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GENUS MICROMERIA: A REVIEW ARTICLE

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Abstract

Micromeria (Family Lamiaceae) is widespread across Europe, Asia, Africa and North America, with a center of diversity in the Mediterranean region and the Canary Islands. More than 78 species of Micromeria have been known, famous examples is: *M. fruticose*.Genus Micromeria comprises plants of different chemical nature. Based on previous studies, Micromeria species is considered as a rich source of essential oils, mainly; monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpenes hydrocarbons, and oxygenated sesquiterpenes. About ten species of Micromeria have been identified to grow widely in Lebanon, of which *Micromeria fruticosa* is the most common and abundant. Several pharmacological activities were reported including antimicrobial, antioxidant, anticancer, and antidepressant effect. This is a review article where we thoroughly discuss the chemical nature and classes of all isolated metabolites from Micomeria plant especially *Micromeria fruticosa* and their reported biological activities in an attempt to inspire the researchers to isolate and structural elucidate the compounds that could have valuable use in drug discovery and medical application.

Keywords

Micromeria, fruticosa, taxonomy, chemistry, pharmacology

1. INTRODUCTION

Plants have been widely used to treat different disorders in discovering drugs, and as cosmeceuticals [(Davis SC, Perez R., 2009), (Uniyal SK, Singh KN, Jamwal P, Lal B., 2006)].However, the astounding advantages of synthetic drugs have, in turn, overshadowed herbal and alternative medicine [(Losoya Z., 2013), (Mckenna J. , 1998)]. Herbal medicine has been popularly used by 78% of the population (within Latin America and Asia) and has been found with low adverse effects [(Losoya Z., 2013), (Mckenna J. , 1998), (Doughari J., 2007)].

Historically, the health benefits of plants had demonstrated great inspiration for alternative medicinal treatments that are both effective and natural (Doughari J., 2007). While some countries have resorted to other treatment methods, developing countries and impoverished populations have frequently used natural medications [(El Astal Z, Ashour A, Kerrit A., 2005), (Abu-Irmaileh BE, Afifi FU., 2003), (Newman DJ, Gragg GM., 2012)].

Nowadays, both developed and developing countries have returned to using natural herbal products because of the unpromising results of using synthetic drugs towards treating serious viral infections (such as AIDS), common types of cancers, and other diseases. Moreover, in addition to their adverse side effects, synthetic drugs that are used to treat chronic diseases have significant complications [(Patwardhan B, Vaidya AD, Chorghade M., 2004), (Gurib-Fakim A., 2006)].

Family Lamiaceae

Taxonomical Classification

Lamiaceae (Mint Family) is a flowering plant that has roughly 230 genera and greater than 7,000 species (Patwardhan B, Mashelkar RA., 2009). The most famous genera are Salvia (900 spp.), Scutellaria (360 spp.), Stachys (300 spp.), Plectranthus (300 spp.), Hyptis (280 spp.), Teucrium (250 spp.), Vitex (250 spp.), Thymus (220 spp.), and Nepeta (200 spp).

1.1. General Features of Lamiaceae Shape

The stems usually, but not uniquely, have a square cross-sectional. Its flowers are bilaterally symmetrical with 5 petals and 5 sepals. Lamiaceaeare commonly bisexual and they appear to have one whorl of flowers even though they are comprised of two clusters).The leaves are either decussated (crossing one another) or whorled. These plants are most frequently shrubs or trees but could also be vines. This family includes the characteristically aromatic herbs used in cooking such as rosemary, oregano, thyme, basil, mint, marjoram, sage, and lavender. Its aromaticity along with the simplicity of propagation through stem cutting explains why this family has frequently been cultivated (Patwardhan B, Mashelkar RA., 2009).

1.2. Classification of Lamiaceae

Lamiaceae is divided into two groups:

a. The first group is represented by the subfamily Nepetoideae. This group can be additionally partitioned into several tribes like Menthae, Salviia, Lavanduleae, Nepeteae, and Ocimeae (Patwardhan B, Mashelkar RA., 2009). Plants of this group are mostly aromatic and contain rosmarinic acid as a common secondary metabolite.

b. The second group is represented by the subfamilies Chloanthoideae, Caryopteridoideae, Lamioideae, Scutellarioideae, Wenchengioideae and Ajugoideae. These plants are distinguished by a low concentration of essential oil, the presence of iridoid glycosides, and lack of rosmarinic acid.

1.3. Medicinal Values of Lamiaceae

Nowadays, many of the Lamiaceae plants are word widely harvested, mainly for their culinary use and therapeutic potential. Plants belonging to this family have been widely used to treat different ailments as gastrointestinal disorders, migraines, and disorders of the upper respiratory tract as well as cardiovascular diseases (Takhtajan A., 1997). Many plants are authentic medications mentioned within numerous pharmacopeias and serve as important

raw materials within the pharmaceutical, cosmetic, fragrance, and food manufacturing. [(Bisset NG, Wichtl M, Eds., 2001), (Blumenthal R, Ed., 1999)].

Overview on Chemical Composition of Plants of Lamiaceae

Relying on Lamiaceae in folk and customary medicine is attributed to the existence of monoterpenes in essential oils and various phenolic compounds. Because the variance in the essential oil composition is highly variable, its pharmacological activity is firmly related to certain chemical nature. Nevertheless, its phenolic constituents are highly presented amongst the species. The main phenolic compounds in Lamiaceae plants are lipophilic flavonoids. Several studies on different types of this Family have successfully isolated and identified many active compounds that belonged mainly to monoterpene hydrocarbons, sesquiterpenes hydrocarbons, and their oxygenated derivatives besides alcohols, and aliphatic aldehydes. Along the way, other phenolic miscellaneous and nonvolatile compounds were also found.[(S. Nejad Ebrahimi,J. Hadian,M.H.Mirjalili, A. Sonboli, M. Yousefzadi, 2008), (Mehmet Hakki Alma, Ahmet Mavi, Ali Yildirim, Metin Digrak, and Toshifumi Hirata, 2003), (E2-Moujir, L., Gutiérrez-Navarro, A. M., San Andrés, L. and Luis, J. G, 1996), (Mamadalieva NZ, Herrmann F, El-Readi MZ, Tahrani A, Hamoud R, Egamberdieva DR, Azimova SS, Wink, 2011)].

Genus Micromeria

Micromeria (Family Lamiaceae) are found throughout North America, Europe, Africa, and Asia, with many varieties found within the Mediterranean region and Canary Islands [(Bahramikia S., Yazdanparast R., 2012), (Kew World checklist of Selected Plant Families, n.d.), (weicaoshu)]. Micromeria is also referred to as part of the genus Satureja, Greekrootsmīkros (small) and meris (portion)are a testament to the size of their leaves and flowers [(Genus: MicromeriaBenth, 2007), (Quattrocchi, Umberto., 2000)].This perennial or dwarf shrub lives in warm rocky and dry open habitats [(Silic C., 1979)]. In accordance with their shape and phylogenetic relationships, the Micromeria species are divided into Cymularia, Eumicromeria, and Pseudomelissa [(V. Slavkovskal, M. Couladis, S. Bojovic, O. Tzakou, M. Pavlovic4, B. Lakusic, And R. Jancic., 2005)].

Micromeria Species

Not less than 78 species of Micromeria have been found.Well known examples include *M. fruticosa, M. cilica, M. barbata, M. Juliana, M. thymifolia, M. cristata, M. croatica, M. myrtifolia, M. nervosa, M. albanica, and M. persica* [(Micromeria.), (GRIN Species Records of Micromeria.)].

Chemistry of Genus Micromeria

Genus Micromeria include plants of various chemical nature. Micromeria species are reported as a rich source of such essential oils as monoterpenes, sesquiterpenes, and their oxygenated derivatives. However, their concentrations fluctuate according to subspecies. For instance, species of section Pseudo Melissa contained an enormous amount of oil (>0.5%) mainly oxygenated monoterpenes, while Eumicromeria speciesonly had trace amounts of oil (<0.5 %) of different terpene compounds [(V. Slavkovskal, M. Couladis, S. Bojovic, O. Tzakou, M. Pavlovic4, B. Lakusic, And R. Jancic., 2005)].

Even further, major compounds in the essential oils also differ from one species to another. *M. fruticose*[(Fleisher Z., Fleisher A., 1991), (Baser K. H. C., Kirimer N., O" zek T., Tu"men G., Karaer F., 1996)], *M. dolichodonta* [(Baser K. H. C., Kirimer N., Duman H., 1997a)], and M. *capitellata* [(Baser K. H. C., Kirimer N., Tumen G., 1998)] were distinguished by an enormous amount of oil (0.6%– 4%) principally oxygenated terpenes of the menthane type (78%–91%), mainly pulegone (15%–80%). While *M. biflora* was detected to be a rich source of oxygenated monoterpenes geranial and neral (41.3% - 25.3%)[(Mallavarapu G. R., Srinivasaiyer R., Karna S., 1997)], while pinene (8.3%–13.9%) and bornane (5.0%–26.0%) were the dominant oxygenated monoterpenes in *M. carmine* [(Baser K. H. C., Kirimer N., O" zek T., Tumen G., 1995)].

Besides, Micromeria is reported to be a source of alcohols, aliphatic aldehydes, phenolic compounds mainly chlorogenic and ellagic acids, in addition to flavonoids mainly hesperetin, naringin and quercetin [(Mohammad Al-Hamwi, Maha Aboul-Elaa, Abdalla El-Lakany, Nassim El-Achi, Noha Ghanem, Bassem El Hamaoui, Youssef Bakkour and Fawaz El-Omar., 2015)].

Genus Micromeria in Lebanon

About ten species of Micromeria have been identified to grow widely in Lebanon (M. Al-Hamwi, Y. Bakkour, M. Abou-Ela, A. El- Lakany, M. Tabcheh and F. El-Omar., 2011), (Georges Tohme, 2007)]. Table 1 below shows the photos and descriptions of these species collected from different regions:

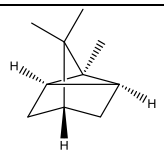
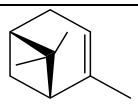
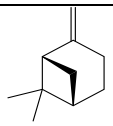
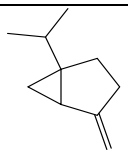
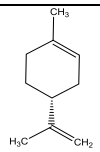
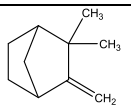
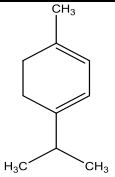
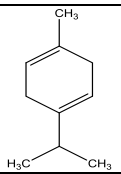
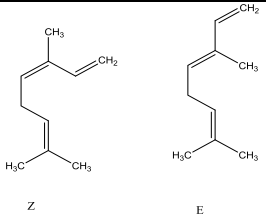
Table 1: Micromeria species grown widely in Lebanon

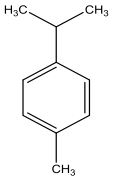
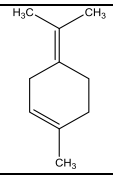
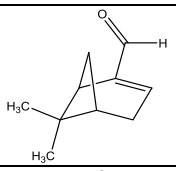
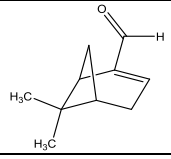
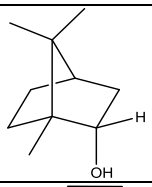
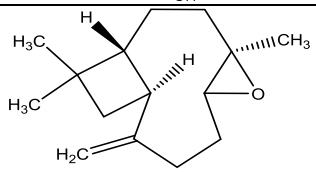
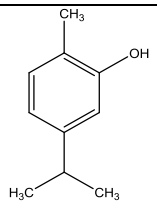
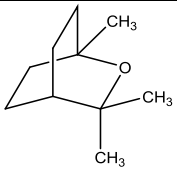
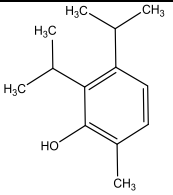
Plant species	Brief description	Photo	Location	Environment
M. amana	- Green plant with rigid stem 5-15 cm; - Sessile and narrow leaves; - Sharp fruits, - Pubescent calyx. - Flowering period:Extended between 6-9		Qammouaa	Rocky at high Altitude
M. graeca	- Pubescent with rigid stem 20-60 cm long; - Narrow, sessile leaves; - Oblong fruits, - Pink flowers. - Flowering period: Extended between 5-7		Ehmej, Chabrouh, Harrisa, Qob Elias	Rocky ground
M. juliana	Pubescent plant - Rigid stem 20-60; - Erect, linear sessile leaves, 5-8 cm; - Sharp fruits, - Pink flower, corolla bigger than calyx - Flowering period: Extended between 5-7		Ehmej, Chnanaair	Woodland
M. libanotica	- Filiform stem 5-20 cm long - Ovate leaves with rounded leaf bases, - Pink corolla. - Flowering period: Extended between 6-9		Faara, Sir, Makmel, Cedars Pass	Rocky at high Altitude
M. myrtifolia	- Pubescent with rigid stem 20-60cm; - Deflexed ovate sessile leaves; - Pink flower, calyx 2.5mm. - Flowering period: Extended between 4-9		Zahleh, Sfeiri, Helouch, Nabaa-Tasseh	Stony ground

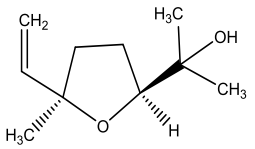
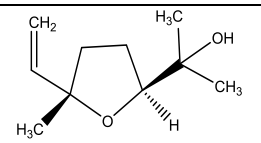
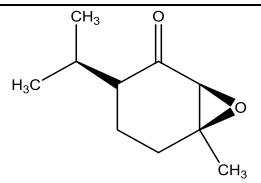
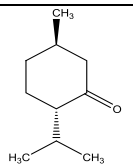
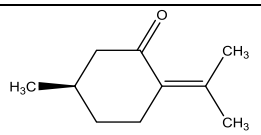
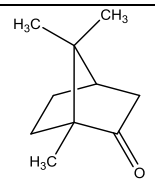
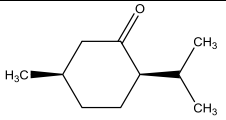
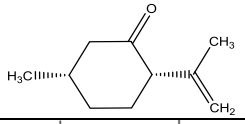
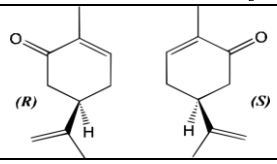
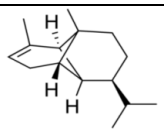
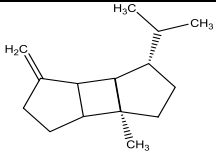
M. nervosa	- Pubescent with rigid stem 20-40cm; - Ovate; narrow sub-sessile leaves; - Pink flower, feathery calyx; - Sharp fruits. - Flowering period: Extended between 2-7		DeirZahrani, Qasmyeh, Cana, Sarada	Stony ground
M. serpyllifolia	- Pubescent with rigid stem 50-100cm; - Petiolate leaves 15cm; - White flower twice the calyx 2-2.5 mm. - Flowering period: Extended between 6-12		Soysseh, KarmChbat	Stony ground
M. nummulariifolia	- Spreading plant 5-10 cm; -Ovate-subulate, sessile leaves; - Pink purple flower, feathery calyx with long teeth. - Flowering period: Extended between 6-9		Aayouness Simane	Rocky ground (altitude)
M. barbata	- Aromatic; 50-100cm; - petiolate leaves 1-5 cm; - White flowers; pubescent calyx, 3-4 mm. - Flowering period: Extended between 6-1		El-Bostan, Qammouaa, Ehden, Cana	Rocky ground
M. fruticosa	- Aromatic, dwarf perennial, evergreen shrubs. - Opposite grey, egg shaped leaves - Small white flowers - Full flowering period: Extended between 5-7		Beqaa valley	Rocky (altitude)

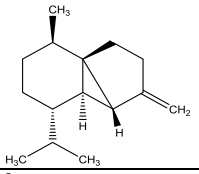
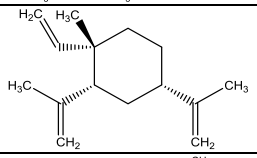
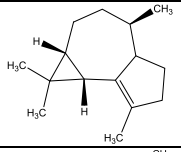
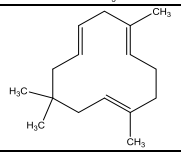
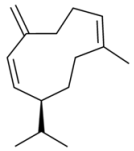
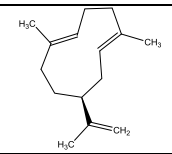
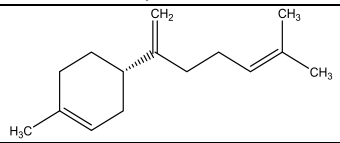
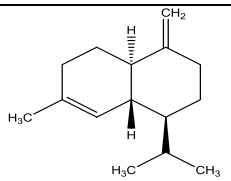
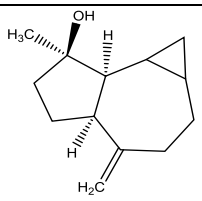
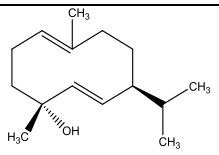
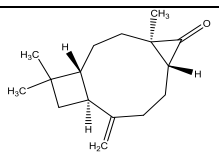
Previously identified compounds from genus Micromeria
The following is a quick review of the identified chemical compounds found withinthe genus Micromeria:

Table 2: Volatile components isolated from Micromeria species:[(M. Al-Hamwi et al., 2011), (Nihaya Salameh, Naser Shraim, and NidalJaradat, 2018), (SemaÇARIKÇI, 2013), (V. Slavkovska et al, 2005), (GordanaStojanovic, Ivan Plic and JasnaUrsic-Jankovic, 2006), (Kirimer N, Ozek T, Baser KHC et al, 1993), (Phokas G, Patouha VVG, Katsiotis S, 1980), (Stojanovic G, Palic I, Ursic JJ, Vajs V, Dokovic D, 1999) and (Ibrahim M. Abu-Reidaha, David Arraez-Romana, Mohammed Al-Nurid, Ismail Waradd,Antonio Segura-Carreteroa., 2019), (Naglaa Gamil Shehab and Eman Abu-Gharbieh , 2012), (abdullatif azab , 2016)]

Compound	Species (Reference)	Structure
a. MONOTERPENE HYDROCARBONS		
Tricyclene	*M. fruticosa* *M. thymifolia* *M. dalmatica* *M. pulegium* *M. albanica* *M. myrtifolia*	
α-Pinene	*M. thymifolia* *M. myrtifolia* *M. albanica* *M. pulegium* *M. fruticosa* *M. cristata* *M. juliana*	
β-Pinene	*M. fruticosa* *M. cristata* *M. juliana* *M. albanica* *M. myrtifolia*	
Sabinene	*M. albanica* *M. fruticosa* *M. dalmatica* *M. thymifolia* *M. myrtifolia* *M. juliana*	
Limonene	*M. fruticosa* *1.2% content* *M. thymifolia* *M. dalmatica* *M. pulegium* *M. albanica* *M. Juliana* *M. myrtifolia*	
Camphene	*M. cristata* *M. albanica* *M. thymifolia* *M. dalmatica* *M. pulegium*	
α-Terpinene	*M. fruticosa* *M. thymifolia* *M. dalmatica* *M. pulegium* *M. albanica* *M. Juliana* *M. myrtifolia*	
ϒ-Terpinene	*M. fruticosa* *M. myrtifolia* *M. cristata* *M. pulegium* *M. juliana* *M. albanica*	
Ocimene	*M. fruticosa* *M. thymifolia* *M. pulegium* *M. albanica*	 Z E

P-Cymene	*M. cristata* *M. fruticosa* *M. thymifolia* *M. juliana* *M. dalmatica* *M. pulegium* *M. albanica*	
Terpinolene	*M. fruticose 0.4%* *M. juliana* *M. cristata* *M. myrtifolia*	
b. OXYGENATED MONOTERPENES		
ALDEHYDES		
α-Campholenal	*M. fruticosa* *M. juliana* *M. cristata*	
Myrtenal	*M. Juliana* *M. cristata*	
ALCOHOLS		
Borneol	*M. fruticosa* *M. pulegium* *M. juliana* *M. cristata major 35.3%*	
α-Terpineol	*M. fruticosa 0.1%* *M. Cilicia* *M. thymifolia* *M. pulegium* *M. juliana* *M. cristata* *M. dalmatica*	
Thymol	*M. fruticosa 1.6% content* *M. thymifolia* *M. dalmatica* *M. cristata* *M. Juliana* *M. thymifolia*	
ETHERS		
1, 8-Cineole	*M. thymifolia* *M. juliana* *M. cristata* *M. fruticosa* *M. myrtifolia*	
Methyl-ethyl Carvacrol	*M. fruticosa* *M. juliana* *M. cristata*	
OXIDES		

cis-Linalool oxide	*M. fruticosa*	
Trans-Linalool oxide		
Piperitone oxide	*M. thymifolia* *M. dalmatica* *M. pulegium* *M. juliana* *M. albanica 44%* *M. cristata* *M. myrtifolia* *M. fruticosa*	
KETONES		
Menthone	*M. fruticosa 0.5%* *M. thymifolia* *M. dalmatica* *M. pulegium* *M. juliana* *M. albanica*	
Pulegone	*M. juliana major 8.6%* *M. fruticosa major 58.5% content* *M. thymifolia* *M. dalmatica* *M. albanica* *M. myrtifolia major 4.3%*	
Camphor	*M. fruticosa* *M. cristata major 12.4%*	
Isomenthone	*M. fruticosa 3.9%* *M. thymifolia* *M. juliana* *M. albanica* *M. myrtifolia* *M. cristata*	
cis-Isopulegone	*M. fruticosa 3.2%* *M. thymifolia* *M. dalmatica*	
Carvone	*M. cristata*	
c. SESQUITERPENES HYDROCARBONS		
α-Copaene	*M. thymifolia* *M. pulegium* *M. Juliana* *M. myrtifolia* *M. fruticosa*	
β-Bourbonene	*M. thymifolia* *M. pulegium* *M. Juliana* *M. cristata* *M. myrtifolia* *M. fruticosa 0.1%*	

β-Cubebene	*M. thymifolia* *M. pulegium* *M. Juliana* *M. myrtifolia*	
β-Elemene	*M. thymifolia* *M. dalmatica* *M. pulegium* *M. juliana* *M. myrtifolia*	
α-Gurgunene	*M. cristata*	
α-Humulene	*M. thymifolia* *M. pulegium* *M. juliana* *M. cristata* *M. fruticosa 0.2%*	
Germacerene D	*M. fruticosa 0.5%* *M. thymifolia* *M. dalmatica* *M. pulegium* *M. juliana* *M. albanica* *M. myrtifolia*	
Germacerene A	*M. croatica*	
β-Bisabolene	*M. fruticosa*	
ϒ-Cadinene	*M. fruticosa* *M. croatica* *M. thymifolia* *M. dalmatica* *M. pulegium* *M. juliana* *M. albanica*	
d. OXYGENATED SWSQUITERPENES		
ALCOHOLS		
Spathulenol	*M. fruticosa 0.2 %* *M. croatica* *M. thymifolia* *M. dalmatica* *M. pulegium* *M. juliana* *M. albanica* *M. cristata*	
Germacrene-D-4-ol	*M. fruticosa* *M. Juliana* *M. myrtifolia*	
Caryophyllene Oxide	*M. fruticosa 0.9%* *M. pulegium* *M. Juliana major 19.4%* *M. albanica* *M. cristata major 6.4%* *M. myrtifolia major33.9%*	
PHENYL PROPANOIDS		

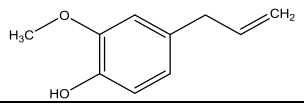
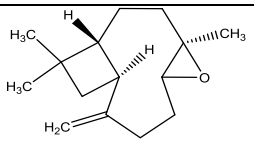
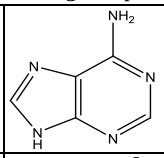
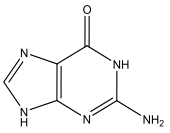
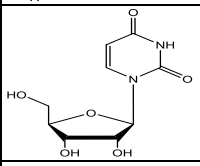
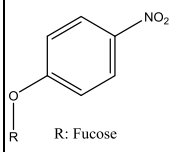
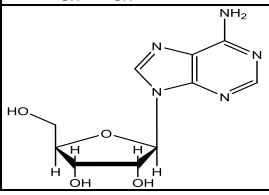
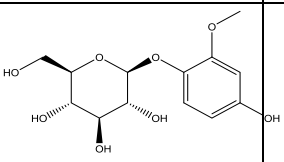
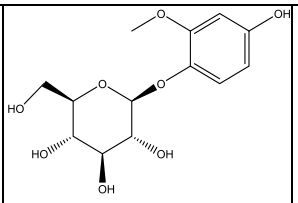
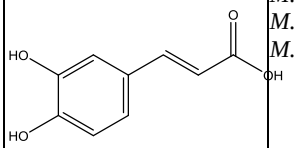
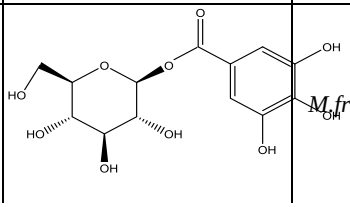
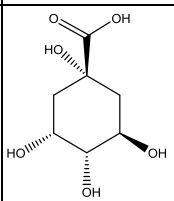
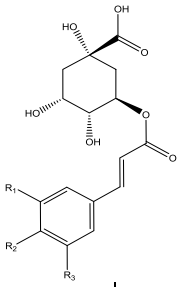
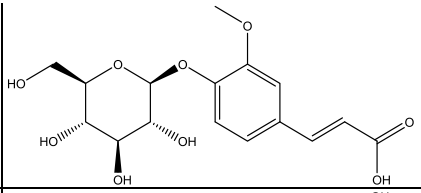
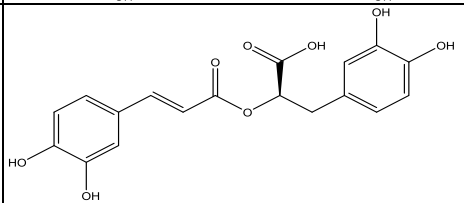
Eugenol	*M. fruticosa* *M. pulegium*	
OTHERS		
Caryophyllene	*M. persica* *M. fruticosa*	

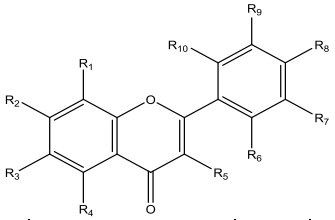
Table 3: Major secondary compounds identified in Micromeria species [(Mohammad Al-Hamwi, Maha Aboul-Elaa, Abdalla El-Lakany, Nassim El-Achi, Noha Ghanem, Bassem El Hamaoui, Youssef Bakkour and Fawaz El-Omar., 2015), (Eman Abu-Gharbieh and Naglaa G Ahmed., 2016)& (Ibrahim M. Abu-Reidaha, David Arraez-Romana, Mohammed Al-Nurid, Ismail Waradd,Antonio Segura-Carreteroa., 2019), (Sanda Vladimir-Knežević, Biljana Blažeković, Maja BivalŠtefan, AntunAlegro,TamásKőszegi, and József Petrik., 2011), (Niklova M., Aneva I., Berkov S., 2016), (Fatiha Brahmi, Naima Guendouze, Didier Hauchard, Phillipe Okusa,LéocadieKamagaju, KhodirMadani& Pierre Duez, 2017)]

Nitrogen containing compounds					
Adenine		*M.fruticosa*	Guanine		*M.Fruticosa*
Uridine		*M.fruticosa*	*p*-nitrophenylfucoside		*M.fruticosa*
Adenosine		*M.fruticosa*	*Iso*-stachioside		*M.fruticosa*
Simple phenolic acid derivatives					
(iso) tachioside		*M.fruticosa*	Caffeic acid		*M. graeca*, *M. dalmatica* *M. fruticosa*
Glucogallin		*M.fruticosa*	Quinic acid		*M.fruticosa*



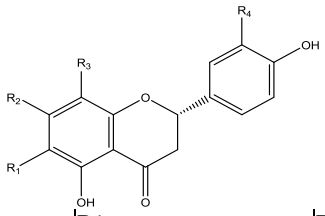
Name		R_1	R_2	R_3
5-*p*-coumaroylquinic acid		H	OH	H
Chlorogenic acid	*M. graeca* *M. thymifolia* *M.fruticosa*	OH	OH	H
3-*O*-Feruloylquinic acid	*M.fruticosa*	H	OH	OCH_3
Ferulic acid 4-*O*-glucoside	*M.fruticosa*			
Rosmarinic acid	*M.fruticosa*			*M.Fruticosa* *M. graeca* *M. thymifolia* *M. Juliana* *M. croatica*

Flavonoid derivatives

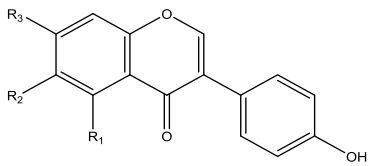


Compound name		R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9
Rutin	*M. fruticosa*	H	OH	H	OH	*O*-rutinose	H	H	OH	OH
5,6-DiOH-7,3',4'-triOCH_3		H	OCH_3	OH	OH	H	H	H	OCH_3	OCH_3
Quercetin		H	OH	H	OH	OH	H	H	OH	OH
Isorhamnetin		H	OH	H	OH	OH	H	H	OH	OCH_3
Apigenin 7-*O*-rutinoside		H	*O*-Rutinose	H	OH	H	H	H	OH	H
Diosmetin 7-*O*-rutinoside		H	*O*-Rutinose	H	OH	H	H	H	OCH_3	OH
Apigenin 7-*O*-glucuronide	*M. fruticosa* *M. graeca*	H	*O*-Glucouronic	H	OH	H	H	H	OH	H
Chrysoeriol	*M. fruticosa*	H	OH	H	OH	H	H	H	OH	OCH_3
7-methylsudachitin		OCH_3	OCH_3	OCH_3	OH	H	H	OCH_3	OH	H
Linarin		H	*O*-Rutinose	H	OH	H	H	H	OCH_3	H
Luteolin		H	OH	H	OH	H	H	H	OH	OH

Apigenin	*M. graeca* *M. dalmatica* *M. fruticosa*	H	OH	H	OH	H	H	H	OH	H
Kaempferol	*M. fruticosa*	H	OH	H	OH	OH	H	H	OH	H
Daizein		H	OH	OH	H	H	H	H	OH	H
Genstein		OH	H	OH	H	H	H	H	OH	H
Glycitein		H	OCH_3	OH	H	H	H	H	OH	H
Quercetin-3-*O*-glucoside		H	OH	H	OH	Glc.	H	H	OH	OH



Compound		R1	R2	R3	R4
Naringenin	*M. fruticosa*	H	OH	H	H
Thymonin		OH	OCH_3	OCH_3	OCH_3



Aglycones:

Compound name		R1	R2	R3
Daidzein		H	H	OH
Genstein	*M. fruticosa*	OH	H	OH
Glycitein		H	OCH_3	OH

Iridoid derivatives:

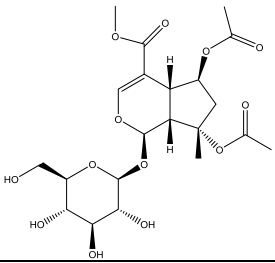
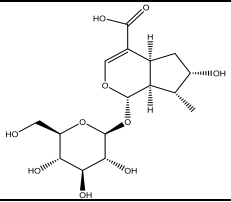
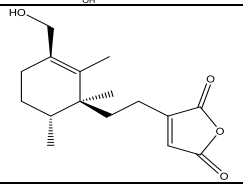
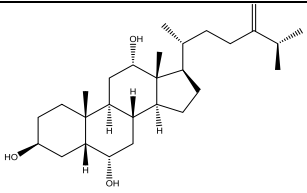
Acetylbarlerin	*M. fruticosa*	
Loganic Acid		
Micromeriol		
Nervosane		

Table 4: Summary of the Reported Pharmacological activities of Micromeria species.

Plant extract	Plant species	Biological activity	Ref.
Essential oil Ethanolic	*M. fruticosa*	Antimicrobial and antioxidant activity	(Mohammad Al-Hamwi, Maha Aboul-Elaa, Abdalla El-Lakany, Nassim El-Achi, Noha Ghanem, Bassem El Hamaoui, Youssef Bakkour and Fawaz El-Omar., 2015)
Volatile oil	*M. fruticosa*	exhibited antilipase and antiamylase activity	(Nihaya Salameh, Naser Shraim , and NidalJaradat, 2018)
Essential oil Ethanolic	*M. fruticosa*	Antimicrobial; anaesthetic,antioxidant, antirheumatic, sedative, antiseptic, common colds, CNS stimulant, the remedy of heart diseases, and abortifacient.	(N. G. Shehab and E. Abu-Gharbieh, 2012)
Essential oil Aqueous	*M. fruticosa*	Both: antitumor. Aqueous extract: analgesic (Treatment of diarrhea, abdominal pains, colds, and wounds, heart disorders, elevated blood pressure, eye infections)	
Essential oil	*M. fruticosa*	Potentiation of Insecticidal, effect added to essential oils of other plants.	
Acetone	*M. fruticosa*	Synergism tomany plant extracts, antibacterial and acaricidal.	
Essential oil	*M. fruticosa*	Boosts the effect of essential oils of other plants, Insecticidal.	
Roots	*M. fruticosa*	Allelopathic: the release of metabolites by the roots of green plants in soil.	
Methanolic	*M. fruticosa*	Myeloperoxidase, antispasmodic, eye infections,diarrhea fatigue,cardiovascular diseases, anti-inflammatory, elevated blood pressure, common colds and wounds remedy)	
Essential oil	*M. fruticosa*	Anti-microbial. Potentiation of current antibiotics	
Aqueous	*M. fruticosa*	Anti-inflammatory, gastroprotective (Wound healing, treatment of diarrhea and antispasmodic	
Essential oil	*M. fruticosa*	Anti-biofilm formation (*Streptococcusmutans*), antimutagenic, antioxidant.	
Ethanolic	*M. fruticosa*	Antimicrobial, antioxidant (Treatment of diarrhea, abdominal pains, colds, skin infections, and wounds)	
Aqueous	*M. fruticosa*	Potential cytotoxic effect on U-87 MG cells.	(Kubra Koc1, OzlemOzdemir, Omer Faruk Kizilkaya, MeryemSengul and Hasan Turkez, 2016)
Essential oil Aqueous	*M. fruticosa*	Interesting anticancer effectson Human Colon Tumor cells in addition to Mammary Carcinoma F7.	(Shehab NG, Abu-Gharbieh E., 2012)
Aqueous	*M. fruticosa*	marked analgesic effect concomitant to inflammatory pain and non-inflammatory reactions	(M. Gulluce, M. Sokmen, F. S¸ahin, A. Sokmen, A. Adiguzel, and H. Ozer),2004
Aqueous	*M. fruticosa*	Anti-inflammatory and gastroprotective activities	(Abu-Gharbieh E, Shehab NG, Khan SA., 2013)
Ethanolic xtract	*M. graeca*	Examined against 4 pathogenic bacteria, two strains of *S. aureus*, *P. aeruginosa*, and *E. coli*. The extract alone revealed a weak antibacterial activity, when combined with antibiotics, the extract reestablished the effects of streptomycin and cefotaxime on resistant strains.	(Fatiha Brahmi, Naima Guendouze, Didier Hauchard, Phillipe Okusa,LéocadieKamagaju, KhodirMadani& Pierre Duez, 2017)
Essential oil	*M. barbata*	Gave a significant antifungal activity when tested against strains of fungi and yeast. An identical result was obtained against antifungal resistant strains.	(K. El Omari, M. Hamze, S. Alwan, C. Jama, N.E. Chihib., 2016)
Five different extracts and its main	*M. cilicica*	Pulegone and several extracts revealed antimicrobial activity against most of the nine tested microorganisms(*Micrococcus luteus*, *Enterobacter aerogenes*, *Staph. aureus*,	(Mehmet Ozturk, UfukKolak, GulactıTopcu, SevilOksuz, B. M. Iqbal Choudhary, 2011)

component pulegone		*Salmonella typhimurium*, *Bacillus subtilis*, *Bacillus cereus*, *E. coli*, *Ps. aeruginosa*, *Streptococcus mutants* and *C. albicans)*and one type of yeast causing infection to humans	
Essential oil	*M. thymifolia*	Showed an interesting antimicrobial activity when examined against four Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella enterica*, and human pathogen *Burkholderiacepacia*A), four Gram-positive bacteria (*Enterococcus fecalis*, *Staphylococcus aureus*, *Bacillus subtilis*, and *Listeria innocua*), and two fungi (*Candida albicans* and *Saccharomyces cerevisiae*).	(Marija A. Marin Miroslav M. NovakovićVele V. Tešević, BrankaS.Vuković-Gačić., 2015)
Methanolic extracts	*M. Juliana* *M. dalmatica* *M. cristata* *M. frivaldszkyana*	Using DPPH assay, all extracts exhibit significant antioxidant activity, the highest activity was for *M. dalmatica*.	(Milena Nikolova, InaAneva, Peterzhelev., 2017)
Ethanolic extracts	*M. croatica* *M. thymifolia* *M. Juliana*	Using five different methods, all the extracts showed interesting antioxidant activity with that of *M. croatica* was the best. The study revealed that the quenching effect of the plants against free radicals is correlated to their phenolic acid and tannin content.	(Sanda Vladimir-Knežević, Biljana Blažeković, Maja BivalŠtefan, AntunAlegro,TamásKőszegi, and József Petrik., 2011)
Acetone extract	*M. nervosa*	Significant free radical quenching activity compared to that of L, α-tocopherol, and BHT.	(Mohammed F. Abdelwahab , Mohammed H. Hussein, Hazem H. Kadry., 2015)
Ethanolic extract	*M. barbata*	Showed its superiority as DPPH radical scavenging activity compared to the commonly used synthetic antioxidant.	(Noha Ghanem, Bassem El Hamaoui, Nassim El-Achi, Youssef Bakkour, SaerAlwan, Fatima Houmaisi, John Hanna El-Nakat and Fawaz El-Omar, 2014)
Ethanolic extract	*M. fruticosa*	The activity of DPPH radical is inhibited when subjected to the extract in a dose-dependent manner at which the IC50 of the extract was 50 µg/mL, which was interestingly below that of BHT (91.40 µg/mL)	(Mohammad Al-Hamwi, Maha Aboul-Elaa, Abdalla El-Lakany, Nassim El-Achi, Noha Ghanem, Bassem El Hamaoui, Youssef Bakkour and Fawaz El-Omar., 2015)
Aacetone and methanolic extracts	*M. cilicica*	showed antioxidant activity following the four test systems (DPPH, ABTS, superoxide anion radical-scavenging, and β-carotene quenching system), the most significant effect was for the acetone extract.	(Mehmet Ozturk, UfukKolak, GulactıTopcu, SevilOksuz, B. M. Iqbal Choudhary, 2011)
Aqueous extract	*M. pulegium*	Significantly inhibits human GR-M melanoma cell line cultures,	(Haveric, Anja, Hindija Čakar, Jasmina, Hadzic, Maida, Haveric, Sani,n., 2018)
Methanolic extract	*M. myrtifolia*	Interesting decrease in cell viability of RD and L20B cell lines when tested at maximum concentrations, a significant decrease occurred at1000µg/ml in comparison with the negative control.	(Khulood W. Al-SamarraeiEbtehal H. Al-Naimy Raghad K. Al-lihaibiRafal S. Al-Ani, 2016)
Ethanolic extract	*M. fruticosa*	high inhibitory activity against MCF7 and A549 cancer cell lines with IC50 below 30µg/ml and significantly boosted the activity of cisplatin at low doses.	(Al-Hamwi M, Aboul-Ela M, El-Lakany A, Nasreddine S., 2021)
Methanolic extract	*M. myrtifolia*	Showed antidepressant activity through different *in-vitro* and *in-vivo* experimental models of depression.	(Esra KüpeliAkkol, Fatma Tu˘gçeGüra˘gaçDereli and MertIlhan, 2019)

2. CONCLUSION

Reviewing the literature survey on Micromeria species, the researchers considered them as a rich source of polyphenolic compounds and essential oils, which are bioactive compounds that extremely attract scientific interest and manifest a wide scope of pharmacological effect. Because of the diversity in their chemical constituents and reported pharmacological activities including anti-inflammatory, antimicrobial, antifungal, antioxidant, and anti-cancer, Micromeria species are considered as a rich source of raw materials that can be used for organic synthesis and drug production.

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