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FURTHER CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF THE IRANIAN LABIATAE FAMILY

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ABSTRACT

A very important medicinal plant family is the Labiatae family, also known as the mint family. Plants in this family are herbs or shrubs often with an aromatic smell. They are common in the Maltese Islands and other Mediterranean countries for the fact that some of them produce a high amount of essential oil that enables them to survive the hot summer season. Some examples from this family include mints, thyme, tulsi, spearmint and coleus. It is widely cultivated for medicinal, traditional and folk medicine, perfumery, culinary and ornamental purposes. Also they are used as culinary and ornamental plants. Medicinal constituents include the strong aromatic essential oil, tannins, saponins and organic acids. This family contains a wide variety of chemicals. A wide range of compounds such as terpenoids, iridiods, phenolic compounds and flavonoides have been reported from the members of the family. The oil is obtained by steam distillation. In aromatherapy, the oil is used for its soothing effects. The plant has sedative, diuretic, tonic, antispasmodic and antiseptic properties.

KEYWORDS: biologically active compounds, plant; phytochemical; plant biologically active compounds.

INTRODUCTION

Lamiaceae or Labiatae, also called as the mint family, is a family of flowering plants. It had traditionally been considered closely related to Verbenaceae,[1] but in the 1990s, phylogenetic studies showed that many genera classified in Verbenaceae belong instead in Lamiaceae.[2][3] The enlarged Lamiaceae contains about 236 genera and 6,900 to 7,200 species. The largest genera are *Salvia* (900), *Scutellaria* (360), *Stachys* (300), *Plectranthus* (300), *Hyptis* (280), *Teucrium* (250), *Vitex* (250), *Thymus* (220) and *Nepeta* (200).[4]

Phlomis species

The genus *Phlomis* comprises of the family Lamiaceae, being represented by 17 species in the flora of Iran among which 10, including *Phlomis* cancellata, are endemic.[5][6] Recently result showed some species of *Phlomis* are used in folk medicine as a stimulant or tonic and for wound healing, and many studies have shown various biological properties, including anti-inflammatory, immunosuppressive, antimicrobial and antimutagenic activities. Previous chemical investigations on different species of *Phlomis* have identified flavonoids and triterpenes.[7]

Phlomis cancellata Bunge

The essential oils obtained by hydrodistillation of the leaves and stems and by diethyl ether extract of aerial parts of *Phlomis cancellata* Bunge. endemic in Iran, were analyzed by GC and GC/MS. The oils obtained from the leaves of *P. cancellata* were rich in especially germacrene D (40.5%) and β-caryophyllene (18.6%). The other main component of the leaf oil was bicyclogermacrene (10.1%), whereas the stem oil contained mainly β-selinene (34.7%), germacrone (20.4%), germacrene B (17.0%) and γ-elemene (15.4%). The major components of the diethyl ether extract were germacrene D (19.7%), hexadecanoic acid (16.0%) and 6, 10, 14-trimethylpentadecan-2-one (14.1%). All of the oils were rich in sesquiterpene hydrocarbons.[7]

Phlomis persica Boiss. and *Phlomis olivieri* Benth.

The waterdistilled essential oils from aerial parts of *Phlomis persica* Boiss. and *Phlomis olivieri* Benth., which are endemic to Iran, were analyzed by GC and GC/MS. The oil of *P. persica* was found to contain germacrene D (38.2%), bicyclogermacrene (16.3%) and α-pinene (13.3%) as major constituents. The oil of *P. oliveri* was characterized also by higher amount of germacrene D (26.4%) and bicyclogermacrene (12.7%).

Both oils consisted mainly of sesquiterpene hydrocarbons.[8]

***Phlomis pungens* Willd.**

The composition of the essential oil from *Phlomis pungens* of Iran was analyzed by GC and GC/MS. Twenty-four compounds were identified in the oil of *P. pungens*, representing 91.7% of the total oil with germacrene D (24.5%), bicyclogermacrene (14.1%), α-pinene (13.5%) and (E)-β-farnesene (13.4%) as major constituents. The oil of *P. pungens* consisted of mainly sesquiterpenes.[9]

***Salvia* Species**

Salvia is a fascinating plant genus and one of the widespread members of the Labiatae (Lamiaceae) family, Some of these species feature prominently in the pharmacopoeias of many countries throughout the world. The range of traditional applications of the herbs in domestic medicine seems to be endless.[10] *Salvia* species are important because of their medicinal, traditional and economical uses.[11]

***Salvia aethiopis* L.**

The composition of the oils from leaves and flowers of *Salvia aethiopis* L. has been analysed by a combination of GC and GC/MS. During the flowering period, the oil consisted mainly of sesquiterpenes. The major components of the oil of *S. aethiopis* were β-caryophyllene (24.6%), α-copaene (15.5%) and germacrene D (13.5%).[12]

***Salvia brachysiphon* Stapf.**

The composition of the essential oils from *Salvia brachysiphon* Stapf. which are endemic to Iran, obtained by hydrodistillation were analyzed by GC and GC/MS. In the oil of *S. brachysiphon*, also β-caryophyllene (28.1%), α-pinene (20.6%), limonene (11.5%) and β-pinene (10.6%) were found to be the major constituents.[13]

***Salvia choloroleuca* Rech. F. & Aell.**

The aerial parts of *Salvia choloroleuca* was collected from Fasham, province of Tehran. Air-dried parts of *S. choloroleuca* were subjected to hydrodistilaton. The essential oil isolated by hydrodistillation from *S. choloroleuca* was obtained in yield of 0.45% (w/w). *S. choloroleuca* oil contained bicyclogermacrene (17.0%), germacrene D (15.7%), β-pinene (11.4%), α-pinene (9.7%), sabinene (9.6%), β-caryophyllene (5.2%) and spathulenol (5.1%) among the twenty-nine constituents characterized, comprising 97.3% of the total components detected. Sesquiterpenes comprised 50.8% and monoterpenes consisted of 46.3% of the oil.[14]

***Salvia compressa* Vent.**

The water distilled oils from the aerial parts of *Salvia compressa* Vent. collected from two different localities were analyzed by GC and GC/MS. The main components found in the oil of sample A, collected at Tange Malavi were β-caryophyllene (21.4%), α-pinene (18.4%) and caryophyllene oxide (13.2%), while in the oil of the sample B collected at Mamolan to Pole Dokhtar, β-caryophyllene (21.1%), 3-thujopsanone (15.3%), germacrene D (12.6%), bicyclogermacrene (11.6%) and nerol (10.7%) were the most abundant constituents. Both oils were richer in sesquiterpenes than monoterpenes.[15]

In another study, Ms Aboee-Mehrizi et al analyzed the hydrodistilled volatile oil from aerial parts of *Salvia compressa* by GC/MS. Eight components of the oil of *S.compressa* were characterized, representing 97.4% of the total components detected. The major constituent was identified as α- Pinene (70.9%), Borneol (7.1%), and Camphen (5.9%). Result showed that this endemic *S. compressa* species can be exploited as a source of biologically active constituent α- Pinene.[16]

***Salvia eremophila* Boiss.**

The water-distilled essential oil produced from the aerial parts of *Salvia eremophila* Boiss. was analyzed by GC/MS. Twenty-eight compounds were identified representing 96.0% of the total components detected with α-pinene (24.3%), bornyl acetate (18.9%), camphene (16.0%) and borneol (14.3%) as the major constituents.[17]

Also, the essential oil composition and in vitro antioxidant and antimicrobial activity of the essential oil and methanol extract of *Salvia eremophila* were evaluated in this research. GC and GC/MS analysis of the plant essential oil resulted in the identification of 28 compounds representing 99.2% of the oil. Borneol (21.8%), α-pinene (18.8%), bornyl acetate (18.6%) and camphene (6.5%) were detected as the major components consisting 65.8% of the oil. The plant essential oil and methanol extract were also subjected to screenings for the evaluation of their antioxidant activities using 2, 2-diphenyl-1-picrylhydrazyl (DPPH) and β-carotene-linoleic acid tests. While the plant essential oil showed only weak antioxidant activities, its methanol extract was considerably active in both DPPH (IC_{50}= 35.19 μg/ml) and β-carotene-linoleic acid (inhibition percentage: 72.4%) tests. Appreciable total phenolic content (101.2 μg/mg) was also detected for the plant methanol extract as gallic acid equivalent in the Folin-Ciocalteu test. The plant was also screened for its antimicrobial activity and good to moderate inhibitions were recorded for its essential oil and methanol extract against most of the tested microorganisms.[18]

***Salvia glutinosa* L.**

The aerial parts of *Salvia glutinosa* afforded in addition to lupeol, α- and β- amyrin a furanosesquiterpene, its structure being established by high field NMR techniques. The relative configuration at C-1, C-10, C-4, C-5 and C-6 of 6β-tigloyloxyglechomafuran (**Fig 1**) was determined by the observed NOE'S.[19]

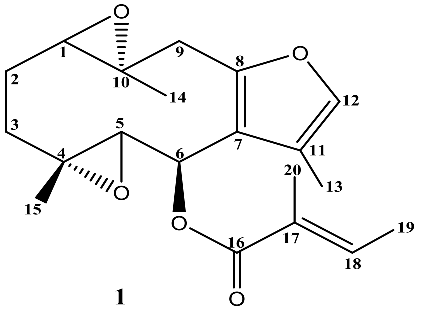

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Figure 1: Chemical structures of *6β-tigloyloxyglechomafuran* from *Salvia glutinosa* L. (1)

Furthermore, the volatile oil of *Salvia glutinosa* L. was tested against Gram-positive and Gram-negative bacteria. Antibacterial activity of methanolic extract of *S. glutinosa* showed by disc diffusion method using four bacteria in four different concentrations of the extract. The results showed *S. glutinosa* had its most effect on Gram-positive bacteria *Staphylococcus aureus*, and its effect was less on Gram-negative bacteria. The results showed that *S. glutinosa* has antibacterial activity. The effect was weak, but further investigation of other microorganisms on their antimicrobial activities is needed.[20]

***Salvia hydrangea* DC. ex Benth.**

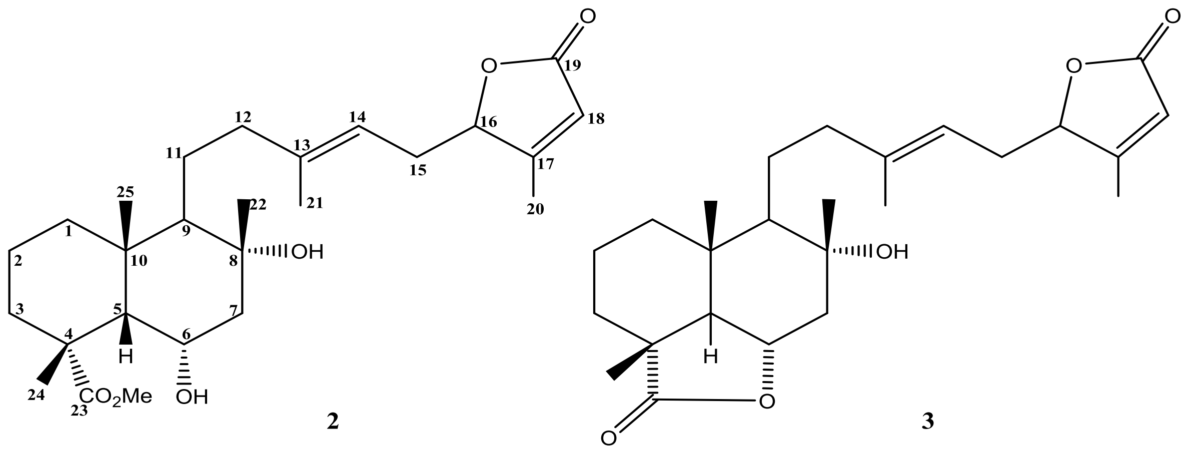
The composition of the essential oil of *Salvia hydrangea* DC. ex Benth. was analyzed by GC and GC/MS. The major constituents were spathulenol (23.1%), 1, 8-cineole (12.3%), α-pinene (10.0%) and β-caryophyllene (99%).[21]

In another study, the essential oils were obtained from the aerial parts of *S. hydrangea* and two other species and analyzed by GC/MS. The antimicrobial activity of essential oil from *Salvia* species may well be due to the presence of synergy between six tested compounds (linalool, 1, 8-cineole, α-pinene, β-pinene, β-caryophyllene and limonene) and other constituents of the oils with various degrees of antimicrobial activity. Among these, linalool and 1, 8-cineole (*Salvia hydrangea* oil contained 1, 8-cineole (15.2%)) had the highest antimicrobial activity.[22]

In addition, Bahadori & Mirzaei evaluated the phytochemical and biological effects of *S. hydrangea*. Total flavonoid and phenolic contents and brine shrimp lethality potential of the extracts were also determined. Findings showed moderate to high flavonoid and phenolic contents that *Salvia hydrangea* contain important metabolites and could be suggested for discovery of biologically active natural compounds.[11]

***Salvia hypoleuca* Benth.**

A $CHCl_3$ extract of the aerial parts of *Salvia hypoleuca* Benth. Has been shown to contain several C_{25}-terpenoids with previously unknown carbon skeleton, two crystalline compounds, molecular formula $C_{25}H_{40}O_6$ and $C_{25}H_{36}O_5$ (**Fig 2**). The nature of the all oxygen function of the first compound was established and the second compound was also an alcohol as shown by the IR spectrum, which further displayed hand for two γ-lactones. Furthermore, the ^{13}C NMR spectrum of **2** was in good agreement with the proposed stereochemistry. However, the configuration at C-16 and the absolute one were not determined; they named the free acid which corresponds to **2** and **3** salvileucolide.[23]



2 **3**

Figure 2: Chemical structures of Sesterterpenes from *Salvia hypoleuca* Benth. (2, 3)

In addition, Rustaiyan & Koussari also studied the more polar fractions of *Salvia hypoleuca* which afforded several further sesterterpenes, the salvileucolide methyl ester derivatives **7**, **8a**, **8b** and **9** as well as the isomeric epoxides **5a-5c** and the hydroperoxide **4** derived from salvileucolide-6,23-lactone and sesterterpene with a further new carbon skeleton, the keton **6** (**Fig 3**).[24]

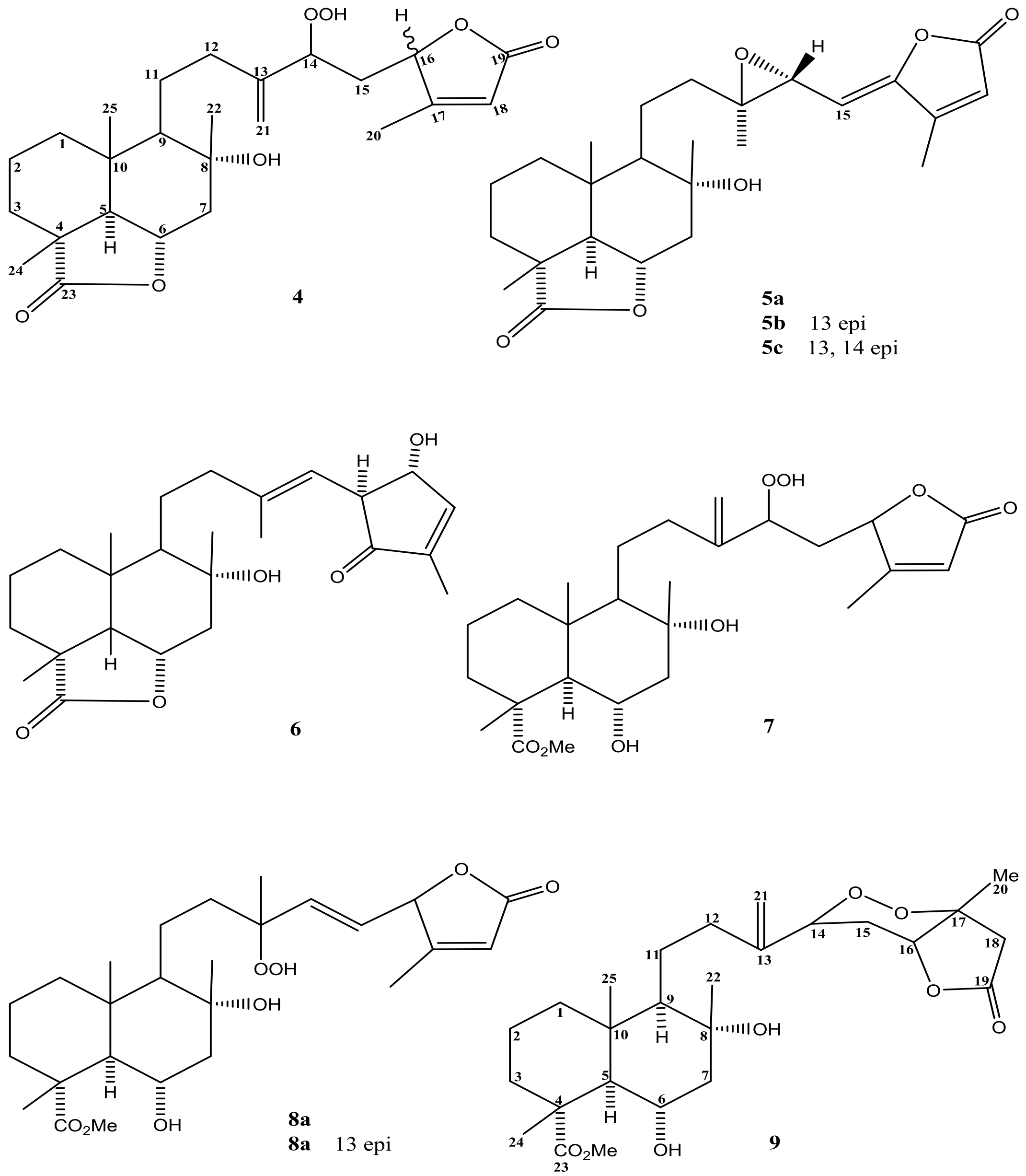


Figure 3: Chemical structures of further Sesterterpenes from *Salvia hypoleuca* Benth. (4-9)

In another study, the roots of *S. hypoleuca* were hydrodistilled in a Celevenger-type apparatus. Among 19 volatile compounds identified by GC/MS, hexadecanoic acid (27.4%) and viridiflorol (14.9%) were the major components.[25]

***Salvia indica* L.**

Chemical composition of the essential oil from the aerial parts of *Salvia indica* obtained by hydrodistillation were analyzed by GC and GC/MS. Twenty four components representing 95.9% of the oil of *S. indica* were identified of which α-pinene (17.0%), 1,8-cineole (13.4%) and β-pinene (11.3%) were the major constituents.[26]

***Salvia leriifolia* Benth.**

The essential oils obtained by hydrodistillation of the stem, leaf and flower *Salvia leriifolia* Benth. were analyzed by GC and GC/MS. Thirty-four compounds representing 92.4% of the stem oil of *Salvia leriifolia* were identified among them ß-pinene (19.0%), germacrene D (11.0%) and ô-cadinene (10.5%) were the major ones. The leaf oil of the plant was characterized by higher amount of ß-pinene (31.5%), 1, 8-cineole (24.7%) and ot-pinene (17.5%) among the thirty components comprising 98.9% of the total oil detected. Twenty-seven compounds representing 95.9% of the flower oil of the plant were identified among them y-terpinene (62.2%) and p-cymene (11.1%) were the major ones. The stem oil of the plant consisted mainly both monoterpenes and sesquiterpenes, while in leaf and flower oils monoterpenes predominated over sesquiterpenes.[27]

In addition, phytochemical investigation of the choloroform ($CHCl_3$) extract of *Salvia leriifolia* afforded 8(17), 12E, 14- labdatrien-6, 19- olide **(10)** that was found to prossess antibacterial activity against

Staphylococous aureus. Its structure was determined by a combination of spectral method (**Fig 4**).[28]

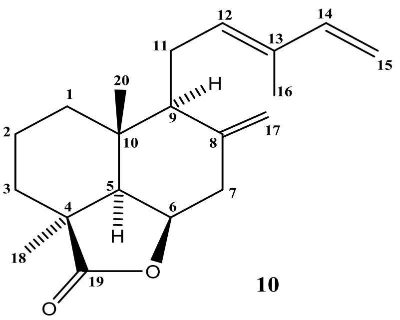


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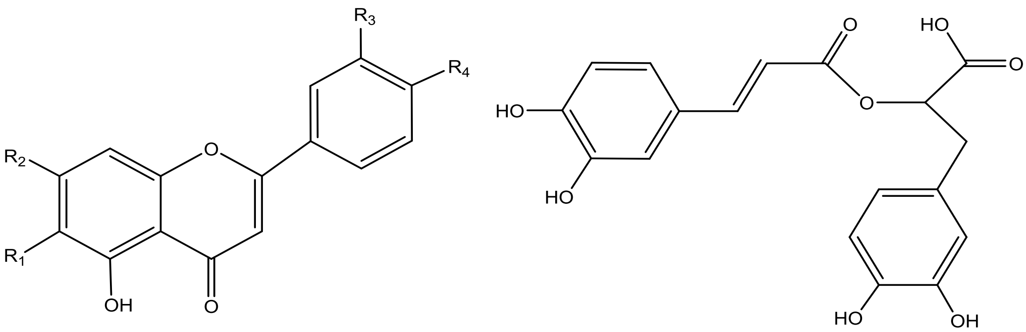
Figure 4: Chemical structures of Labdane Diterpenoid from *Salvia leriifolia* Benth. (10)

***Salvia limbata* C.A. Mey.**

The composition of the essential oils from aerial parts of *Salvia limbata* have been analyzed by a combination of GC and GC/MS. In the oil of *S. limbata*, α-pinene (23.7%), β-pinene (18.7%) and sabinene (14.5%) were found to be the major constituents; its oil consisted mainly of monoterpenes.[29]

In another study, the composition of the essential oils from *Salvia limbata* C.A. Mey. (syn. *S.chrysadenia*), obtained by hydrodistillation were analysed by GC and GC/MS. Germacrene D (24.5%), (Z)-ocimene (14.2%) and bicyclogermacrene (11.7%) were the main components among the thirty-eight constituents characterized in the oil of *S. limbata* representing 98.8% of the total components detected.[30]

In addition, the ethyl acetate and methanol extracts of the flowered aerial parts of *S. limbata* contained six flavones and rosmarinic acid that separated by using several chromatographic methods. The isolated compounds were identified as ladanein **(11)**, salvigenin **(12)**, luteolin 7-methyl ether **(13)**, cirsiliol **(14)**, eupatorin **(15)**, luteolin 7-O-glucoside **(16)** and rosmarinic acid **(17)** (**Fig 5)** which some of these flavonoids have been reported to show antibacterial and cytotoxic activities.[31]



	R_1	R_2	R_3	R_4
11	OH	OMe	H	OMe
12	OMe	OMe	H	OMe
13	H	OMe	OH	OH
14	OMe	OMe	OH	OH
15	OMe	OMe	OH	OMe
16	H	Glu	OH	OH

17

Figure 5: Structures of the Isolated Flavones and Rosmarinic Acid from *S. limbata*. (11–17)

***Salvia multicaulis* Vahl.**

The composition of the oils from leaves and flowers of *Salvia multicaulis* Vahl. Analyzed by GC and GC/MS. During the flowering period, the oil of *S. multicaulis* contained monoterpenes more than sesquiterpenes, also α-Pinene (26.0%), 1, 8-cineole + limonene (20.0%) and camphor (19.0%) were the predominant compounds among the 16 characterized in this oil which comprising 94.6% of the total components detected.[12]

In another study, the essential oil of aerial parts of *S. multicaulis* was isolated by hydrodistillation and analyzed by combination of capillary GC and GC/MS. The in vitro antimicrobial activity of the essential oil was studied against eight Gram-positive and Gram-negative bacteria (*Bacillus subtilis*, *Bacillus pumulis*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*) and three fungi (*Candida albicans*, *Saccharomyces cerevisiae* and *Aspergillus niger*). The results of antibacterial activity tests of the essential oil according to the disc diffusion method and MIC values indicated that all the samples have moderate to high inhibitory activity against the tested bacteria except for *P. aeruginosa* which was totally resistant. In contrast to antibacterial activity, the oil exhibited of *S. multicaulis* showed weak activity antifungal property.[32]

In addition, the essential oil of the aerial part of *S. multicaulis* analysis showed greatest antimicrobial activity against *Staphylococcus epidermidis* (5.3 µg/ml) and *S. cerevisiae* (9.3 µg/ml). The ethyl acetate showed greatest antimicrobial activity against *Bacillus subtilis* (106.7 µg/ml), *Candida albicans* (5.3 µg/ml) and ether extract showed greatest antimicrobial activity against

Klebseilla pneumoniae (10.7 µg/ml) and *Saccharomyces cerevisiae* (10.7 µg/ml).[33]

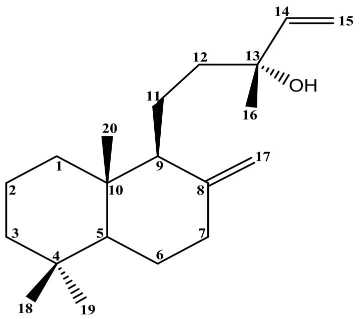
Salvia palaestina **Benth.**

The composition of the essential oils from aerial parts of *Salvia palaestina* Benth. analyzed by a combination of GC and GC/MS. The essential oils consisted sesquiterpenes predominated over monoterpenes. β-Caryophyllene (36.4%) was the predominant compound in the oil of *S. palaestina*.[29]

Salvia persepolitana **Boiss.**

The essential oils obtained by hydrodistillation of the aerial parts of *Salvia persepolitana* Benth. analyzed by GC and GC/MS. Manool (37.3%) was the main component among the twenty-three constituents characterized in the oil of *S. persepolitana* representing 90.0% of the total components detected.[34]

In other study, Purification of chloroform extract of aerial parts of *S. persepolitana* carried out by column chromatography on silica gel with a gradient of *n*-hexan/ethyl acetate. At the end of chromatography, the column was eluted by methanol. Further purification was carried out by column chromatography (smaller columns) and thin layer chromatography (glass plates) in *n*-hexane-ethyl acetate as solvent for several times and yielded pure compounds. The structure of purified natural products was elucidated by using Nuclear Magnetic Resonance (NMR) spectroscopy and Mass spectrometry. The chloroform extract of *S. persepolitana* yielded two known diterpenoids as manool **(18)** and sclareol **(19)** and one known flavonoid namely ladanein **(20) (Fig 6)**. The amount of purified sclareol was 3% (18 g) of the total plant weight, so *S. persepolitana* can be a good sourse for sclareol.[35]



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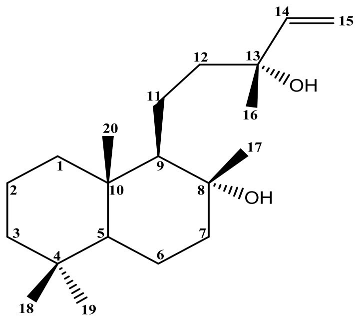

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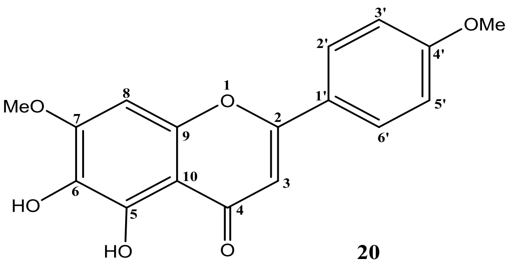

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Figure 6: Structures of the *Salvia persepolitana* Boiss. (18-20)

Salvia reuterana **Boiss.**

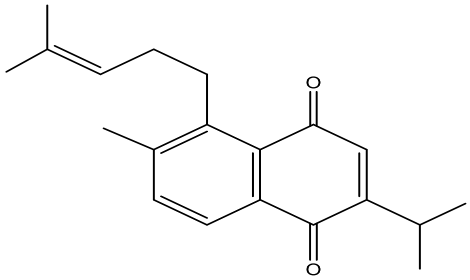
Salvia reuterana is a medicinal herb with various therapeutic usages. The aim of the present review is to take account of pharmacological properties of *Salvia reuterana*. The literature with respect to various pharmacological properties of *Salvia reuterana*. *S. Reuterana* possesses neurological, antimicrobial, antioxidant, chemotherapeutic, and antidiabetic properties and can be used as an alternative for treatment of several disorders.[36]

The essential oils obtained by hydrodistillation of the leaves, stems and flowers of *Salvia reuterana* (Lamiaceae) were analysed by GC and GC/MS. Germacrene D and β-caryophyllene were the major constituents in all the three oils: (28.5, 27.7 and 32.5%) and (15.5, 11.4 and 16.6%), respectively. Bicyclogermacrene (10.2 and 13.2%) was also prodominated in the stem and flower oils. The composition of the oils was mostly quantitativel rather than qualitatively different. All the oils consisted mainly of sesquiterpenes and a small percentage of non-terpenoid compounds. In all the three oils, monoterpenes were in a concentration less than 0.5%. Antibacterial activity was determined by the measurement of growth inhibitory zones.[37]

In another study, evaluated the chemical compositions of the essential oils of *S. reuterana* Boiss. and its antimicrobial properties. Volatile fractions were isolated by simultaneous distillation-extraction technique. The analysis of the essential oils was performed using the GC and GC/MS. The in vitro antimicrobial activities against 10 bacterial strains were evaluated using the disk diffusion and micro-well dilution techniques. Twenty-six compositions were identified in leaves and 31 in flowers of the essential oil of *S. reuterana*. The lowest concentration of *S. reuterana* essential oil was highly effective in inhibiting the growth of *Candida albicans*. *A. niger* was the most resistant microbes against the extract of flowers and leaves of the species of the essential oils. *Staphylococcus aureus* was highly resistant to the essential oil of flowers and leaves of *S. reuterana* but it showed sensitivity to the extract of flowers and leaves of *S. reuterana*. Considering the relatively high antimicrobial activities of the species, the effective compounds in the flowers can be used for antibacterial purposes.[38]

***Salvia rhytidea* Benth.**

The composition of the essential oils from aerial parts of *Salvia rhytidea* Benth. have been analyzed by a combination of GC and GC/MS. During the fowering period, oils consisted mainly of monoterpenes. The major components of the oil of *S. rhytidea* were β-phellandrene (22.7%) and sabinene (13.5%).[39] Sahandinone **(21)**, 12-deoxysalvipisone **(22)**, miltirone **(23)**, 7α-acetoxyroyleanone **(24)**, and labda-7, 14-dien-13-ol **(25) (Fig 7)** were isolated from the roots of *Salvia rhytidea* Benth. The ^{13}C-NMR spectroscopic data were revised for the quaternary carbons of both Sahandinone and miltirone with the help of HMBC spectra in respect to the spectral data previously reported in the literature. Sahandinone and miltirone very potent anticancer agents were isolated in high yields from the roots of the plant. The biological activities of the plants' constituents were reported in the literature as antimicrobial, cytotoxic and antimalarial.[40] Also the methanolic extract of *S. rhytidea* Benth. was rich in flavonoids and tannins.[41]



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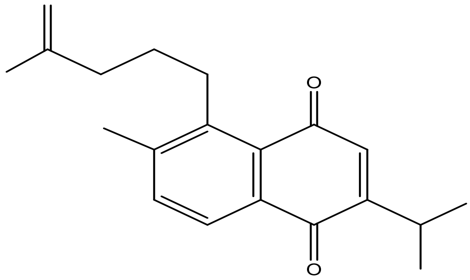

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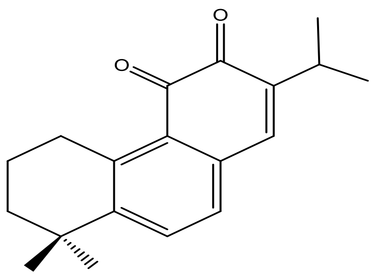

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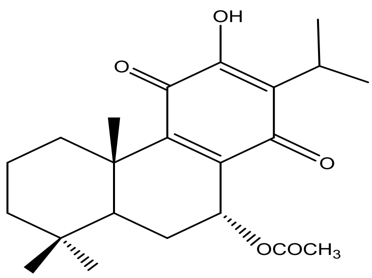

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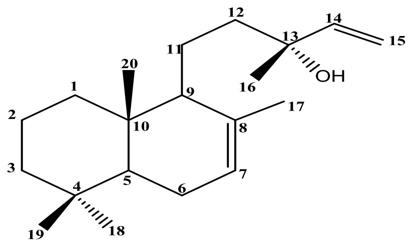

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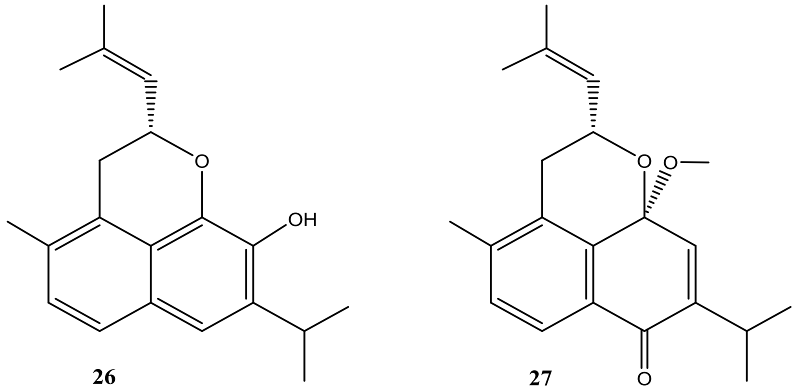
Figure 7: Structures of the *Salvia rhytidea* Boiss. (21-25)

***Salvia sahendica* Boiss. & Buhse.**

The essential oil of the aerial parts of *Salvia sahendica* Boiss. et Buhse. has been analyzed by a combination of GC and GC/MS. Among the 24 components identified in this oil, α-pinene (29.4%) and β-pinene (34.8%) were found to be the major constituents.[42]

In a screening of Iranian plants for antiprotozoal activity, an n-hexane extract of the roots of *Salvia sahendica* potently inhibited the growth of *Plasmodium falciparum* K1 strain. Subsequent HPLC-based activity profiling led to the identification of seven known and one new abietane-type diterpenoid. Structure elucidation was achieved by analysis of spectroscopic data including 1D and 2D NMR. The absolute configuration of sahandol **(26)** and sahandone **(27)** were assigned by comparison of experimental ECD spectra with calculated ECD data, using time-dependent density functional theory and methanol as the solvent **(Fig 8)**. In vitro biological activity against *P. falciparum* and *Trypanosoma brucei rhodesiense* STIB 900 strain and cytotoxicity in rat myoblast (L6) cells were determined. The IC_{50} values of the compounds ranged from 0.8 µM to over 8.8 µM against *P. falciparum*, and from 1.8 µM to over 32.3 µM against *T. brucei rhodesiense*. The cytotoxic IC_{50} values ranged from 0.5-15.5 µM. Selectivity indices for *P. falciparum* were 0.1 to 18.2, and 0.1 to 1.2 for *T. brucei rhodesiense*.[43]



26 27

Figure 8: Structures of the *Salvia sahendica* Boiss. & Buhse. (26, 27)

***Salvia sclareopsis* Bornm. Ex Hedge.**

The composition of the essential oils from *Salvia sclareopsis* Bornm. Ex Hedge. which is endemic to Iran obtained by hydrodistillation were analyzed by GC and GC/MS. The oil was rich in β-caryophyllene (22.5%) and germacrene D (15.5%).[44] The antioxidant properties were measured by DPPH and β-carotene linoleaic acid tests. The result of DPPH assays showed that leaves are higher antioxidant campared with other organs, while in β-carotene linoleaic acid assay all organs have same antioxidant acivity.[45]

***Salvia syriaca* L.**

Rustaiyan reports in 1987 were shown the extract of the aerial parts of *Salvia syriaca* afforded a polar sesterterpene lactone **(28)** with four hydroxy groups. Acetylation gave a triacetate **(Fig 9)**.[46]

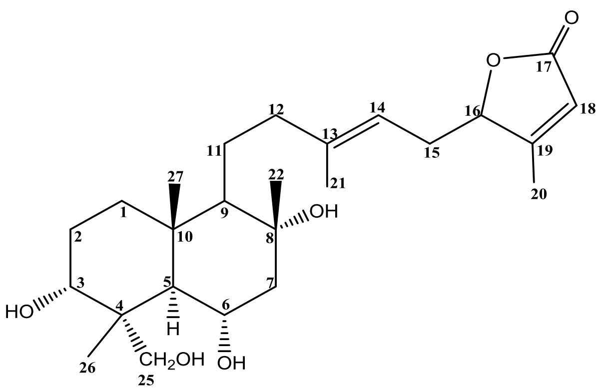


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Figure 9: Structures of the *Salvia syriaca*. (28)

Eidi et al in 2011 reported the ethanolic extract exhibited antinociceptive activity against writhing-induced by acetic acid. In xylene ear edema test, *Salvia syriaca* L. ethanolic extract showed significant activity in the mice and this plant has antinociceptive and anti-inflammatory effect on the mice.[47]

Salvia urumiensis

The essential oil isolated by hydrodistillation from the aerial parts of *Salvia urumiensis* was obtained in yields of 0.25% (w/w). Twenty-nine constituents, representing 87.0% of the total components in the oil of *S. urumiensis*, were characterized by spathulenol (14.6%) and -pinene (14.0%), bornyl acetate (7.7%), and germacrene D (5.2%).[48]

***Salvia verbascifolia* M.Bieb.**

The composition of the essential oils from *Salvia verbascifolia* M.Bieb. obtained by hydrodistillation were analyzed by GC and GC/MS. The oils of *S. verbascifolia* were rich in β-caryophyllene (18.5%), germacrene D (34.1%) and caryophyllene oxide (10.3%).[13]

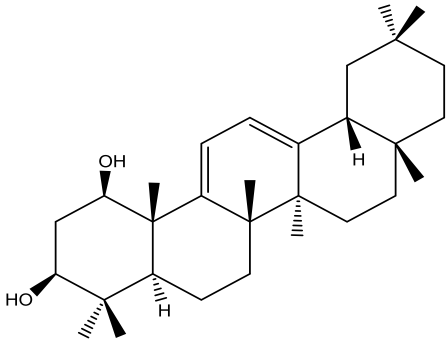
***Salvia verticillata* L.**

The essential oils of *Salvia verticillata* from two regions of Iran were obtained by GC and GC/MS. 1, 8-cineole (19.0%), germacrene D (17.0%) and α-pinene (15.8%) were the main components in the essential oil of *S. verticillata* that collected from Gachsar region and β-caryophyllene (12.0%), germacrene D (10.7%) and spathulenol (10.0%) found to be the major constituents in those which were harvested from Khalkhal region.[49]

In another report, Compositions of the essential oils were identified and analysed using GC and GC/MS and by measuring the Retention Index and Massspectrums.The antibacterial effects of essences were surveyed on two bacteria using tubed dilution method to determine the MIC and MBC. Acquired analysis showed that efficiency of the essences in *Salvia verticillata* was 0.92. The essence of *Salvia verticillatahas* the most antibacterial effects upon *Escherichia coliand* the least one on *Staphylococcus aureus*. As a result, the essences of this herb have considerable antibacterial effects and can be desirably replaced in lieu of synthetic antibiotics, which bacteria become more resistance apropos of them.[50]

Salvia xanthocheila **Boiss.**

From the chloroform extract of the aerial parts of *Salvia xanthocheila*, one new triterpene, together with two known diterpenes, two known flavonoids and a phytosterol was isolated. On the basis of comprehensive spectroscopic analyses, including electron ionisation mass spectra, ^{1}H-NMR, ^{13}C-NMR, 1-D nuclear Overhauser effect, distortionless enchancement by polarisation transfer, H, H correlation spectroscopy, heteronuclear multiple quantum coherence, rotating frame Overhauser enhancement spectroscopy spectra and comparison with spectral data of known compounds, the structure of new compounds was established as 1β, 3β-dihydroxy-olean-9(11), 12-dienyl **(29)**. The five known compounds were 7α-acetoxyroyleanone **(30)**, taxodione **(31)**, salvigenin **(32)**, apigenin-7, 4'-dimethyl ether **(33)** and β-sitosterol **(34)**, respectively **(Fig 10)**. These known structures are isolated from the aerial parts of *S. xanthocheila* for the first time.[51]



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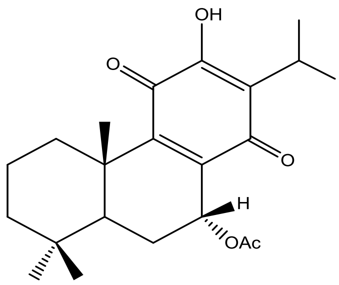

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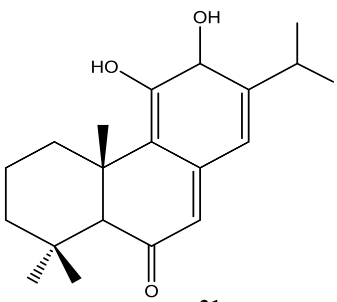

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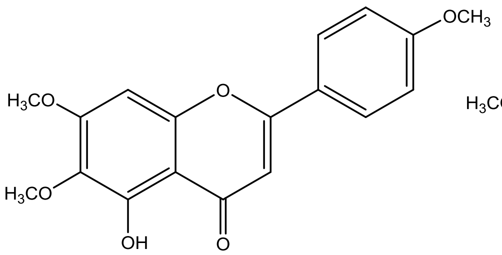

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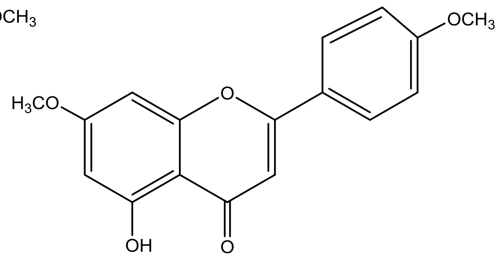

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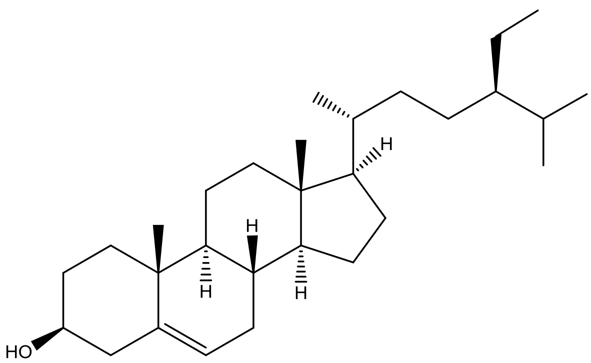

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Figure 10: Structures of the *Salvia xanthocheila*. (29-34)

***Scutellaria* species**

Scutellaria (Lamiaceae), commonly known as 'Skullcaps', has been extensively used in Traditional Chinese Medicine (TCM). Recently, much emphasis has been given to this genus due to the rich source of bioflavonoids that contribute to its biological properties. Therefore, different species of *Scutellaria* are being explored worldwide.[52] *Scutellaria* is represented in the flora of Iran by twenty species including eight endemics with known antiproliferative potentials.[5] [6] [53]

***Scutellaria litwinowii* Bornm. & sint.ex Bornm.**

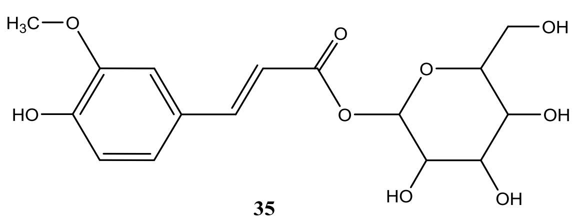
Scutellaria litwinowii Bornm. & Sint. ex Bornm. is one of the Iranian species of *Scutellaria.* There are widespread reports about the cytotoxic and antitumor effects of some species of genus *Scutellar*. The apoptotic effects of *S. litwinowii* on 2 myeloid cell lines, apoptosis-proficient HL60 cells and apoptosis-resistant K562 cells, were analyzed that It could be concluded that *S. litwinowii* induced apoptosis in both apoptosis-proficient and apoptosis-resistant leukemic cells.[53]

Also the report of Afsharzadeh demonstrates that S. *litwinowii* extract protects PC12 cells against serum/glucose-deprivation-induced cell death by antioxidant mechanisms, which indicates the potential therapeutic application of *S. litwinowii* in managing cerebral ischemic and neurodegenerative disorders.[54]

The composition of the essential oil from *Scutellaria litwinowii* Bornm. & sint.ex Bornm.(syn. *S. chorassanica*) obtained by hydrodistillation was analysed by GC and GC/MS. The oil of *S. litwinowii* was characterized by higher amount of (E)-β-farnesene (20.3%) and germacrene D (16.9%) among the thirty-two components comprising 91.9% of the total oil detected.[55]

***Scutellaria pinnatifida* A. Hamilt**

Phytochemical analysis of the methanolic and dichloromethane extracts of the aerial parts of *Scutellaria pinnatifida* led to the isolation of a phenylpropanoid, 1-o-feruloyl-β-D-glucose **(35)**, two known flavonoids including luteolin-7-o-glucoside **(36)** and apigenin-7-o-glucoside **(37)**, three known phenylethanoid glycosides composed of syringalide A **(38)**, phlomisethanoside **(39)** and verbascoside **(40)**, and oleic acid **(41) (Fig 11)**. The extracts were also evaluated for their radical scavenging activity and insecticidal property by 2, 2-diphenyl-1-picryl-hydrazyl (DPPH) assay and contact toxicity method, respectively. Among the extracts, the methanol extract showed the most potent free radical scavenging activity with an IC_{50} value of 0.044 ± 0.350 mg/mL which could be attributed to the presence of the isolated phenolic compounds. In the case of insecticidal activity, the n-hexane extract displayed the most potent activity and caused 10%, 15%, and 40% mortality to *Oryzaephilus mercator* at the concentration of 5, 10, and 15 mg/mL after 4 h of exposure.[56]



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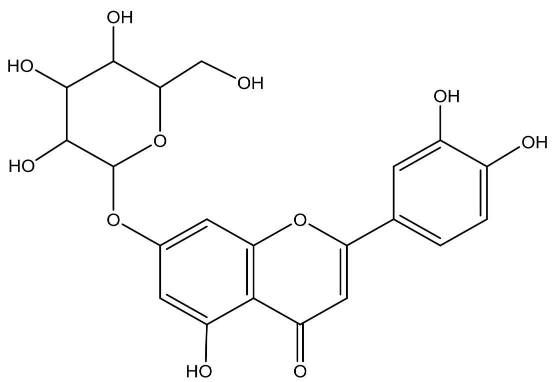

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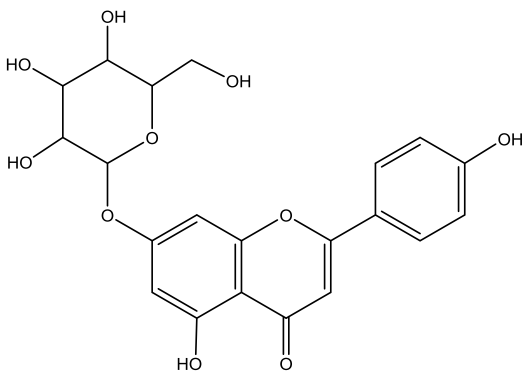

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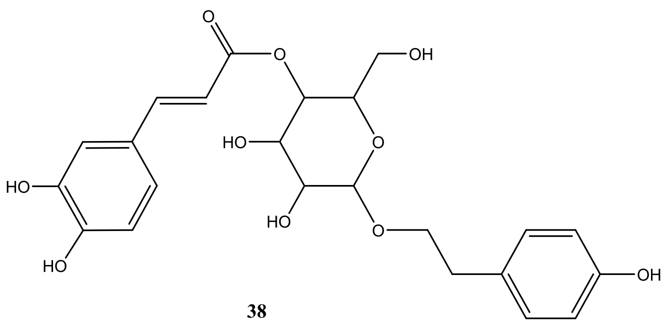

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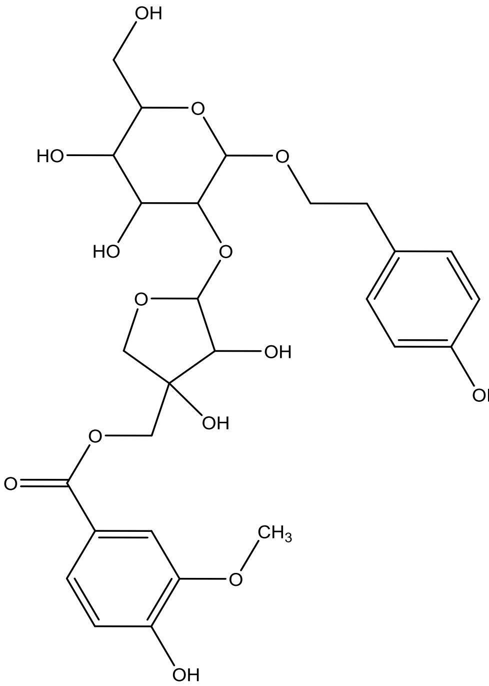

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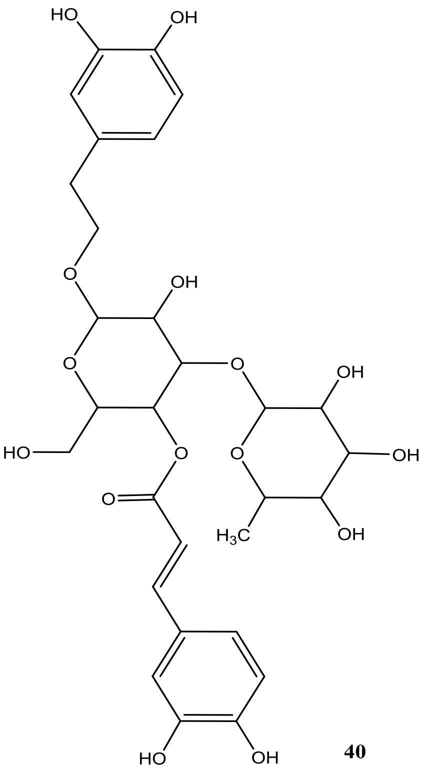

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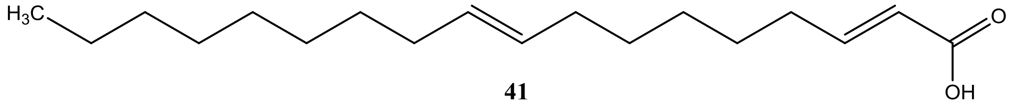

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Figure 11: Structures of the *Scutellaria pinnatifida*. (35-41)

Sashourpour reported that the extracts of *S. pinnatifida*, significantly inhibit the harmful effects of toxic α-synuclein aggregates and can be used to treat amyloid-related disorders.[57]

In another report, Water-distilled essential oil from the aerial parts of *S. pinnatifida* was analyzed by GC and GC/MS. Methyl chavicol (81.9%) was the main component among the 11 constituents characterized in the oil of *S. pinnatifida* representing 100% of the total components detected.[58]

Stachys species

Stachys genus with medicinal properties and high polymorphic features has been considered one of the largest genera of Lamiaceae.[59] *Stachys* species are used as food plants by the larvae of some *Lepidoptera* species, including the moths *Coleophora auricella*, *C. lineolea*, and *C. wockeella*, all recorded on *St. Officinalis*.[60]

Stachys acerosa Boiss.

The oil obtained by hydrodistillation of the aerial parts of *Stachys acerosa* Boiss., which is endemic to Iran, was analyzed by GC/MS. There were twenty components including cis-chrysanthenyl acetate (41.0%) and linalool (23.5%), comprising 92.1% of the total oil detected. The oil was richer in oxygenated monoterpenes than sesquiterpenes.[61]

In another study, the essential oil of the aerial parts of *St. acerosa*, which belongs to the Lamiaceae family and grows in central Iran, was obtained by a hydrodistillation method and analyzed by GC and GC/MS apparatus. Fourteen compounds representing 98.8% of the oil were identified. Among them N-methylisatin (30%), α-pinene (25%), sabinene (12.3%), and 2-hydroxyacetophenone (11.2%) were the major constituents of the oil, which were obtained in 0.1% yield.[62]

Stachys asterocalyx Rech. f.

Water-distilled essential oil from the aerial parts of *Stachys asterocalyx* Rech. f. which is endemic to Iran was analyzed by GC and GC/MS. The major components of the oil of *Stachys asterocalyx* were α-bisabolol (25.1%) and linalool (18.0%).[63]

Stachys byzanthina C. Koch.

The chemical composition of the oil obtained by hydrodistillation of the aerial parts of *Stachys byzanthina* C. Koch. was investigated by GC and GC/MS analysis. Twenty-four components representing 88.5% of the total oil were identified, of which sesquiterpenes; α- copaene (16.5%), spathulenol (16.1%), β- caryophyllene (14.3%) and β- cubebene (12.6%) were the major components.[64]

In another study, the oil obtained by hydro-distillation and steam distillation of the aerial parts of *St. byzanthina* grown in Iran were analyzed by GC/MS. Both hydrodistilled and steam distilled essential oils of the aerial parts of *St. byzantina* were rich in sesquiterpenes such as α-copaene (16.6% and 10.4%), spathulenol (16.1% and 18.5%) and β-caryophyllene (14.3% and 13.5%), respectively.[65]

In another report, Anti-inflammatory effects of acetone and methanolic extract of aerial parts of *St. byzanthina* was investigated. In the carrageenan-induced paw edema, both extract revealed dose-related inhibitory effects on carrageenan-induced rat paw edema over the dose range 50-200 mg/kg. The anti-inflammatory activities of these extract was similar to a high dose of indomethacin (5 mg/kg) in both carrageenan-induced paw edema and formalin-induced paw licking. In conclusion, the present data provide further evidence for an important role of extract of *St. byzanthina* in the inhibition of pain and inflammatory processes.[66]

***Stachys benthamiana* Boiss.**

The composition of the essential oil from *Stachys benthamiana* Boiss. obtained by hydro-distillation was analyzed by GC and GC/MS. Twenty compounds were identified in the oil of *St. benthamiana*, representing 91.2% of the total oil, with germacrene D (16.8%), linalool (16.6%) and β-caryophyllene (11.0%) as the major constituents. The endemic oil of *St. benthamiana* consisted mainly of sesquiterpenes.[67] Saeedi in 2008 reported that methanol extracts of *St. benthamiana* have a potential as source of antibacterial agent of natural origin.[68]

***Stachys inflata* Benth.**

The essential oils obtained by hydrodistillation of three different stages of growth, per-flowering, flowering and post-flowering of *Stachys inflata* Benth. were analyzed by GC and GC/MS. Twenty-eight components were identified in the pre-flowering oil and flowering oil, and twenty-four components in the post-flowering oil, representing 98.3%, 91.9% and 90.1% of their total oils, respectively. All three samples were characterized by higher amounts of germacrene D (30.3%, 32.9% and 15.4%) and limonene (16.4%, 15.6% and 13.1%), respectively. The other main component in the pre-flowering oil was α-pinene (18.5%) and in the post-flowering oil, bicyclogermacrene (14.3%), spathulenol (13.6%) and α-pinene (12.1%) were predominated.[69]

In another study, Composition and antioxidant and antimicrobial activities of essential oil and methanol extract polar and nonpolar sub fractions of *St. inflata* were determined. GC and GC/MS analyze of the essential oil showed 45 constituents representing 95.4% of the oil, the major components linalool (28.5%), α-terpineol (9.4%), spathulenol (8.4%) and (2*E*)-hexenal (4.6%) constituted 51.0% of it. Essential oil and extracts were also tested for their antioxidant activities using 2, 2-diphenyl-1-picrylhydrazyl (DPPH) and β-carotene/linoleic acid assays. In the DPPH test, IC_{50} value for the polar sub fraction was 89.5 μg/ml, indicating an antioxidant potency of about 22% of that of butylated hydroxytoluene (IC_{50} = 19.7 μg/ml) for this extract. In β-carotene/linoleic acid assay, the best inhibition belonged to the nonpolar sub fraction (77.0%). Total phenolic content of the polar and nonpolar extract sub fractions was 5.4 and 2.8% (w/w), respectively. The plant also showed a week antimicrobial activity against three strains of tested microorganisms. Linalool and α-terpineol were also tested as major components of the oil and showed no antioxidant but considerable antimicrobial activities.[70]

In another report by Ahmadvand et al in 2017 that identified the various antioxidative activities of ethanol and methanol extracts, and chemical composition of *Stachys inflata* Benth. leaves essential oil. Ethanol and methanol extracts of *St. inflata* Benth. leaves were primarily prepared. The total antioxidant capacity of sample was assessed by phosphomolybdate method. Total phenol content and total flavonoid content were determined by Folin-Ciocalteu and Zhishen methods. The component of *St. inflata* Benth. leaves essential oil was analyzed with gas chromatography/mass spectrometry (GC/MS). It was demonstrated that the total antioxidant capacity of ethanol and methanol extracts of *St. inflata* Benth. leaves were 4.30± 0.17; 3.63± 0.23 mg of ascorbic acid equivalents/g of extract. Moreover, the total phenol content ethanol and methanol extracts of *St. inflata* Benth. leaves were 830.334± 26.41; 384.29± 13.37 mg of gallic acid equivalents /g of extract, and flavonoid content ethanol and methanol extracts of *St. inflata* Benth. leaves were 17.09± 0.154; 31.18± 1.03 mg of quercetin equivalents /g of extract. GC/MS data and retention indices of *St. inflata* Benth. leaves essential oil samples were used to identify 54 constituents. These compounds make up a total of 48.8% essential oil. Phenol, 2-methyl-5(1-methyleth; Phenol, 5-methyl-2-)1methyleyth; 2-pentadecanone and hexadecanoic acid are the major compounds of *St. inflata* Benth. leaves essential oil. This study indicated that *St. inflata* Benth. leaves essential oil has remarkable antioxidant properties. Furthermore, *St. inflata* Benth. leaves essential oil was identified as an easily accessible source of natural antioxidants such as Phenol,2-methyl-5(1-methyleth; Phenol,5-methyl-2-)1methyleyth; 2-pentadecanone,6,10,14-trimet; Veridi florol; 2-cycohexen-1-on,2-methyl-5-and 1H-cycloprop[e]azulen-7-ol,dec. It may also be suitable to be used in food and pharmaceutical applications. This study demonstrated that *St. inflata* Benth. leavesare easily accessible sources of natural antioxidants. Therefore, they may be suitable to be used in food and pharmaceutical applications.[71]

***Stachys lavandulifolia* Vahl.**

The constituents of the oil obtained by hydrodistillation of *Stachys lavandulifolia* Vahl. grown in Iran were analyzed using GC and GC/MS. Fifty-five compounds were observed, of which 44 could be identified. The major components found in the oil were α-pinene (20.1%), β-pinene (12.1%) and spathulenol (7.2%).[72]

The results of the research by Rahzani et al shown that *St. lavandulifolia* possesses marked anti-oxidative stress activity and it can be useful as a supplement in the management of diseases related to oxidative stress.[73]

***Stachys multicaulis* Benth.**

Water-distilled essential oil from the aerial parts of *Stachys multicaulis* Benth. Growing Wild in Iran was analyzed by GC and GC/MS. Bicyclogermacrene (23.0%), spathulenol (20.7%), germacrene D (12.4%) and caryophyllene oxide (11.1%) were the predominant compounds in the oil of *St. multicaulis*.[63]

The antioxidant activities of *St. multicaulis* have been determined by using 1, 1-diphenyl-2-picrylhydrazyl (DPPH) as well as by flow injection analysis-luminol chemiluminescence (FIA-CL). The extracts were shown to possess a significant scavenger activity against DPPH free radical and an inhibitory effect on H_2O_2- or HOCl-luminol chemiluminescence and the results concluded that the extract have a potential source of antioxidants of natural origin.[74]

***Stachys obtusicrena* Boiss.**

Water-distilled essential oil from the aerial parts of *Stachys obtusicrena* Boiss. which is endemic to Iran was analyzed by GC and GC/MS. In the oil of *St. obtusicrena*, α-pinene (34.6%), germacrene D (8.0%) and bicyclogermacrene (7.8%) were found to be the major constituents.[63]

***Stachys persica* Gmel.**

The oils obtained by hydro-distillation and steam distillation of the aerial parts of *Stachys persica* Gmel. grown in Iran were analyzed by GC/MS. The essential oil obtained by hydrodistillation of the aerial parts of *St. persica* was characterized by a high amount of non-terpenoid components of which methyllinoleate (27.7%), hexadecanoic acid (9.8%) and 6,10,14-trimethyl-2-pentadecanone (9.2%) were the major constituents, whereas the steam distilled oil of the plant contained hexadecanoic acid (27.2%), carvacrol (9.4%) and eugenol (5.2%).[65]

***Stachys pilifera* Benth.**

The oil obtained by hydrodistillation of the aerial parts of *Stachys pilifera* Benth. which are endemic to Iran, was analyzed by GC/MS. Thirty compounds representing 88.9% of the oil of *St. pilifera* were identified, among them *cis*-chrysanthenyl acetate (25.2%) and *trans*-verbenol (19.7%) being the major ones. The oil was richer in oxygenated monoterpenes than sesquiterpenes.[61]

***Stachys turcomanica* Trautv.**

The composition of the essential oil from *Stachys turcomanica* obtained by hydro-distillation was analyzed by GC and GC/MS. Twenty-eight compounds were identified in the oil of *Stachys turcomanica* representing 93.0% of the total oil with germacrene D (17.4%), 7-epi-α-selinene (10.5%), βelemene (9.2%) and β-pinene (8.6%) as the major constituents.[30]

***Stachys schtschegleevii* Sosn.**

The composition of the essential oil obtained by hydro-distillation from the leaves of *Stachys schtschegleevii* Sosn. before the flowering stage analyzed by GC and GC/MS. Forty-five compounds representing 98.7% of the total oil were identified, of which α-pinene (36.4%), germacrene D (18.6%), limonene (8.2%), and piperitone (6.2%) were the major constituents. Furthermore, antibacterial activity of the entire oil and its two main monoterpenes was evaluated against six Gram-positive and Gram-negative bacteria. The oil exhibited moderate activity against the tested bacteria.[75]

In another study, the results showed the various *Stachys* species (especially *St. byzantina* and *St. persica*) are valuable sources of natural compounds with important biological properties. Nine *Stachys* plants were collected from different regions of Iran. Cytotoxic activities of methanol, 80% methanol and dichloromethane (DCM) extracts of these plants were assessed on three human cancer cell lines (HL-60, K562 and MCF-7 cells) with the MTT assay, while antioxidant and antimicrobial activities were determined on methanol extracts by DPPH and nutrient broth micro-dilution assays, respectively. DCM extract of *St. pilifera* Benth. had the lowest IC_{50} in three cancer cell lines ranging from 33.1 to 48.2 µg/ml, followed by the 80% methanol extract of *St. persica* S.G.Gmel. ex C.A.Mey. (IC_{50} range: 62.1–104.1 µg/ml) and DCM extract of *St. byzantina* C. Koch (IC_{50} range: 62.7–131.0 µg/ml). *St. byzantine*, *St. lavandulifolia* Vahl., *St. acerosa* Boiss., *St. obtusicrena* Boiss. and *St. persica* showed lowests IC_{50} values in the DPPH scavenging assay (135.1, 162.6, 164.7, 169.4 and 172.4 µg/ml, respectively), while their total phenolic contents were 23.9, 18.2, 18.6, 20.4, 27.8 mg equivalent of Gallic acid in 1 g dry plant, respectively. The methanol extracts of *St. byzantina* and *St. persica* inhibited all six tested Gram-negative and Gram-positive bacterial strains.[76]

***Teucrium* species**

Teucrium is a genus of mostly perennial plants in the family Lamiaceae. Members of the genus are commonly known as germanders. *Teucrium* species are rich in essential oils. Some (notably *Teucrium fruticans*) are valued as ornamental plants and as a pollen source, and some species have culinary and medical value.[77]

Teucrium persicum Boiss.

The composition of the essential oil from the aerial parts of *Teucrium persicum* Boiss. obtained by hydrodistillation was analyzed by GC and GC/MS. Epi-α-Cadinol (23.2%) and α-pinene (17.3%) were the main components among the thirty-one constituents characterized in the oil of *T. persicum* representing 95.9% of the total components detected.[78]

Teucrium persicum is an Iranian endemic plant belonging to the Lamiaceae family which has traditionally been used to relieve abdominal pains. Tafrihi in 2014 have used a highly invasive prostate cancer cell line, PC-3, which is an appropriate cell system to study anti-tumor properties of plants. A methanolic extract obtained from *T. persicum* potently inhibited viability of PC-3 cells. The viability of SW480 colon and T47D breast cancer cells was also significantly decreased in the presence of the *T. persicum* extract. Flow cytometry suggested that the reduction of cell viability was due to induction of apoptosis. In addition, the results of wound healing and gelatin zymography experiments supported anti-cell invasion activity of *T. persicum.* Interestingly, sublethal concentrations of *T. persicum* extract induced an epithelial-like morphology in a subpopulation of cells with an increase in E-Cadherin and β-Catenin protein levels at the cell membrane. These results strongly suggest that *T. persicum* is a plant with very potent anti-tumor activity.[79]

In another study, a new guaiane type skeleton sesquiterpenoid named guaiasistanol (6α, 10α-epoxy-4α-hydroxyguaiane) **(42) (Fig 12)** was isolated from chloroform part of the *Teucrium persicum* extract, also chrysothol. This compound was evaluated for inhibitory activity against acetylcholinesterase and it showed a moderate activity with 28% inhibition.[80]

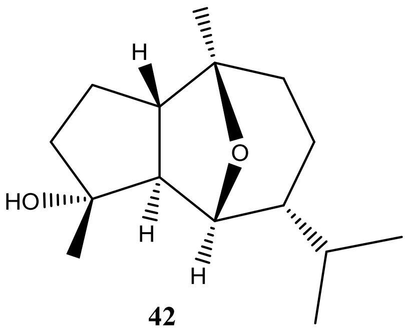

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Figure 12: Structures of the *Teucrium persicum* Boiss. (42)

***Teucrium Stocksianum* Boiss.**
The essential oil of the aerial parts of *Teucrium Stocksianum* Boiss. subsp. *Stocksianum* from Iran was analyzed by capillary GC, GC/MS techniques. The major constituents were α-Pinene (36.6%), β-pinene (14.1%) and β- Cubebene (5.0%).[81]

***Thymus* species**
In Iran 14 species of *Thymus* are present, among which 4 are endemic.[6] *Thymus* species have several folkloric uses, especially for flavoring purposes. Thymol and carvacrol are the major compounds in most of the *Thymus* essential oils. The therapeutic potential of thyme rests on contents of thymol, carvacrol, flavonoids, eugenol, aliphatic phenols as well as luteolin, saponins, and tetra methoxylated flavones. The essential oil of thyme has antibacterial, antiseptic, antifungal, anti-parasitic and antioxidant activity.[82] [83] It is used in folk medicine as diaphoretic, antimyotic, antiseptic and sedative and for treatment of insomnia.[84]

***Thymus caucasicus* Wind. Ex Ronniger subsp. *Grossheimii* (Ronniger) Jalas.**
Chemical composition of the essential oil from the aerial parts of *Thymus caucasicus* obtained by hydrodistillation was analyzed by GC and GC/MS. Twenty three compounds representing 90.5% of the oil of *T. caucasicus* including 1, 8-cineole (15.4%) and (E)-nerolidol (13.8%) as the main constituents were identified.[26] Also in another study in 2009, Seventeen compounds were identified that the essential oil of *T. caucasicus* includes thymol (34.2%), methyl chavicol (25.1%) and γ-terpinene (12.7%) as the major constituents.[85]

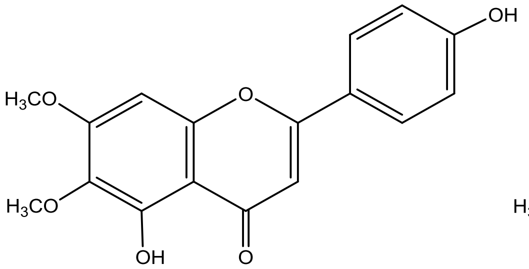
***Thymus kotschyanus* Boiss. & Hohen.**
A comparison of the chemical composition, antioxidant and antibacterial activity of the essential oils obtained from the leaves of *Thymus kotschyanus* Boiss. & Hohen. was carried out. The oils were obtained by hydrodistillation and were analyzed by GC and GC/MS. Twenty - nine components 96.6% of the *T. kotschyanus* oil have been identified. In the oil of *T. kotschyanus* leave, carvacrol (24.4%), β-caryophyllene (14.5%), γ-terpinene (12.4%), α-phellandrene (10.8%), p-cymene (9.8%) and thymol (6.8%) were the predominant compounds. Antioxidant activity was tested according to the DPPH radical scavenging method with measurement of sample concentration providing 50% inhibition (IC_{50}). Antibacterial activity was determined by measurement of the minimum inhibitory concentration (MIC) using the broth dilution method. The essential oil showed free radical scavenging and antibacterial activity.[86]

In another study, The essential oils of the aerial parts of *T. kotschyanus* Boiss. obtained by hydrodistillation (HD) and microwave oven distillation (MD) were analyzed by GC and GC/MS. 39 componentswere identified in the essential oil of this plant (95.0% in HD and 94.8% in MD). The components of theessential oil extracted by MD were similar to those obtained by HD. *T. kotschyanus* essential oil was characterizedby a high amount of carvacrol (64.6% in HD and 44.7% in MD). Other major compounds were identified asp-cymene, γ-terpinene and L-Borneol. Thymoquinone was absent in HD method. Although the time of MDwas 12 times less than HD, but the percentage of essential oil was only 15% less (1.2% in MD and 1.4% inHD). Moreover, the amount of carvacrol as the main component of the plant essential oil, in MD was 20% lessthan HD.[87]

***Zhumeria majdae* Rech.**
Zhumeria majdae Rech. known locally by the name Mohre-Khosh.[5] This plant is used for its pleasant scent and also as a drug by the natives in southern region of Iran.[88] The studies of *Z. majdae* was collected from

south of Iran in 1983 and 1992, showed the the presence of Camphor and Linalool as two monoterpenes, triterpene and two flavonoids 6-methoxyapigenin 7-methyl ether (Cirsimaritin) **(43)** and 6-methoxyluteolin 4- methyl ether (Desmethoxycentaureidin) **(44)** were investigated by NMR and GC/MS spectra. [89] [90] It should be noted that two diterpene quinones with rearranged abietane skeletons, 12, 16-dideoxy aegyptinone B **(45)** and 12-deoxy-salvipisone **(46)** with manool **(47)** **(Fig 13)** from the roots of *Z. majdae* have been isolated.[91]

In another study, the stem oil of *Z. majdae* analyzed by GC and GC/MS that Manool (37.1%) and α-cedrol (6.0%) were the main constituents.[92]



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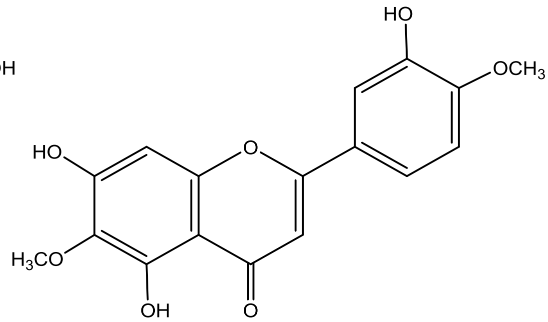

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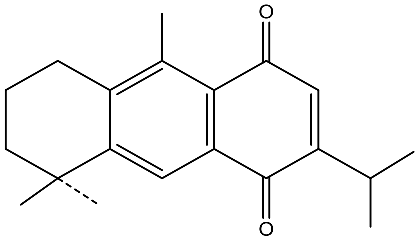

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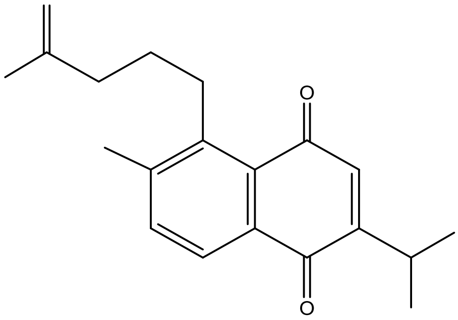

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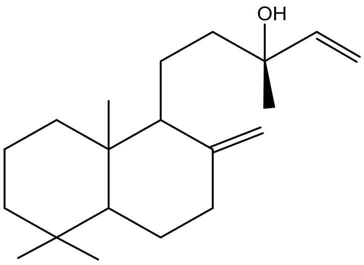

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Figure 13: Structures of the *Zhumeria majdae* Rech. (43-47)

***Ziziphora capitata* L.**

The genus *Ziziphora* is represented in the flora of Iran by four species[5] that have been used as sedative, stomachic and carminative.[93]

The compositions of the *Ziziphora capitata* L. SUBSP. *capitata* are as follow; Ninteen components were identified in the oil of the plant which represented about 98.8% of the total composition that Germacrene D (31.1%) and Z-β-ocimene (15.4%) were the major components of the oil. The oil of *Ziziphora capitata* consists of six monoterpene hydrocarbons (35.1%), nine sesquiterpene hydrocarbons (49.4%), three oxygenated sesquiterpenes (8.4%) and one aliphatic acid (5.9%) that showed *Z. capitata* is rich in sesquiterpenes and the oil was insensitive against Gram-positive and Gram-negative bacteria except against *Shigella flexneri*.[94]

***Ziziphora clinopodioides* Lam.**

The compositions of the *Ziziphora clinopodioides* Lam. From two different locations were analyzed. Twenty components were identified in the oil of sample A (oil from Lorestan) which represented about 100% of the total composition of the oil that consist of eight oxygenated monoterpenes (72.1%), nine monoterpene hydrocarbons (24.5%) and three sesquiterpenes (3.4%). Thymol (53.6%), *p*-cymene (10.5%), carvacrol (8.7%), γ-terpinene (6.7%) and 1, 8-cineole (5.4%) were the major components of the oil of the plant.

Twenty-six components were identified in the oil of sample B (oil from Qom), making up 96.2% of total composition that consist of 12 oxygenated monoterpenes (72.1%), ten monoterpene hydrocarbons (14.1%), three sesquiterpenes (9.1%) and one aliphatic alcohol (0.9%). 1, 8-cineole (21.6%) and terpinen-4-ol (18.2%) were the major components in this oil followed by linalool (7.9%), pulegon (7.7%) and α-terpineol (5.3%). Also the antibacterial assays showed that the oils of both samples from *Z. clinopodioides* inhibited the growth of all bacteria.[94]

***Ziziphora persica* Bunge.**
The composition of the essential oil from *Ziziphora persica* Bunge. was obtained by hydro-distillation and analyzed by GC and GC/MS. The oil of *Z. persica* was characterized by high amount of pulegone (27.8%), neomenthol (22.5%) and *p*-menth-3-en-8-ol (18.1%) among the 34 components, comprising 94.7% of the total oil detected.[95]

CONCLUSIONS
In this review, we will be discussing the constituents and biological activities of some of the genus of the Iranian Labiatae family namely: *Phlomis*; *Piatychaeta*; *Salvia*; *Scutellaria*; *Stachys*; *Teucrium*; *Thymus*; *Zhumeria* and *Ziziphora*.

CONFLICT OF INTEREST
The authors declare no conflicts of interest.

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