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REVIEW ARTICLE: THE PHARMACOLOGICAL POTENTIAL OF THE GENUS MICROMERIA

Al-Harith Mohammed AL-Samawi[1], Amina El-Shaibany[1]* and Mahmoud Mahyoob Alburyhi[2]

[1]Pharmacognosy, Department of Pharmacognosy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.

[2]Pharmaceutics and Industrial Pharmacy, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.

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***Corresponding Author**
Amina El-Shaibany
Pharmacognosy, Department of Pharmacognosy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.

ABSTRACT

The genus Micromeria, belonging to the family Lamiaceae, comprises numerous species distributed across North America, Europe, Africa, and Asia, with a notable presence in the Mediterranean region and Canary Islands. This review article explores the pharmacological potential of Micromeria species, focusing on their antimicrobial, antioxidant, cytotoxic, and enzyme inhibitory activities. Essential oils and extracts from species such as *Micromeria hortensis*, *Micromeria khuzestanica*, and *Micromeria montana* demonstrate significant antimicrobial properties, attributed to high levels of carvacrol and thymol. Antioxidant activity is similarly robust, primarily due to oxygenated monoterpenes. Cytotoxic studies reveal potent activity against various cancer cell lines, suggesting potential applications in cancer therapy. Additionally, Micromeria species exhibit strong inhibitory effects on acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), enzymes implicated in Alzheimer's disease. This review underscores the importance of further research to isolate and characterize the active compounds in Micromeria, paving the way for their potential therapeutic applications.

KEYWORDS: Micromeria, Lamiaceae, antimicrobial, antioxidant, cytotoxic, acetylcholinesterase inhibition, butyrylcholinesterase inhibition, carvacrol, thymol, medicinal plants.

INTRODUCTION

The selection of medicinal plants requires considerable experience. Statistical studies conducted in Australia and the US indicated that almost 48.5% and 34% of individuals, respectively, had used at least one unconventional therapy (Kim et al., 2007). In developing countries, about 65–80% of the world population depends primarily on plants for their healthcare due to poverty and lack of access to modern medicine (Calixto, 2005). It is well known that in many developing countries, people suffer from a lack of safe modern drugs. Therefore, evaluating effective plants for the treatment of diseases such as diabetes has been recommended.

In the last decade, many researchers have reported the efficacy of herbal medicines in various diseases. According to statistical data reported multiple times, approximately 25% of the active compounds in currently prescribed synthetic drugs were first identified in plant resources. Moreover, 20,000 plants have been used for medicinal purposes, with around 4,000 being commonly used. Among these, 10% currently have commercial importance (Kim et al., 2007; Momtaz & Abdollahi, 2010).

Genus Micromeria

Micromeria (Family Lamiaceae) is found throughout North America, Europe, Africa, and Asia, with many varieties located in the Mediterranean region and Canary Islands (Bahramikia & Yazdanparast, 2012). Micromeria is also sometimes classified as part of the genus Satureja. The name Micromeria derives from the Greek roots *mīkros* (small) and *meris* (portion), reflecting the small size of their leaves and flowers (Genus: Micromeria Benth, 2007; Quattrocchi, 2000). This perennial or dwarf shrub thrives in warm, rocky, and dry open habitats (Silic, 1979).

Pharmacology of Genus Micromeria

Antimicrobial Activity

Studies on the antimicrobial activity of 37 different plant species have been reported. According to the literature, **Micromeria hortensis** and **Micromeria montana** are among the most commonly evaluated species for their antimicrobial properties. Most studies have tested these species against both Gram-negative and Gram-positive bacteria, as well as fungi. In some studies, the focus was solely on their antifungal activities.

The presence and concentration of carvacrol have been identified as significant indicators of antimicrobial activity. Plant species with high levels of thymol and carvacrol generally exhibit strong antimicrobial properties (Bektas Tepe & Mustafa Cilkiz, 2016). For instance, *M. hortensis* oil, known for its natural antibacterial properties, shows potential for use in food packaging, particularly for products that are prone to oxidation and microbial contamination (Shojaee-Aliabadi et al., 2013).

Antioxidant Activity

According to literature data, the β-carotene bleaching assay is the most commonly used antioxidant test system. Another frequently employed method is the determination of free radical scavenging potential. Among the free radicals tested, DPPH, ABTS, TBARS, superoxide, and nitric oxide are the most commonly evaluated.

Reports indicate that essential oils from **Micromeria hortensis**, **Micromeria khuzestanica**, and **Micromeria montana** generally exhibit significant antioxidant activity. This activity is largely attributed to their high content of oxygenated monoterpenes, particularly carvacrol and thymol. Additionally, polar phytochemicals are also noted as biologically active compounds contributing to this antioxidant potential.

Due to their substantial antioxidant activity, Micromeria species are considered valuable sources for consumption. Their importance, particularly in the food industry and ethnopharmacology, has been strongly emphasized in these studies (Bektas Tepe & Mustafa Cilkiz, 2016).

Cytotoxic Activity

According to the literature survey, cytotoxic activities of 12 Micromeria species have been evaluated, including *M. atropatana Bung.*, *M. hortensis*, *M. intermedia CA Mey*, *M. kitaibelii Wierzb. ex Heuff.*, *M. khuzestanica*, *M. montana*, *M. punctata subsp. punctata K. Schum.*, *M. sahendica Bornm.*, *M. spicigera*, and *M. thymbra L.* Cytotoxicity of the essential oils and/or extracts of these species has been tested on various cell lines, such as J774 macrophage, 5637, KYSE, Fem-X Human Malignant Melanoma, Vero, SW480, MCF7, JET3, A549, THP-1, and HT29/219 (Bektas Tepe & Mustafa Cilkiz, 2016).

The cytotoxic activity of *M. hortensis* on the J774 macrophage cell line was tested by Moradi et al. (2008). The study found that it was toxic at higher concentrations (IC50 value = 45.13

μM) than those needed to inhibit parasite cell growth. *M. intermedia* was evaluated by Sadeghi et al. (2013), who reported an IC50 value of 156 μg/ml against the 5637 and KYSE cell lines. Stanojkovic et al. (2013) assessed the cytotoxic activity of *M. kitaibelii* methanol extract, which showed strong activity against Fem-X Human Malignant Melanoma cells (IC50 value = 39.66 μg/ml) and moderate activity against other cancer cell lines (IC50 values of 138.06 μg/ml against MDA-MB-361 and 173.15 μg/ml against HeLa).

Another species, *M. khuzestanica*, was studied by Yousefzadi et al. (2014). Its essential oil significantly reduced cell viability in Vero, SW480, MCF7, and JET 3 cells in a dose-dependent manner, with IC50 values of 31.2, 62.5, 125, and 125 μg/mL, respectively. The cytotoxicity potential of *M. punctata* subsp. *punctata* on human monocytic leukemia cells (THP-1) and erythrocytes was evaluated by Tariku et al. (2010), revealing high toxicity on THP-1 cells (CC50 value = 0.013–350 nL/mL with a selectivity index between 0.001 and 28) and erythrocytes (LC50 value = 0.35–1.52 μg/ml).

M. sahendica was also investigated by Yousefzadi et al. (2012), who found that its essential oil significantly reduced cell viability in MCF7, Vero, SW480, and JET 3 cells with IC50 values of 15.6, 125.0, and 250.0 μg/ml, respectively. *M. odora* and *M. parvifolia* were tested by Mongelli et al. (1996) using a dichloromethane extract, showing promising activity against brine shrimp (LC50 value = 5200 μg/ml). Saab et al. (2012) evaluated *M. thymbra* using the MTT assay in Vero cells, finding it exhibited the highest selectivity index (SI).

Most studies have focused on crude extracts and essential oils. However, specific active phytochemicals responsible for cytotoxic activity have been reported only in a few studies. Stanojkovic et al. (2013) identified rosmarinic acid as capturing the G2/M phase cell cycle in Fem-X cells, showing that both the methanol extract and rosmarinic acid exhibited significant cytotoxic activity. Gohari et al. (2012) reported on brine shrimp lethality and tested four cancerous cell lines (HT29/219, Caco (2), NIH-3T3, and T47D), identifying key compounds with cytotoxic properties.

Acetylcholinesterase (AChE) and Butyrylcholinesterase (BChE) Inhibitory Activities

Acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) are key enzymes involved in Alzheimer's disease. Several studies have evaluated the inhibitory activities of various Micromeria species on these enzymes.

Orhan et al. (2008) investigated the AChE and BChE inhibitory activities of the essential oil obtained from *M. cuneifolia*. The essential oil demonstrated very high inhibitory activity (over 80%) against AChE.

The AChE inhibitory activity of *M. khuzestanica* was also examined by Basiri et al. (2007). This study focused on the protective effect of *M. khuzestanica* essential oil against the toxicity of malathion, a commonly used organophosphorus (OP) compound. Malathion inhibited erythrocyte AChE and increased hepatic cell glucose-6-phosphate (GP) and phosphoenolpyruvate carboxykinase (PEPCK) activities. Co-administration of *M. khuzestanica* essential oil resulted in the restoration of malathion-induced changes in hepatic cell GP and PEPCK activities, as well as blood AChE levels and glucose levels. The study concluded that the oil interferes with malathion-induced stimulation of hepatic glycogenolysis and gluconeogenesis through its antioxidant potential and increased AChE activity.

Silva et al. (2009) assessed the AChE inhibitory activity of *M. montana* essential oil. The study highlighted the strong AChE inhibitory potential of the oil, suggesting its potential for developing AChE inhibitors from natural products.

CONCLUSION

The genus Micromeria holds significant pharmacological potential, particularly in antimicrobial, antioxidant, cytotoxic, and enzyme inhibitory activities. The high content of oxygenated monoterpenes, carvacrol, and thymol in these species contributes to their biological activities. Further studies on specific active phytochemicals responsible for these activities and their mechanisms of action are warranted to fully explore the medicinal potential of Micromeria species.

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