorsal face slightly convex; ventral face with 3-5 narrow, whitish, longitudinal ribs; pericarp mucilaginous when wet; pappus absent or when present than as a small scarious corona or an auricle c. 4 species distributed in Europe, N. Africa, eastwards to North- East Asia, 3 species have been recorded from Libya.

+Capitula radiate 1. *C. recutita*

-Capitula discoid or disciform

+ capitula heterogamous; marginal florets female;

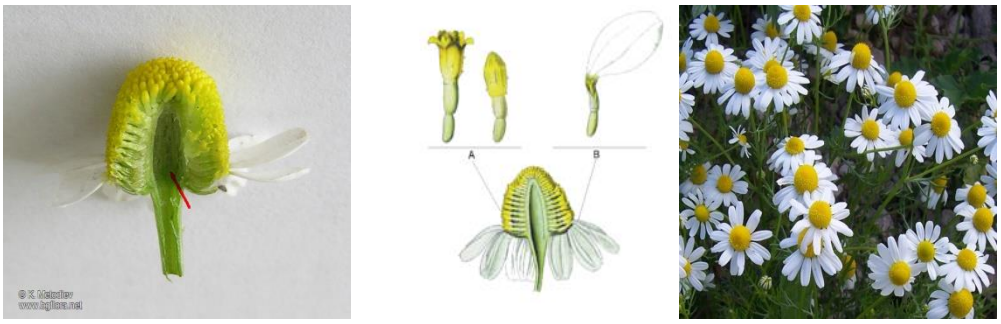
Tubular florets 5-lobed 2. *C.pubescens*

-Capitula homogamous; tubular florets 4- lobed 3. *C.pubescens* (Jafri and El-gadi, 1983).

2.1.2.1 *Chamomilla recutita* (L). Rauschert (syn. *Matricaria recutita* L. *M. suaveolens* L.)

Fragrant, glabrous annual; stem (2) 10-60 cm, erect or ascending, much branched above. Leaves 40-70 mm long, segments acute, well separated. Peduncles 3-10 cm. Capitula (1-) 8-120 (- more), 10-25 mm in diam.; involucral bracts oblanceolate, obtuse or acute, 2.5-3.5 mm with pale, scarious margin. Ligule 12-25, 6-9×2-3mm soon reflexed, rarely absent. Tubular florets 5- lobed, yellow; upper part of the tube campanulate above a marked constriction. Cypsela 1mm, pale greyish-brown, with 4-5 ribs on the ventral surface; pappus short, coronate or absent but

sometime in cypselas of ray florets, irregularly toothed auricle equalling the length of the cypsela.



A: Disc florets B: Ray florets

Figure 2: Images showing *Chamomilla recutita* flowers

Www. Bgflora.net. https://en.wikipedia.org/wiki/ *Matricaria chamomilla*. http://calphotos.berkeley.edu/cg

Distribution: Most of Europe, but probably native only in the south and east. It appears now naturalized in N. Africa**.**

In Libya: Reported to be grown in Misurata (Jafri and El-gadi, 1983).

2.1.2.2 *Chamomilla aurea* (Loefl.) Gay ex Cosson and Kralik (Syn. *Matricaria aurea* (Loefl.) Schultz Bip).

Stem 4-25 cm, slender, decumbent or ascending and often flexuous, branched from the base, glabrous below, sometimes very sparsely pubescent below the capitulum. Leaves (5-) 10-40 (-60) × (3-) 6-15 mm, 2-3-pinnatisect, linear-oblanceolate in outline; ultimate segments capillary, mucronate. Peduncles 0.5-2.5 cm long. Capitula 1-60, 1-3 per branch, 4-7 mm in diam.; involucral bracts ovate, ± obtuse, 2.5-3.5 mm, with brown scarious margin. Florets all tubular; corolla c. 1 mm, 4-lobed, yellow. Cypsela 0.6-0.9 × 0.15-0.2 mm (excl. pappus), pale to dark-

brown, with 3(-5) whitish, prominent ribs on the adaxial surface; pappus usually as long as the corolla or slightly shorter, auriculiform, scarious.

Figure 3: Images showing *Chamomilla aurea* flower heads.

Flowerslnlsrael.com www.maltawildplants.com

Distribution: Mediterranean region, S.W. Asia eastwards to Western Himalayas.

In Libya: Reported to be grown in Greian (JafrI and El-gadi, 1983).

2.2 Chemical part (*Chamomilla recutita*)

2.2.1 Volatiale oil compounds

2.2.1.1 Monoterpenes: α-pinene, α-terpinene, myrcene, geraniol, sabinene (Pizard et.,al 2006).

2.2.1.2 Sesquiterpenes: α-bisabolol, α-bisabolol oxide A, α-bisabolol oxide B, α-bisabolol oxide C, α-bisabolone oxide, chamazulene, spathulenol, Caryophyllene epoxide, β-bisabolene, trans-β-farnesene, trans-α- farnesene, β-selinene, germacrene D, germacrene A, bicyclogermacrene, cadinene, α-muurolene, calamenene, β- caryophyllene (Motl et.,al 1983; Ahmed et.,al 1993).

2.2.1.3 Spiroethers: Cis (Z)-enyne dicycloether cis-2-[hexadiyne)- (2,4)-ylidene]-1,6-dioxaspiro-[4,4]-nonene), trans (E)-enyne dicycloether trans-2-[hexadiyne)- (2,4)-ylidene]-1,6-dioxaspiro-[4,4]-nonene (Becker, 1981).

2.2.2 Flavonoids

2.2.2.1 Flavon aglycons: Apigenin, luteolin, chrysoseriol.

2.2.2.2 Flavon glycosides: Luteolin-7-glucoside, luteolin-4 glucoside, chrysoseriol-7-glucoside, apigenin-7-glucoside (apigetrin) apigenin-7-(6’’-O-acetyl)-glucoside, apigenin-7-(6’’-O-apiosyl)-glucoside (apiin) (Carle and Isaac; 1985).

2.2.2.3 Flavonol aglycones: Quercetin, chrysosplenol, chrysosplenitin, eupatoletin, eupalitin

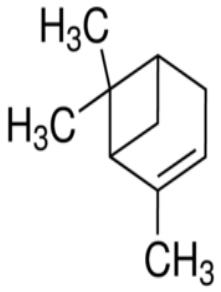
2.2.2.4 Flavonol glycosides: Quercetin-7-glucoside (quercimeritrin), quercetin-3-rutinoside, quercetin-3-galactoside (Kunde and Isaac; 1979).

2.2.3 Coumarines: Herniarin, umbelliferone, isoscopoletin, esculetin, scopoletin (Kotov et.,al 1991).

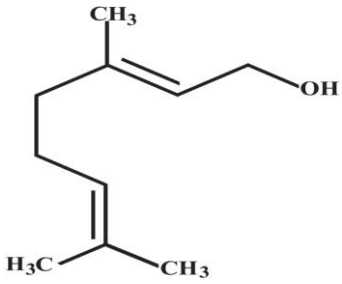
2.2.4 Phenyl carboxylic acid: Synergic acid, vanillic acid, anisic acid, caffeic acid (Maha et.,al 2012).

2.3 Chemical part (*Chamomilla aurea*)

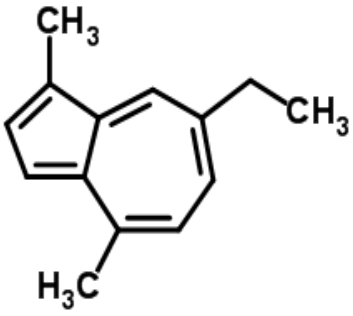
The main constituents of the volatile oil are α-bisabolol and it is oxides, bisabolene, acetylene, and azulenes. The phenolic compounds are coumarins (herniarin and umbelliferone), flavonoids: apigenin, apigenin-7-O-glucoside, luteolin, luteolin-7- O-glucoside, quercetin, rutin, naringenin. Phenolic acid: chlorogenic acid and caffeic acid (Esam Qnais. 2011; Nasir. 2014; Pino et.,al 2000; Matos et.,al 1993).



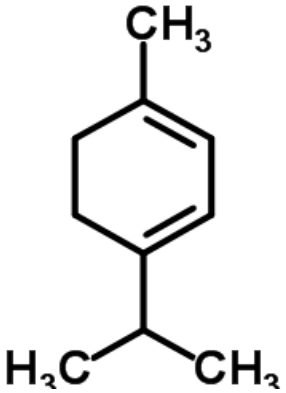
α-pinene



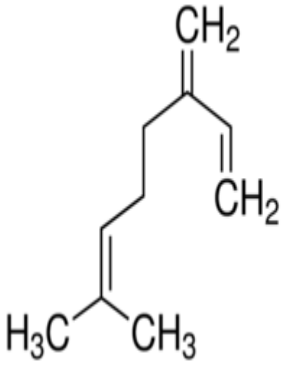
Geraniol



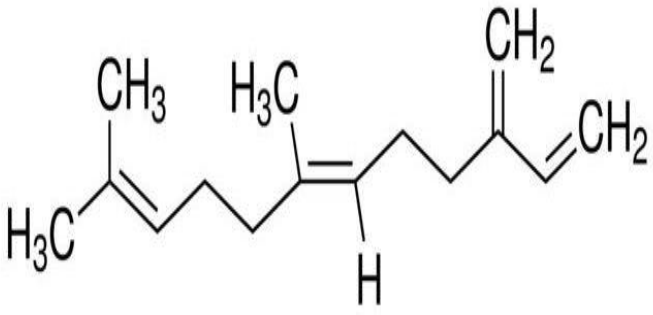
Chamazulene



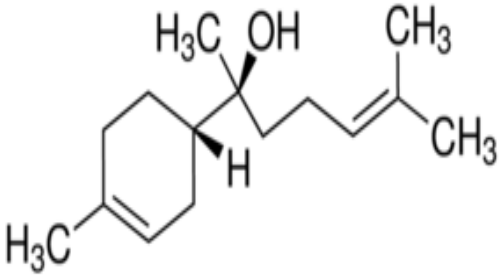
α-terpinene



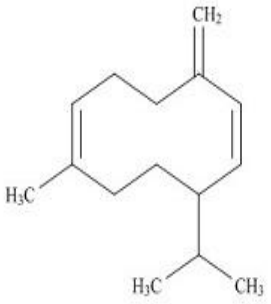
Myrcene



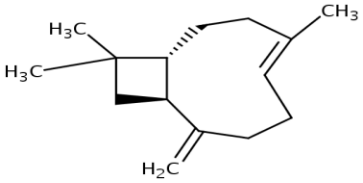
Trans-β- farnesene



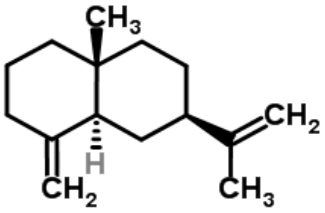
α-bisabolol



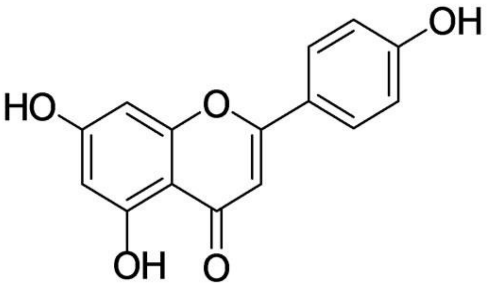
Germacrene D



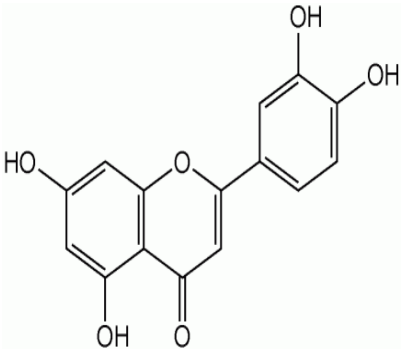
β-caryophyllene



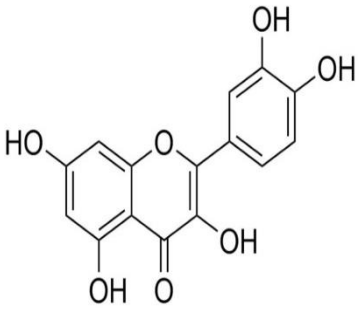
β-selinene



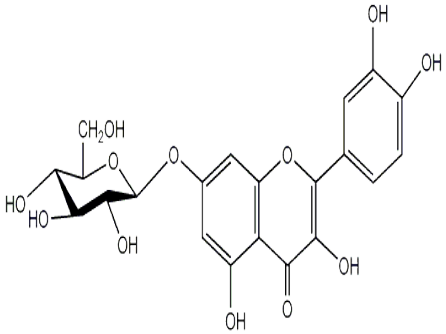
Apigenin



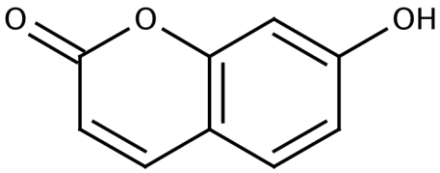
Luteolin



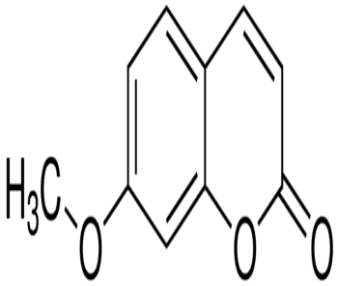
Quercetin



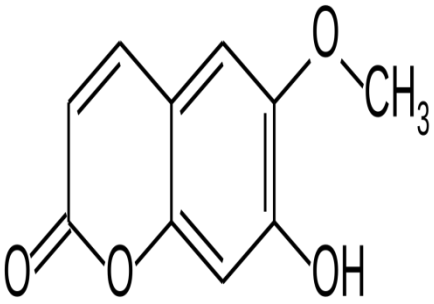
Quercetin-7-glucoside



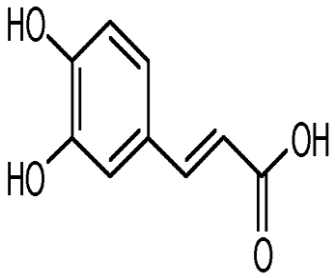
Umbelliferone



Herniarin



Scopoletin



Caffeic acid

Figure 4: Some compounds found in *Chamomilla* species

2.3 Pharmacological activities (*Chamomilla recutita*)

2.3.1 Anti-inflammatory and antiphlogistic properties:

The flowers of chamomile contain 1–2% volatile oils including alpha-bisabolol, alpha-bisabolol oxides A & B, and matricin (usually converted to chamazulene) and other flavonoids which possess anti-inflammatory and antiphlogistic properties. A study in human volunteers demonstrated that chamomile flavonoids and essential oils penetrate below the skin surface into the deeper skin layers. This is important for their use as topical antiphlogistic (anti-inflammatory) agents. One of the chamomile's anti-inflammatory activities involve the inhibition of LPS-induced prostaglandin E release and attenuation of cyclooxygenase (COX-2) enzyme activity without affecting the constitutive form, COX- (Srivastava et al., 2010; Miguel et al., 2015).

2.3.2 Antibacterial, antifungal, antiviral activities:

The antibacterial and antiviral effects of chamomile have been well documented. An ethanolic extract of German chamomile inhibited the growth of herpes and poliovirus. Compounds in the essential oil of chamomile were effective against *Staphylococcus* and *Candida*. Among the chamomile are essential oil components; α bisabolol has the strongest activity against Gram-positive and Gram-negative bacteria. Chamazulene also has strong antimicrobial activity. Spiroethers have weak activity against Gram-positive bacteria but were inactive against gram-negative bacteria. German chamomile esters and lactones show activity against *Mycobacterium tuberculosis* and *M. avium*. Chamazulene, α bisabolol, flavonoids and umbelliferone display antifungal properties against *Trichophyton mentagrophytes, T. rubrum* and *Candida albicans* (Nogueira et al., 2008; Lu et al., 1998).

2.3.3 Wound healing activity:

The efficacy of the topical use of chamomile to enhance wound healing was evaluated in a double-blind trial on 14 patients who underwent dermabrasion of tattoos. The effects on drying and epithelialization were observed, and chamomile was judged to be statistically Efficacious in producing wound drying and in speeding epithelialization (Nayak et al., 2007; Martins et al., 2009).

2.3.4 Treatment of gastrointestinal disorders:

Methanol extracts of *Chamomilla recutita* (flowers) and *Ginkgo biloba* (leaves) have a MIC > 100 micro g/mL against the gram-negative bacterium Helicobacter pylori (HP) (Mahady et al., 2005; Albrecht et al., 2014).

2.3.5 Common cold:

Common cold (acute viral nasopharyngitis) is the most common human disease. It is a mild viral infectious disease of the upper respiratory system. Typically common cold is not life-threatening, although it is complications (such as pneumonia) can lead to death, if not properly treated. Studies indicate that inhaling steam with chamomile extract has been helpful in common cold symptoms; however, further research is needed to confirm these findings (Saller et al., 1990).

2.3.6 Eczema:

Topical applications of chamomile have been shown to be moderately effective in the treatment of atopic eczema. It was found to be about 60% as effective as 0.25% hydrocortisone cream. Roman chamomile of the Manzana type (Kamillosan (R)) may ease discomfort associated with eczema when applied as a cream containing chamomile extract (Patzelt-Wenczler and Ponce; 2000).

2.3.7 Colic/Diarrhea conditions:

An apple pectin-chamomile extract may help shorten the course of diarrhea in children as well as relieve symptoms associated with the condition. Two clinical trials have evaluated the efficacy of chamomile for the treatment of colic in children (Sebai et al., 2014).

2.3.8 Diabetes:

Studies suggest that chamomile ameliorates hyperglycemia and diabetic complications by Suppressing blood sugar levels, increasing liver glycogen storage and inhibition of sorbitol in the human erythrocytes (Eddouks et al., 2005).

2.3.9 Anxiety and seizure:

Chamomile has been reported in the treatment of generalized anxiety disorder (GAD). But the reports seem contradictory as an earlier report suggests that German chamomile showed significant inhibition of GAD activity (Murti et al., 2012).

2.3.10 Osteoporosis:

Osteoporosis is metabolic bone disease resulting from low bone mass (osteopenia) due to excessive bone resorption. The aqueous extracts derived from *Chamomilla recutita* may form the basis to design "functional foods" for the prevention of osteoporosis (Kassi et al., 2004).

2.3.11 Immunomodulatory activity:

Intragastric and parenteral administration of heteropolysaccharides of *Chamomilla recutita* L. is found to normalize developing of the immune response to air cooling and enhance (but do not normalize) this process upon immersion cooling. The immunomodulating effect of the heteropolysaccharides upon cooling is attributed to initiation of immunostimulating properties of heavy erythrocytes (macrocytes), activation of immunoregulation cells of peripheral blood, and increased sensitivity of effector cells to helper signals (Gupta et al., 2010).

2.3.12 Cardiovascular conditions:

It has been suggested that regular use of flavonoids consumed in food may reduce the risk of death from coronary heart disease in elderly men. A study assessed the flavonoid intake of 805 men aged 65–84 years who were followed up for 5 years. Flavonoid intake (analyzed in tertiles) was significantly inversely associated with mortality from coronary heart disease and shown an inverse relation with an incidence of myocardial infarction (Srivastava et al., 2010).

2.3.13 Anticancer activity:

Most evaluations of tumor growth inhibition by chamomile involve studies with apigenin which is one of the bioactive constituents of chamomile. Studies on preclinical models of skin, prostate, breast and ovarian cancer have shown promising growth inhibitory effects. In a recently conducted study, chamomile extracts were shown to cause minimal growth inhibitory effects on normal cells, but shown significant reductions in cell viability in various human cancer cell lines. The aqueous and methanolic extracts of chamomile showed differential apoptosis in

cancer cells but not in normal cells at similar doses **(**Srivastava and Gupta, 2007; Miraj and Alesaeid; 2016).

2.3.14 Pharmacological activities of *Chamomilla aurea*

Phytochemical analysis of essential oil from *Chamomilla aurea* shows several chemical compounds many of which have an important antimicrobial and antioxidants activity. The essential oils of *C. aurea* show inhibitory activity against gram-positive bacteria which was significantly higher than against gram-negative ones.

Chamomilla aurea hydroalcoholic extract is effective to protect against acute colitis in the acetic acid model. And also is found to be used for hypoglycaemic treatments. Chamomile oil obtained from *C. aurea* also possesses anti-inflammatory activity and investigations. Reveal that it is also used as an antispasmodic and analgesic agent (Humaira et., al 2016; Ali-Shtayeh et., al 2008; Minaiyan et al., 2011; Yaniv et al., 1987).

2.4 Traditionally uses In Libya:

Flowers of *Chamomilla* are used as inhalation in flu, cough, and as the sedative, tonic, diuretic. It is also known to be effective in the treatment of various gastrointestinal disorders such as antispasmodic, intestinal colic, flatulence, ulcer and diarrhea (Yousef et al., 2016).

2.5 Dosage formulation: Chamomile is formulated in many dosage forms. It comes as a topical cream, topical ointment, topical lotion, oral inhalation, powder, tea, solution for bath, and infusion and as a volatile oil known as the essential oil (Wald and Brendler, 1998 ; Liang and Huang, 1999).

2.5.1 Dosage forms recommended doses and duration of therapy

2.5.1.1 Usual adult dosage:

2.5.1.1.1 A. Dermatitis: For treatment of dermatitis apply cream or lotion topically 4 times daily.

2.5.1.1.2 B. Tension: For treatment of tension associated with the disorder of nervous system use:

1. Liquid extract (1:1 in 45%-70% ethanol), 1 to 4 ml orally 3 times daily.
2. Tea powder, orally 1-4 cups of tea daily or as needed.

2.5.1.1.3 C. GI- discomfort: The average daily dose for treatment of any GI-discomfort is 2-8g, 3 times a day of fluid extracts (1:1 in 45 % ethanol). Dose 1-4ml orally three times daily (Wald and Brendler, 1998).

2.5.1.2 Usual pediatric dosage

2.5.1.2.1 Dermatitis, cream, topical: Apply 4 times daily.

2.5.1.2.2 Tension, tea, and oral 1 to 4 times daily, amount dependent on age.

2.5.1.2.3 GI- doses: 2g, 3times daily or fluid extract of 0.6-2ml as single dose. Internal use is only in patients older than 3 years (Liang and Huang, 1999).

Figure 5: Preparation of chamomille

https://www.desertcart.ae/products/ https://www.mabouticbienetre.com/ http://www.hsconline.co.u

CHAPTER THREE

Experimental

3.1 Materials and methods

3.1.1 Instruments and chemicals used

Instruments: Clevenger apparatus, Camag TLC tanks, Camag TLC plate heater III, and UV source.

Chemicals: Methanol, toluene, dichloromethane, hydrochloric acid, and p-dimethylaminobenzaldehyde, almost all were from Sigma Aldrich.

3.1.2 Plant materials

Two drugs were collected for study from different areas in Libya.

The flowers of *Chamomilla recutita* with voucher number D68107361 were collected in March 2016 from Misurata city in Libya and identified and authenticated by Dr. Mohamed Nouri Abohedra Botany department, Tripoli University.

The flowers of *Chamomilla aurea* with voucher number D681073603 were collected in April 2017 from Greian city in Libya and identified and authenticated by Dr. Mohamed Nouri Abohedra Botany department, Tripoli University.

3.2 Obtaining volatile oil

50 gram of *Chamomilla recutita* and *C. aurea* were weighed and placed in Clevenger apparatus in 500 ml water for 3 hours to obtain the volatile oil.

3.3 TLC studies

Five pieces of capitula *Chamomilla recutita* and *C. aurea* were macerated in 5 ml dichloromethane, filtered and the obtained extract was spotted on TLC plate. The mobile phase used is dichloromethane: Methanol: Toluene 4: 2: 2. After development plates were placed on Camag TLC plate heater III at 87°C and then sprayed with 1% p- dimethylaminobenzaldehyde in

99 ml methanol and 1ml hydrochloric acid. To view spots the sprayed plates were again heated at 120°C.

3.4 Chamazulene test

Five pieces of capitula *Chamomilla recutita* and *C. aurea* were macerated in 5 ml dichloromethane, filtered and to the obtained extract a few drops of 1% p-dimethylaminobenzaldehyde in 99 ml methanol and 1ml hydrochloric acid was added.

CHAPTER FOUR

4.0 Results

4.1 The amount of volatile oils

50 gram of *Chamomilla recutita* and *C. aurea* capitula were water distilled using Clevenger apparatus to obtain volatile oils.

Table 1: Showing amount and color of volatile oil obtained.

	Chamomilla recutita	*Chamomilla aurea*
Amount of volatile oil	% 0.6 ml/g	% 0.1 ml/g
Color	pale-blue	pale- yellow

4.2 TLC results

After spraying plates with1% p-dimethylaminobenzaldehyde in 99 ml methanol and 1ml hydrochloric acid, blue spots for *Chamomilla recutita* and yellow-brownish spots for *C. aurea* were detected.

4.3 Chamazulene test

In addition of 1% P-dimethylaminobenzaldehyde in 99 ml methanol and 1 ml hydrochloric acid, *Chamomilla recutita* gave a positive test indicating the presence of chamazulene, While *C. aurea* gave a negative result.

Figure 6: Images showing obtaining volatile oil of *Chamomilla recutita*

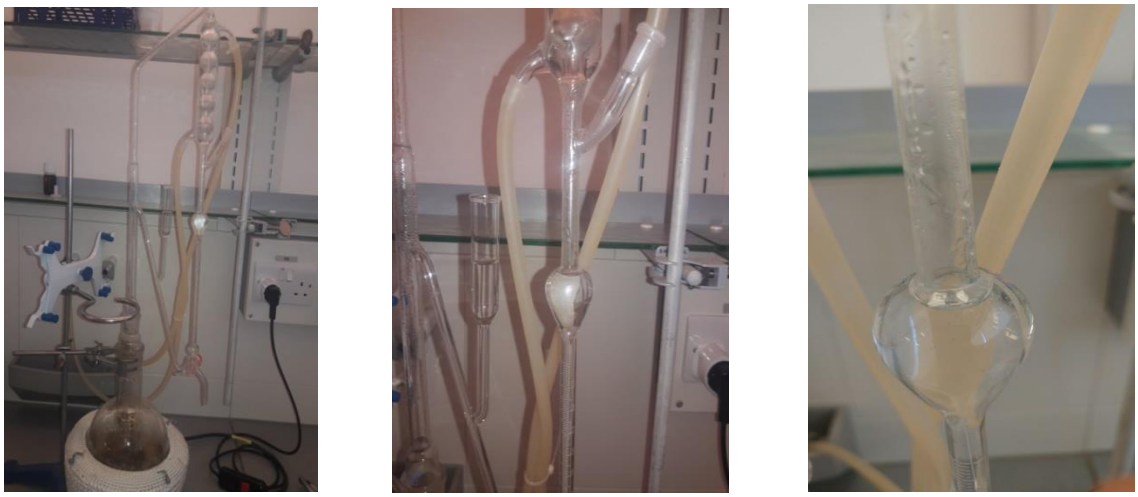


Figure 7: Images showing obtaining volatile oil of *Chamomilla aurea*

Figure 8: Images showing TLC studies

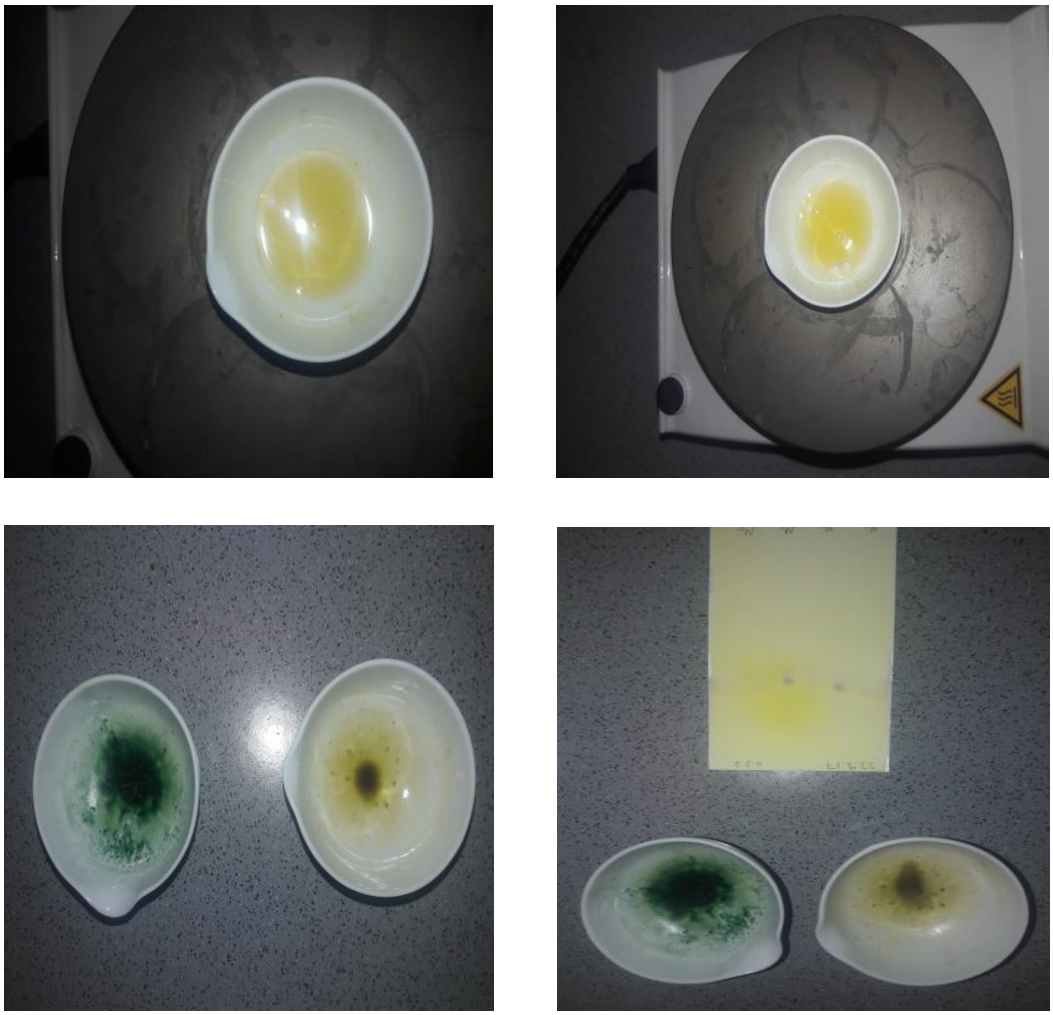


Figure 9: Images showing chamazulene test

CHAPTER FIVE

Conclusion

Chamazulene is a very important compound medicinally with a strong anti-inflammatory, antiseptic, antimicrobial, antispasmodic properties isolated from *Chamomilla* genus. The colors of this essential are not always blue because of the lack of chamazulene. It is a chemical race and especially *Chamomilla* species growing in Mediterranean countries belong to this race. In this study we decided to compare two *Chamomilla* species used in Libyan traditional medicine. *Chamomilla recutita* and *C. aurea* grows in different regions in Libya both species have seen to differ in some respects.

In this study volatile oil was obtained by water distillation using Clevenger apparatus. According to our results the percentage obtained of volatile oil from *C. recutita* is % 0.6 ml/g and was found to contain chamazulene with a positive blue in TLC and chamazulene test. While the percentage of volatile oil obtained from *C. aurea* was % 0.1 ml/g and gave brownish yellow spots in TLC and a negative chamazulene test.

Therefore, *Chamomilla recutita* is the species of *Chamomilla* that is recommended to be used medicinally. This is evident from the traditional use of *C. recutita* over that of *C. aurea*.

REFERENCES

Ahmed, A., Ahmed, Jakupovic j., Maha. A. Abou Elela., Ahmed A. Seif El-Din and Nadia S. Hssein. (1993). Two bisabolene from *Matricaria chamomilla*. *Natural products letter* 3 (4): 277-281.

Albrecht U, Muller V, Schneider B, Stange R. (2014). Efficacy and safety of an herbal medicinal product containing myrrh, chamomile and coffee charcoal for the treatment of gastrointestinal disorders: a non-interventional study. *BMJ Open Gastroenterology*. 1 (1): 000015.

Ali-Shtayeh MS, Jamous RM, Al-Shafi e' JH et al. (2008). Traditional knowledge of wild edible plants used in Palestine (Northern West Bank): a comparative study. *Journal of Ethnobiology and Ethnomedicine* 12: 4-13.

Carle R, and Isaac, O. (1985). Dtsch. Apoth. Ztg. 125 Nr. 43/Suppl. 1, 2-8.

Eddouks M, Lemhadri A, Zeggwah NA, Michel JB. (2005). The Potent hypoglycaemic activity of the aqueous extract of Chamamelum nobile in normal and streptozotocin-induced diabetic rats. Diabetes Res Clin Pract; 67: 189–195.

Esam Qnais. (2011). The analgesic effect of the ethanolic extract of *Matricaria aurea*. Department of Biology and Biotechnology, Faculty of Science, the Hashemite University, Zarqa – JORDAN. *Turk J Biol* 35. 347-352.

Gupta Vikas, Mittal Payal, Bansal Parveen, Khokra L. Sukhbir, Kaushik Dhirender. (2010). Pharmacological Potential of *Matricaria recutita*-A Review. *International Journal of Pharmaceutical Sciences and Drug Research* 2 (1): 12-16.

Humaira Rizwana., Mona S., Alwhibi and Dina A. Soliman. (2016). Antimicrobial Activity and Chemical Composition of Flowers of *Matricaria aurea* a Native Herb of Saudi Arabia. *International Journal of Pharmacology*, 12: 576-586.

Jafri, **S.M.H** and El-gadi A. (1983). Flora of Libya, Asteraceae, Department of Botany, Faculty of Science, Al-Faateh University, Tripoli.

Kassi E., Papoutsi Z., Fokialakis N., Messari I, Mitakou S., Moutsatsou p. (2004). Greek plant extracts exhibit selective estrogen receptor modulator (SERM)-like properties. *J Agric Food Chem*. 52 (23): 6956-61.

Kotov, AG. Khvorost, PP., Komissarenko, NF. (1991). Coumarins of *Matricaria recutita*. *Khim.Prir. Soedin*. 6: 853–4.

Kunde, R., Isaac, O. (1979). Flavones of chamomile (*Matricaria chamomilla* L.) and a new acetylated apigenin-7-glucoside. *Planta Med*., 37, 124.

Liang Y., Huang Y. (1999). Suppression of inducible Cox and inducible NO synthase by apigenin and related flavonoids in mouse macrophages. *Carcinogenesis*. 20 (10): 1945-52.

LU, T., C.L. Cantrell, S.L. Robbs, S.G. Franzblau and N.H. Fischer, (1998). Antimycobacterial *Matricaria* esters and lactones from Asteraceae species, *Planta Med*., 64: 665-667.

Mahady GB., Pendland SL., Stoia A., Hamill FA., Fabricant D., Dietz BM., Chadwick LR. (2005). In vitro susceptibility of *Helicobacter pylori* to botanical extracts used traditionally for the treatment of gastrointestinal disorders. *Phytother Res*.; 19 (11): 988-91.

Maha Aboul Ela., Abdalla El-Lakany, and Mohamed Ali Hijazi. (2012). Phytochemicals - A Global Perspective of Their Role in Nutrition and Health, General introduction to family Asteraceae**.** Dept. Of pharmacognosy, Faculty of Pharmacy, Beirut Arab University, Beirut, Lebanon. DOI: 10.5772/28956.

Malik Hassan Mehmood., Siraj Munir., Uzair Ali Khalid., Mudassir Asrar and Anwarul Hassan Gilani. (2015). Antidiarrhoeal, antisecretory and antispasmodic activities of *Matricaria chamomilla* are mediated predominantly through K^+-channels activation. *Journal ListBMC Complement Altern Medv*.15; PMC4410481.

Martins MD., Marques MM.**,** Bussadori SK., Martins MA., Pavesi VC., Mesquita-Ferrari RA., Fernandes KP. (2009). Comparative analysis between *Chamomilla recutita* and corticosteroids on wound healing. An in vitro and in vivo study. *Phytother Res*. 23 (2): 274-8.

Matos, FJ., Machado MI., Alencar JW et al. (1993). Constituents of Brazilian chamomile oil. *Journal of Essential Oil Research* 5: 337-339.

Miraj Sepide and Alesaeid Samira. (2016). A systematic review study of therapeutic effects of *Matricaria recutita* chamomile (chamomile). *Electron Physician*. 8 (9): 3024–303.

Miguel, FG. Cavalberio, AH. Spinola, NF. Ribeiro, DL., Barcelos, GR., Antunes, LM. (2015). Vethod alidation of an RP-HPLC-DAD Method for chamomile (*Matricaria chamomilla*). Preparation and assessment of the marker, apigenin-7-glucside, safety and anti-inflamatory effect. *Evid Based Complement Alternat Med*. Doi 10.1155/2015/82843.

Minaiyan, M., Dehkordi, N.G., Mahzouni, P., Roknabady, M.A. (2011). Effect of Matricaria aurea (Loefl.) Shultz-Bip. Hydro alcoholic Extract of Acetic Acid-Induced Acute Colitis in Rats. *Iran. J. Basic Med. Sci*., 14 (1) 67-74.

Motl, O., Repcak, M., Ubik, K. (1983). Further components of chamomile oil. *Arch. Pharm*., 316, 908.

Murti Krishna., Panchal A Mayank., Gajera Vipul and Solanki Jinal. (2012). Pharmacological properties of *Matricaria recutita*: A Review. *Pharmacologia* 3 (8): 348-351.

Nasir Ali Siddiqui. (2014). Chemical constituents of essential oil from flowers of *Matricaria aurea* grown in saudi Arabia. Department of Pharmacognosy. *Indian Journal of Drugs,* 2 (4), 164-168.

Nayak BS, Raju SS., Rao AV. (2007**).** Wound healing activity of *Matricaria recutita* L. extract. *J Wound Care*. 16 (7): 298-302.

Nogueira JC., Diniz Mde F, Lima EO. (2008). In the vitro antimicrobial activity of plants in Acute Otitis Externa. *Braz J Otorhinolaryngo*l; 74 (1): 118-24.

Patzelt-Wenczler R, Ponce-Pöschl E. (2000). Proof of efficacy of Kamillosan® cream in atopic eczema. Eur. *J Med Res*. 5: 171–175.

Pino, JA., Marbot R., Agiiero J et al. (2000). Essential oil of chamomile *Chamomilla recutita*

Pizard, A., Alyari, H., Shakiba.M.R., Zehtab-Salmasi,S, and Mohammadi, A. (2006). "Essential oil content and composition of German chamomile (*Matricaria chamomilla* L.) at Different Irrigation Regimes. *Journal of Agronomy* 5 (3): 451-455.

Becker H., Reichling, J. (1981). Lst die phytotherapie mit Baldrian und kamille noch zeitgemaess? Teil II. *Dtsch. Apoth. Ztg*, 121, 1285-1290.

Saller, R., Beschomer M, Hellenbrecht D. (1990). Dose dependency of symptomatic relief of complaints by chamomile steam inhalation in patients with common cold. *Eur J Pharmacol*. 183: 728–729.

Sebai, H., Jabri MA., Souli A., Rtibi K., Selmi S, Tebourbi O. (2014). Antidiarrheal and antioxidant activities of chamomile (*Matricaria recutita* L.) decoction extract in rats. J *Ethnopharmacol*. 152 (2): 327–32.

Sharafzadeh Shahram and Alizadeh Omid. (2011). German and Roman Chamomile. Department of Agriculture, Firoozabad Branch, Islamic Azad University, Firoozabad, Iran. *Journal of Applied Pharmaceutical Science* 01 (10): 01-05.

Singh Ompal., Khanam Zakia., Misra Neelam, and Srivastava Kumar Manoj. (2011). Chamomile (*Matricaria chamomilla* L.): An overview. *Pharmacogn Rev*. 5 (9): 82–95.

Srivastava K Janmejai., Shankar Eswar, and Sanjay Gupta. (2010). Chamomile: A herbal medicine of the past with bright future. Department of Urology & Nutrition, Case Western Reserve University, Cleveland, Ohio 44106. *Mol Med Report*. 1; 3 (6): 895–901.

Srivastava JK. Gupta S. (2007). Antiproliferative and apoptotic effects of chamomile extract in various human cancer cells. *J Agric Food Chem*.; 55 (23): 9470-8

Viapiana Agnieszka., Struck-Lewicka Wictoria. Pawel Konieczynski., Wesolowski Marek, and Kaliszan Roman. (2016). An approach based on HPLC-fingerprint and Chemometrics to quality consistency evaluation of *Matricaria chamomilla* L. Commercial samples. PMCID: PMC5073126.

Wald G., Brendler T. (1998). PDR for Herbal Medicines. Lst ed. Montville, (NJ) Medical Economics Company Publishers 07645-1742.

Yaniv, Z., Dafni, A., Friedman, J., and Palevitch, D. (1987). Plants used for the treatment of diabetes in Israel. *J Ethnopharmacol*. 19 (2): 145-51.

Yousef, A. Taher., Amel, M. Hamza., Awatef M. Samud., Jamal, S. Elmezogi. (2016). CNS depressant activity of chamomile methanol extract in mice. *Pakistan Journal of Pharmaceutical Research*. Vol. 2: (02): pp 98-102.