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Chapter 3

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

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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, Teucrioideae, 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*

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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
M. spicata	Brazil	For the expulsion of parasitic worms, mainly *Ascaris lumbricoides*	[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]
	India	The plant is typically used in the treatment of loss of appetite, common cold, bronchitis, sinusitis, fever, nausea, and vomiting	[10]
M. pulegium	Brazil	For expulsion of parasitic worms; mainly *Ascaris lumbricoides*, *Entamoeba histolytica*, and *Giardia lamblia*; 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]

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Species	Region	Indications	Reference
M. rotundifolia	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, choleretic, antispasmodic, anti-inflammatory, sedative, hypotensive, and insecticidal	[21]
M. longifolia	Iran	Different parts of the plant (leaves, flower, stem, bark, and seeds) have been used as antimicrobial, carminative, stimulant, antispasmodic, antirheumatic, anticatarrhal, 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]
M. piperita	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
M. arvensis	India	Possess abortifacient property	[10]
M. australis	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]
M. haplocalyx	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].

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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 spermatogenetic 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 μL/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
M. spicata	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]
M. pulegium	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
	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]
M. rotundifolia	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]
M. longifolia	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
M. spicata			
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, *p*-coumaric, ferulic, and rosmarinic acids	Finland	[106]
	Protocatechuic and vanillic acids	China	[107]
	4-Hydroxy benzoic, caffeic, *p*-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]

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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]
M. piperita			
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, *p*-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, *p*-coumaric, sinapic, shikimic, rosmarinic acids	Mexico	[98]
	Rosmarinic, caffeic, gallic, syringic, *p*-hydroxybenzoic, o-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]
M. pulegium			
Phenolic acids	Caffeic acid	Egypt	[123]
	Caffeic, vanillic, and ferulic acids	Greece	[104]
	4-Hydroxy benzoic, caffeic, *p*-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]

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Class of compounds	Identified compounds	Origin	Reference
M. rotundifolia			
Phenolic acids	Caffeic, *p*-hydroxybenzoic, ferulic, and *p*-coumaric acids	Spain	[126]
	Caffeic, *p*-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]
M. longifolia			
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]
M. australis			
Phenolic acids	Rosmarinic, chlorogenic, and caffeic acids	Australia	[26]
Flavonoids	Neoponcirin, narirutin, biochanin A, apigenin, hesperetin, and naringenin	Australia	[26]
M. haplocalyx			
Phenolic acids	Rosmarinic, caffeic acid	China, Finland	[27, 129]
	Cis-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 C_{18}: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 (•OH) [25, 138],

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the hydroalcoholic extract of *M. piperita* [139] and peppermint essential oil [140] as scavengers of nitric oxide (•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 ($O_2^{\bullet -}$) 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 $ABTS^+$		
M. spicata, *M. piperita*, *M. longifolia*, *M. pulegium*, *M. rotundifolia*	Ethanolic	[99, 144, 148]
M. longifolia, *M. viridis*	Essential oil	[6]
M. spicata, *M. pulegium*, *M. rotundifolia*	Essential oil	[51, 71, 147]
Measurement of lipid peroxidation inhibition		
M. pulegium	Water Essential oil	[69]
M. aquatica, *M. pulegium*, *M. suaveolens*, *M. piperita*	Methanolic	[145, 149]
M. longifolia	Methanolic	[149]
M. arvensis, *M. villosa*	Methanolic	[145]
M. piperita	Essential oil	[140]
M. spicata, *M. pulegium*, *M. rotundifolia*	Ethanolic	[150]
Measurement of iron chelating activity		
M. spicata	Ethanolic	[142]
M. piperita	Ethanol/water	[139]
M. aquatica, *M. arvensis*, *M. piperita*, *M. pulegium*, *M. rotundifolia*, *and M. villosa*	Methanolic	[145]

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

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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 Hadjlaoui 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 Hadjlaoui 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 μL/L) [157, 158]. Similarly, the essential oil of *M. microphylla* gave remarkable activity against this insect (LC_{50}, 0.2 μL/L) in fumigation bioassays and in contact bioassays (24 h; LC_{50}, 0.01 mg/cm^2) [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 μL/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 μL/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 μL/L) was a slightly better fumigant than *M. spicata* (LD_{50}, 33.1 μL/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 μg/mL [165]. Similarly, in Yi and Wetzstein [166] study, spearmint and peppermint methanolic extracts significantly inhibited SW-480 colon cancer cell growth (IC_{50s}: 143.6 ± 25.6 μg/mL for spearmint and 92.3 ± 17.8 μg/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 μg/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

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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 μg/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 × (10 μg/μL) to 100 × (100 μg/μL)).

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 μg/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 μg/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 μg/mL) [171] and human laryngeal epidermoid carcinoma (IC_{50} = 94 μg/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 μg/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 μg/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 μg/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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