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Chemical Composition and Biological Activities of *Mentha* Species

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Additional information is available at the end of the chapter

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Abstract

The genus *Mentha* L. (Lamiaceae) is distributed all over the world and can be found in many environments. *Mentha* species, one of the world's oldest and most popular herbs, are widely used in cooking, in cosmetics, and as alternative or complementary therapy, mainly for the treatment of gastrointestinal disorders like flatulence, indigestion, nausea, vomiting, anorexia, and ulcerative colitis. Furthermore, it is well documented that the essential oil and extracts of *Mentha* species possess antimicrobial, fungicidal, antiviral, insecticidal, and antioxidant properties. The economic importance of mints is also evident; mint oil and its constituents and derivatives are used as flavoring agents throughout the world in food, pharmaceutical, herbal, perfumery, and flavoring industry. To provide a scientific basis for their traditional uses, several studies have been conducted to determine the chemical composition of mints and assess their biological activities. This chapter describes the therapeutic effects and uses of *Mentha* species and their constituents, particularly essential oils and phenolic compounds; some additional biological activities will also be considered.

Keywords: *Mentha* sp., therapeutic effects, uses, composition, biological activities

1. Introduction

Mentha is a member of the Lamiaceae which was originally described and named by Jussieu (1789) who gave the family name Lamiaceae, due to the distinctive flowers with a prominent liplike lower petal. This family has almost cosmopolitan distribution, from temperate to tropical regions, but is primarily found in the Mediterranean Basin. Members of this family may be annual or perennial herbs, shrubs, and small trees. The Lamiaceae are closely allied

to the Verbenaceae, and, in a recent family revision, several genera have been transferred to Lamiaceae [1]. As a result, the circumscription of the Lamiaceae has been changed to include eight subfamilies: Ajugoideae, Chloranthaceae, Lamioideae, Nepetoideae, Pogostemonoideae, Scutellarioideae, Teucroideae, and Viticoideae. Nevertheless, over 47% of the Lamiaceae fall within the subfamily Nepetoideae [2].

This family includes about 260 genera and more than 7000 species. Their characteristic features include the stems which are quadrangular (square) in cross-section and the bisexual, zygomorphic bilaterally symmetrical flowers, composed of five united and deeply lobed petals and five united sepals; typically, the lower petal is larger than the others. The fruit is dry and woody, a schizocarp or drup. The distinctive strongly aromatic leaves are opposite with successive pairs at right angles (i.e., decussate) with margins entire or lobed. Many species of this family, such as mints, have important commercial uses for the culinary, pharmaceutical, herbal, and ornamental industries [1].

Throughout history, a number of mint species have been used around the globe for various properties. Peppermint oil is one of the world's oldest herbal medicines. The gathering of dried peppermint dates back to at least 1000 BC, and its use is documented in the ancient Egypt, Greece, and Rome; in traditional Chinese medicine, the use of a local mint species, *Mentha haplocalyx* Briq. called "bo he," has long been documented [3]. Peppermint (*Mentha piperita* L.) was not officially described until 1696, when the English botanist John Ray (1628–1705) first discovered this pepper-flavored mint. Entering the London Pharmacopoeia in 1721, peppermint has since been cultivated for its essential oil throughout Asia, Europe, and North America [4]. Mint history is colored by stories from ancient mythology. Proserpine, Pluto's wife, was said to have transformed a hated rival into a mint plant. Both the Latin "mentha" and the Greek "minthe" have come to be associated with metamorphosed beauty [5].

The taxonomy of the genus *Mentha* has been in a state of flux, with more than 3000 names published since 1753, most of them being synonyms or unresolved names [2], often referring to cultivars. The genus *Mentha* L. is widely distributed on all continents (except in South America and Antarctica). The centers of variety of this genus that groups spontaneous and cultivated forms are Europe, Australia, Central Asia, and North Africa [6].

Most *Mentha* grows best in wet environments and moist soils. Mints will grow 10–120 cm tall and can spread over an indeterminate-sized area. Due to the tendency to spread unchecked, mints are considered invasive. All mints prefer, and thrive in, cool, moist spots in partial shade. But, in general, mints tolerate a wide range of conditions and can also be grown in full sun. They are fast growing, extending their reach along surfaces through a network of runners [7]. According to the latest taxonomic treatment, the genus *Mentha* comprises 61 species [8] and about 100 varieties and cultivars, divided into five sections: *Audibertia*, *Eriodontes*, *Mentha*, *Preslia*, and *Pulegium*. The systematic of the genus is not fully elucidated because of the strong morphologic variations, levels of ploidy ($2n = 2x = 24$ to $2n = 6x = 96$) and hybridizations that can be intra- and interspecific and between spontaneous and cultivated forms [6].

Within the section *Mentha*, it has been suggested that the five basic species, *Mentha arvensis* L., *Mentha aquatica* L., *Mentha spicata* L., *Mentha longifolia* (L.) Huds, and *Mentha suaveolens* Ehrh. (Figure 1), have given rise to 11 naturally occurring and named hybrids. However, *M. spicata*

and possibly *M. longifolia* are also of hybrid origin and incongruence of nuclear and plastid DNA-based phylogenies indicates that all species of this section may have experienced some extension of reticulate gene flow during their evolution [9].

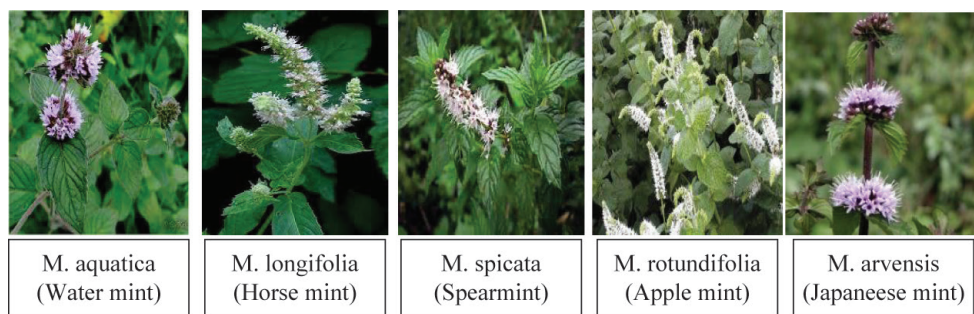


Figure 1. The five basic species comprising the genus *Mentha* [10].

Šarić-Kundalić et al. [9] suggest a differentiation of the section *Mentha* into three basic lines, *capitatae*, *spicatae*, and *verticillatae*, based on inflorescence characters. The line “*capitatae*” includes all species with compact, headlike inflorescence; the type of species is *M. aquatica*. The “*spicatae*” species have a spike as shown by *M. spicata*, *M. longifolia*, and *M. suaveolens*. The third line is represented by *M. arvensis* having an inflorescence vertically partitioned into whorls.

2. Therapeutic effects and uses

Besides its culinary uses, mint is also used in traditional systems of medicine. Mints are mainly used to cure gastrointestinal disorders, but the spectrum of medical activities is broader [9]. Mint was originally used as a medicinal herb to treat stomachache and chest pains, and it is commonly used in the form of tea as a home remedy to stimulate digestion; alleviate stomach pain; and treat biliary disorders, dyspepsia, enteritis, flatulence, gastritis, gastric acidities, aerophagia, intestinal colic, and spasms of the bile duct, gallbladder, and gastrointestinal tract [7, 10, 11]. Mint also aids digestion, notably of fats; in recent years, it has been often recommended for treating obesity. Mint tea is also a strong diuretic [7].

The essential oil from *Mentha* spp. is used topically to treat oral mucosal inflammation and also an antimicrobial and an ingredient in many analgesic creams. Approved for internal use, the oil from *Mentha* spp. is also used to treat bile duct discomfort, irritable bowel syndrome, myalgia and neuralgia, inflammation of the oral mucosa, discomfort from menstrual cramps, secondary amenorrhea and oligomenorrhea, and diverticulitis and is used as an anti-inflammatory and expectorant [4, 12].

Other therapeutic effects attributed to a series of *Mentha* species are summarized in **Table 1**.

Species	Region	Indications	Reference
<i>M. spicata</i>	Brazil	For the expulsion of parasitic worms, mainly <i>Ascaris lumbricoides</i>	[13]
	Morocco	Leaf and stem infusion for headache and tiredness	[14]
	India	Stimulant, carminative, antispasmodic, fever, remedy in infantile troubles; the boiled leaves extract is used to relieve hiccup, flatulence, giddiness and as remedy for inflammation, bronchitis, to control vomiting during pregnancy	[15]
	Turkey	Three or four cups daily between meals can relieve gastrointestinal complaints. This herb is considered stimulant, carminative, antispasmodic, and antidote for poisons. It has been reported as a remedy for inflammation, fevers, bronchitis, infantile troubles, vomiting in pregnancy, and hysteria	[16]
	India	The boiled leave extract was counseled in the viral hepatitis, as analgesic known for its ability to enhance memory. Leaves are given for fever and bronchitis and are used as lotion in aphthae, as stomachic and diuretic, for gas pain, rheumatism, toothache, muscle pain, and mouthwash	[11]
	France	Acquires a very powerful action on the nervous system	[17]
<i>M. pulegium</i>	India	The plant is typically used in the treatment of loss of appetite, common cold, bronchitis, sinusitis, fever, nausea, and vomiting	[10]
	Brazil	For expulsion of parasitic worms; mainly <i>Ascaris lumbricoides</i> , <i>Entamoeba histolytica</i> , and <i>Giardia lamblia</i> ; renal calculus; fever; bad cold; cough; bronchitis; bellyache; and bad cold	[13]
	Algeria	Stomachic, carminative, antiemetic, antispasmodic, tonic, antitussive, and insecticidal	[18]
	Iran	Antiseptic for treatment of cold, sinusitis, cholera, food poisoning, bronchitis, and tuberculosis	[19]

Species	Region	Indications	Reference
<i>M. rotundifolia</i>	Iran	In the treatment of flatulent dyspepsia and intestinal colic	[7]
	Spain	Hypotensive	[20]
	Morocco	Leaf and stem decoction was used in cold and for system digestive	[14]
	France	Tonic, stimulative, stomachic, carminative, analgesic, choleric, antispasmodic, anti-inflammatory, sedative, hypotensive, and insecticidal	[21]
<i>M. longifolia</i>	Iran	Different parts of the plant (leaves, flower, stem, bark, and seeds) have been used as antimicrobial, carminative, stimulant, antispasmodic, antirheumatic, antiscorbutic, wound healing, deworming, insect repellent, antiemetic, sedative, diuretic, aphrodisiac, blood purifier and for the treatment of headaches, digestive disorders, tonsillitis, diarrhea, dysentery, abdominal disorders, constipation, gall stone, jaundice, toothache, flatulence, asthma, cough, dyspnea, common cold, fever, headache, general weakness, and bladder and kidney stones	[22]
<i>M. piperita</i>	India	Peppermint oil (as well as peppermint leaf) has been used internally as an antispasmodic (upper gastrointestinal tract and bile ducts) and to treat irritable bowel syndrome, catarrh of the respiratory tract, and inflammation of the oral mucosa. Externally, peppermint oil has been used for myalgia and neuralgia To relieve menstrual cramps and used externally for neuralgia, myalgia, headaches, migraines, and chicken pox	[23]
	India	Peppermint plants have been used for many conditions, including loss of appetite, common cold, bronchitis, sinusitis, fever, nausea, vomiting, and indigestion	[10]
	Finland	Peppermint uses include irritable bowel syndrome, flatulence, indigestion, nausea, vomiting, cough, and bronchitis	[24]
	USA	The odors of peppermint serve as central nervous system stimulant and are used to decrease fatigue	[25]

Species	Region	Indications	Reference
<i>M. arvensis</i>	India	Possess abortifacient property	[10]
<i>M. australis</i>	Australia	Decoctions were used to treat colds and coughs while inhaling the crushed mint to relieve headaches; the plant is also used as an abortifacient	[26]
<i>M. haplocalyx</i>	China	Various parts of the plant are used to treat sores and rashes on the skin, headache, red eyes, common cold, superficial visual obstructions, sore throat, mouth ulcers, and distension and oppression in the chest and the hypochondrium	[27, 28]

Table 1. Traditional indications of some *Mentha* species.

Mint is also used for buccodental prevention. During the middle ages, powdered mint leaves were used to whiten teeth [7]. Fresh mint leaves are used in chewing, for mouth burns; in decoction, it is used as mouthwashes to reduce gingival pain [29]. Mint is used in making oral dentifrices as it can provide overall freshness in breath. More studies are being done as to whether or not it directly contributes to preventing caries and plaque; however, it is confirmed that it does create an unfavorable environment for bacteria [23]. Moreover, peppermint applied to the gums of teething babies can help relieve distress and clean teeth [4].

Mint oil and its constituents and derivatives are also used as flavoring agents throughout the world in food, pharmaceutical, perfumery, and flavoring industry [23]. Essential oils isolated from *Mentha* plants have a long history of use as improving the flavor of foods like confectionaries (such as candies and chewing gums) and beverages. Mint flavor, which includes spearmint, peppermint, and corn mint, is probably the third most important flavor used after vanilla and citrus. As a result, *Mentha* plants are among the most important commercial herbs cultivated for dry leaf production in Germany, Spain, Poland, Bulgaria, Egypt, Morocco, Greece, Israel, United Kingdom, Turkey, Nigeria, and China [12, 30].

3. Adverse and toxic effects

Although some healthcare professionals believe that herbal medicines, such as the essential oil from *Mentha* spp., are relatively safe as they are “natural,” recent publications have highlighted potentially severe side effects [4]. Contact allergy to the leaves of *Mentha spicata* has been reported, and cases of contact cheilitis from its essential oil, as toothpaste flavoring, have been described. The main allergens appear to be carvone and limonene. Spearmint and peppermint tea can cause iron deficiency anemia [16]. Besides, the essential oil from peppermint is associated with adverse effects such as heartburn, nausea, vomiting, allergic reactions, flushing, and headaches [4]. Potentially toxic compounds in peppermint are pulegone and menthol. Pulegone and its metabolite menthofuran, the probable hepatotoxic compounds in pennyroyal mint (*Mentha pulegium* L.), are also found in peppermint in much smaller proportions [23].

On the basis of recent rodent chronic studies [31], target organs for pulegone and menthofuran are the liver and kidney, and a plausible mechanism for toxicity is the formation of reactive metabolites, which is also supported by in vitro experimental data. According to the Committee of Experts on Flavoring Substances (CEFS), provisional consumption limits were established for pulegone at 20 mg/kg in food and beverages [32].

Menthol causes hepatocellular changes in rats. Inhalation of menthol can cause apnea and laryngeal constriction, a risk for infants. Contact sensitivity to menthol and peppermint with oral symptoms including burning mouth syndrome, recurrent oral ulceration, or a lichenoid reaction has been reported. The excessive inhalation of mentholated preparation has caused reversible nausea, anorexia, cardiac problems, ataxia, and other central nervous system (CNS) problems. Peppermint oil is contraindicated in obstruction of the bile ducts, gallbladder inflammation, and severe liver failure [23].

Dose-dependent hepatotoxicity and nephrotoxicity were reported for *M. piperita* and *M. spicata* in rats as well as decreased plasma testosterone and increased plasma LH and FSH levels affecting spermatogenic activity; extensive degenerative changes in germinal epithelium and spermatogenesis arrest were observed in testicular biopsies. The exact *Mentha* compounds that cause these effects are not known [33].

In Wistar rats, depending on dosage, the *M. longifolia* leaves' essential oil increased the population of neutrophils, monocytes, and large unstained cells; the liver-body weight ratio; and the serum cholesterol, HDL cholesterol, triglyceride, inorganic phosphate, total and conjugated bilirubin, alkaline phosphatase activity, total proteins, and albumin; it reduced the serum urea and atherogenic index. The oil, at 500 $\mu\text{L}/\text{kg}$ of body weight, also increased the kidney-body weight ratio [22].

Due to the major decrease of the potentially harmful pulegone and menthone by oven-drying, it is recommended that this herb should be oven-dried or cooked before consumption in order to reduce toxicity. Eating of the raw plant should be discouraged, particularly in patients with a history of liver disease or those taking cytochrome P450-inducing drugs [22].

4. Composition of *Mentha* species

The majority of studies on mint constituents focus on essential oils. Indeed, these compounds are widely used in different industries. Moreover, major polyphenols have also been investigated for interesting biological properties.

4.1. Essential oils

Essential oils are natural and volatile secondary metabolites characterized by a strong odor and a complex composition. They are usually obtained by steam or hydro-distillation from various aromatic plants, generally localized in temperate to warm countries like Mediterranean and tropical countries where they represent an important part of the traditional pharmacopoeia [34].

Several species of *Mentha* are cultivated for the production of essential oil. Indeed, mint oils are among the most important essential oils produced in the world, and their values are exceeding 400 million of US dollar/year. For instance, *M. canadensis* L. produces corn mint oil which represents the most important source of (-) menthol; *M. piperita* L. produces peppermint oil, constituted of menthol, menthone, and menthyl acetate as main components; *M. spicata* ssp., *M. viridis* (native spearmint), and *M. gracilis* (scotch spearmint) produce mostly carvone-rich oils, although different compositions have been reported; *M. citrata* is a source of linalool and linalyl acetate; *M. pulegium* produces the so-called pennyroyal oil, which is a pulegone-rich oil; the composition of *M. aquatica* oils is dominated by menthofuran [21]; *M. haplocalyx* could be classified into six chemotypes, including linalool, pulegone, menthone, carvone, menthol, and piperitenone oxide [35].

Peppermint leaves typically contain 1.2–3.9% (v/w) of essential oil, with more than 300 identified compounds. The terpenic class is the most represented, comprising about 52% of monoterpenes and 9% of sesquiterpenes, whereas other groups, such as aldehydes (9%), aromatic hydrocarbons (9%), miscellaneous (8%), lactones (7%), and alcohols (6%), have been shown to be present in a smaller proportion. Among monoterpenes, menthol is the major constituent (35–60%), followed by menthone (2–44%), menthyl acetate (0.7–23%), 1,8-cineole (eucalyptol) (1–13%), menthofuran (0.3–14%), isomenthone (2–5%), neomenthol (3–4%), and limonene (0.1–6%), whereas β -caryophyllene is the main sesquiterpene (1.6–1.8%) [36]. Most of peppermint oil medicinal properties are ascribed to menthol, their major active component, while esters, such as menthyl acetate, provide the familiar minty taste and associated aroma [4].

Table 2 presents published compositions of some widespread mint essential oils with a more limited commercial interest, including *M. pulegium*, the source of the essential oil “pennyroyal” rich in pulegone; *M. spicata*, dominated by carvone; and *M. rotundifolia* and *longifolia* of varied composition.

Species	Component	Origin (% in the oil)	Reference
<i>M. spicata</i>	Carvone	Tunisia (50), China (47–65), Greece (59), Japan(62), Israel(58), India (73), Portugal (76),South Africa (55), India (50–77), Serbia (50), Pakistan (60–63), Turkey (50), Algeria (59), Morocco (29), India (49), Algeria (49)	[6, 35, 37–51]
	Pulegone	Brazil (55)	[52]
	Piperitenone oxide	Greece (36)	[53]
	Piperitone	Turkey (22–28)	[54]
<i>M. pulegium</i>	Pulegone	Portugal (35), Algeria (39), Japan (51), Switzerland (20–35),Greece (45–50), Portugal (78–81), Uruguay (73), Morocco (80),Iran (38), Greece (33–76), India (66–83), Bulgaria (27–50), Egypt (44), Algeria (4–87), Spain (41–42), Tunisia (61),Iran (41), Morocco (70), Algeria, Bejaia (70); Algeria, Bouira (71)	[41, 47, 55–72]

Species	Component	Origin (% in the oil)	Reference
<i>M. rotundifolia</i>	Menthone	Portugal (36)	[73]
	Piperitone	Austria (70), Iran (38)	[19, 74]
	Piperitenone	Greece (84–97)	[75]
	Menthol	Tunisia (41–52), Greece (61–78)	[76, 77]
	Carvone	Argentina (43), Finland (62),	[78, 79]
	Trans-piperitone oxide	Italy (41), Japan (18–26)	[80, 81]
	Cis-piperitone oxide	Algeria (28–31)	[82]
	Piperitol	Spain (58)	[83]
	Piperitenone oxide	Japan (46), Japan (8–84), Morocco (0.9–56), Algeria (24–39)	[38, 84–86]
	Lippione	Senegal (80)	[87]
	Pulegone	Morocco (85), Tunisia (32)	[88, 89]
	2,4(8),6-p-Menthatrien-2,3-diol	Cuba (15)	[90]
	Menthol	Morocco (41)	[91]
	Piperitenone	Algeria (55)	[86]
	Trans-piperitone epoxide	Algeria, Bejaia (30)	[71]
<i>M. longifolia</i>	Piperitone	Yugoslavia (39)	[92]
	Pulegone	Tunisia (47), Senegal (52 and 42)	[12, 68]
	Cis-piperitone epoxide	Turkey (18)	[93]

Table 2. Major constituents of the essential oils of some *Mentha* species described in the literature.

4.2. Phenolic compounds

Phenolic compounds, secondary metabolites ubiquitously distributed in plants, include a large group of biologically active compounds, with over 8000 molecules, either small or large and complex molecules, presenting at least one aromatic ring with one or more hydroxyl groups attached. These compounds often appear in their natural sources as esters and glycosides [94].

Species of the genus *Mentha* have been reported to contain a range of components, including cinnamic acids and aglycon, glycoside, and/or acylated flavonoids [95]. Triantaphyllou et al. [96] reported that water extracts from *Mentha* contain esters of phenolic acids and flavonoid derivatives and glycosidic flavonoids hydroxylated in position 3 or 5.

Regarding phenolic acids, the genus *Mentha* is particularly rich in caffeic acid and its derivatives, chlorogenic and rosmarinic acid [24, 25, 36, 94, 95, 97–99], the latter accounting for 60–80% of total phenolic compounds. In addition, seven salvianolic acids have been described

in *Mentha* plants, such as salvianolic acid H/I, salvianolic acid E, salvianolic acid B, and isosalvianolic acid A (caffeate trimers) [30].

Mentha plants are rich in flavonoids, particularly in flavones and flavanones. Luteolin and its derivatives are the main flavones described in *Mentha* species [30]. The components eriocitrin, luteolin-7-*O*-glucoside, naringenin-7-*O*-glucoside, isorhoifolin, eriodictyol, luteolin, and apigenin were identified in aqueous extracts from *Mentha* species, hybrids, varieties, and cultivars [95]. Besides, Areias et al. [97] have reported the main component in aqueous *Mentha* extracts to be the glycoside eriocitrin.

In an older study, external lipophilic methylated flavonoids have been extracted from dried leaves of *Mentha aquatica*, *M. spicata*, *M. x piperita*, and *M. citrata*. Twenty flavonoids have been identified. 5,6-Dihydroxy-7,8,3',4'-tetramethoxyflavone was identified as major flavonoid of *M. spicata* and *M. x piperita* and 5-hydroxy-6,7,8,4'-tetramethoxyflavone (gardenin B) as a major compound of *M. citrata* and *M. aquatica* [100].

The phenolic composition of other species of different origins is summarized in **Table 3**.

Class of compounds	Identified compounds	Origin	Reference
<i>M. spicata</i>			
Phenolic acids	Rosmarinic acid	Japan	[101]
	Veratric acid	China	[102]
	Vanillic, homovanillic, hydroxybenzoic, syringic, 4-hydroxy cinnamic, trans-hydroxy cinnamic, 2-hydroxy cinnamic, and ferulic acids	Greece	[103]
	Gallic acid	Greece	[104]
	Protocatechuic acid	China	[105]
	Gallic, chlorogenic, caffeic, vanillic, syringic, <i>p</i> -coumaric, ferulic, and rosmarinic acids	Finland	[106]
	Protocatechuic and vanillic acids	China	[107]
	4-Hydroxy benzoic, caffeic, <i>p</i> -coumaric, chlorogenic, and rosmarinic acids	Algeria	[99]
Flavonoids	Diosmetin, diosmin, diosmin-7-glucoside	India	[108]
	6,4'-trihydroxy-7,3'-dimethoxyflavone	Spain	[109]
	5-Desmethoxynobiletin, 5,6-dihydroxy-7,8,3',4'-tetramethoxyflavone, thymonin, sideritiflavone	Japan	[101]
	5-Hydroxy-3',4',6,7-tetramethoxyflavone and thymonin	China	[102]
	Naringenin, luteolin	Greece	[103]
	Apigenin, rutin, catechin	Greece	[104]
	Chrysoeriol, 5, 6-dihydroxy-7, 8, 3', 4'-tetramethoxyflavone and nodifloretin	China	[105]
	Rutin, quercetin, luteolin	Greece	[110]

Class of compounds	Identified compounds	Origin	Reference
	Rutin, scopoletin	Czech Republic	[111]
	Catechin, epicatechin, rutin, myricetin, luteolin, apigenin, naringenin	Malaysia	[112]
	Rutin, naringin, luteolin, diosmin, naringenin, kaempferol, and diosmetin	Algeria	[99]
Lignans	Spicatolignan A and spicatolignan B	China	[113]
<i>M. piperita</i>			
Phenolic acids	Rosmarinic acid	France	[114]
	Rosmarinic, caffeic, and lithospermic acids	Poland	[115]
	Rosmarinic and lithospermic acids	Poland	[116]
	Rosmarinic, salvianolic, and dehydro-salvianolic acids		[117]
	Caffeic, syringic, gallic, vanillic, <i>p</i> -coumaric, and ferulic acids	USA	[25]
	Caffeic acid, salvianolic acid B, protocatechuic acid glucoside, isosalvianolic acid A, prolithospermic acid, salvianolic acids (E and H/I), danshensu	Iran	[118]
	Protocatechuic acid glucoside, caffeic, chlorogenic, rosmarinic, prolithospermic acids, salvianolic acid H/I, isosalvianolic acid A, salvianolic acid B, salvianolic acid E, and danshensu	Different origins	[24, 30]
	Caffeic, vanillic, ferulic, and chlorogenic acids	Iran	[119]
	Caffeic, <i>p</i> -coumaric, sinapic, shikimic, rosmarinic acids	Mexico	[98]
	Rosmarinic, caffeic, gallic, syringic, <i>p</i> -hydroxybenzoic, <i>o</i> -coumaric, and cinnamic acids	Croatia	[120]
	Caffeic, chlorogenic, 3-O-caffeoylquinic acids, salvianolic acid B, and salvianolic acid L	Portugal	[94]
Flavonoids	Luteolin 7-O-rutinoside, isorhoifolin, eriodictyol 7-O-glucoside, hesperidin, eriocitrin, narirutin, diosmin	France	[114]
	5,6-Dihydroxy-7,8,3',4'-tetramethoxyflavone, sorbifolin, thymosin, thymonin, sideritoflavone, ladanein, xanthomicrol, acacetin, salvigenin, 5-O-demethylnobiletin	France	[121]
	Luteolin 7-O- β -glucuronide, luteolin 7-O-rutinoside, isorhoifolin, eriodictyol, eriodictyol 7-O- β -glucoside, hesperidin, eriocitrin, narirutin, naringenin-7-O- β -glucoside	Poland	[115]
	Luteolin 7-O-glucuronide	Poland	[116]
	Luteolin 7-glucoside, luteolin 7-O-rutinoside, isorhoifolin, pebrellin, eriodictyol 7-O-glucoside, eriodictyol-7-rutinoside, 5,6-dihydroxy-7,8,3',4'-tetramethoxyflavone	Portugal	[97]

Class of compounds	Identified compounds	Origin	Reference
	Luteolin O-diglucuronide, luteolin O-glucuronide, methylated luteolin-glucuronide, luteolin-glucopyranosyl-rhamnopyranoside, eriodictyol-glucopyranosyl-rhamnopyranoside	Poland	[117]
	Luteolin, luteolin 7-O-neohesperidoside, tricetin 3'-O-glucoside, 5'-O-rhamnoside, pebrellin, hesperidin, eriocitrin, narirutin, eriodictyol-7-rutinoside, gardenin D, isosafrole, kaempferol 7-O-rutinoside, 4'-methoxykaempferol-7-O-rutinoside	USA	[122]
	Catechin, (-)-epigallocatechin gallate	USA	[25]
	Luteolin O-diglucuronide, luteolin O-glucuronide, luteolin O-rutinoside, eriocitrin, narirutin, diosmin, myricetin O-glucoside	Iran	[118]
	Luteolin-di-O-glucuronide, eriocitrin, luteolin-O-glucuronide, luteolin-O-rutinoside, narirutin, apigenin-O-rutinoside, diosmin, luteolin-O-glucuronide, myricetin-O-glucoside	Different origins	[24]
	Rutin	Iran	[119]
	Catechin, quercetin-4'-glucoside, (-)-epicatechin	Croatia	[120]
	Gallocatechin-gallate, rutin, quercetin, naringin, hesperidin	Mexico	[98]
	Luteolin-7-O-rutinoside, luteolin-7-O-glucuronide, luteolin-O-diglucuronide, eriodictyol-O-rutinoside and eriodictyol-O-hexoside, naringenin-7-O-rutinoside, eriodictyol-7-O-rutinoside	Portugal	[94]
Lignans	Medioresinol, medioresinol sulfate	Iran	[118]
Stilbenes	Trans-resveratrol	Croatia	[120]
<i>M. pulegium</i>			
Phenolic acids	Caffeic acid	Egypt	[123]
	Caffeic, vanillic, and ferulic acids	Greece	[104]
	4-Hydroxy benzoic, caffeic, <i>p</i> -coumaric, chlorogenic, and rosmarinic acids	Algeria	[99]
Flavonoids	Diosmin	France	[124]
	Thymonin, jaceosidin, pectolinaringenin, ladanein, sorbifolin, pedalitin, 5,6,4'-trihydroxy-7,3'-dimethoxyflavone; 5,6-dihydroxy-7,3',4'-trimethoxyflavone; 5-hydroxy-6,7,3',4'-tetramethoxyflavone, apigenin, luteolin, chrysoeriol	Algeria	[125]
	Acacetin 5-O- α -L-rhamnopyranosyl(1-2)-O- α -L-rhamnopyranoside, 7-O- α -rutinosides of apigenin and luteolin, vicenin, 5-hydroxy-6,7,3',4'-tetramethoxyflavone	Egypt	[123]
	Luteolin, diosmin, and kaempferol	Algeria	[99]
	Apigenin, luteolin, naringenin, catechin	Greece	[104]

Class of compounds	Identified compounds	Origin	Reference
<i>M. rotundifolia</i>			
Phenolic acids	Caffeic, <i>p</i> -hydroxybenzoic, ferulic, and <i>p</i> -coumaric acids	Spain	[126]
	Caffeic, <i>p</i> -coumaric, chlorogenic, and rosmarinic acids	Algeria	[99]
Flavonoids	Apigenin, luteolinidin, elargonidin, cyanidin, delphinidin, petunidin, luteolin	Spain	[126]
	Thymonin, thymosin, 5,6-dihydroxy-7,8,3',4'-tetramethoxyflavone, jaceosidin, hispidulin, ladanein, sorbifolin, nodifloretin, apigenin, luteolin, genkwanin	Algeria	[125]
	Esculetin	Czech Republic	[127]
	Luteolin, diosmin, naringenin, kaempferol, and diosmetin	Algeria	[99]
<i>M. longifolia</i>			
Phenolic acids	Rosmarinic, salvianolic acid L, dedihydro-salvianolic acid	Poland	[117]
Flavonoids	Luteolin-glucuronide, luteolin-diglucuronide, luteolin-glucopyranosyl-rhamnopyranoside, eriodictyol-glucopyranosyl-rhamnopyranoside, methylated luteolin-glucuronide	Poland	[117]
	5-Hydroxy-6,7,3',4'-tetramethoxyflavone	Turkey	[128]
<i>M. australis</i>			
Phenolic acids	Rosmarinic, chlorogenic, and caffeic acids	Australia	[26]
Flavonoids	Neoponcirin, narirutin, biochanin A, apigenin, hesperetin, and naringenin	Australia	[26]
<i>M. haplocalyx</i>			
Phenolic acids	Rosmarinic, caffeic acid	China, Finland	[27, 129]
	<i>Cis</i> -salvianolic acid J, salvianolic acid J, lithospermic acid, rosmarinic acid, lithospermic acid B, magnesium lithospermate B, sodium lithospermate B, and danshensu	China	[130]
Flavonoids	Isoraifolin, luteolin-7-glucoside, menthoside	China	[27]
	Eriocitrin, luteolin-7-O-glucoside	Finland	[129]

Table 3. Phenolic composition of *Mentha* species reported in the literature.

4.3. Other compounds

Various other classes of compounds have been characterized and quantified in the mints. *M. spicata* and *M. piperita* contain different trace elements [46, 131]. Maffei and Scannerini [132] studied the variability of the triacylglycerol, diacylglycerol, and free fatty acids in some *Mentha* species. They found a high level of C₁₈:3 only in the leaves of certain species (*M. longifolia*, *M. crispa*, and *M. sachalinensis*). Among the major components found in peppermint

leaves are fatty acids such as linoleic, linolenic, and palmitic acid [98]. In addition, recent studies identified two new ceramides from the methanolic extract of *M. longifolia*, longifoamides A and B [10].

Triterpenoids and steroids were also isolated from mints. So, two triterpenoids ursolic acid and uvaol and three steroids stigmast-5-en-3- β -yl formate, stigmast-5-en-3-one, and β -sitosterol were isolated from the aerial parts of *M. longifolia* subsp. *noeana* [128].

On the other hand, different pigments were identified and quantified in *Mentha* species. The analysis of *M. spicata* revealed the presence of xanthophylls (neoxanthin, violaxanthin, and lutein, zeaxanthin), carotenes (α -carotene) [133], and chlorophylls (chlorophylls a and b) [134, 135]. Carotenoids (lutein and β -carotene isomers) were determined in dry peppermint tea, but only lutein was found in infusion [36]. Among vitamins, α -tocopherols and ascorbic acid were present in mints [36, 98, 135].

Mint was also reported to contain sugars, saponins, alkaloids, anthraquinones, and quinines [136], but these absolutely surprising HPTLC-based phytochemical data as well as the identity/purity of investigated samples should be thoroughly verified.

5. Biological activities

The research over the past several years has shown that mint and its constituents possess different biological activities including antioxidant, antimicrobial, insecticidal, anticancer, and anti-inflammatory properties [10].

5.1. Antioxidant activity

Various types of compounds from aromatic and medicinal plants are receiving particular attention due to their radical scavenging properties. Reactive oxygen species (ROS) are chemical species formed in the body during metabolism that are highly reactive and may have one or more unpaired electrons. Oxidative stress, i.e., an imbalance between ROS and antioxidant defenses, has deleterious effects, such as the peroxidation of membrane lipids and the attack on biomolecules (proteins, membrane enzymes, carbohydrates, and DNA) [137].

Various *Mentha* species and their extracts or essential oils have been shown to possess antioxidant activity [30]. Phenolic acids (e.g., rosmarinic and caffeic acids), flavones (e.g., luteolin derivatives), and flavanones (e.g., eriocitrin derivatives) are possibly the major antioxidants. Vitamin antioxidants (e.g., ascorbic acid and carotenoids) are minor contributors to the overall antioxidant potential. In essential oils, unsaturated terpenes having a cyclohexadiene structure (e.g., terpinene) and minor cyclic oxygenated terpenes (e.g., thymol) may contribute to antioxidant potential, while acyclic unsaturated oxygenated monoterpenes (e.g., linalool) may act as pro-oxidants [36].

Mentha extracts are widely known to act as free radical scavengers in vitro. The acetonic extract and essential oil of peppermint act as scavengers of hydroxyl radical (\bullet OH) [25, 138],

the hydroalcoholic extract of *M. piperita* [139] and peppermint essential oil [140] as scavengers of nitric oxide ($\bullet\text{NO}$), and the ethanolic and water extracts of *M. pulegium* [141] as scavengers of hydrogen peroxide (H_2O_2). Besides, different fractions of the ethanol extract of *M. spicata* [142]; the ethanolic extracts from *M. spicata*, *M. pulegium*, and *M. rotundifolia* [99]; the methanolic extract of *M. pulegium* [68, 143] and *M. longifolia* [68] were shown to quench superoxide ($\text{O}_2\bullet^-$) radicals.

Mentha plants have also been reported for antioxidant activities in several functional tests. The DPPH test, a test widely used to measure the ability to donate hydrogen atoms [41], was applied to measure the antioxidant capacities of *Mentha* species extracted by different solvent systems; these include the ethanol extracts of *M. longifolia*, *M. piperita* [144], *M. pulegium* [73, 99, 141, 144], *M. spicata*, and *M. rotundifolia* [96, 144]; the methanol extracts from *M. pulegium* [68, 69, 143, 145], *M. longifolia* [68, 93], *M. aquatica*, *M. arvensis*, *M. piperita*, *M. rotundifolia*, and *M. villosa* [145]; the water extracts from *M. pulegium* [69, 73, 141]; and the acetonic extracts from peppermint [25] and *M. spicata* [146]. DPPH was also used to evaluate the antioxidant activity of the essential oils from *M. aquatica* [92], *M. longifolia* [6, 68, 92, 93], *M. spicata* [6, 46, 51], *M. pulegium* [68, 69, 72, 73], *M. rotundifolia* [89, 147], and *M. piperita* [46, 92, 138, 140].

Other tests are less used in literature to evaluate the antioxidant potential/radical scavenger capacity of *Mentha* species polar extracts and essential oils (**Table 4**).

Species	Type of extract	Reference
Test measuring the quenching of ABTS⁺		
<i>M. spicata</i> , <i>M. piperita</i> , <i>M. longifolia</i> , <i>M. pulegium</i> , <i>M. rotundifolia</i>	Ethanolic	[99, 144, 148]
<i>M. longifolia</i> , <i>M. viridis</i>	Essential oil	[6]
<i>M. spicata</i> , <i>M. pulegium</i> , <i>M. rotundifolia</i>	Essential oil	[51, 71, 147]
Measurement of lipid peroxidation inhibition		
<i>M. pulegium</i>	Water Essential oil	[69]
<i>M. aquatica</i> , <i>M. pulegium</i> , <i>M. suaveolens</i> , <i>M.</i> <i>piperita</i>	Methanolic	[145, 149]
<i>M. longifolia</i>	Methanolic	[149]
<i>M. arvensis</i> , <i>M. villosa</i>	Methanolic	[145]
<i>M. piperita</i>	Essential oil	[140]
<i>M. spicata</i> , <i>M. pulegium</i> , <i>M. rotundifolia</i>	Ethanolic	[150]
Measurement of iron chelating activity		
<i>M. spicata</i>	Ethanolic	[142]
<i>M. piperita</i>	Ethanol/water	[139]
<i>M. aquatica</i> , <i>M. arvensis</i> , <i>M. piperita</i> , <i>M. pulegium</i> , <i>M. rotundifolia</i> , and <i>M. villosa</i>	Methanolic	[145]

Species	Type of extract	Reference
Measurement of iron(III) to iron(II) reducing activity		
<i>M. spicata</i>	Ethanolic	[142]
<i>M. longifolia</i>	Methanolic	[151]
<i>M. piperita</i>	Essential oil	[138]
<i>M. pulegium</i>	Ethanolic, water	[141]
Measurement of total antioxidant activity (TAA) by the phosphomolybdenum method		
<i>M. spicata</i>	Acetone, acetone/water methanol, methanol/water, ethanol, ethanol/water	[146]
<i>M. piperita</i>	Essential oil	[138]
<i>M. pulegium</i>	Ethanol, water	[141]
Measurement of oxygen radical absorbance capacity (ORAC)		
<i>M. piperita</i>	Acetonic	[25]
Kit Radicaux Libres (KRL) assay		
<i>M. spicata</i> , <i>M. pulegium</i> , <i>M. rotundifolia</i>	Essential oils	[51, 71]
Clinical tests measuring the ferric reducing ability of plasma (FRAP test)		
<i>M. longifolia</i>		[151]
<i>M. pulegium</i>	Water, ethanolic	[73, 141]
<i>M. pulegium</i>	Essential oil	[73]
<i>M. rotundifolia</i>	Essential oil	[89]

Table 4. Different methods applied to evaluate the antioxidant properties of *Mentha* species.

The most studied species are *M. spicata*, *M. piperita*, *M. longifolia*, *M. pulegium*, *M. rotundifolia*, *M. arvensis*, and *M. aquatica*. *M. piperita* and *M. spicata* extracts showed good antioxidant activities in several in vitro assay systems compared to other species [95, 99, 144, 149]. The antioxidant compounds present in these extracts act as hydrogen- or electron-donating agents and/or metal chelators. Moreover, as expected from their composition, the polar extracts of *Mentha* species showed much better activity than the essential oils [6, 41, 69, 93].

5.2. Antimicrobial activity

The antibacterial and antifungal activities of *Mentha* species have been studied on various bacteria and fungi [30]. These studies indicate that essential oils are more efficient antifungals and antibacterials compared to the polar extracts [6, 68, 73]. *Mentha* essential oils showed remarkable antimicrobial activity against bacteria and other microorganisms, such as yeasts and periodontopathogens [4], mainly due to the presence of oxygenated monoterpenes in their chemical compositions [22]. Bactericidal and bacteriostatic activities are observed in the 1/1 to 1/1000 (V/V) and 1–5 mg/mL concentration ranges, respectively.

Thus, *M. rotundifolia* oils showed effect against *Bacillus subtilis*, *B. cereus*, *Escherichia coli*, *Proteus mirabilis*, *Salmonella typhimurium*, and *Staphylococcus aureus* [21, 88, 89, 152]. The pulegone-rich essential oil of *M. suaveolens* efficiently inhibited all the microorganisms (20 stains) tested by Oumzil et al. [85]. Furthermore, according to Brahmi et al. [71], *M. rotundifolia* essential oils exhibited stronger antimicrobial effect than *M. pulegium* oils against all the microorganisms studied (three Gram⁺, three Gram⁻, two fungal, and one yeast). Nevertheless, *M. pulegium* oil showed good antimicrobial activity against 11 bacteria (3 Gram⁺ and 8 Gram⁻) and 2 yeasts [72].

M. pulegium presents an appreciable activity toward all microorganisms (five Gram⁺, five Gram⁻, and six fungal strains) tested by Hadjilaoui et al. [68] and *Streptococcus pyogenes* [47]. Similarly, they showed the best bacteriostatic and bactericidal effect compared to tested medicinal and aromatic plants from other genera [70]. Besides, the essential oil of the flowering aerial parts of *M. pulegium* showed a significant activity against microorganisms especially Gram-positive bacteria [19].

The essential oil of *M. spicata* has an appreciable activity against *Streptococcus pyogenes* [47], *E. coli*, *S. aureus*, *S. pyogenes* [46], and *C. albicans* [46, 51]. Oils of *Mentha longifolia* showed strong antimicrobial activity against all 16 microorganisms tested by Hadjilaoui et al. [68] and against *Escherichia coli*, *Shigella sonnei*, and *Micrococcus flavus*. These bacteria were also inhibited by the essential oils from *M. aquatica* and *M. piperita* [92]. Of the *Mentha* essential oils tested by Hussain et al., the oil from *M. arvensis* showed relatively higher antimicrobial activity [45]; the essential oils of *Mentha officinalis* totally inhibited *E. coli*, *Bacillus aureus*, *Streptococcus lactis*, and *S. aureus* [153].

Besides, the essential oils from *Mentha* spp. have been considered a safe ingredient for the development of antibiofilm agents that could find a role in the pharmaceutical industry [4].

The antibacterial or antifungal activity of *Mentha* plant polar extracts have been studied to a much lesser extent; bactericidal and bacteriostatic activities are observed in the 2–4 mg/mL and 100–250 µg/mL concentration ranges, respectively, and at 6 µg/disk. The extracts were shown to possess antibacterial and antifungal activity [30]. Methanolic extracts of *M. viridis* and *M. pulegium* showed slight antimicrobial capacity against *S. enteritidis* and *E. coli*, respectively [104]; infusions of *M. piperita* and *M. spicata* were active on *Vibrio parahaemolyticus* [154]. Fractions from *M. spicata* ethanol extract showed effective antibacterial activity against *Escherichia coli*, *Salmonella paratyphi*, *Shigella boydii*, *Staphylococcus aureus*, and *Vibrio cholerae* [142]. Peppermint tea extracts were active against *Chlamydia pneumoniae* [24].

5.3. Insecticidal activity

Mint is also known to exhibit insecticidal activity against a wide variety of insects. *Mentha* has been used as insecticides mainly in the form of essential oils [155]. *M. spicata*, *M. pulegium*, and *M. rotundifolia* oils demonstrated insecticidal properties against adults of *Rhyzopertha dominica*, in contact and fumigation bioassays and repellency [51, 71]. *M. pulegium* and *M. rotundifolia* oils were also very toxic in the first 24 h in a contact toxicity bioassay against the same pest [156].

M. arvensis oil was toxic against *Sitophilus oryzae* (LC_{50} , 45.5 $\mu\text{L/L}$) [157, 158]. Similarly, the essential oil of *M. microphylla* gave remarkable activity against this insect (LC_{50} , 0.2 $\mu\text{L/L}$) in fumigation bioassays and in contact bioassays (24 h; LC_{50} , 0.01 mg/cm²) [159], and the ethanolic extract of *M. longifolia* was also efficient against it (24.2% repellency) [160]. Additionally, *M. pulegium* oil was toxic against *Sitophilus granarius* (contact LD_{50} , 9.1 $\mu\text{L/mL}$) [72], and *M. longifolia* essential oil has 100% repellence against *Sitophilus zeamais* [22].

Varma and Dubey [158] reported complete inhibition of *Tribolium castaneum*, through the treatment of wheat samples with *M. arvensis* essential oil. The essential oil of *M. microphylla* gave remarkable activity against adults of this insect (LC_{50} , 4.5 $\mu\text{L/L}$) in fumigation bioassays [159]. Furthermore, the insecticidal properties of *M. longifolia* essential oil against this pest have been attributed to piperitenone oxide (LC_{50} , 9.95 mg/L) [22]. In another study, Lee et al. [157] observed that *M. piperita* (LD_{50} , 25.8 $\mu\text{L/L}$) was a slightly better fumigant than *M. spicata* (LD_{50} , 33.1 $\mu\text{L/L}$) against *T. castaneum*. Besides, in both contact and fumigation assays, the *M. rotundifolia* oil samples rich in pulegone and menthone, compared to other chemotypes, exhibited superior insecticidal activity against the adults of the same insect [161].

Mentha essential oils and polar extracts showed also insecticidal properties toward other insect species. The ethanolic extract of *M. longifolia* was efficient against third- and fourth-instar larvae of *Culex pipiens* (LC_{50} -26.8 ppm). *M. arvensis* oil efficiently repelled (85%) *Callosobruchus chinensis* [160]. Feeding on *M. longifolia* caused death in *Chrysolina herbacea* [22]. *M. pulegium* L. oil also caused 100% mortality of *Mayetiola destructor* [162]. Studies have shown that essential oils of spearmint were effective against *Lycoriella ingenua* at 20×10^{-3} mg/mL [10]; fumigation allowed controlling all stages of *Callosobruchus maculatus*; and the egg stage was the most susceptible stage [163]. Also, compared to *M. pulegium*, a *M. suaveolens* hydrosol showed higher insecticidal activity toward an insect pest of citrus, *Toxoptera aurantii* [164].

5.4. Cytotoxicity

Several studies have indicated that *Mentha* plants contain constituents with cytotoxic properties that may find use in developing anticancer agents. For example, *M. arvensis*, *M. longifolia*, *M. spicata*, and *M. viridis* methanolic and aqueous extracts showed antiproliferative effect against various cancer cell lines in vitro at a concentration of 100 $\mu\text{g/mL}$ [165]. Similarly, in Yi and Wetzstein [166] study, spearmint and peppermint methanolic extracts significantly inhibited SW-480 colon cancer cell growth (IC_{50} : 143.6 ± 25.6 $\mu\text{g/mL}$ for spearmint and 92.3 ± 17.8 $\mu\text{g/mL}$ for peppermint). The cytotoxic effect of the essential oil of *M. pulegium* on ovarian adenocarcinoma (SK-OV-3), human malignant cervix carcinoma (HeLa), and human lung carcinoma (A549) cell lines has been shown by other investigators (IC_{50} s ranging from 14.10 to 59.10 $\mu\text{g/mL}$) [167]. In an in vitro screening for the tumoricidal properties of international medicinal herbs, *M. spicata* and *M. piperita* exhibited extremely weak tumoricidal effects ($LC_{50} > 5.0$ mg/mL), while *M. pulegium* showed a weak activity (LC_{50} , 1.2–2.5 mg/mL) [168].

The cytotoxicity of essential oils from four *Mentha* species (*M. arvensis*, *M. piperita*, *M. longifolia*, and *M. spicata*) was tested on breast cancer (MCF-7) and prostate cancer (LNCaP) cell lines

using the MTT assay. The tested *Mentha* essential oils showed prominent cytotoxic activity against both cancer cell lines (IC_{50} s ranging from 43.5 ± 2.1 – 95.7 ± 4.5 $\mu\text{g/mL}$) [45].

In another study, aqueous extract of *M. spicata* significantly reduced the proliferation of Wehi-164 and U937 cells dose and time dependently (LD_{50} s ranging from 4.63 to 5.97 mg/mL) [169]. Jain et al. [170] examined the possible molecular mechanisms underlying the cytotoxicity and anticarcinogenic potential of *Mentha piperita* leaf extracts on six human cancer (HeLa, MCF-7, Jurkat, T24, HT-29, MIA PaCa-2). The chloroform and ethyl acetate extracts showed significant dose- and time-dependent anticarcinogenic activity, leading to G1 cell cycle arrest and mitochondrial-mediated apoptosis, perturbation of oxidative balance, upregulation of Bax gene, elevated expression of p53 and p21 in the treated cells, and acquisition of senescence phenotype (effective doses ranging from $10 \times (10 \mu\text{g}/\mu\text{L})$ to $100 \times (100 \mu\text{g}/\mu\text{L})$).

Lv et al. [25] also evaluated the antiproliferative activity of a peppermint extract against the human tumor cell line HT-29 (effective doses 250 and 500 $\mu\text{g/mL}$). Similarly, the cytotoxic effect of *Mentha piperita* essential oil was assessed against four human cancer cells. It was found to be significantly active against human lung carcinoma SPC-A1, human leukemia K562, and human gastric cancer SGC-7901 cells, with IC_{50} values of 10.9, 16.2, and 38.8 $\mu\text{g/mL}$, respectively [138].

M. longifolia methanolic extract and *M. piperita* ethanolic extract presented a cytotoxic activity, respectively, against human breast cancer ($IC_{50} = 191.2$ $\mu\text{g/mL}$) [171] and human laryngeal epidermoid carcinoma ($IC_{50} = 94$ $\mu\text{g/mL}$) [172]. Besides, peppermint extract showed cytotoxicity against four human tumor cell lines (MCF-7, NCI-H460, HeLa, and HepG2; IC_{50} s ranging from 98 ± 9 to 226 ± 11 $\mu\text{g/mL}$) [94].

5.5. Anti-inflammatory properties

Mentha extracts contain numerous constituents which could have anti-inflammatory effects. In vitro, the anti-inflammatory activity of the *M. piperita* essential oil has been determined by 5-lipoxygenase (5-LOX) inhibition assay (IC_{50} s ranging from 0.03 ± 0.01 – 0.08 ± 0.01 $\mu\text{g/mL}$) [140]. It could also effectively inhibit nitric oxide (*NO) and prostaglandin E2 (PGE2) production in lipopolysaccharide (LPS)-activated RAW 264.7 macrophages [138]. Lv et al. [25] using J774A.1 mouse macrophage cells showed that peppermint extracts were efficient in inhibiting IL-1 and COX-2 expression and have inhibitory effect on IL-6 and MCP-1 (IC_{50} s ranging from 50 to 100 $\mu\text{g/mL}$).

In vivo, pretreatment of albino mice and female Wistar rats with *M. suaveolens* methanol extract induced an anti-inflammatory effect [173]. The anti-inflammatory effects of aqueous, chloroform, ethyl acetate, and hexane extracts of *M. spicata* ethyl acetate and aqueous fractions were both effective in reducing the chronic and acute inflammation of *Wistar albino* rats [11]. In addition, edema reduction was also observed by topic use of *M. aquatica* L. alcohol extract on Male CD-1 mice [174]. The *M. piperita* essential oil exhibited potent anti-inflammatory activities in a croton oil-induced mouse ear edema model. The oil reduced the edematous response by 5.77, 7.37, and 30.24% at the dose of 200, 400, and 800 μg , respectively [138].

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References

- [1] De Judicibus M. Botanical notebook. UoM Custom Book Centre; Printed by Custom Book Centre, University of Melbourne, March 2010 Australia. 2011. 232 p.
- [2] Lawrence B.M. Mint: the genus *Mentha*. Medicinal and aromatic plants -industrial profiles. CRC Press/Taylor & Francis, Boca Raton, FL; 2007.
- [3] Qing W. *Mentha's* historical textual research and clinical new application, Journal of Haidian University. 2002;02.
- [4] Peixoto I.T.A., Furlanetti V.F., Anibal P.C., Duarte M.C.T., Höfling J.F. Potential pharmacological and toxicological basis of the essential oil from *Mentha* spp. Rev Ciênc Farm Básica Apl. 2009;30(3):235–239.
- [5] Sutour S. Study of the chemical composition of essential oils and extracts of mints from Corsica and Kumquants. Doctorat thesis in organic and analytical chemistry. University of Corsica. 2010; 221 p.
- [6] Mkaddem M., Bouajila J., Ennajar M., Lebrihi A., Mathieu F., Romdhane M. Chemical composition and antimicrobial and antioxidant activities of *Mentha (longifolia* L. and *viridis*) essential oils. Journal of Food Science. 2009;74: 358–363.
- [7] Abbaszadeh B., Valadabadi S.A., Farahani H.A., Darvishi H.H. Studying of essential oil variations in leaves of *Mentha* species. African Journal of Plant Science. 2009;3(10): 217–221.
- [8] Kew. 2010. The Plant list: <http://www.theplantlist.org/tpl/search=Mentha+species>
- [9] Saric-Kundalic B., Fialova S., Dobes C., Olzant S., Tekelova D., Grancai D., Reznicek G., Saukel J.. Multivariate numerical taxonomy of *Mentha* species hybrids varieties and cultivars. Sci Pharm. 2009;77: 851–876.
- [10] Kunnumakkara A.B., Chung J.G., Koca C., Dey S. Mint and its constituents. In Aggarwal B.B., Kunnumakkara A.B.: Molecular targets and therapeutic uses of spices. World Scientific, Singapore; Hackensack, NJ; 2009; pp.373–401.

- [11] Arumugam P., Gayatri Priya N., Subathra M., Ramesh A. Anti-inflammatory activity of four solvent fractions of ethanol extract of *Mentha spicata* L. investigated on acute and chronic inflammation induced rats. *Environmental Toxicology and Pharmacology*. 2008;**26**: 92–95.
- [12] Diop S.M., Guèye M.T., Ndiaye I., Ndiaye E.B., Diop M.B., Heuskin S., Fauconnier M.L., Lognay G. Chemical composition of essential oils and floral waters of *Mentha longifolia* (L.) Huds. from Senegal. *American Journal of Essential Oils and Natural Products*. 2016;**4**(1): 46–49.
- [13] Di Stasi L.C., Oliveira G.P., Carvalhaes M.A., Queiroz-Junior M., Tien O.S., Kakinami S.H., Reis M.S. Medicinal plants popularly used in the Brazilian tropical atlantic forest. *Fitoterapia*. 2002;**73**: 69–91.
- [14] El-Hilaly J., Hmammouchi M., Lyoussi B. Ethnobotanical studies and economic evaluation of medicinal plants in Taounate province (Northern Morocco). *Journal of Ethnopharmacology*. 2003;**86**: 149–158.
- [15] Kumar A., Chattopadhyay S. DNA damage protecting activity and antioxidant potential of pudina extract. *Food Chemistry*. 2007;**100**: 1377–1384.
- [16] Akdogan M., Tamer M.N., Cure E., Cure M.C., Korolu B.K., Delibat N. Effect of spearmint (*Mentha spicata* Labiatae) teas on androgen levels in women with Hirsutism. *Phytotherapy Research*. 2007;**21**: 444–447.
- [17] Bruneton J. *Pharmacognosy phytochemistry. Medicinal plants*, fourth ed. Tec and Doc, Paris; 2009;1269 p.
- [18] Delille L. *The medicinal plants of Algeria*. Berti Editions, Alger; 2007;240 p.
- [19] Mahboubi M., Haghi G. Antimicrobial activity and chemical composition of *Mentha pulegium* L. essential oil. *Journal of Ethnopharmacology*. 2008;**119**: 325–327.
- [20] Bello R., Calatayud S., Beltran B., Primo-Yufera E., Esplugues J. Cardiovascular effects of the methanol and dichloromethanol extracts from *Mentha suaveolens* Ehrh. *Phytotherapy Research*. 2001;**15**: 447–448.
- [21] Sutour S., Bradesi P., de Rocca-Serra D., Casanova J, Tomi F. Chemical composition and antibacterial activity of the essential oil from *Mentha suaveolens* ssp. *Insularis* (Req.) Greuter. *Flavour and Fragrance Journal*. 2008;**23**: 107–114.
- [22] Mikaili P., Mojaverrostami S., Moloudizargari M., Aghajanshakeri S. Pharmacological and therapeutic effects of *Mentha Longifolia* L. and its main constituent, menthol. *Ancient Science of Life*. 2013;**33**: 129–136.
- [23] Balakrishnan A. Therapeutic uses of peppermint—a review. *Journal of Pharmaceutical Sciences and Research*. 2015;**7**(7): 474–476.
- [24] Kapp K., Hakala E., Orav A., Pohjala L., Vuorela P., Püssa T., Vuorela H., Raal A. Commercial peppermint (*Mentha × piperita* L.) teas: antichlamydial effect and polyphenolic composition. *Food Research International*. 2013;**53**:758–766.

- [25] Lv J., Huang H., Yua L., Whent M., Niu Y., Shi H., Wang T.T.Y., Luthria D., Charles D., Yu L.C. Phenolic composition and nutraceutical properties of organic and conventional cinnamon and peppermint. *Food Chemistry*. 2012;**132**: 1442–1450.
- [26] Tang K.S.C., Konczak I., Zhao J. Identification and quantification of phenolics in Australian native mint (*Mentha australis* R. Br.). *Food Chemistry*. 2016;**192**: 698–705.
- [27] Bensky D., Clavey S., Stoger E. Chinese herbal medicine: materia medica, 3rd ed. Eastland Press, Inc., Seattle, WA, USA; 2004;47–49pp.
- [28] Chinese Pharmacopoeia Commission. Pharmacopoeia of the People's Republic of China. 1. China Medical Science Press. 2010;pp 278–279.
- [29] Lamendin H., Toscano G., Requirand P. Buccodental phytotherapy and aromatherapy. *EMC-Dentisterie* 2004;**1**: 179–192.
- [30] Kapp K. Polyphenolic and essential oil composition of *Mentha* and their antimicrobial effect. Academic Dissertation. Faculty of Pharmacy of the University of Helsinki. 2015;90 p.
- [31] NTP 2011. Toxicology and carcinogenesis studies of pulegone (CAS No. 89-82-7) in F344/N rats and B6C3F1 mice (gavage studies). *Natl Toxicol Program Tech Rep Ser*. 2011;563: 1–201.
- [32] European Commission. Regulation (EC) No 1334/2008 of the European Parliament and of the 550 Council of 16 December 2008 on flavourings and certain food ingredients with flavouring properties for 551 use in and on foods and amending Council Regulation (EEC) No 1601/91, Regulations (EC) No 2232/96 552 and (EC) No 110/2008 and Directive 2000/13/EC. *Official Journal of the European Union Lex*. 2008;354:34.
- [33] Akdogan M., Ozguner M., Kocak A., Oncu M., Cicek E. Effects of peppermint teas on plasma testosterone, follicle-stimulating hormone, and luteinizing hormone levels and testicular tissue in rats. *Urology*. 2004;**64**: 394–398.
- [34] Bakkali F., Averbeck S., Averbeck D., Idaomar M. Biological effects of essential oils—a review. *Food and Chemical Toxicology*. 2008;**46**: 446–475.
- [35] Zhao D., Xu Y.W., Yang G.L., Husaini A.M., Wu W. Variation of essential oil of *Mentha haplocalyx* Briq. and *Mentha spicata* L. from China. *Industrial Crops and Products*. 2013;**42**: 251–260.
- [36] Riachi L.G., De Maria C.A.B. Peppermint antioxidants revisited. *Food Chemistry*. 2015;**176**: 72–81.
- [37] Adam K., Sivropoulou A., Kokkini S., Lanaras T., Arsenakis M. Antifungal activities of *Origanum vulgare* subsp. *hirtum*, *Mentha spicata*, *Lavandula angustifolia*, and *Salvia fruticosa* essential oils against human pathogenic fungi. *Journal of Agricultural and Food Chemistry*. 1998;**46**: 1739–1745.
- [38] Miyazawa M., Watanabe H., Umemoto K., Kameoka H. Inhibition of acetylcholinesterase activity by essential oils of *Mentha* species. *Journal of Agricultural and Food Chemistry*. 1998;**46**: 3431–3434.

- [39] Oka Y., Nacar S., Putievsky E., Ravid U., Yaniv Z., Spiegel Y. Nematicidal activity of essential oils and their components against the root-knot nematode. *Phytopathology*. 2000;**90**: 710–715.
- [40] Chowdhury J.U., Nandi N.C., Uddin M., Rahman M. Chemical constituents of essential oils from two types of spearmint (*Mentha spicata* L. and *M. cardiaca* L.) introduced in Bangladesh. *Bangladesh Journal of Scientific and Industrial Research*. 2007;**42**: 79–82.
- [41] Mata A.T., Proenc C., Ferreira A.R., Serralheiro M.L.M., Nogueira J.M.F., Araújo M.E.M. Antioxidant and anti-acetylcholinesterase activities of five plants used as Portuguese food spices. *Food Chemistry*. 2007;**103**: 778–786.
- [42] Mkolo N.M., Olowoyo J.O., Sako K.B., Mdakane S.T.R., Mitonga M.M.A., Magano S.R. Repellency and toxicity of essential oils of *Mentha piperita* and *Mentha spicata* on larvae and adult of *Amblyomma Hebraeum* (Acari: Ixodidae). *Science Journal of Microbiology*. 2011;7 p.
- [43] Chauhan R.S., Kaul M.K., Shahi A.K., Kumar A., Ram G., Tawa A. Chemical composition of essential oils in *Mentha spicata* L. accession [IIIM(J)26] from North-West Himalayan region, India. *Industrial Crops and Products*. 2009;**29**: 654–656.
- [44] Sokovic M.D., Vukojevic J., Marin P.D., Brkić D.D., Vajs V., Van Griensven L.J. Chemical composition of essential oils of *Thymus* and *Mentha* species and their antifungal activities. *Molecules*. 2009;**14**(1): 238–249.
- [45] Hussain A.I., Anwar F., Nigam P.S., Ashraf M., Gilani A.H. Seasonal variation in content, chemical composition and antimicrobial and cytotoxic activities of essential oils from four *Mentha* species. *Journal of the Science of Food and Agriculture*. 2010;**90**(11): 1827–1836.
- [46] Kizil S., Hasimi N., Tolan V., Kiliç E., Yuksel U. Mineral content, essential oil components and biological activity of two *Mentha* species (*M. piperita* L., *M. spicata* L.). *Turkish Journal of Field Crops*. 2010; **15**(6): 148–153.
- [47] Boukhebt H., Chaker A.N., Belhadj H., Sahli F., Ramdhani M., Laouer H., Harzallah D. Chemical composition and antibacterial activity of *Mentha pulegium* L. and *Mentha spicata* L. essential oils. *Der Pharmacia Lettre*. 2011;**3**: 267–275.
- [48] Znini M., Bouklah M., Majidi L., Kharchouf S., Aouniti A., Bouyanzer A., Hammouti B., Costa J., Al-Deyab S.S. Chemical composition and inhibitory effect of *Mentha spicata* essential oil on the corrosion of steel in molar hydrochloric acid. *International Journal of Electrochemical Science*. 2011;**6**: 691–704.
- [49] Govindarajan M., Sivakumar R., Rajeswari M., Yogalakshmi K. Chemical composition and larvicidal activity of essential oil from *Mentha spicata* (Linn.) against three mosquito species. *Parasitology Research*. 2012;**110**: 2023–2032.
- [50] Allali H., Chikhi I., Dib M.E., Muselli A., Fekih N., Meliani N., Kamal M.A., Tabti B., Costa J. Antioxidant activity and chemical analysis of *Mentha spicata* cultivated from

west northern region of Algeria by headspace solid phase micro-extraction and hydro-distillation. *Natural Products: An Indian Journal*. 2013;**9**(6): 258–263.

- [51] Brahmi F., Adjaoud A., Marongiu B., Falconieri D., Yalaoui-Guellal D., Madani K., Chibane M. Chemical and biological profiles of essential oils from *Mentha spicata* L. leaf from Bejaia in Algeria. *Journal of Essential Oil Research*. 2016;<http://dx.doi.org/10.1080/10412905.2015.1118411>.
- [52] Gonçalves R.S., Battistin A., Pauletti G, Rota L., Serafini L.A. Antioxidant properties of essential oils from *Mentha* species evidenced by electrochemical methods. *Revista Brasileira de Plantas Medicinai*s. 2009;**11**(4): 372–382.
- [53] Koliopoulos G., Pitarokili D., Kioulos E., Michaelakis A., Tzakou O. Chemical composition and larvicidal evaluation of *Mentha*, *Salvia*, and *Melissa* essential oils against the West Nile virus mosquito *Culex pipiens*. *Parasitology Research* 2010;**107**: 327–335.
- [54] Telci I., Demirtas I., Bayram E., Arabaci O., Kacar O. Environmental variation on aroma components of pulegone/piperitone rich spearmint (*Mentha spicata* L.). *Industrial Crops and Products*. 2010;**32**: 588–592.
- [55] Fujita Y., Fujita S.I. Essential oil of *Mentha pulegium* and *M. grattefossei* view from the standpoint of comparative biochemistry. *Nippon Kagaku Zasshi*. 1967;**88**: 767–768.
- [56] Sticher O., Fluck H. The composition of genuine, extracted and distilled essential oils of some *Mentha* species. *Pharmaceutica Acta Helvetiae*. 1968;**43**: 411–446.
- [57] Sivropoulou A., Kokkini S., Lanaras T., Arsenakis M.. Antimicrobial activity of mint essential oils. *Journal of Agricultural and Food Chemistry*. 1995;**43**: 2384–2388.
- [58] Reis-Vasco E.M.C., Coelho J.A.P., Palavra A.M.F. Comparison of pennyroyal oils obtained by supercritical CO₂ extraction and hydrodistillation. *Flavour and Fragrance Journal*. 1999;**14**: 156–160.
- [59] Lorenzo D., Paz D., Dellacassa E., Davies P., Vila R., Canigueral S. Essential oils of *Mentha pulegium* and *Mentha rotundifolia* from Uruguay. *Brazilian Archives Boilogy and Technology*. 2002;**45**(4): 519–524.
- [60] Aghel N., Yamini Y., Hadjiakhoondi A., Pourmortazavi S.M. Supercritical carbon dioxide extraction of *Mentha pulegium* L. essential oil. *Talanta*. 2004;**62**: 407–411.
- [61] Bouchra C., Achouri M., Idrissi Hassani LM., Hmamouchi M. Chemical composition and antifungal activity of essential oils of seven Moroccan Labiatae against *Botrytis cinerea* Pers: Fr. *Phytochemistry*. 2003; 89: 165–69.
- [62] Kokkini S., Handilou E., Karouscou R. Clinal variation of *Mentha pulegium* essential oils along the climatic gradient of Greece. *Journal of Essential Oil Research*. 2004;**16**: 588–593.
- [63] Agnihotri V.K., Agarwal S.G., Dhar P.L., Thappa Baleshwar R.K., Kapahi B.K., Saxena R.K., Qazi G.N. Essential oil composition of *Mentha pulegium* L. growing wild in the north-western Himalayas India. *Flavour and Fragrance Journal*. 2005;**20**: 607–610.

- [64] Stoyanova A., Georgie V., Kula J., Majda T. Chemical composition of the essential oil of *Mentha pulegium* L. from Bulgaria. *Journal of Essential Oil Research*. 2005;17: 475–477.
- [65] El-Ghorab A.H. The chemical composition of *Mentha pulegium* L. essential oil from Egypt and its antioxidant activity. *Journal of Essential Oil Bearing Plants*. 2006;9: 183–195.
- [66] Beghidja N., Bouslimani N., Benayache F., Benayache S., Chalchat J. Composition of the oils from *Mentha pulegium* grown in different areas of the east of Algeria. *Chemistry of Natural Compounds*. 2007;43: 481–483.
- [67] Diaz-Maroto M.C., Castillo N., Castro-Vazquez L., Gonzalez-Vinas M.Á., Perez-Coello M.S. Volatile composition and olfactory profile of pennyroyal (*Mentha pulegium*) plants. *Flavour and Fragrance Journal*. 2007;22: 114–118.
- [68] Hajlaoui H., Trabelsi N., Noumi E., Snoussi M., Fallah H., Ksouri R., Bakhrouf A. Biological activities of the essential oils and methanol extract of two cultivated mint species (*Mentha longifolia* and *Mentha pulegium*) used in the Tunisian folkloric medicine. *World Journal of Microbiology and Biotechnology*. 2009;25: 2227–2238.
- [69] Kamkar A., Jebelli Javan A., Asadi F., Kamalinejad M. The antioxidative effect of Iranian *Mentha pulegium* extracts and essential oil in sunflower oil. *Food and Chemical Toxicology*. 2010;48: 1796–1800.
- [70] Ait-Ouazzou A., Lorán S., Arakrak A., Laglaoui A., Rota C., Herrera A., Pagán R., Conchello P. Evaluation of the chemical composition and antimicrobial activity of *Mentha pulegium*, *Juniperus phoenicea*, and *Cyperus longus* essential oils from Morocco. *Food Research International*. 2012;45: 313–319.
- [71] Brahmi F., Abdenour A., Bruno M., Silvia P., Alessandra P., Danilo F., Yalaoui-Guellal D., Elsebai M.F., Madani K., Chibane M. Chemical composition and *in vitro* antimicrobial, insecticidal and antioxidant activities of the essential oils of *Mentha pulegium* L. and *Mentha rotundifolia* (L.) Hudson growing in Algeria. *Industrial Crops and Products*. 2016;88: 96–105.
- [72] Abdelli M., Moghrani H., Aboun A., Maachi R. Algerian *Mentha pulegium* L. leaves essential oil: chemical composition, antimicrobial, insecticidal and antioxidant activities. *Industrial Crops and Products*. 2016;94: 197–205.
- [73] Teixeira B., Marques A., Ramos C., Batista I., Serrano C., Matos O., Neng N.R., Nogueira, J.M.F., Saraiva J.A., Nunes M.L. European pennyroyal (*Mentha pulegium*) from Portugal: chemical composition of essential oil and antioxidant and antimicrobial properties of extracts and essential oil. *Industrial Crops and Products*. 2012;36: 81–87.
- [74] Zwaving J.H., Smith D. Composition of the essential oil of Austrian *Mentha pulegium*. *Phytochemistry*. 1971;10: 1951–1953.
- [75] Kokkini S., Handilou E., Karousou R., Lanaras T. Variations of pulegone content in pennyroyal (*Mentha pulegium* L.) plants growing wild in Greece. *Journal of Essential Oil Research*. 2002;14: 224–227.

- [76] Marzouk B., Fredj M.B.H., Chraief I., Mastouri M., Boukef K., Marzouk Z. Chemical composition and antimicrobial activity of essential oils from Tunisian *Mentha pulegium* L. Journal of Food, Agriculture and Environment. 2008;**6**: 78–82.
- [77] Petrakis E.A., Kimbaris A.C., Pappas C.S., Tarantilis P.A., Polissiou M.G. Quantitative determination of pulegone in pennyroyal oil by FT-IR spectroscopy. Journal of Agricultural and Food Chemistry. 2009;**57**: 10044–10048.
- [78] De la Torre C.P., Torres O.A. Essential oil of *Mentha rotundifolia*. Arch Biochim Quim Farm. 1977;**20**: 85–88.
- [79] Galambosi B., Aflatuni A., Sorvari K. Effect of cultivation techniques on mint oils in northern Finland. Perfumer and Flavorist. 1998;**23**: 27–31.
- [80] Avato P., Sgarra G., Casadoro G. Chemical composition of the essential oils of *Mentha* species cultivated in Italy. Scientia Pharmaceutica. 1995;**63**: 223–230.
- [81] Umemoto K., Arai T., Nii H., Furukawa K. Chemical constituents of wild mints. Part XX. Essential oil of self-pollinated plants of *Mentha aquatica* with sesquiterpene alcohols as major components. Nippon Nogei Kagaku Kaishi. 1994;**68**: 1567.
- [82] Brada M., Bezzina M., Marlier M., Lognay G.C. Chemical composition of the leaf oil of *Mentha rotundifolia* (L.) from Algeria. Journal of Essential Oil Research. 2006;**18**: 663–665.
- [83] Perez Raya M.D., Utrilla M.P., Navarro M.C., Jiménez J. CNS activity of *Mentha rotundifolia* and *Mentha longifolia* essential oil in mice and rats. Phytotherapy Research. 1990;**4**: 232–234.
- [84] Fujita S., Nakano T., Fujita Y. Studies on the essential oils of the genus *Mentha*. Part X. On the components of the essential oils of *Mentha rotundifolia* (Linn.) Huds. Nippon Nogei Kagaku Kaishi. 1977;**51**: 699–702.
- [85] Oumzil H., Ghoulemi S., Rhajaoui M., Ildrissi A., Fkih-Tetouani S., Faid M., Ben-jouad A. Antibacterial and antifungal activity of essential oils of *Mentha suaveolens*. EHRH Phytotherapy Research. 2002;**16**: 723–731.
- [86] Brada M., Bezzina M., Marlier M., Carlier A., Lognay G. Variabilité de la composition chimique des huiles essentielles de *Mentha rotundifolia* du Nord de l'Algérie. Journal of Biotechnology, Agronomy, Society and Environment. 2007;**11**: 3–7.
- [87] Koyalta D., Sanokho A., Miralles J., Bassene E. Essential oil composition of three Senegalese mint species, 4. Rivista Italiana EPPOS. 1993;**4**: 544–547.
- [88] El Arch M., Satrani B., Farah A., Bennani L., Boriky D., Fechtal M., Blaghen M., Talbi M. Chemical composition, antimicrobial and insecticide activities of *Mentha rotundifolia* essential oil from Morocco. Acta Botanica Gallica. 2003;**150**: 267–274.
- [89] Riahi L., Elferchichi M., Ghazghazi H., Jebali J., Ziadi S., Aouadhi C., Chograni H., Zaouali, Y., Zoghalmi N., Mliki A. Phytochemistry: antioxidant and antimicrobial activities of the essential oils of *Mentha rotundifolia* L. in Tunisia. Industrial Crops and Products. 2013;**49**: 883–889.

- [90] Pino J.A., Rosado A., Fuentes V. Chemical composition of the leaf oil of *Mentha rotundifolia* (L.) Hudson from Cuba. *Journal of Essential Oil Research*. 1999;**11**: 241–242.
- [91] Derwich E., Benziane Z., Boukir A. Antibacterial activity and chemical composition of the leaf essential oil of *Mentha rotundifolia* from Morocco. *Electronic Journal of Environmental Agricultural and Food Chemistry*. 2010;**9**: 19–28.
- [92] Mimica-Dukic N., Bozin B., Sokovic M., Mihajlovic B., Matavulj M. Antimicrobial and antioxidant activities of three *Mentha* species essential oils. *Planta Medica*. 2003;**69**:413–419.
- [93] Gulluce M., Sahin F., Sokmen M., Ozer H., Daferera D., Sokmen A., Polissiou M., Adiguzel A., Ozkan H. Antimicrobial and antioxidant properties of the essential oils and methanol extract from *Mentha longifolia* L. ssp. *longifolia*. *Food Chemistry*. 2007;**103**: 1449–1456.
- [94] Pereira E., Pimenta A.I., Calhelha R.C., Antonio A.L., Verde S.C., Barros L., Santos-Buelga C., Ferreira I.C.F.R. Effects of gamma irradiation on cytotoxicity and phenolic compounds of *Thymus vulgaris* L. and *Mentha x piperita* L. *LWT—Food Science and Technology*. 2016;**71**: 370–377.
- [95] Dorman H.J.D., Kosar M., Kahlos K., Holm Y., Hiltunen R. Antioxidant properties and composition of aqueous extracts from *Mentha* species, hybrids, varieties, and cultivars. *Journal of Agricultural and Food Chemistry*. 2003;**51**: 4563–4569.
- [96] Triantaphyllou K., Blekas G., Boskou D. Antioxidative properties of water extracts obtained from herbs of the species Lamiaceae. *International Journal of Food Sciences and Nutrition*. 2001;**52**: 313–317.
- [97] Areias F.M., Valentao P., Andrade P.B., Ferreres F., Seabra R.M. Phenolic fingerprint of peppermint leaves. *Food Chemistry*. 2001;**73**: 307–311.
- [98] Pérez M.G.F., Rocha-Guzmán N.E., Mercado-Silva E., Loarca-Piña G., Rosalía Reynoso-Camacho R. Effect of chemical elicitors on peppermint (*Mentha piperita*) plants and their impact on the metabolite profile and antioxidant capacity of resulting infusions. *Food Chemistry*. 2014;**156**: 273–278.
- [99] Brahmi F., Hauchard D., Guendouze N., Madani K., Kiendrebeogo M., Kamagaju L., Stévigny C., Chibane M., Duez P. Phenolic composition, *in vitro* antioxidant effects and tyrosinase inhibitory activity of three Algerian *Mentha* species: *M. spicata* (L.) *M. pulegium* (L.) and *M. rotundifolia* (L.) Huds (Lamiaceae). *Industrial Crops and Products*. 2015;**74**: 722–730.
- [100] Voirin B., Bayet C., Faure O., Jullien F. Free flavonoid aglycones as markers of parentage in *Mentha aquatica*, *M. citrata*, *M. spicata* and *M. x piperita*. *Phytochemistry*. 1999;**50**: 1189–1193.
- [101] Yamamura S., Ozawa K., Ohtani K., Kasai R., Yamasaki K. Antihistaminic flavones and aliphatic glycosides from *Mentha spicata*. *Phytochemistry*. 1998;**48**(1): 131–136.

- [102] Zheng J., Zhao D.S., Wu B., Wu L.J. Study on chemical constituents in the herb of *Mentha spicata*. Zhongguo Zhong Yao Za Zhi= Zhongguo Zhongyao Zazhi= China Journal of Chinese Materia Medica. 2002;27(10): 749–751.
- [103] Fiamegos Y.C., Nanos C.G., Vervoort J., Stalikas C.D. Analytical procedure for the in-vial derivatization-extraction of phenolic acids and flavonoids in methanolic and aqueous plant extracts followed by gas chromatography with mass-selective detection. Journal of Chromatography. 2004;1041: 11–18.
- [104] Proestos C., Chorianopoulos N., Nychas G.J.E., Komaitis M. RP-HPLC analysis of the phenolic compounds of plant extracts: investigation of their antioxidant capacity and antimicrobial activity. Journal of Agricultural and Food Chemistry. 2005;53: 1190–1195.
- [105] Chen G., Gao H., Zheng J., Wu B., Yang X., Wu L. Study of chemical constituents in active parts of *Mentha spicata* III. Zhongguo Zhong Yao Za Zhi= Zhongguo Zhongyao Zazhi= China Journal of Chinese Materia Medica. 2006; 31(7): 560–562.
- [106] Kivilompolo M., Hyotylainen T. Comprehensive two-dimensional liquid chromatography in analysis of Lamiaceae herbs: characterisation and quantification of antioxidant phenolic acids. Journal of Chromatography. 2007;1145: 155–164.
- [107] Song Y., Chen G.T., Sun B.H., Huang J., Li X., Wu L.J. Study of chemical constituents in active parts of *Mentha spicata* Shenyang Yaoke Daxue Xuebao. 2008; 25(9): 705–707.
- [108] Sankara Subramanian S., Nair A.G.R. Flavonoids of the leaves of *Mentha spicata* and *Anzsochzlus carnosus*. Phytochemistry. 1972;11: 452–453.
- [109] Tomas-Barberan F.A., Husain S.Z., Gil M.I. Distribution of methylated flavones in the Lamiaceae. Biochemical Systematics Ecology. 1988;16(1): 43–46.
- [110] Papageorgiou V., Mallouchos A., Komaitis M. Investigation of the antioxidant behavior of air- and freeze-dried aromatic plant materials in relation to their phenolic content and vegetative cycle. Journal of Agricultural and Food Chemistry. 2008;56: 5743–5752.
- [111] Adam M., Dobias P., Eisner A., Ventura K. Extraction of antioxidants from plants using ultrasonic methods and their antioxidant capacity. Journal of Separation Science. 2009;32: 288–294.
- [112] Bimakr M., Abdul Rahman R., Saleena Taip F., Ganjloo A., Md Salleh L., Selamat J., Hamid A., Zaidul I.S.M. Comparison of different extraction methods for the extraction of major bioactive flavonoid compounds from spearmint (*Mentha spicata* L) leaves. Food and Bioproducts Processing. 2011;89: 67–72.
- [113] Zheng J., Chen G.T., Gao H.Y., Wu B., Wu L.J. Two new lignans from *Mentha spicata* L. Journal of Asian Natural Products Research. 2007;9(3–5): 431–435.
- [114] Guedon D.J., Pasquier B.P. Analysis and distribution of flavonoid glycosides and rosmarinic acid in 40 *Mentha piperita* clones. Journal of Agricultural and Food Chemistry. 1994;42: 679–684.

- [115] Fecka I., Turek S. Determination of water soluble polyphenolic compounds in commercial herbal teas from Lamiaceae: peppermint, melissa, and sage. *Journal of Agricultural and Food Chemistry*. 2007;**55**: 10908–10917.
- [116] Fecka I., Raj D., Krauze-Baranowska M. Quantitative determination of four water-soluble compounds in herbal drugs from Lamiaceae using different chromatographic techniques. *Chromatographia*. 2007;**66**: 87–93.
- [117] Krzyzanowska J., Janda B., Pecio L., Stochmal A., Oleszek W., Czubacka A., et al. Determination of polyphenols in *Mentha longifolia* and *M. piperita* field-grown and *in vitro* plant samples using UPLC-TQ-MS. *Journal of AOAC International*. 2011;**94**(1): 43–50.
- [118] Hadjmohammadi M., Karimiyan H., Sharifi V. Hollow fibre-based liquid phase micro-extraction combined with high-performance liquid chromatography for the analysis of flavonoids in *Echinophora platyloba* DC and *Mentha piperita*. *Food Chemistry*. 2013;**141**: 731–735.
- [119] Farnad N., Heidari R., Aslanipour B. Phenolic composition and comparison of antioxidant activity of alcoholic extracts of peppermint (*Mentha piperita*). *Journal of Food Measurement and Characterization*. 2014;**8**: 113–121.
- [120] Mekinic I.G., Skroza D., Ljubenkov I., Simat V., Mozina S.S., Katalinic V. *In vitro* antioxidant and antibacterial activity of Lamiaceae phenolic extracts: a correlation study. *Food Technology and Biotechnology*. 2014;**52**(1): 119–127.
- [121] Voirin B., Saunois A., Bayet C. Free flavonoid aglycones from *Mentha piperita*: developmental, chemotaxonomical and physiological aspects. *Biochemical Systematics and Ecology*. 1994;**22**(1): 95–99.
- [122] Gao B., Lu Y., Qin F., Chen P., Shi H., Charles D., et al. Differentiating organic from conventional peppermints using chromatographic and flow injection mass spectrometric (FIMS) fingerprints. *Journal of Agricultural and Food Chemistry*. 2012;**60**: 11987–11994.
- [123] Shalaby N.M.M., Moharram F.A., El-Toumy S.A.A., Marzoyk M.S.A., Ahmed A.A.E. Phytochemical and pharmacological studies of *Mentha pulegium* L. *Bulletin of Faculty of Pharmacy, Cairo University, Department of Natural Products, National Research Centre, Cairo, Egypt*. 2000;**38**(2): 143–151.
- [124] Ramos T., Groubert A., Pellecuer J. Diosmine analysis from several plant origins. *Institut National de la Recherche Agronomique, Faculté de Pharmacie, Université Montpellier I, Montpellier, Fr. Colloques, 69 (Polyphenols 94)*; 1995. pp. 311–12. CODEN: COLIEZ ISSN: 0293-1915.
- [125] Zaidi F., Voirin B., Jay M., Viricel M.R. Free flavonoid aglycones from leaves of *Mentha pulegium* and *Mentha suaveolens* (Labiatae). *Phytochemistry*. 1998;**48**(6): 991.
- [126] Marin Pares E. A pharmacognostic study on *Mentha rotundifolia* (L.) Hudson Circle Farm. 1983;**41**(279): 133–152.

- [127] Dobias P., Pavlikova P., Adam M., Eisner A., Benova B., Ventura K. Comparison of pressurised fluid and ultrasonic extraction methods for analysis of plant antioxidants and their antioxidant capacity. *Central European Journal of Chemistry*. 2010;**8**(1):87–895.
- [128] Ertaş A., Gören A.C., Haşimi N., Tolan V., Kolak U. Evaluation of antioxidant, cholinesterase inhibitory and antimicrobial properties of *Mentha longifolia* subsp. *noeana* and its secondary metabolites. *Records of Natural Products*. 2015;**9**(1): 105–115.
- [129] Kosar M., Dorman H.J.D., Baser K.H.C., Hiltunen R. Screening of free radical scavenging compounds in water extracts of *Mentha* samples using a postcolumn derivatization method. *Journal of Agricultural and Food Chemistry*. 2004;**52**(16): 5004–5010.
- [130] She G.M., Xu C., Liu B., Shi, R.B. Polyphenolic acids from mint (the aerial of *Mentha haplocalyx* Briq.) with DPPH radical scavenging activity. *Journal of Food Science*. 2010;**75**(4): C359–C362.
- [131] Choudhury R.P., Kumar A., Garg A.N. Analysis of Indian mint (*Mentha spicata*) for essential, trace and toxic elements and its antioxidant behavior. *Journal of Pharmaceutical and Biomedical Analysis*. 2006;**41**: 825–832.
- [132] Maffei M., Scannerini S. Fatty acid variability in some *Mentha* species. *Biochemical Systematics and Ecology*. 1992;**20**(6): 573–582.
- [133] Raju M., Varakumar S., Lakshminarayana R., Krishnakantha T.P., Baskaran V. Carotenoid composition and vitamin A activity of medicinally important green leafy vegetables. *Food Chemistry*. 2007;**101**: 1598–1605.
- [134] Curutchet A., Dellacassa E., Ringuelet J.A., Chaves A.R., Vina S.Z. Nutritional and sensory quality during refrigerated storage of fresh-cut mints (*Mentha × piperita* and *M. spicata*). *Food Chemistry*. 2014;**143**: 231–238.
- [135] Dambrauskienė E., Viškėlis P., Karklelienė R. Productivity and biochemical composition of *Mentha piperita* L. of different origin. *Biologija*. 2008;**54**(2): 105–107.
- [136] Padmini E., Prema K., Geetha B.V., Rani M.U. Comparative study on composition and antioxidant properties of mint and black tea extract. *International Journal of Food Science and Technology*. 2008;**43**: 1887–1895.
- [137] de Sousa Barros A., de Moraes S.M., Travassos Ferreira P.A., Pinto Vieira I.G., Craveiro A.A., dos Santos Fontenelle R.O., de Menezes J.E.S.A., Ferreira da Silva F.W., de Sousa H.A. Chemical composition and functional properties of essential oils from *Mentha* species. *Industrial Crops and Products*. 2015;**76**: 557–564.
- [138] Sun Z., Wang H., Wang J., Zhou L., Yang, P. Chemical composition and anti-inflammatory, cytotoxic and Antioxidant activities of essential oil from leaves of *Mentha piperita* grown in China. *PLoS One*. 2014;**9**(12).
- [139] Ebrahimzadeh M.A., Nabavi S.M., Nabavi S.F. Antioxidant and antihemolytic activities of *Mentha longifolia*. *Pharmacologyonline*. 2010;**2**:464–471

- [140] Tsai M.L., Wu C.T., Lin T.F., Lin W.C., Huang Y.C., Yang C.H. Chemical composition and biological properties of essential oils of two mint species. *Tropical Journal of Pharmaceutical Research*. 2013;**12**(4): 577–582.
- [141] Brahmi F., Boulekbache-Makhlouf L., Yalaoui-Guellal D., Chibane M., Madani K. Comparative study on the antioxidant effect of aqueous and ethanolic extracts of *Mentha pulegium* L. grown at two different locations. *PhytoChem BioSub Journal*. 2014;**8** (3): 138–149.
- [142] Arumugam P., Murugan R., Subathra M., Ramesh A. Superoxide radical scavenging and antibacterial activities of different fractions of ethanol extract of *Mentha spicata* (L.). *Medicinal Chemistry Research*. 2010;**19**: 664–673.
- [143] Karray-Bourouai N., Ksouri R., Falleh H., Rabhi M., Abdul Jaleel C., Grignon C., Lachaâl M. Effects of environment and development stage on phenolic content and antioxidant activities of *Mentha pulegium* L. *Journal of Food Biochemistry* 2010;**34**: 79–89.
- [144] Nickavar B., Alinaghi A., Kamalinejad M. Evaluation of the antioxidant properties of five *Mentha* species. *Iranian Journal of Pharmaceutical Research*. 2008;**7**(3): 203–209.
- [145] Benabdallah A., Rahmoune C., Boumendjel M., Aissi O., Messaoud C. Total phenolic content and antioxidant activity of six wild *Mentha* species (Lamiaceae) from northeast of Algeria. *Asian Pacific Journal of Tropical Biomedicine*. 2016;**6**(9): 760–766.
- [146] Brahmi F., Madani K., Dahmoune F., Rahmani T., Bousbaa K., Oukmanou S., Chibane, M. Optimization of solvent extraction of antioxidants (phenolic compounds) from Algerian mint (*Mentha spicata* L.). *Pharmacognosy Communications*. 2012;**2** (4):72–86.
- [147] Brahmi F., Madani K., Djerrada N., Idir S., Harfi F., Chibane M., Brada M. Assessment of the chemical composition and *in vitro* antioxidant activity of *Mentha rotundifolia* (L.) Huds essential oil from Algeria. *Journal of Essential Oil Bearing Plants*. 2016;**19**(5): 1251–1260, DOI: 10.1080/0972060X.2015.1108878.
- [148] Arumugam P., Ramamurthy P., Santhiya S.T., Ramesh A. Antioxidant activity measured in different solvent fractions obtained from *Mentha spicata* Linn.: an analysis by ABTS⁺ decolorization assay. *Asia Pacific Journal of Clinical Nutrition*. 2006;119–124.
- [149] Lopez V., Martín S., Gómez-Serranillos M.P., Carretero M.E., Jäger A.K., Calvo M.I. Neuroprotective and neurochemical properties of mint extracts. *Phytotherapy Research*. 2010;**24**: 869–874.
- [150] Brahmi F., Madani K., Stévigny C., Chibane M., Duez P. Algerian mint species: HPTLC quantitative determination of rosmarinic acid and *in vitro* inhibitory effects on linoleic acid peroxidation. *Journal of Coastal Life Medicine*. 2014;**2**(12):986–992.
- [151] Raj J.X., Bajppai P.K., Kumar P.G., Murugan P.M., Kumar J., Chaurasia O.P., et al. Determination of total phenols, free radical scavenging and antibacterial activities of *Mentha longifolia* Linn. Hudson from the cold desert, Ladakh, India. *Pharmacognosy Journal*. 2010;**2**: 470–475.

- [152] Ladjel S., Gherraf N., Hamada D. Antimicrobial effect of essential oils from the Algerian medicinal plant *Mentha rotundifolia* L. Journal of Applied Sciences Research. 2011;7(11): 1665–1667.
- [153] Justin K., Protais M., Rose N., Viateur U. Chemical composition and in vitro antibacterial activity of the leaf essential oil of *Mentha officinalis* from Rwanda. Journal of Chemistry Chemical Engineering. 2012;6: 401–409.
- [154] Yano Y., Satomi M., Oikawa H. Antimicrobial effect of spices and herbs on *Vibrio parahaemolyticus*. International Journal of Food Microbiology. 2006;111: 6–11.
- [155] Kumar P., Mishra S., Malik A., Satya S. Insecticidal properties of *Mentha* species: a review. Industrial Crops and Products. 2011; 34(1): 802–817.
- [156] Benayad N., Ebrahim W., Hakiki A., Mahjouba Mosaddak M. Chemical characterization and insecticidal evaluation of the essential oil of *Mentha suaveolens* L. and *Mentha pulegium* L. growing in Morocco. Scientific Study and Research. 2012;13(1): 027–032.
- [157] Lee S.E., Lee B.H., Choi W.S., Park B.S., Kim J.G., Campbell B.C. Fumigant toxicity of volatile natural products from Korean spices and medicinal plants towards the rice weevil *Sitophilus oryzae* (L.). Pest Management Science. 2001;57: 548–553.
- [158] Varma J., Dubey N.K. Efficacy of essential oils of *Caesulia axillaris* and *Mentha arvensis* against some storage pests causing biodeterioration of food commodities. International Journal of Food Microbiology. 2001;68: 207–210.
- [159] Mohamed M.I.E., Abdelgaleil A.M.S. Chemical composition and insecticidal potential of essential oils from Egyptian plants against *Sitophilus oryzae* (L.) (Coleoptera: Curculionidae) and *Tribolium castaneum* (Herbst) (Coleoptera: Tenebrionidae). Applied Entomology and Zoology. 2008;43: 599–607.
- [160] Kumar A., Shukla R., Singh P., Singh A.K., Dubey N.K. Use of essential oil from *Mentha arvensis* L. to control storage moulds and insects in stored chickpea. Journal of the Science of Food and Agriculture. 2009;89: 2643–2649.
- [161] Kasrati A., Alaoui Jamali C., Bekkouche K., Spooner-Hart R., Leach D., Abbad A. Chemical characterization and insecticidal properties of essential oils from different wild populations of *Mentha suaveolens* subsp. timija (Briq.) Harley from Morocco. Chemistry & Biodiversity. 2015;12: 823–831.
- [162] Lamiri A., Lhaloui S., Benjilali B., Berrada M. Insecticidal effects of Hessian fly against *Mayetiola destructor* (Say). Field Crops Research. 2001;71: 9–15.
- [163] El Nagar T.F.K., Abdel Fattah H.M., Khaled A.S., Aly S.A. Efficiency of peppermint oil fumigant on controlling *Callosobruchus maculatus* F. infesting cow pea seeds. Life Science Journal. 2012;9(2): 375–383.
- [164] Zekri N., Handaq N., El Caidi A., Zair T., El Belghiti M.A. Insecticidal effect of *Mentha pulegium* L. and *Mentha suaveolens* Ehrh. hydrosols against a pest of citrus *Toxoptera aurantii* (Aphididae). Research on Chemical Intermediates. 2015;1–11, <http://dx.doi.org/10.1007/s11164-015-2108-0>.

- [165] Sharma V., Shabir H., Moni G., Kumar S.A. *In vitro* cancer activity of extracts of *Mentha* spp. against human cancer cells. *Indian Journal of Biochemistry and Biophysics*. 2014;**51**(5): 416–419.
- [166] Yi W., Ywetzstein H. Anti-tumorigenic activity of five culinary and medicinal herbs grown under greenhouse conditions and their combination effects. *Journal of Science and Food Agriculture*. 2011;**91**: 1849–1854.
- [167] Shirazi F.H., Ahmadi N., Kamalinejad M. Evaluation of northern Iran *Mentha pulegium* L. cytotoxicity. *Daru Journal of Pharmaceutical Sciences*. 2004;**2**(3): 106–110.
- [168] Mazzio E.A., Soliman K.F.A. *In vitro* screening for the tumoricidal properties of international medicinal herbs. *Phytotherapy Research*. 2009;**23**: 385–398.
- [169] Hajjghasemi F., Hashemi V., Khoshzaban F. Cytotoxic effect of *Mentha spicata* aqueous extract on cancerous cell lines *in vitro*. *Journal of Medical Plants Research*. 2011;**5**(20): 5142–5147.
- [170] Jain D., Pathak N., Khan S., Venkata Raghuram G., Bhargava A., Samarth R., Kumar Mishra P. Evaluation of cytotoxicity and anticarcinogenic potential of *Mentha* leaf extracts. *International Journal of Toxicology*. 2011;**30**(2): 225–236.
- [171] Al-Ali K.H., El-Beshbishy H.A., El-Badry A.A., Alkhalaf M. Cytotoxic activity of methanolic extract of *Mentha longifolia* and *Ocimum basilicum* against human breast cancer. *Pakistan Journal of Biological Science*. 2013;**16**(23): 1744–1750.
- [172] Abirami S.K.G., Nirmala P. A comparative—*in vitro* study of anticancer effect of *Mentha piperita*, *Ocimum Basilicum* and *Coleus aromaticus* against human laryngeal epidermoid carcinoma (HEP-2) cell lines. *Journal of Medical Plants and Studies* 2014;**2**(1): 2320–3862.
- [173] Moreno L., Bello R., Primo-Yufera E., Esplugues J. Pharmacological properties of the methanol extract from *Mentha suaveolens* Ehrh. *Phytotherapy Research*. 2002;**16**: S10–S13.
- [174] Conforti F., Sosa S., Marrelli M., Menichini F., Statti G.A., Uzunov D., Tubaro A., Menichini F., Loggia R.D. *In vivo* anti-inflammatory and *in vivo* antioxidant activities of Mediterranean dietary plants. *Journal of Ethnopharmacology*. 2008;**116**(1): 144–151.

