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Review Article

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CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF SELECTED GENERA OF THE IRANIAN LABIATAE (LAMIACEAE) FAMILY- A REVIEW (PART ONE)

Prof. Abdolhossein Rustaiyan[1*], Afsaneh Faridchehr PhD.[2], Mahdieh Ariaee Fard MSc.[3] and Zahra Sadat Aghakhah Razlighi MSc.[4]

[1,2,4]Department of Chemistry, Faculty of Basic Sciences, Science and Research Branch Islamic Azad University, Tehran, Iran.

[3]Faculty of Pharmaceutical Chemistry, Department of Phytochemistry and Essential Oils Technology, Islamic Azad University, Pharmaceutical Sciences Branch (IAUPS), Tehran, Iran.

***Corresponding Author: Prof. Abdolhossein Rustaiyan**

Department of Chemistry, Faculty of Basic Sciences, Science and Research Branch Islamic Azad University, Tehran, Iran.

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ABSTRACT

Lamiaceae or Labiatae is a family of flowering plants commonly known as the mint or deadnettle family. Many of the plants are aromatic in all parts and include widely used culinary herbs, such as basil, mint, rosemary, sage, savory, marjoram, oregano, hyssop, thyme, lavender, and perilla. Some species are shrubs, trees (such as teak), or rarely, vines. Many members of the family are widely cultivated, for not only their aromatic qualities but also their ease of cultivation, since stem cuttings readily propagate them. References such as Phytochemistry, Journal of Essential Oil Research, Flavour and Fragrance Journal and Journal of Herbal Drugs etc. used to search scientific contribution until 2017, using relevant keywords. Literature focusing on Essential Oil, Chemical Composition and their chemical structure and in short we refere to the Biological Activities from the some genus. Treatments with Essential Oil from genera in this review have shown positive result in biological activities such as traditionally used in rheumatism, anti-bacterial effects, free radical scavenging and activity in cancer cell line. In this review, we will be discussing the constituents and biological activities of some of the genera of the Iranian Labiatae family namely: *Ajuga*; *Ballota*; *Cyclotrichium*; *Eremostachys*; *Hymenocrater*; *Marrubium*; *Melissa*; *Mentha*; *Micromeria*; *Nepeta*; *Ocimum* and *Perovskia*.

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

INTRODUCTION

The family has a cosmopolitan distribution.[1] The enlarged Lamiaceae contains about 236 genera and has stated to contain aproximately 7000 species. The largest genera are *Salvia* (900), *Scutellaria* (360), *Stachys* (300), *Plectranthus* (300), *Hyptis* (280), *Teucrium* (250), *Vitex* (250), *Thymus* (220), and *Nepeta* (200). *Clerodendrum* was once genera of over 400 species,[2] but by 2010, it had narrowed to about 150.[3] The family Labiatae has traditionally considered closely related to the Verbenaceae; in the 1990s, phylogenetic studies suggested that many genera classified in the Verbenaceae should classified in the Lamiaceae [4] [5] or to other families in the order Lamiales.

The alternate family name Labiatae refers to the fact that the flowers typically have petals fused into an upper lip and a lower lip (labia in Latin). The flowers are bilaterally symmetrical with five united petals and five united sepals. They are usually bisexual and verticillastrate (a flower cluster that looks like a whorl of flowers, but actually consists of two crowded clusters). Although this still considered an acceptable alternative name, most botanists now use the name Lamiaceae in referring to this family. The leaves emerge oppositely, each pair at right angles to the previous one (decussate) or whorled. The stems are frequently square in cross section, [6] but this is not found in all members of the family, and is sometimes found in other plant families.

Ajuga Species

Ajuga chamaecistus Ging. ssp. *chamaecistus*

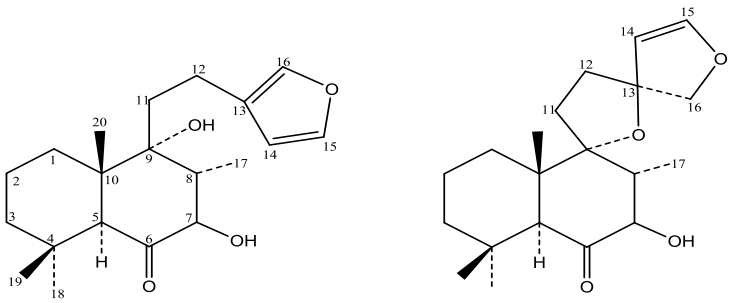
The hydro-distilled oil from the aerial parts of *Ajuga chamaecistus* Ging. ssp. *chamaecistus* was analyzed by GC and GC/MS. Nineteen compounds were identified representing 96.3% of the oil, with β-pinene (15.0%) and linalool (14.5%) as major constituents.[7]

Chemical investigations of some *Ajuga* species have shown flavonoids and neo-clerodane diterpenoids.[8-10] Studies on the aerial parts of *A. multiflora* revealed that one flavonoid and two iridoid glycosides were isolated and identified as apigenin, 8-o-acetylharpagide and harpagide based on spectroscopic evidence.[11]

***Ballota* Species**

***Ballota aucheri* Boiss**

From the *Ballota* genera already found furanolabdanes, which have reported from seven species. Two new labdanes, 7β, 9α-dihydroxy-15-16-epoxy labda-13 (16), 14-Dien-6-one **(1)** and 7β-hydroxy-9α, 13, 15, 16-bis-epoxy labd-14-en-6-one **(2)** were isolated from the aerial parts of *Ballota aucheri* (**Fig 1**).[12]

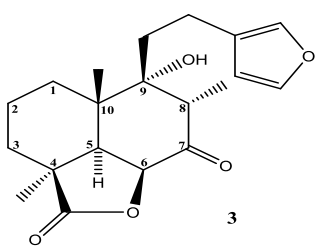


1 **2**

Figure 1: Chemical structures of Furanolabdanes in *Ballota aucheri*.

In another study, the aerial parts of *B. aucheri* afforded ballotinone **(3)**, five new labdanes **(4, 5,6a-c)** and balloaucherolide **(7)**, a seco-labdane (**Fig 2**).[13]

In addition, the aerial parts of *B. aucheri* contained, in addition to the known diterpenes **8** and **9**, a further furolabdane **(10)**, the seco derivative **11** as well as the dimer **12** (Persianone) (**Fig 2**).[14]



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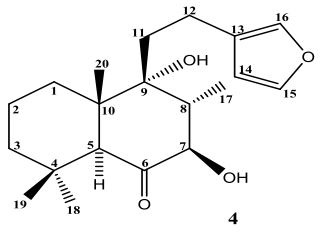

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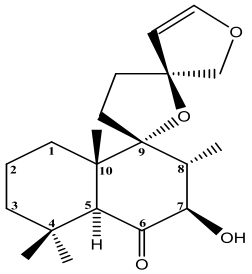

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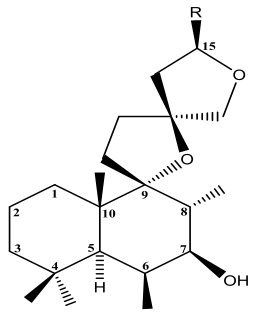
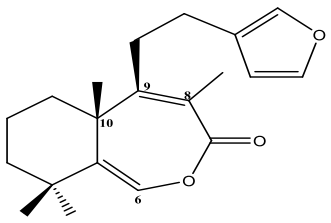


	6a	**6b**	**6c**
R	OMe	OMe	OEt
		15 epi	



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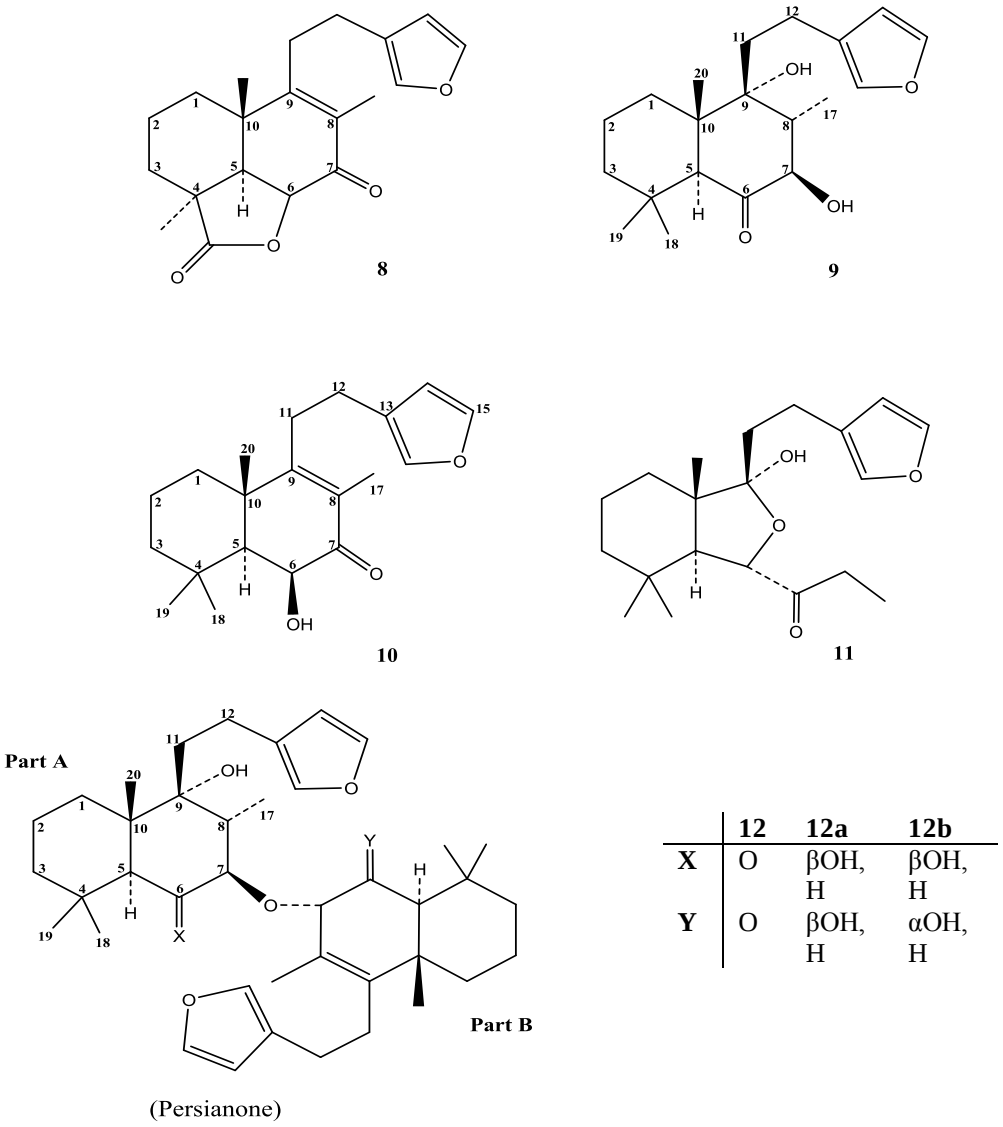


	12	12a	12b
X	O	βOH, H	βOH, H
Y	O	βOH, H	αOH, H

Figure 2: Chemical structures of *Ballota aucheri*.

In another study, the comparison of the essential oil from *B. aucheri* obtained by hydro-distillation was analyzed by GC and GC/MS. α-Cadinol (21.0%) and dehydroaromadendrane (11.8%) were the main components among the 37 constituents characterized in the oil of *B. aucheri*, representing 82.5% of the total components detected.[15]

Ballota nigra

Chemical composition of the essential oil from the aerial parts of *Ballota nigra* obtained by hydro-distillation was analyzed by GC and GC/MS. β-pinene (39.0%) and α-pinene (34.5%) were the main components among 12 constituents characterized in the oil of *B. nigra*, representing 99.3% of the total compounds detected.[16]

***Cyclotrichium* Species**

***Cyclotrichium leucotrichum* (Stapf. ex Rech.f.)**

The genera *Cyclotrichium leucotrichum* is representing in the flora of Iran by four species including three that are endemic.[17] [18] Only a few reports on the analysis of oils of *Cyclotrichium* species have been published.[19-22]

The water-distilled oils from the aerial parts of *Cyclotrichium leucotrichum* (Stapf. ex Rech.f.) was analyzed by GC and GC/MS. Linalool (38.7%), limonene (15.4%) and spathulenol (12.6%) were the predominant compounds in the oil of *Cyclotrichium leucotrichum*. The oil of the plant consisted mainly of monoterpenes.[23]

***Cyclotrichium straussii* (Bornm.) Rech.f.**

The composition of the essential oils from a Labiatae species of Iran was analyzed by GC and GC/MS. β-pinene (33.8%) and 1, 8-cineole (14.7%) were the main components among the 18 constituents characterized in the oil of *Cyclotrichium strausii* representing 93.2% of the total components detected.[22]

***Eremostachys* Species**

***Eremostachys labiosa* Bunge**

The Iranian flora comprises 15 species of *Eremostachys*, among which five are endemic.[17] Phytochemical studies on a few species of *Eremostachys* revealed the presence of alkaloids, coumarins, flavonoids,[24] phenyl ethanoid glycosides,[25] iridoid glycosides [26] and monoterpene glycosides.[27] [28]

The essential oils obtained by hydro-distillation of the flower, leaf and stem of *E. labiosa* Bunge. was analyzed by GC and GC/MS. The chief constituents found in the aerial part of *E. labioa* were 6,10,14-trimethyl 2-pentadecanone (22.3%), 1,8-cineole (21.7%) and α-pinene (16.5%), while the main components identified in the stem oil were α-phellandrene (28.6%), β-phellandrene (11.4%), α-pinene (10.1%) and tetradecane (10.0%). The composition of both oils differs quantitatively and qualitatively.[29]

***Eremostachys macrophylla* Montbr. & Auch.**

The essential oils obtained by hydro-distillation of the flower, leaf and stem of *Eremostachys macrophylla* Montbr. & Auch, was analyzed by GC and GC/MS. The major compounds in the flower oil of *E. macrophylla* were 1,8-cineole (19.0%) and germacrene D-4-ol (10.6%), whereas the leaf oil contained α-pinene (30.0%), 1,10-di-epi cubenol (22.7%), elemol (13.3%) and bornyl acetate (11.0%).The stem oil of the plant was dominated also by 1,10-di-epi cubenol (34.4%) and elemol (24.0%).[29]

In another study, the volatile constituents of the aerial parts of *E. macrophylla* were growing in the wild in Iran have examined by GC/FID and GC/MS. Altogether, 16 compounds were identified, constituting approximately 96.4% of the oil. The oil of *E. macrophylla* consisted mainly of germacrene D (47.1%), germacrene-B (17.8%), γ-elemene (9.1%), myrcene (6.7%), β-elemene (2.7%), and β-phellandrene (2.6%).[30]

In another study, the aerial part extracts of *Eremostachys macrophylla* that has been traditionally used in wound healing, snake bites, rheumatism and joint pains, investigated for general toxicity, anti-proliferative, free radical scavenging and anti-bacterial effects. Moreover, preliminary phytochemical investigations were carried out on the extracts.[31]

***Hymenocrater* Species**

***Hymenocrater calycinus* (Boiss.) Benth.**

Nine species of the genera *Hymenocrater* are found in Iran, of which four are endemic: *H. yazdianus* Rech.f., *H. oxyodontus* Rech.f., *H. platystegius* Rech.f. and *H. incanus* Bounge.[17] [32]

Water-distilled essential oils from aerial parts of *Hymenocrater calycinus* (Boiss.) Benth. collected from three different locations of Bojnourd (Iran) village of Yekeh-Shakh (sample A), village of Nodeh (sample B) and Golestan forest (sample C), were analyzed by GC and GC/MS. α-Pinene (10.5%) and sabinene (10.5%) were the major constituents of sample A. The main constituents found for sample B were spathulenol (35.4%) and abietatriene (13.4%). In sample C, β-caryophyllene (32.8%) and caryophyllene oxide (16.1%) were the most abundant compounds.[33]

In another study, aerial part of plants which growing in Baladeh-Noor and Orost-Sari regions were collected and the essential oils were extracted by hydro-distillation using Clevenger apparatus. GC and GC/MS apparatuses carried out the analysis of the composition of the essential oils. 54 compounds were identified in the essential oils of *H. calycinus* populations. Most components of the plant were identified in the Baladeh-bala site (36 compounds), while the highest yields was observed in the Orost site (1.27%). Hexadecanoic acid, Spathulenol and 6, 10, 14- Trimethyl-2-pentadecanone were dominant components of essential oils in three sites.[34]

***Hymenocrater elegans* Bunge**

The composition of the essential oil from *Hymenocrater elegans* Bunge. obtained by hydro-distillation was analyzed by GC and GC/MS. Nineteen compounds were identified in the oil of *H. elegans* representing 92.0% of the total oil with spathulenol (49.5%) and caryophyllene oxide (12.9%) as the major constituents.[35]

In another study, the composition of the essential oil obtained from the dried aerial parts of *Hymenocrater elegans* Bunge. analyzed by GC and GC/MS. Forty-five components have been identified in the oil of *H. elegans*. The major constituents of the oil were manoyl oxide (22.7%), sclareol (12.4%) and 1, 8-cineole (8.3%). The antimicrobial activity of *H. elegans* oil studied using the disk diffusion method and determination of MIC values. The *H. elegans* oil exhibited concentration-dependent antibacterial activity on *Bacillus subtilis, Staphylococcus aureus, Escherichia coli* and *Salmonella typhi*. The essential oil did not show antifungal activity against fungi.[36]

In another study, *H. elegans* Bunge collected from Firoozkooh. Dried leaves of the plant were steam distilled in a Kaiser-Lang apparatus for 45 min. The oil produced at the yield of 0.1% (based on dry weight). GC and GC/MS analysis of this oil revealed the presence of 33 compounds, among which germacrene D (10.2%), β-caryophyllene (9.7%), α-humulene (9.6%), β-bourbonene (7.1%) and germacrene-B (6.9%) were the major constituents.[37]

***Hymenocrater platystegius* Rech.f.**

GC and GC/MS analyzed water-distilled essential oils from the leaves and stems of Hymenocrater platystegius, which is endemic to Iran. Seventeen compounds representing 91.7% of the leaf oil and 10 compounds representing 90.7% of the stem oil of *H. platystegius*

were identified. Both oils were rich in α-pinene (16.7% and 18.6%) and spathulenol (17.1% and 17.9%). The other main component of the leaf oil was 1, 8-cineole (12.9%), and of the stem oil, *cis*-calamenene (11.27%).[38]

In another study, the essential oil composition of the aerial parts of *H. platystegius* Rech.f, GC and GC/MS studied a plant endemic to Iran. The oil obtained by hydro-distillation of air-dried samples. The yield of the oil was 0.1% (w/w) and it had a pale yellow color with a distinct sharp odor. Forty-two compounds identified representing about 99.8% of the total oil. Monoterpene hydrocarbons (45.3%) constituted the principal fraction, followed by oxygen-containing monoterpenes (26.7%). The main components were found to be Ot-pinene (20.6%), 1, 8-cineole (18.6%), β-pinene (9.9%), ô-cadinene (4.2%), myrcene (3.5%) and linalool (3.3%).[39]

***Hymenocrater yazdianus* Rech.f.**

Water-distilled essential oils from the leaves of *Hymenocrater yazdianus*, which is endemic to Iran, was analyzed by GC and GC/MS. Fifty-five components of the leaf oil of *H. yazdianus* were characterized, representing 95.1% of the total components detected. The major constituents were identified as 1, 8-cineole (17.6%), β-caryophyllene (13.9%), α-pinene (10.6%) and caryophyllene oxide (10.4%). The antibacterial activity of the stem, leaf and flower oils of *H. yazdianus* against seven Gram-positive and Gram-negative bacteria were determined using the MIC method. The growth inhibitory zone (mm) was also measured.[40]

***Marrubium* Species**

***Marrubium crassidens* Boiss**

The composition of the essential oils from the aerial parts of *Marrubium crassidens* Boiss. obtained by hydro-distillation was analyzed by GC and GC/MS. The oil of *M. crassidens* characterized by higher amount of β-caryophyllene (20.3%), germacrene D (12.9%), caryophyllene oxide (11.1%) and cubenol (11.0%) among the fourteen compounds comprising 91.7% of the total oil detected. The oils consisted mainly of sesquiterpenes.[41]

In another study, methanol extract from aerial parts of *M. crassidens* assessed for its anti-proliferative activity in the breast cancer cell line MCF-7 through MTT bioassay using cell viability and cytotoxicity indices. The antioxidant property of *M. crassidens* extract together with its phenolic and flavonoids content evaluated, as well. According to data obtained in the study, *M. crassidens* exhibited anti-proliferative activity with a gradual rise in cytotoxicty effect setting out on 240 µg/mL concentration of the extract. Moreover, the IC_{50} value for antioxidant activity of the extract was determined as 40 µg/mL and values for the total phenolic and flavonoids calculated as 512.64 mg gallic acid equivalent and 212.73 mg quercetin equivalent per 100 g of dry plant material. Generally, the observed antiproliferative and antioxidant properties of *M. crassidens* could be certified to the high amounts of phenolic and flavonoid content detected in the extract.[42]

In another study, Methanolic extract of *M. crassidens* Boiss has potent antioxidative effects and can have cardio-protective effects on Ischemia/Reperfusion (I/R) injuries in heart. The extract prepared by maceration. The isolated rat hearts were perfused by Krebs-Henseleit solution enriched with the extract (0, 10, 50, and 100µg/ml), using the langendorff method. After 15 minutes stabilization, the hearts subjected to 30 minutes regional ischemia and then 120 minutes reperfusion. During the experiments, hemodynamic functions recorded and cardiacarrhythmias were determined. At the end, the infarct size measured. *M. crassidens* has protective effects against I/R injuries in isolated rat hearts and the protective effects could be related to antioxidative activities of the extract.[43]

In another study, the volatile composition of *M. crassidens* has studied. The investigated taxa are *M. crassidens* Bioss. which is native in Iran. The essential oil was obtained by hydro-distillation in a modified Clevenger-type apparatus and their analysis was performed by GC and GC/MS. Twenty-two components in the oil of *M. crassidens* representing 90.5% of the total oil was identified. The essential oils were characterizied by a high amount of sesquiterpens with germacrene D (14.2%), bicyclogermacrene (14.2%), β-caryophyllene (29.0%) and spathulenol (5.6%) as the major constituents of *M. crassidens*.[44]

Marrubium propinquum* and *Marrubium parviflorum

Two species of genera *Marrubium* studied for their volatile components. The essential oils were extracted from aerial parts of the plants through hydro-distillation using a Clevenger apparatus. Later, CG and CG/MS analysis were applied to assess the chemical components of the essential oils. Analysis of the *M. propinquum* essential oil resulted in the identification of 22 components, representing 79.6% of the total essential oil that principally contained oleic acid (19.0%), β-caryophyllene (7.4%) and m-tolualdehyde (5.2%). In the case of *M. parviflorum*, 20 components were identified, representing 83.8% of the *M. parviflorum* essential oil, among them oleic acid (11.8%), α-pinene (10.2%) and germacrene D (9.8%) were the main compounds. Regarding the results of this study in both essential oils after the non-terpenoids, sesquiterpene hydrocarbons possessed the uppermost portion of the oils. We found some similarities and differences between *M. propinquum* and *M. parviflorum* essential oils and in comparison with other species of genera *Marrubium* that might be due to different parameters such as agrotechnical factors.[45]

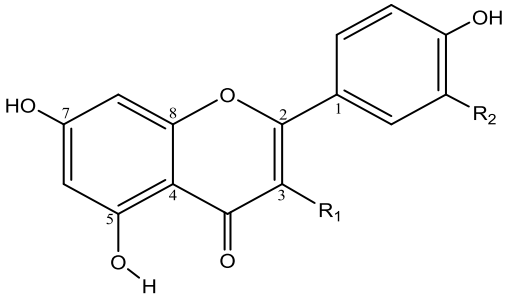
***Melissa* Species**

***Melissa officinalis* L.**

Melissa officinalis L. is a medicinal herb having used in traditional medicine all over the world. *M. officinalis* is a plant cultivated in some parts of Iran. The leaves of lemon balm, *M. officinalis* L, used in Iranian folk medicine for their digestive, carminative, antispasmodic, sedative, analgesic, tonic, and diuretic properties, as well as for functional gastrointestinal disorders. Various studies have shown that *M. officinalis* L. possesses high amount of antioxidant activity through its chemical compounds including high amount of flavonoids, rosmaric acid, gallic acid, phenolic contents. Many studies confirmed the antioxidative effects of *M. officinalis*; thus, its effect in preventing and treating oxidative stress-related diseases might be reliable.[46]

Chemical composition of the essential oil from the aerial parts of *M. officinalis* (lemon balm) obtained by hydro-distillation were analyzed by GC and GC/MS. Cedrane (14.1%) and 2,2,8,8-tetramethy-l-5-nonanone (12.6%) were the main components among 24 constituents characterized in the oil of *M. officinalis* representing the 89.6% of the total components detected. In addition, the extract samples subjected to screening by using DPPH and linoleic acid assay. Methanol extract tested against antioxidant activity by using DPPH and linoleic acid assay. It was found that methanol extract *M. officinalis* exhibited great antioxidant activity.[47]

In another study, analyzing the volatile oils by hydro-distillation method along with characterizing major flavonoids of *M. officinalis* flowers growing wild in the north of Iran was the aim of this study. Hence, the study led to the identification of 37 oil compositions by a combination HP-5 GC/FID and GC/MS analytical techniques. The results revealed that the major oil components for *M. officinalis* was β-caryophyllene (24.4%), followed by geranial (8.6%), 1, 8-cineole (6.9%), neral (6.7%), dehydroaromedendrene (5.8%) and thymol (4.8%), accounting for 91.3% of the total components. The essential oils of *M. officinalis* inhibited mildly the DPPH radicals identified by approximately equal amount of monoterpenes (42.2%) and sesquiterpenes (43.7%). Furthermore, based on high amount of total flavonoid content in EtOAc extract of flowers (49.2 ± 1.0 mg/g) and consequently the potent antioxidant activity (inhibition of the DPPH radicals, IC_{50}= 25.2 ± 0.6 µg/mL), two major flavonoids (apigenin **(13)** and quercetin **(14)**) have been isolated from flowers of *M. officinalis* by using Column Chromatography method. The structures of **1** and **2** were established by analysis of NMR spectroscopic data and comparison with their literature data (**Fig 3**).[48]



Apigenin (13): R_1= H, R_2: H

Quercetin (14): R_1: OH, R_2: OH

Figure 3: Chemical structures of flavonoids in *Melissa officinalis* L.

In another study, the volatile constituents of the essential oil of wild *M. officinalis* L. obtained from the Kurdistan province of Iran extracted by headspace/solid-phase micro-extraction and was analyzed by gas chromatography and gas chromatography/mass spectrometry. Of 14 compounds in the oil, 12 (85.7%) was identified. The main components were as follows: (E)-citral (37.2%), neral (23.9%) and citronellal (20.3%). Some physicochemical properties, such as the logarithm of calculated octanol–water partitioning coefficients ($\log K_{ow}$), total biodegradation (TB_d in mol/h and g/h), water solubility (S_w, mg/L at 25°C) and median lethal concentration 50 (LC_{50}), were calculated for all compounds from *M. officinalis* L.[49]

In another study, the essential oil of leaves (0.32% yield, w/v) was obtained by steam distillation with a Clevenger apparatus and analyzed by capillary GC and GC/MS. 18 substances were identified. The main components of the essential oil were geraniol (44.2%), citronellol (23.3%), β-caryophyllene (5.6%), citronellal (4.7%), spathulenol (3.4%), geranyl acetate (3.3%) and γ-murolene (2.1%).[50]

In another study, the identification of chemical constituents of the essential oils were carried out using gas chromatography/mass spectrometry analysis and antimicrobial activity of the essential oils was evaluated by disc diffusion assay as well as determination of MIC and minimal bactericidal concentration against four important food-borne bacteria: *Salmonella typhimorium, Escherichia coli, Listeria monocytogenes* and *Staphylococcus aureus*. Antioxidant activity of the essential oils was also determined by 2, 2-diphenyl-1-picrylhydrazyl, 2, 2-azinobis 3-ethylbenzo thiazoline-6-sulfonic acid and β-carotene bleaching tests. The major compounds of *M. officinalis* essential oil were citronellal (37.3%), thymol (11.9%), citral (10.1%) and β-caryophyllene (7.2%). The underlying results indicated strong antimicrobial effects of the oils against tested bacteria. *Staphylococcus aureus* with the lowest MIC value (0.12 mg/mL) for oil was the most sensitive bacterium; In addition, the results of the antioxidant activity showed that the essential oils had notable

antioxidant properties. The essential oils are appropriate alternatives as potential sources of natural preservative agents with the aim of being applied in food industries.[51]

In another study, the cytotoxicity of *M. officinalis* extract identified on Madin-Darby canine kidney (MDCK) cell culture by MTT assay. The virus was inoculated to the cells (multiplicity of infection = 0.1) in two protocols. In protocol 1, the *M. officinalis* extracts at concentrations of 0.005, 0.050, 0.010, 0.100 and 0.500 mg/mL incubated with the virus for one hour pre-inoculation. In second protocol, the mentioned concentrations of *M. officinalis* extracts added to the cells one-hour post infection. Furthermore, the antiviral effect of oseltamivir with different concentrations tested as the positive controls. The 50% tissue culture infective dose, neutralizing index and hemagglutination titer were determined. The medicine oseltamivir and *M. officinalis* extracts were not toxic for MDCK at concentrations less than 1 mg/mL. All utilized concentrations of *M. officinalis* extracts were vigorously efficient to decrease the viral yield in both experiments. The 50% tissue culture infective dose of the groups containing up to 0.100 mg/mL of *M. officinalis* extracts in the first experiment in compare with 0.050 mg/mL in the second experiment reduced to zero. Although hemagglutination tests showed little titers, the viral quantity significantly decreased in both experiments. By the way, the medicine oseltamivir could completely suppress viral replication in MDCK.[52]

In another study, the essential oil of different parts of this plant extracted and analyzed by GC/MS. The ticks placed on the filter paper in the bottom of a petri dish (9 mm), and contact toxicity assay then performed by contacting the extract with the ticks. The essential oil of leaves showed the most potent insecticidal effect while the stem essential oil demonstrated the weakest effect. The lowest concentration of essential oil from the leaves showed more considerable insecticide activity compared to the highest concentration of stem and flower essential oils. *M. officinalis* is an effective insecticide with potent effect against *T. urticae* and it could be suggested as a natural pesticide against *T. urticae*.[53]

Mentha Species

Mentha aquatic L.

The genera *Mentha* are represented in the flora of Iran by six species, of which *M. Mozaffarianii* is an endemic plant.[17] [18]

The essential oil obtained by hydro-distillation of the stem and leaf of *Mentha aquatic* L. was analyzed by GC and GC/MS. Twenty compounds, representing 88.1% of the stem oil of *M. aquatic* were identified; among them β-caryophyllene (22.4%), viridiflorol (11.3%) and 1, 8-cineole (10.9%) were the major. The leaf of the plant was characterized by higher amount of piperitenone oxide (25.7%) and also β-caryophyllene (12.0%) and 1, 8-cineole (10.3%), among the 29 components, comparising 95.4% of the total oil, detected.[54]

In another study, the antibacterial activity of *M. aquatica* essential oil tested against *Staphylococcus aureus*, *Lactobacillus reuteri*, *Bifidobacterium animalis* and *Clostridium perfringens* using agar well and disc diffusion techniques. Results showed the antibacterial activity of essential oil at 1500 and 2500 ppm examined in industrial liquid kashk during the storage at 4°C for 20 days. Essential oil reduced the *S. aureus* viable count below 5 log CFU g^{-1} after 4 days; however, the population of *C. perfringens*, *L. reuteri* and *B. animalis* decreased <1 log CFU g^{-1} during the storage time. The least deteriorative effect on the lactic acid bacteria related to *M. aquatica*. As revealed by organoleptic studies, kashk samples containing *M. aquatica* essential oil at 1500 and 2500 ppm were the most preferred samples.[55]

Mentha mozaffarianii Jamzad

The composition of the essential oils from *Mentha mozaffariani* Jamzad, which is endemic to Iran, was obtained by hydro-distillation and analyzed by GC and GC/MS. 20 compounds were identified in the oil of *M. mozaffarianii*, representing 83.6% of the total oil, with 1, 8-cineole (53.5%) being the major constituent. oil was richer in oxygenated monoterpenes than sesquiterpenes.[56]

Mentha longifolia (L.) Huds.

An essential oil composition of *Mentha longifolia* (L.) Huds. analyzed by GC and GC/MS. Twenty-three components were identified representing 99.3% of the oil. Carvone (61.8%) and limonene (19.4%) were the most abundant constituents.[57]

In another study, the essential oils obtained by hydro-distillation from the flower, leaf and stem of *M. longifolia* L. analyzed by GC and GC/MS. Piperitenone oxide (73.1% and 52.5%) and piperitenone (11.2% and 27.2%) were the main constituents in the flower and leaf oils of *M. longifolia*, respectively. The stem oil of the plant characterized by higher amounts of *cis*-piperitone oxide (25.8%) and borneol (13.5%). All oils consisted mainly of oxygenated monoterpenes and small percentage of sesquiterpenes.[58]

In another study, were dried aerial parts of 12 accessions of Iranian mints, three of which belonged to *M. longifolia* (L.) Huds. used, These were water distilled, and the essential oils analyzed by GC/FID and GC/MS. Results indicated a significant variation in oil composition within the accessions. *cis*-Carveol (53.5–78.2%) was found as the main constituent in the oils of three *M. longifolia* accessions.[59]

***Micromeria* Species**

***Micromeria persica* Boiss**

The *Micromeria* genera are represented in Iran by three species: *M. persica* Boiss., *M. hedgei* Rech. f. and *M. myrtifolia* Boiss. et Hohen. of which *M. persica* and *M. hedgei* are endemic plants.[17] [18]

Some *Micromeria* species are used in folk medicine for different purposes. In Spain *M. graeca* is used for stomach pains; *M. biflora* is used for treating disorders of the digestive tract; in Turkey *M. fruticosa* is used to relieve headache*; M. herpyllomorpha* and *M. varia* are used in the Canary Islands as a capillary tonic.[60]

Essential oils isolated by hydro-distillation from the aerial parts of *M. persica* Boiss. collected from province of Hamedan (Iran) before flowering and full flowering stage were analyzed. The main constituents were thymol (33.1% and 28.6%), gterpinene (28.7% and 17.5%), limonene (5.0% and 20.7%), 1, 8-cineole (14.2% and 0.2%), and p-cymene (7.0% and 17.5%) before flowering and full flowering stage, respectively.[61]

In another study, Water-distilled essential oil from the aerial parts of *M. persica* Boiss. which is endemic to Iran was analyzed by GC and GC/MS. Twenty-four components representing 96.1% of the oil of *M. persica* were identified of which linalool (15.2%), α-pinene (15.0%) and (E)-nerolidol (13.8%) were found to be the major constituents.[38]

In another study, The chemical composition of the essential oils from aerial parts of *M. persica* were extracted using hydro-distillation method and analyzed using GC and GC/MS. Fifty-two compounds were identified in the essential oils of aerial parts of *M. persica*. The main chemical compositions were n-hexadecanoic acid (14.9%), thymol (9.5%), linoleic acid (8.0%), carvacrol (5.6%), (E)-nerolidol (5.5%), linolenic acid (5.5%), α-cadinol (2.7%), linalool (2.7%), borneol (2.6%), caryophyllene oxide (2.3%) and pulegone (2.0%). Presence of borneol, thymol, carvacrol and pulegone suggests the potential of this plant as a flavouring source in the food industry, being used in perfumery and cosmetics industry, vitamin E synthesis and exhibit strong fungicidal, antibacterial and antimicrobial activities.[62]

In another study, the aerial parts of *M. persica* collected as samples from four regions of Fars province in Iran were dried. Then, the essence of the dried samples extracted by water distillation in the Clevenger machine, and identification of compounds made using the GC/MS machine. In Kuh-e Zireh, Firuzabad, Bezyn defile in Darab and Ghir to Firuzabad regions, the numbers of recognized compounds were 30, 45, 50 and 25 respectively. The main essence compounds of the four examined populations were Germacrene D, Bicyclogermacrene, spathulenol, and δ-cadinene. Geographical position and ecological parameters of habitat, such as height, annual rainfall, and climate, can change the quality and quantity of the essential oil's compounds in *M. persica*.[63]

***Micromeria hedgei* Rech. f.**

Micromeria hedgei belongs to the Lamiaceae family and is a rare endemic and endangered species that used in traditional medicine in Iran. In this regard, essential oil composition and antimicrobial activity of wild and cultivated *M. hedgei* reported for the first time. Essential oils isolated via hydro-distillation from the aerial parts of *M. hedgei* were analyzed by a combination of capillary GC and GC/MS. The major constituents were geranial (18.0 and 22.6%), neral (13.8 and 15.9%), geraniol (13.1 and 10.7%), nerol (7.6 and 6.0%), E-caryophyllene (6.5–3.8%), carvacrol (6.2 and 5.2%), geranyl acetate (5.7 and 3.0%), caryophyllene oxide (4.7 and 3.8%), thymol (3.1 and 3.6%) and α-humulene (3.2 and 3.2%) in wild and cultivated *M. hedgei*. Antimicrobial activity of essential oils was investigated by disc diffusion method. Essential oil showed good antimicrobial activity against five medically important pathogens compared with standard antibiotics.[64]

***Nepeta* Species**

Nepeta is a genus of flowering plants in the family Lamiaceae also known as catmints. The genus name is reportedly in reference to *Nepeta*, an ancient Etruscan-city. The genus is native to Europe, Asia and Africa and has naturalized in North America. The genera *Nepeta* that belongs to the Lamiaceae family consists of about 280 species. In Iran 67 species are present, among which 39 are endemics. *Nepeta* species are still used in the traditional medicine of many countries as diuretic, diaphoretic, vulnerary, antitussive, antispasmodic, antiasthmatic, tonic, febrifuge, emmenagogue and sedative agents.[65]

This family contains a wide variety of chemicals, a wide range of compounds such as terpenoids, iridiods, phenolic compounds and flavonoids have been reported from the members of the family.[66-68] Some of the short chain terpenoids in essential oils are responsible for odor and taste in these plants. Lavandula species contain several pleasant-smelling terpenoid compounds and used in perfumes and for deterring moth damage in stored clothing. Lebdan diterpenoids are found in 20 genera of the family including *Ballota*, *Coleus*, *Lagichilus*, *Leonotice*, *Marrubium* and *Sideritis*. Coleon compounds (tri-cyclic diterpenoids), found in leaves and inflorescence of Plectoranthus and other genera, have some antioxidant properties. Iridoides are also found in the family and have taxonomic importance. The family is also a rich source of plant species containing large amounts of phenolic acids.[69]

***Nepeta asterotricha* Rech. f.**

The chemical constituents from the root, leaf and aerial part of *Nepeta asterotricha* Rech.f., growing in Iran, were obtained by hydro-distillation and analyzed by GC

and GC/MS. The root oil characterized by higher amount of 4aα, 7β, 7aα-nepetalactone (26.2%), linalool (10.2%), 1, 8-cineole (10.2%) and terpinen-4-ol (9.2%). Thirty-two constituents representing 97.6% of the chromatographical leaf oil were identified of which 1, 8-cineole (21.0%), 4aα, 7β, 7aα-nepetalactone (15.0%); terpinen-4-ol (14.3%) and linalool (7.7%) were the major components. The main components of the aerial parts oil were 1, 8-cineole (26.1%), terpinen-4-ol (14.8%), 4aα, 7α, 7β- nepetalactone (8.7%) and cis-sabinene hydrate (8.6%). The antimicrobial effects of root, leaf and aerial part essential oils from *N. asterotricha* studied against seven Gram-positive and Gram-negative bacteria and three fungi by disc diffusion method. The results of the bioassays showed the interesting antimicrobial activity, in which the Gram-positive bacteria, *Bacillus cereus* and *Staphylococcus aureus*, were the most sensitive to the oils, as well the oils exhibited a remarkable antifungal activity against all the tested fungi.[70]

In another study, Thirty-five compounds representing 93.0% of the stem oil of *N. asterotricha* identified among which terpinen-4-ol (22.8%) and γ-terpinene (14.1%) were the major ones. The flower oil of the species was characterized by higher amounts of terpinen-4-ol (24.8%), 4aα, 7aβ-nepetalctone (18.2%) and 1, 8-cineole (11.6%) among the thirty-three components comprising 98.5% of the total oil detected. The antibacterial activity of the stem, leaf and flower oils of *N. asterotricha* against seven Gram-positive and Gram-negative bacteria were determined using the MIC method. The growth inhibitory zone (mm) was also measured.[40]

In another study, Samples plants of *N. asterotricha* extracted by hydro-distillation (Clavanger type), the essential oil yield was 1.8%. The quantitative and qualitative analyses of the oils performed by GC and GC/MS, respectively. The major component identification were terpinolene (21.2%), n-dodecanol (18.6%) and n-undecane (12.0%).[71]

Fallah Iri Sofla, studied on chemical composition and antibacterial activity of the essential oil of *N. asterotricha* from Iran, the essential oil was isolated by steam distillation of the stems of the plant and the oil was obtained with 0.6% yield, which was analyzed by capillary GC and GC/MS. Studies of essential oil revealed terpinene-4-ol (18.7%), linalool (14.9%), γ-terpinene (8.7%),cis-sabinene hydrate (8.6%),4aα-7ß-7aα-nepetalactone (7.4%) and 1, 8-cineole (5.6%), as the major constituents.[72]

***Nepeta binaludensis* Jamzad.**

The composition of the essential oil of *Nepeta binaludensis* investigated by means of GC, GC/MS and ^{1}H-NMR spectra of the main compounds. 1, 8-cineole (42.0%) was the most abundant component in the oil. However in addition nepetalactone (25.0%), linalool (4.0%), α-terpineol (4.0%) and β-pinene (3.0%) were detected in the oil of *N. binaludensis*.[73]

In another study, Essential oils of the plant aerial parts, which collected from two regions Dowlat Abad and Freizi, were slightly yellow and the yields were 0.5% (v/w) in both regions. Eighteen components representing 95.2% and 97.5% of the total oils of these regions identified, respectively. The major constituent of the oxygenated monoterpene-rich oils was 1, 8-Cineole (77.8% and 73.2% respectively).[74]

In another study, the essential oil of the aerial parts of *N. binaludensis* Jamzad obtained by hydro-distillation and analyzed by GC, GC/MS and then ^{13}C-NMR spectra of the main compounds. Sixty-five components, representing 97.42% of the oil identified. The major components of the oil were 1, 8-cineole (68.3%), α-terpineol (5.2%), β-pinene (4.7%), δ-terpineol (2.5%), α-pinene (1.5%). The minimum inhibitory concentrations (MICs) and minimum cidal concentrations (MCCs) of the essential oil and its major component, 1, 8-cineole, as authentic compound were determined using broth dilution method against four bacteria and one fungus. The essential oil was moderately active against *Bacillus cereus* (3.1 mg/mL), *Escherichia coli* (3.1 mg/mL), *Staphylococcus aureus* (6.2 mg/mL) and *Candida albicans* (12.5 mg/mL) with the same MIC and MCC values in each case. Another Gram-negative bacteria, Pseudomonas aeroginosa, appeard not to be susceptible to inhibitory effects of the essential oil. The obtained MIC and MCC values for 1, 8-cineole was closely near to the essential oil values.[75]

***Nepeta bornmuelleri* Hausskn. ex Bornm**

The essential oil from the aerial parts of *Nepeta bornmuelleri* was obtained by hydro-distillation. The oil was analyzed by capillary gas chromatography, using flame ionization and mass spectrometric detected.

Twenty-eight compounds were identified in the oil *N. bornmuelleri* with 4aβ, 7α, 7aβ-nepetalactone (64.0%) and 1, 8-cineole (7.1%) as main components.[76]

In another study, the essential oils of leaves, flowers, stems and roots of the plant were separately extracted using hydro-distillation method and analyzed by GC and GC/MS. In the leaf and flower oils, 38 and 19 components were identified, representing 98.% and 94.5% of the total oils, with 4aβ,7α,7aβ-nepetalactone (29.2% and 26.8%), 1,8-cineole (19.6% and 14.6%), 4aα,7α,7aα-nepetalactone (6.6% and 19.5%) and β-pinene (18.9% and 11.4%) as the main constituents, respectively. The stem oil was characterized by higher amount of 4aβ, 7α, 7aβ-nepetalactone (39.8%), caryophyllene oxide (24.1%) and 1, 8-cineole (12.8%) among the 9 components comprising 95.8% of the total oil. Furthermore, 12 compounds were identified in the root oil, representing 99.3% of the total oil. 4aβ, 7α, 7aβ-Nepetalactone (73.2%) and 4aα, 7α, 7aα-nepetalactone (13.4%) isomers were found to be the major constituents. As a result, nepetalactone was the dominant component in the essential oils of *N. bornmuelleri*.[77]

***Nepeta bracteata* Benth**

Nepeta bracteata is a medicinal plant that wildly grows in Province of Khorasan (Iran). The indigenous people as a folkloric medicine in Khorasan Province use this herb. The result of this study indicated that the indigenous people for treatment of many diseases, including asthma, cold, headache and stress, use the aerial parts, especially the flowers of *N. bracteata*. In addition, this herb has used as a sedative. The flowers of *N. bracteata* are used for treatment of respiratory diseases, including asthma, lungspasms, seasonalallergies and cough due to cold.[78]

In another study, the oil of *N. bracteata* Benth. was obtained by hydro distillation. The oil was analyzed by capillary gas chromatography, using flame ionization and mass-spectrometric detection. Twenty-eight compounds were characterized in the oil of *N. bracteata* with spathulenol (14.0%), caryophyllene oxide (12.3%), bicyclogermacrene (11.4%) and β-caryophyllene (11.2%) as the main constituents. The oil of *N. bracteata* consisted of mainly of sesquiterpenes, while nepetalactone was not detected in this oil.[76]

***Nepeta cataria* L.**

In another study, the chemical composition of the essential oils from *Nepeta cataria* has been analyzed by GC/MS. The analysis of the essential oils indicated that 4aα, 7α, 7aβ-nepetalactone (55-58%) and 4aα, 7β, 7aα-nepetalactone (30-31.2%) were the major compounds of the essential oils at all developmental stages. The results showed that the tested essential oils exhibited antimicrobial activities against the food-borne pathogens at concentrations of 0.125-2 µL/mL. Based on these results, the essential oil of *N. cataria* can possibly be used in food products as a natural preservative agent.[79]
In another study, the chemical composition of essential oils from *N. cataria* analyzed by GC/MS. The antimicrobial activity of the essential oil evaluated by broth micro-dilution in 96 well plates, which were incubated at 30°C for 24-48 h (fungi) or at 37°C for 24 h (bacteria). The analysis of the essential oils indicated that 4aα, 7α, 7aβ-nepetalactone (55-58%), and 4aα, 7β, 7aα-nepetalactone (30-31.2%) were the major compounds of the essential oils at all developmental stages. The tested essential oils exhibited antimicrobial activities against the tested bacteria at concentrations of 0.125-4 µL/mL. Moreover, the oils entirely inhibited the growth of *Candida* species at a concentration less than 1 µL/mL.[80]

The essential oil of *N. cataria* was extracted by hydro-distillation and the composition of the volatile oil was characterized by GC/FID and GC/MS. The inhibitory effects of essential oil at concentrations of 0, 150, 300, 600, and 1200 μlL^{-1} on seed germination and seedling growth of *Hordeum spontaneum* Koch, *Taraxacum officinale*, *Avena fatua* L. and three crop seeds including *Lipidium sativum*, *Nepeta cataria* and *Ocimum basilicum* were tested. The examined concentrations of *N. cataria* essential oil showed different phytotoxic as well as selective properties on the germination and growth of the studied species. The studied essential oil could be considered as an allelochemical agent in formulation of natural herbicides in future weeds control.[81]

***Nepeta cephalotes* Boiss.**

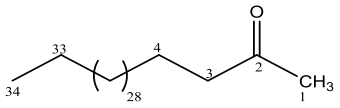
The composition of the essential oil of *Nepeta cephalotes* Boiss. This is endemic to Iran investigated by means of GC, GC/MS and ^{1}H-NMR spectra of the main compounds. Ten compounds were identified in the oil of *N. cephalotes* representing 78% of the total oil with 4aα, 7α, 7aα-nepetalactone (35.1%), and β-pinene (18.2%) and 1, 8-cineole (11.4%) as the major constituents. Nepetalactone and β-pinene were confirmed by their ^{1}H-NMR spectra.[82]

In another study, the essential oil from the aerial parts of *N. cephalotes* obtained by hydro-distillation. The oil was analyzed by capillary gas chromatography, using flame ionization and mass-spectrometric detection. Eight components were identified in the oil of *N. cephalotes* with 4aα, 7α, 7aα-nepetalactone (90.1%) and β-pinene (7.5%) as main constituents.[76]

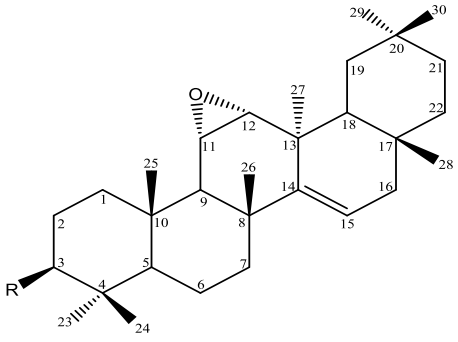
***Nepeta crassifolia* Boiss. & Buhse**

The essential oil of *Nepeta crassifolia* Boiss. & Buhse was prepared by steam distillation and analyzed by GC and GC/MS. Thirty-five substances out of the 52 detected were identified. The major constituents were found to be stereoisomers of nepetalactones (72.8%) and 1, 8-cineole (9.0%). 4aα, 7β, 7aβ-Nepetalactone was isolated and identified by ^{1}H- and ^{13}C-NMR.[83]

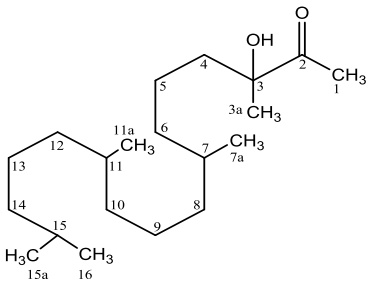
In another study, a long chain ketone (crassifone), a pentacyclic triterpenoid coupled with fatty acid moiety (crassi-foate), and an acyclic diterpenoid (crassifol) have been isolated from the ethanol soluble part of *N. crassifolia* collected from Kangavar, Iran. Structures of all the metabolites elucidated with the aid of spectroscopic techniques, including 2D NMR experiments (**Fig 4**).[84]



Crassifone



R= stearyl (Crassifoate)



Crassifol

Figure 4: Chemical structures of *Nepeta crassifolia Boiss. & Buhse*.

***Nepeta crispa* Willd.**

The composition of the essential oil of *Nepeta crispa* Willd. was investigated by means of GC and GC/MS. 1, 8-cineole (71.0%) was the most abundant component in the oil of *N. crispa*. The other main components were α-pinene (5.0%) and γ-terpineol (4.1%) was found to be the major constituents.[85]

In another study, the oil was analyzed by capillary gas chromatography, using flame ionization and mass spectrometric detection. Twenty-eight components were identified in the oil of *N. crispa* with 1, 8-cineole (62.8%), 4aα-7α-7aα-nepetalactone (10.3%) and 4aβ-7α-7aβ-nepetalactone (9.2%) as main constituents. The oil of *N. crispa* consists of about 20% nepetalactone.[86]

***Nepeta denudate* Benth.**

The composition of the essential oils of *Nepeta denudata* Benth. which is endemic to Iran, was investigated by means of GC, GC/MS and ^{1}H-NMR spectra of the main compounds, 1,8-cineole (48.0%), myrtenol (5.0%), β-pinene (4.6%) and trans-pinocarveol (4.5%) were the main components among the 21 constituents characterized in the oil of *N. denudata*, representing 85.7% of the total components detected. The structure of 1, 8-cineole, nepetalactone and β-pinene were confirmed by their ^{1}H-NMR spectra.[82]

***Nepeta depauperata* Benth.**

The essential oil from flowering aerial parts of *Nepeta depauperata* Benth., an endemic Iranian plant, obtained by steam distillation was analyzed by GC/MS. The constituents identified by their mass spectra and Kovats' indices (KI). Thirty-three compounds consisting 82.5% of the total components identified from the oil obtained with a yield of 0.3%v/w. Among them, spathulenol (31.8%), β-caryophyllene (12.9%) and caryophyllene oxide (10.2%) were the major components of the oil.[87]

The antibacterial and antifungal activities of the total methanolic extract and different sub-fraction of the flowering aerial parts investigated by cup plate method and disc diffusion assay, respectively. The minimum inhibitory concentrations and minimum bactericidal concentrations of the active extract or subfraction determined by micro plate dilution method. The crude extract and chloroform sub-fraction of *N. depauperata* had inhibition activity on the growth of *Staphylococcus aureus*, *Bacillus subtilis* and *Pseudomonas aeruginosa* while no antibacterial activity observed against *Staphylococcus epidermidis*, *Escherichia coli* and *Salmonella typhi*. It concluded from the antifungal assay that just the yeast *C. albicans*, showed a high sensitivity to all the extract and related sub-fractions. No activity was seen against *Aspergillus niger*, *A. fumigatus*, *A. flavus* and *Fusarium oxysporum*. These findings demonstrate that the *N. depauperata* is effective against *S. aureus*, *B. subtilis* and *P. aeruginosa* and could be a natural source of effective natural antifungal compounds against *C. albicans*.[88]

***Nepeta glomerulosa* Boiss.**

The chemical compositions of the essential oil of *Nepeta glomerulosa* Boiss aerial parts, grown in Iran were determined by GC/MS. Fifty-two compounds (97.2%) were determined. The major compounds were geranyl acetate (17.0%), limonene (12.0%), eucalyptol (5.8%), bornyl acetate (5.3%), citronellal (4.9%), spathulanol (4.2%), sabinene (3.9%), β-ocimene (3.9%), β-sesquiphellandrene (2.8%),neryl acetate (2.5%), α-humulene (2.4%), α-pinene (2.3%), humulene oxide (2.2%), norsolanadione (2.1%) and terpinen-4-ol (2.0%). The yield of the oil was 1.1(v/w) %. The essential oil showed antibacterial activity for *Staphylococcus aureus*.[89]

Rustaiyan, study on chemical composition of the volatile oil of *N. glomerulosa Boiss* from Iran, the composition of the volatile oil from aerial parts of *N. glomerulosa* was investigated by means of GC and GC/MS techniques. Of 35 compounds identified, 25 were monoterpenes and 10 sesquiterpenes. The compounds most frequently found in

the oil studied were: 1, 8-cineole (10.4%), geraniol (9.7%), geranyl OAc (9.4) and β-caryophyllene oxide (5.2%).[90]

***Nepeta haussknechtii* Bornm.**

Water distilled essential oils from aerial parts of *Nepeta haussknechtii* Bornm. Was analyzed by GC and GC/MS. Twenty-seven compounds representing 94.2% of the oil of *N. haussknechtii* were characterized. The major components of the essential oil of *N. haussknechtii* were 1, 8-cineole (36.7%) and elemol (11.4%). The oil richer in oxygenated monoterpenes than sesquiterpenes.[91]

***Nepeta heliotropifolia* Lam.**

The composition of the essential oil from *Nepeta heliotropifolia* Lam. Was obtained by hydro-distillation and analyzed by GC and GC/MS. 1, 8-cineole (16.8%), 4aα,7α,7aβ nepetalactone (16.3%), cis-sabinene hydrate (16.1%) and linalool (11.9%) were the main components among the 23 constituents characterized in the oil of *N. heliotropifolia*, representing 92.8% of the total components detected.[56]

***Nepeta hormozganica* Jamzad**

Sonboli study about the composition and antibacterial activity of the essential oil of the aerial flowering parts of *Nepeta hormozganica* Jamzad, Analysis of the oil conducted by GC/FID and GC/MS. Thirty-two components were characterized accounting for 99.4% of the total oil. Oxygenated monoterpenes (87.5%) were found to be the predominant group of compounds, of which 1, 8-cineole (65.0%) and 4aα-7α-7aβ-nepetalactone (13.0%) was the main constituents. The antibacterial activity of the essential oil and its main constituents showed that all of the tested microorganisms were highly inhibited by the essential oil with inhibition zones ranged from 12 to 24 mm. The most sensitive bacteria were *Staphylococcus aureus* and *Staphylococcus epidermidis* with the lowest MIC values of 0.3 and 0.6 mg/mL, respectively. Considering sensitivity screening it is conceivable that the activity of the oil from *N. hormozganica* could be attributed mainly to the synergistic property of 1, 8-cineole and nepetalactone.[92]

***Nepeta ispahanica* Boiss.**

The essential oil from *Nepeta ispahanica* Boiss. obtained by hydro-distillation and mass spectrometric detection. Twenty-seven compounds were characterized in the oil with 1, 8-cineole (71.7%) as the main constituent.[86]

In another study, the composition of the essential oil of *N. ispahanica* Boiss. was investigated by means of GC, GC/MS and ^{1}H-NMR spectra of the main compounds. 1, 8-cineole (66.0%) was the most abundant component in the oil.[73]

In another study, the essential oil obtained from the aerial parts of *N. ispahanica* was analyzed by GC and GC/MS. Thirty-three constituents accounting for 97.1% of the total oil were identified with 1, 8-cineole (78.2%), α-terpineol (2.3%) and 4-terpineol (1.9%) as the main components. Antibacterial activity of the oil and various extracts of the plant was studied against four Gram-positive and three Gram-negative bacteria. The oil inhibited the growth of all of the tested bacteria except *Pseudomonas aeruginosa*. In addition, the antioxidant activity of the samples was tested by using 2, 2-diphenyl-1-picrylhydrazyl (DPPH) assay. The free radical scavenging activity of n-BuOH subfraction of the methanol extract (IC_{50}= 37 µg/mL) was superior to all other extracts, while the oil was the least effective.[93]

***Nepeta laxiflora* Benth.**

Chemical composition of oils and antioxidant activity of the volatile oils and methanol extracts of *Nepeta laxiflora* was analyses by gas chromatography and gas chromatography/mass spectrometry. The most abundant compounds in volatile oils of *N. laxiflora* were α-pinene (19.7%) and 1, 8-cineole (11.8%) The polar subfractions of methanol extracts of *N. laxiflora* showed the highest radical-scavenging activity (IC_{50} = 105.9 ± 1.3 µg). In the β-carotene-linoleic acid system, the inhibition capacity of the nonpolar subfractions of methanol extracts of *N. laxiflora* found with the strongest activity (87.1 inhibitions) which is almost equal to the inhibition capacity of positive control butylated hydroxytoluene. The volatile oils and methanolic extracts of *Nepeta laxiflora* Benth. showed potential antibacterial and antioxidant activities. The results support the traditional usage and also possible use of plant volatile oil and extracts in the food and/or pharmaceutical industry.[94]

***Nepeta makuensis* Jamzad et Mozaffarian**

The chemical composition of the essential oil of *Nepeta makuensis* Jamzad et Mozaffarian, which is endemic to Iran, was analyzed by GC/MS. Twenty-eight components representing 92.9% of the oil were identified of which viridiflorol (17.5%), T-cadinol (10.7%) and spathulenol (9.0%) were the major ones.[95]

***Nepeta meyeri* Benth.**

The essential oil obtained by hydro-distillation of the aerial parts of *Nepeta meyeri* Benth. was analyzed by GC and GC/MS. The oil of *N. meyeri* was made up mainly of oxygenated monoterpenes, of which 4aα, 7α, 7αβ-nepetalactone (68.1%) was the major constituent.[54]

Water-distilled volatile oil from the aerial parts of *N. meyeri* Benth. was analyzed by a combination of GC and GC/MS. Eighteen components were identified, constitute approximately 99.3% of the oil. The main constituents of the essential oil were 4a*α*-7*α*-7a*β*-nepetalactone (53.2%), 1, 8-cineole (29.3%) and camphor (4.1%).[96]

***Nepeta persica* Boiss.**

Essential oil of *Nepeta persica* cultivated in Iran obtained by steam distillation and supercritical (carbon dioxide) extraction methods. The oils were analyzed by capillary gas chromatography using flame ionization and mass spectrometric detections. The compounds identified

according to their retention indices and mass spectra (EI, 70 eV). The effects of different parameters such as pressure, temperature, and modifier volume and extraction times (dynamic and static) on the supercritical fluid extraction (SFE) of *N. persica* oil investigated. The results showed that under the pressure of 20.3 MPa, temperature of 45 °C, methanol of 1.5% v/v), dynamic extraction time of 50 min and static extraction time of 25 min extraction was more selective for the 4αβ, 7α, 7aα-nepetalactone. Twelve compounds identified in the steam-distilled oil. The major components of *N. persica* were 4αβ, 7α, 7aα-nepetalactone (26.5%), *cis*-β-farnesene (4.4%) and 3, 4α-dihydro-4aα, 7α, 7aα-nepetalactone (3.5%). However, by using supercritical carbon dioxide under optimum conditions, only two components have more than 90.0% of the oil. The extraction yield based on steam distillation was 0.08% (v/w). On the other hand, using SFE extraction yield in the range of 0.22-8.9% (w/w) obtained at different conditions. The results show that, in Iranian *N. persica* oil, 4αβ, 7α, 7aα-nepetalactone is a major component.[97] In another study, the extract of aerial parts of the plant administered intraperitoneally to male NMRI mice, at various doses, 30 min before behavioral evaluation. The HE of *N. persica* at the dose of 50 mg/kg significantly increased the percentage of time spent and percentage of arm entries in the open arms of the elevated plus-maze (EPM). This dose of plant extract affected neither animal's locomotors activity nor ketamine-induced sleeping time. The 50 mg/kg dose of the plant extract seemed to be the optimal dose in producing the anxiolytic effects, lower or higher doses of the plant produce either sedative or stimulant effects. At 100 mg/kg, the plant extract increased the locomotors activity. These results suggested that the extract of *N. persica* at dose of 50 mg/kg possess anxiolytic effect with less sedative and hypnotic effects than that of diazepam and causes a non-specific stimulation at 100 mg/kg.[98]

In another study, the essential oils from the flower, leaf, stem and root of *N. persica* Boiss., analyzed by GC and GC/MS, were shown to contain 4aβ,7α,7aβ-nepetalactone (58.5%, 62.3%, 66.2% and 27.1%, respectively), and 4aα,7α,7aβ-nepetalactone (33.0%, 28.3%, 24.9% and 7.6%, respectively). The other main component of the flower and stem oils was α-pinene (3.6% and 4.4%) and of the leaf oil β-ocimene (3.6%). In the root oil, other main constituents were α-pinene (40.4%), α-amorphene (5.3%), γ-cadinene (2.9%), and cis-calamenene (2.5%). Nepetalactone was the major component of the flower, leaf and stem oils, which are thus important sources of nepetalactone. Antibacterial activities of the flower, leaf, stem and root oils were evaluated using the micro-dilution broth method. Inhibitory effects on *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Salmonella typhi* and *Enterococcus faecalis* were recorded. The flower, leaf, stem, and root oils had difference activities against the test microorganisms. The antibacterial property of the essential oils might be ascribed to their high content of nepetalactone isomers.[99]

***Nepeta racemosa* Lam.**

Nepeta racemosa is an herbal and medicinal plant. Chemical profiles of the essential oils and volatile compounds from the aerial parts of *N. racemosa* obtained through hydro-distillation (HD), solvent-free microwave extraction (SFME), microwave assisted hydrodistillation (MAHD) and headspace solid-phase micro-extraction (HS-SPME) methods subsequently investigated by means of GC and GC/MS instruments. Totally, 25, 26, 24, and 24 components identified in the chemical profiles, representing 98.1%, 96.6%, 97.7% and 96.4% of the total compositions when using the HD, HS-SPME, SFME and MAHD methods, respectively. In all samples, oxygenated monoterpenes were the major fractions of the chemical profiles with the exception of chemical composition of the essential oil of *N. racemosa* obtained by using the MAHD approach in which monoterpene hydrocarbons were dominant constituting compounds. In final, 4aα, 7α, 7aα-nepetalactone was the most abundant compound in the chemical profiles of HD, HS-SPME and SFME approaches while 4aα, 7α, 7aβ-nepetalactone oxygenated monoterpene was the most frequent compound in the MAHD profile. The significance of this study relates to the fact that the essential oils, which are rich in monoterpene hydrocarbons and oxygenated monoterpenes could be regarded as powerful food preservatives and novel antioxidants.[100]

The water-distilled essential oil of *N. racemosa* Lam. essential oil of was analyzed by GC and GC/MS. The main consitutents of the oil were found to be 4aα, 7α, 7aα-nepetalactone (64.9%), (Z)-β-ocimene (9.5%), (E)-nerolidol (8.8%) and 4aα, 7α, 7aβ-nepetalactone (7.4%).[101]

***Nepeta rivularis* Bornm.**

The essential oil from the aerial parts of *Nepeta rivularis* Bornm. was obtained by hydro-distillation. The oil was analyzed by capillary gas chromatography, using flame ionization and mass spectrometric detection. Twenty-two components were identified in the oil of *N. rivularis* with 1, 8-cineole (38.5%), sabinene (14.8%), β-pinene (10.7%) and γ-terpinene (5.1%) as the main constituents.[86]

***Nepeta schiraziana* Boiss.**

The stems, flowers and leaves of *Nepeta schiraziana* collected from Sepidan region in north-west of Fars province. The essential oils of stems, flowers and leaves of the plant separately obtained by hydro-distillation and analyzed by GC and GC/MS. In each oils of the stem and flower, fourteen components were identified with 1, 8-cineole (45.6% and 39.4%), germacrene D (17.4% and 15.8%), and β-caryophyllene (11.7% and 10.6%) as the main constituent, respectively. Furthermore, 1, 8-cineole (38.5%), β-caryophyllene (14.2%) and caryophyllene oxide (11.7%) were the major components among the 18

constituents characterized in the leaf oil. As a result, 1, 8-cineole was the dominant compound in the investigated oils while nepetalactone isomers reported in many *Nepeta* species, were not identified in *N. schiraziana*.[102]

***Nepeta sintenisii* Bornm.**

The aerial parts of *Nepeta sintenisii* from Iran subjected to hydrodistillation and the chemical composition of the isolated essential oil analyzed by GC/MS method for first time. Forty constituents (96.5% of the total oil) were identified of which 4aβ, 7α, 7aβ-nepetalactone (23.4%), elemol (16.1%), E-β-farnesene (9.5%), 1, 8-cineole (8.2%), cis-sabinene hydrate (6.5%), β-bisabolene (4.2%) and germacrene D (3.5%) were the main components.[103]

***Nepeta sessilifolia* Bunge.**

Water distilled essential oils from the aerial parts of *Nepeta sessilifolia* Bung. analyzed by GC and GC/MS. Thirty-three compounds representing 97.4% of the *N. sessilifilia*. The major components of the essential oil of *N. sessilifolia* were linalool acetate (14.7%) and linalool (14.2%). The oil was richer in oxygenated monoterpenes than sesquiterpenes.[91]

***Ocimum* Species**

***Ocimum basilicum* L.**

A comparison of the chemical composition and antimicrobial activity of the essential oils obtained from the aerial parts of two types of *Ocimum basilicum* L., *O. basilicum* L. (green type) and *O. basilicum* (purple type) were carried out. The oils obtained by hydro-distillation and analyzed by GC and GC/MS. The main components of the oil of the *O. basilicum* (green type) were methyl chavicol (62.5%), geranial (12.5%) and neral (9.9%) while in the oil of *O. basilicum* (purple type), *trans*-a-bergamotene (17.5%), linalool (17.0%) and 1, 8-cineole (9.0%) were the prominent components. The antimicrobial activity of each oil was determined by measurement of the growth inhibitory zone, against three Gram-positive, one Gram-negative and one fungus using the well diffusion assay.[104]

In another study, Chemical composition, antioxidant, antimicrobial and cytotoxic activities of *O. basilicum* essential oil examined. The main components for *O. basilicum* essential oil were methylchavicol (46.9%), geranial (19.1%), neral (15.1%), geraniol (3.0%), nerol (3.0%), and caryophyllene (2.4%). Inhibitory concentrations (IC_{50}) for reactive oxygen species and reactive nitrogen species (RNS) scavenging were 200-250 µg/mL of *O. basilicum* essential oil. Minimal inhibitory concentration for *Salmonella typhi*, *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, *Aspergillus niger*, and *Candida albicans* were 145 ± 8, 160 ± 7, 45 ± 4, 40 ± 3, 80 ± 9, and 95 ± 7 µg/mL of *O. basilicum* essential oil, respectively. IC_{50} for nasopharyngeal cancer cell line (KB) and liver hepatocellular carcinoma cell line (HepG2) were 45 ± 4 and 40 ± 3 µg/mL of *O. basilicum* essential oil, respectively. Thus, it could be used as an effective source of natural antioxidant and antibacterial additive to protect foods from oxidative damages and foodborne pathogens. Furthermore, it could be promising candidate for antitumor drug design.[105]

***Perovskia* Species**

***Perovskia abrotanoides* Karel.**

The composition of the essential oils from *Perovskia abrotanoides* Karel. obtained by hydro-distillation were analyzed by GC and GC/MS. The oil of *P. abrotanoides* was characterized by a higher amount of 1, 8-cineole (28.0%) and camphor (24.0%), among the 23 components comprising 84.3% of the total oil detected. The oils consisted mainly of monoterpenes predominated.[15]

In another study, the essential oils obtained by hydro-distillation from the stem, leaf, flower and root of *P. abrotanoides* Karel. analyzed by GC and GC/MS. Camphor (41.6%, 32.4%, 26.2% and 32.2%) and 1, 8-cineole (10.2%, 32.1%, 18.0% and 24.5%) were the main constituents in the stem, leaf, flower and root oils of *P. abrotanoides*, respectively. The other main component in the flower oil of the plant was α-pinene (16.0%). The oils consisted mainly of oxygenated monoterpenes and small percentage of sesquiterpenes.[58]

DISCUSSION

In this review, we will be discussing the constituents and biological activities of selected genera of the Iranian Labiatae family namely: *Ajuga*; *Ballota*; *Cyclotrichium*; *Eremostachys*; *Hymenocrater*; *Marrubium*; *Melissa*; *Mentha*; *Micromeria*; *Nepeta*; *Ocimum* and *Perovskia*.

Since the present manuscript is voluminous, we decided to submit up to the genera *Perovskia*. The rest of the genera will be discoussed in part two.

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