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REVIEW ARTICLE

# Phytochemical and nutra-pharmaceutical attributes of *Mentha* spp.: A comprehensive review

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**Abstract** Medicinal plants are considered colossal producers of bioactive therapeutics agents. The genus *Mentha* possesses commercial values owing to its aromatic species. Despite its traditional applications in food flavoring, *Mentha* spp. such as *Mentha piperita* (peppermint), *M. aquatica* (water mint), *M. spicata* (spearmint), and *M. arvensis* (wild mint) are widely used for treating not only cold and fever but also gastro-intestinal and cardiovascular disorders as folk medicines. It has revealed a plethora of biological traits viz. antimicrobial, antioxidant, anticancer, anti-ulcer, anti-diabetic, insecticidal, and anti-inflammatory activities. Generally, the presence of bioactive phytochemicals is the prime reason for the traditional pharmacological activities of *Mentha* spp. A rich source of potential phytoconstituents of *Mentha* spp. is an important agent for designing nutrapharmaceuticals. The current review paper discusses the different phytochemical, traditional medicinal features, and prime therapeutic properties of some of the most commonly used *Mentha* spp. Also, this paper summarizes the role of various metabolites of *Mentha* towards the development of therapeutic drugs in the future.



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**Contents**



## 1. Introduction

*Mentha* (family – Lamiaceae), also known as 'Mint' is distributed across Asia, Europe, Australia, Africa, and North America. It contains about 25 different species and few hybrid plants. Some common species of the genus *Mentha* includes *M. piperita*, *M. aquatica*, *M. spicata*, *M. rotundifolia*, *M. arvensis*, *M. pulegium*, *M. longifolia*, and *M. suaveolens* (Fig. 1). There is a diverse range of taxonomical names in the Lamiaceae family that shows huge morphological changes (Šarić-Kundalić et al., 2009, Mogosan et al., 2017). The specific characteristics are square stems in cross-section as well as zygomorphic, bisexual, and bilateral symmetric flowers containing 5 united and deeply lobed petals and sepals (Nieto, 2017). Plants contain dry woody fruits.

*Mentha* spp. have shown disparate commercial roles in the food, medical, and ornamental industries (Nieto, 2017). It has exhibited its potentiality against intestinal parasites and digestive problems (Hanafy, 2018). Owing to its different medicinal effects, it is also considered a popular herbal therapeutics against flatulence, nausea, ulcerative colitis, anorexia, bronchitis, and liver diseases (Brahmi et al., 2017). It has been revealed that the genus *Mentha* include anti-inflammatory, anti-emetic, antispasmodic, analgesic, anticancer, anti-obesity, anti-diabetic, anti-bloating, and immunomodulatory actions (Farzaei et al., 2017). Furthermore, reports have revealed the antimicrobial and antioxidant effects of essential oil or extract of some *Mentha* spp., viz. *M. spicata*, *M. arvensis, M. rotundifolia, M. suaveolens*, and *M. pulegium* (Brahmi et al., 2016).

*Mentha* spp. have been utilized for culinary applications for many years (Okut et al., 2017). These groups of plants are mainly used to cure gastrointestinal complaints, however, their medical effectiveness is broad (Trevisan et al., 2017). For stomach ache and chest disorders, *Mentha* spp. are generally taken as a tea for home-based therapy. The tea can stimulate digestion, reduce stomach pain, gastritis, dyspepsia, flatulence, enteritis, intestinal colic, gastric acidities, aerophagia, and spasm of the gallbladder, bile duct, and gastrointestinal tract

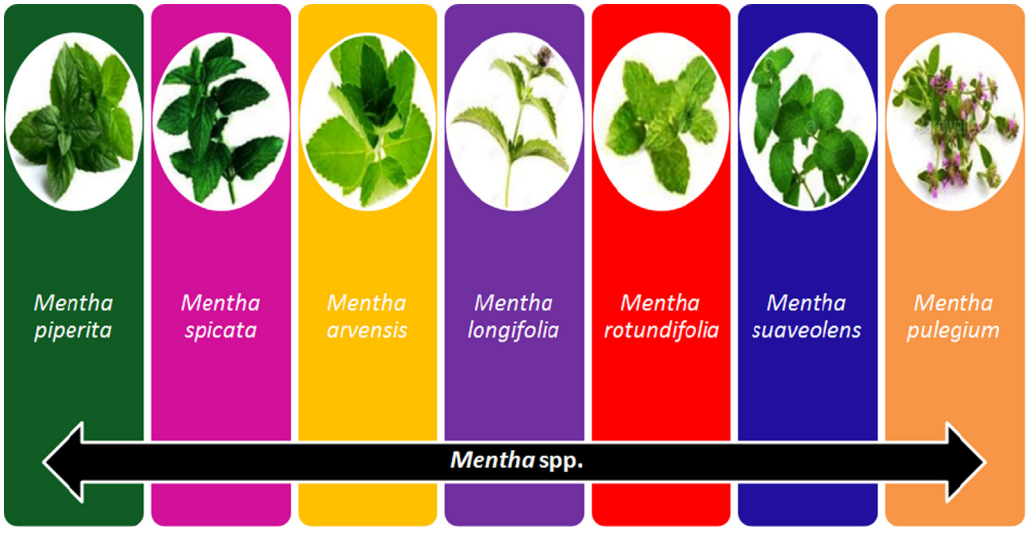


**Fig. 1** Common species of *Mentha*.

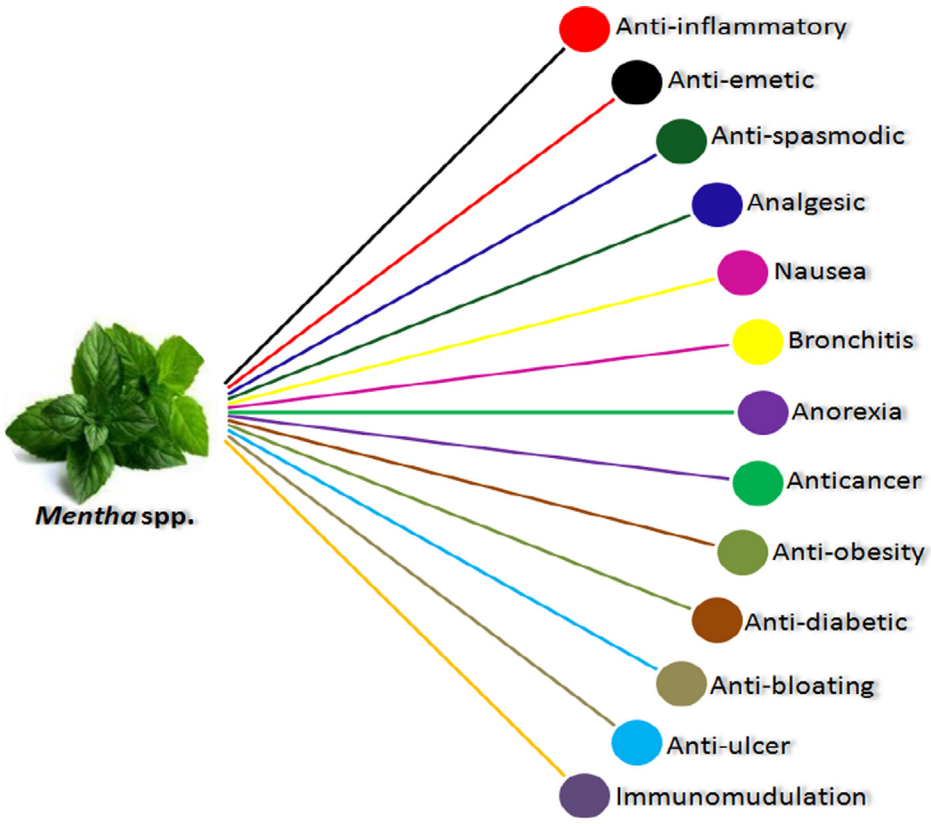


**Fig. 2** Various medicinal applications of *Mentha* spp.

(Abbaszadeh et al., 2009). This plant also helps in lipid digestion. Recently, it has been suggested for its paramount role in reducing obesity. Reports have also shown a strong diuretic effect for mint tea (Abbaszadeh et al., 2009).

*Mentha* spp. are beneficial for buccodental prevention too. The milled powder of *Mentha* spp. leaves were used to whiten teeth throughout the middle centuries (Sunitha and Reddy, 2018). Fresh leaves can be used for chewing and mouth burns. It can also be used as a mouthwash solution to diminish gingival pain (Blass, 1943). Due to its effect on breath freshness, *Mentha* spp. are used in making oral dentifrices and preventing caries and plaque (Balakrishnan, 2015) (Fig. 2).

## 2. Bioactive constituents of *Mentha* spp.-

### *2.1. Essential oils*

Essential oils are complex volatile secondary metabolites that are often obtained from aromatic plants using the hydrodistillation technique (Edris, 2007). *Mentha* spp. oil is one of the crucial essential oils prepared globally with the financial cost of 400 million US dollars per annum. Corn mint oil, for example, can be obtained from *M. arvensis*, which is the most important source of menthol. Other instances are; peppermint oil from *M. piperita*; carvone-rich oil from *M. spicata*, *M. gracilis*, and, *M. viridis*; linalool and linalyl from *M. aquatica*; and pennyroyal oil from *M. pulegium* (Pereira et al., 2016). Besides, *M. haplocalyx* could be categorized into carvone, linalool, menthol, pulegone, piperitenone oxide, and menthone (Muhammad et al., 2015). *M. piperita* leaves include 1.2–3.9% (v/w) of essential oils and more than 300 recognized components. The terpenic group with about 52% of monoterpenes and 9% of sesquiterpenes are the most important components of peppermint leaves. The other classes include aromatic hydrocarbons (9%), lactones (7%), aldehydes (9%), and alcohols (6%). Menthol with about 35–60% is the main constituent of monoterpenes. Other monoterpenes are limonene (0.1–6%), neomenthol (3–4%), isomenthone (2–5%), 1,8-cineole (eucalyptol) (1–13%), menthofuran (0.3–14%), menthyl acetate (0.7–23%), and menthone (2–44%). The main sesquiterpene is β-caryophyllene with a total content of 1.6–1.8% (Sahib et al., 2013). Some of the important metabolites present in the essential oils of *Mentha* spp. are 1,2-epoxyneomenthyl acetate, 1,8-cineole, 3-octanol, 3-octanone, 3-octyl acetate, beta-caryophyllene, carvone, caryophyllene oxide, *cis*-dihydrocarvone, *cis*-sabinene hydrate, decyl acetate, elemol, geraniol, germacrene D, isomenthone, limonene, linalool, menthol, and menthone.

### *2.2. Phenolic compounds*

Secondary metabolites in plants are often phenolic compounds that are a large category of biologically active components (Pliego et al., 2020). It includes over 8000 molecules with at least one aromatic ring containing one or more hydroxyl groups bonded. The natural sources for these compounds are esters and glycosides (Pereira et al., 2016). *Mentha* spp. possess a variety of compounds such as glycoside, cinnamic acids and aglycon, and/or acylated flavonoids (Dorman et al., 2003). The aqueous extract of *Mentha* sp. contained phenolic acid esters and flavonoids derivatives (Triantaphyllou and Dimitrios boskou, 2001). Caffeic acid and its derivatives, chlorogenic,

**Table 1** Various phenolic compounds present in different species of *Mentha*.

| *Mentha* spp. | Phenolic components | Compounds name |
|---|---|---|
| *M. spicata* | Phenolic acids | Protocatechuic acid, homovanillic, hydroxybenzoic, syringic, 4-hydroxy cinnamic, *trans*-hydroxycinnamic, veratric acid, 2-hydroxy cinnamic, caffeic, syringic, ferulic acids, gallic acid, vanillic acids, *p*-coumaric, rosmarinic acids, 4-hydroxy benzoic, caffeic, *p*-coumaric, chlorogenic, and rosmarinic acids |
| | Flavonoids | 5-desmethoxynobiletin, 5,6-dihydroxy-7,8,3′,4′-tetramethoxyflavone, thymonin, sideritiflavone, 6,4′-trihydroxy-7,3′-dimethoxyflavone, 5-hydroxy-3′,4′,6,7-tetramethoxyflavone, diosmetin, diosmin, thymonin, chrysoeriol, 5, 6-dihydroxy-7, 8, 3′, 4′-tetramethoxyflavone, naringenin, rutin, quercetin, nodifloretin, luteolin, and scopoletin |
| *M. piperita* | Phenolic acids | Rosmarinic acid, rosmarinic, caffeic acid, salvianolic, dehydro-salvianolic acids, cinnamic acids, protocatechuic acid glucoside, lithospermic acids, sinapic, shikimic, 3-o-caffeoylquinic acids, *p*-hydroxybenzoic, and o-coumaric |
| | Flavonoids | Rutin, xanthomicrol, catechin, quercetin-4′-glucoside, 5,6-dihydroxy-7,8,3′,4′-tetramethoxyflavone, sorbifolin, thymosin, hesperidin, gallocatechin-gallate, thymonin, sideritoflavone, narirutin, ladanein, luteolin 7-o-rutinoside, isorhoifolin, eriodictyol 7-o-glucoside, 5-o-demethylnobiletin, 4′-methoxykaempferol-7-o-rutinoside, luteolinglucopyranosyl-rhamnopyranoside, eriocitrin, and narirutin |
| *M. pulegium* | Phenolic acids | Caffeic acid, vanillic acid, ferulic acids, 4-hydroxy benzoic, caffeic, *p*-coumaric, chlorogenic, and rosmarinic acids |
| | Flavonoids | Thymonin, jaceosidin, pectolinaringenin, ladanein, sorbifolin, pedalitin, diosmin, luteolin, kaempferol, apigenin, luteolin, naringenin, and catechin |
| *M. rotundifolia* | Phenolic acids | Caffeic, *p*-coumaric, chlorogenic, and rosmarinic acids, *p*-hydroxybenzoic, and ferulic acid |
| | Flavonoids | Thymonin, thymosin, 5,6-dihydroxy-7,8,3′,4′-tetramethoxyflavone, jaceosidin, hispidulin, ladanein, sorbifolin, nodifloretin, apigenin, luteolin, genkwanin, esculetin, apigenin, luteolinidin, elargonidin, cyanidin, delphinidin, petunidin, luteolin, luteolin, diosmin, naringenin, kaempferol, and diosmetin |
| *M. longifolia* | Phenolic acids | Rosmarinic, salvianolic acid, dedihydro-salvianolic Acid |
| | Flavonoids | Eriodictyolglucopyranosyl-rhamnopyranoside, methylated luteolin-glucuronide, luteolin-glucuronide, and 5-hydroxy-6,7,3′,4′-tetramethoxyflavone |
| *M. australis* | Phenolic acids | Rosmarinic, chlorogenic, and caffeic acids |
| | Flavonoids | Narirutin, biochanin A, apigenin, hesperetin, naringenin, and neoponcirin |
| *M. haplocalyx* | Phenolic acids | Rosmarinic, caffeic acid, lithospermic acid B, magnesium lithospermate B, sodium lithospermate B, and danshensu |
| | Flavonoids | Eriocitrin, luteolin-7-*o*-glucoside, and isoraifolin, |

and rosmarinic acid are the main phenolic compounds of the genus *Mentha* (Areias et al., 2001, Dorman et al., 2003, Lv et al., 2012, Kapp et al., 2013, Pérez et al., 2014, Riachi and De Maria, 2015, Pereira et al., 2016). Besides, some salvianolic acids are present in *Mentha* spp. (Kapp, 2015). *Mentha* spp. contain flavonoid too, mainly in the form of flavones and flavanones. The main flavones defined in *Mentha* spp. are luteolin and its derivatives (Kapp, 2015). Some other components including eriocitrin, naringenin-7-O-glucoside, luteolin-7-O-glucoside, eriodictyol, isorhoifolin, luteolin, and apigenin are present in the aqueous extract of *Mentha* spp. (Dorman et al., 2003, Areias et al., 2001). Areias et al. (2001) also demonstrated the presence of glycoside eriocitrin as a chief component in the aqueous extract *Mentha* spp. Besides, in another investigation, hydrophobic methylated flavonoid has been isolated from *M. aquatica*, *M. spicata*, and *M. piperita* leaves. The compound 5,6-dihydroxy-7,8,3′,4′-tetramethoxyflavone was observed as of prime flavonoid of *M. spicata* and *M. piperita*, while 5-hydroxy-6,7,8,4′-tetramethoxyflavone was identified as the main component of *M. aquatica* (Voirin et al., 1999). A list of important phenolic compounds present in *Mentha* spp. is shown in Table 1.

### 2.3. Other components

Different categories of bioactive components have been identified in *Mentha* spp. too. *M. spicata* and *M. piperita* include varied trace elements (Choudhury et al., 2006, Kizil et al., 2010). Maffei (1992) reported the presence of triacylglycerol, diacylglycerol, and free fatty acids in *Mentha* spp. Linoleic, linolenic, and palmitic acid are the main components found in *M. piperita* leaves (Pérez et al., 2014). Besides, reports revealed the presence of ceramides in *M. longifolia* methanol extract (Aggarwal and Kunnumakkara, 2009).

Moreover, triterpenoids and steroids are also present in *Mentha* spp. According to Ertas et al. (2015), ursolic acid and uvaol as triterpenoids and stigmast-5-en-3-β-ylformate, stigmast-5-en-3-one, and β-sitosterol as steroids were purified from the aerial regions of *M. longifolia* subsp. *noeana*. Reports have also shown the presence of different pigments in *Mentha* spp. (Ertaş et al., 2015). *M. spicata* contains xanthophylls (neoxanthin, violaxanthin, lutein, and zeaxanthin), carotenes (α-carotene) (Raju et al., 2007, Curutchet et al., 2014, Dambrauskienė et al., 2008). Lutein and β-carotene isomers as carotenoids have been identified in dry *M. piperita* tea, however, only lutein has shown to exist in infusion (Riachi and De Maria, 2015). Two types of vitamins, α-tocopherols, and ascorbic acid are also reported in *Mentha* spp. (Dambrauskienė et al., 2008, Pérez et al., 2014, Riachi and De Maria, 2015). The presence of sugars, saponins, alkaloids, anthraquinones, and quinines was also been reported in *Mentha* spp. (Padmini et al., 2008).

## 3. Biological activities of *Mentha* spp.-

Antimicrobial or antibiotic drug resistance is a huge concern for worldwide researchers (Khusro et al., 2018a). The use of novel phytomedicines has opened a new avenue in dealing with

antimicrobial resistance and other chronic diseases (Edris, 2007, Sahib et al., 2013, Muhammad et al., 2015, Anwar et al., 2016). The search is focused on the detection of natural bioactive compounds with therapeutical benefits. A majority of medicinal plants has been analyzed for their possible physiological functions such as antioxidant, anti-inflammatory, anticancer, and antimicrobial effects (Menichini et al., 2009, Rashid et al., 2013, Muhammad et al., 2015). *Mentha* spp. and their derivatives have shown promising effects in several aspects (Hussain et al., 2010b, Hussain et al., 2010a). Prime pharmaceutical/biological attributes of common *Mentha* spp. are discussed below:

### 3.1. Anticarcinogenic and cytotoxicity activities

Despite great progress in developing novel methodologies in the prevention and treatment of cancer, it remains a challenging health problem worldwide (Desales-Salazar et al., 2020). Repetitive and uncontrolled proliferation of certain cells in the body which can further turn into malignant tumors cells occur during cancer growth (Aarti and Khusro, 2013, Ochwang'i et al., 2014). Chemotherapy, radiotherapy, and pharmaceutical-based regimens are the currently leading therapeutic strategies against cancer. However, these strategies exhibit several drawbacks and affect the patients' health. Thus, the search for alternative therapeutics is a continuous process (Greenwell and Rahman, 2015).

Herbal medicine has been utilized as the initial source of several drugs for many years. Also, recent research has been oriented in the synthesis of plant-derived nanomaterials in cancer treatment (Sivaraj et al., 2014, Raj et al., 2016). In this regard, the capability of many plant species for their plausible anticancer activity has been tested (Cai et al., 2006, Fouché et al., 2008). *In vitro*, *in vivo*, and pre-clinical trial studies have investigated the anti-tumor activities of *Mentha* spp. against many cancer cell lines (Baliga and Rao, 2010). *Mentha* spp. have been proved as the most effective species against tumor inducer among 120 medicinal plants (Ohara and Matsuhisa, 2002). In another investigation, the anticancer activities of extract and essential oils of *Mentha* spp. were tested against Vero (green African monkey kidney), HeLa (human malignant cervix carcinoma), and HepG2 (human laryngeal carcinoma) cell lines (Alley et al., 1988). Results showed potential anticancer traits of *Mentha* spp. against selected cell lines. Moreover, the hydro-distilled essential oil of some common species such as *M. piperita*, *M. longifolia*, *M. spicata*, and *M. arvensis* have shown significant prohibitory effects against human breast cancer cell line MCF-7 (Hussain et al., 2010a). In a different report, the aqueous extracts of *M. pulegium* were observed as promising antitumor agents (Anwar et al., 2017, Karakaş et al., 2012). Also, *Mentha*-derived extracts exhibited a dose-dependent cytotoxic effect (Khan et al., 2012). The aqueous and methanolic extracts of *M. longifolia* showed anti-tumor and anti-mutagenic effects, indicating the presence of bioactive constituents, which might be useful in the development of novel anticancer agents (Al-Ali et al., 2014).

### 3.2. Antioxidant activities

Plant-derived compounds have received great attention due to their antioxidant properties. The generation of one or more unpaired electrons during highly reactive metabolism cycles results in the release of reactive oxygen species (ROS). The imbalance between ROS production and body antioxidant defense system is called oxidative stress which might lead to detrimental cellular events such as peroxidation of membrane lipids and destruction of bio-macromolecules (Desousa barros et al., 2015). Extracts and essentials of *Mentha* spp. have shown antioxidant activities (Kapp, 2015). Phenolic acids (caffeic acids and rosmarinic), flavones (luteolin derivatives), ascorbic acid, and flavanones (eriocitrin derivatives) are known to show promising antioxidant capacities, whereas vitamin antioxidants such as carotenoids exhibit weak radical scavenging traits. Essential oils show controversial effects; unsaturated and minor cyclic oxygenated terpenes act as antioxidant constituents, while acyclic unsaturated oxygenated monoterpenes contribute to pro-oxidant reactions (Riachi and De Maria, 2015). *In vitro* assays have shown free radical scavenging properties of different *Mentha* spp. extracts. It has been found that the essential oils of *M. piperita* can scavenge hydroxyls radicals (Sun et al., 2014), the hydroalcoholic extracts of *M. piperita* are nitric oxide scavengers (Ebrahimzadeh et al., 2010), while aqueous and ethanolic extracts of *M. pulgium* degrade hydrogen peroxide radicals (Brahmi et al., 2014). Also, the ethanol extract of *M. rotundifolia*, *M. pulegium*, and *M. spicata* as well as the methanol extract of *M. pulegium* and *M. longifolia* are effective quenchers of superoxide radicals (Hajlaoui et al., 2009, Karray-Bouraoui et al., 2010, Fatiha et al., 2015). 2,2-diphenyl-1-picrylhydrazyl (DPPH) is a functional assay in evaluating the antioxidant activity of different plants via measuring the ability to donate hydrogen atoms (Mata et al., 2007). It has been widely applied in assessing the antioxidant capacity of different compounds derived from *Mentha* spp. *M. aquatica*, *M. piperita*, *M. spicata*, *M. longifolia*, *M. arvensis*, and *M. pulegium* are the extensively studied species with pronounced *in vitro* antioxidant activities (Nikavar et al., 2008, López et al., 2010, Fatiha et al., 2015). The radical scavenging components show their effect by chelating metals or acting as electron or hydrogen donating agents. Furthermore, the polar extracts of *Mentha* spp. have shown potential activities in comparison with essential oils, as predicted from their composition (Mata et al., 2007, Gulluce et al., 2007, Kamkar et al., 2010).

### 3.3. Anti-inflammatory properties

It has been reported that several components were extracted from *Mentha* spp. show anti-inflammatory characteristics. This property of essential oils from *M. piperita* has been documented via 5-lipoxygenase (5-LOX) inhibition assay *in vitro* (Tsai et al., 2013). This compound could also prohibit the generation of nitric oxide and prostaglandin E2 in lipopolysaccharide-activated RAW 264.7 macrophages (Sun et al., 2014). Moreover, the extracts of *M. piperita* have shown efficiency in the down-regulation of IL-1, IL-6, and COX-2 genes in J774A.1 mouse macrophage cells (Lv et al., 2012). The treatment of animals with methanolic extracts of *M. suaveolens* has induced anti-inflammatory effects *in vivo* (Moreno et al., 2002). Fractions of various solvents extracts of *M. spicata* have substantially diminished acute and chronic inflammation in Wistar albino rats (Arumugam et al., 2008). Besides, the topical use of alcoholic extracts of *M. aquatica*

successfully reduced edema in Male CD-1 mice (Conforti et al., 2008). The essential oils of *M. piperita* significantly reduced inflammatory response in croton oil-induced mouse ear edema model in a dose-dependent manner (Sun et al., 2014).

### 3.4. Antimicrobial activities

Infectious diseases caused by bacteria, viruses, and fungi are among the serious medical concerns worldwide (Nathan, 2004, Khusro et al., 2018a, Khusro et al., 2018b). Additionally, microorganisms can tolerate adverse environmental circumstances and induce multi-drug resistance despite the availability and applications of effective antibiotics (Ahameethunisa and Hopper, 2010). Also, the use of synthetic drugs in developing and underdeveloped regions are not only cost-effective but also can result in adverse effects. Therefore, the need for novel and non-toxic agents to combat microbial infections is the demand of the current hour. In this context, phytomedicines are considered important pipelines for safe and effective drug development.

The essential oils of *Mentha* spp. have been analyzed for their possible antimicrobial activities (Saba and Anwar, 2018). This effect has mainly been in association with volatile bioactive compounds such as oxygenated monoterpenoids, monoterpene, and sesquiterpene hydrocarbons (Mikaili et al., 2013). The growth of gram-positive and gram-negative bacteria such as *Bacillus subtilis*, *Serratia marcesens*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* was inhibited by *Mentha* essential oils (Bupesh et al., 2007, Saba and Anwar, 2018). The essential oils of *M. pulegium* were found effective against all the tested strains of *Klebsiella* sp. (Jazani et al., 2009). Also, the antibacterial properties of *M. piperita* against strains of *Salmonella* sp., *P. aeruginosa*, *Escherichia coli*, *S. aureus*, *B. subtilis*, *Klebsiella pneumoniae* were reported (Irshad et al., 2011). In another study, the growth of *S. enterica*, *E. coli*, and *P. aeruginosa* was inhibited by *M. longifolia* (Nikšić, 2012). On contrary, a weak antibacterial effect of methanolic extract of *M. piperita* was observed against different strains of *Helicobacter pylori*. The activity of the essential oil is generally dependent on bacterial strains, experiment conditions, and plant varieties (Mahady et al., 2005, Mckay and Blumberg, 2006). The impact of distinct extracts of *M. piperita* was determined against some pathogenic bacteria (*E. coli*, *Proteus vulgaris*, *S. aureus*, *K. pneumoniae*, and *P. aeruginosa*). Results showed pronounced antibacterial properties of aqueous and ethyl acetate extracts of *Mentha* sp. (Dixit, 2013). Similarly, *M. spicata* exhibited a potent antimicrobial effect (Padmini et al., 2010). In another study, the growth of gram-positive and gram-negative bacteria was significantly affected by essential oils obtained from *M. spicata* (Saba and Anwar, 2018). Similarly, the potential antibacterial effects of *M. suaveolens* essential oils were reported against different gram-positive and gram-negative bacteria and revealed that these oils could surge the shelf-life of food products (Ed-Dra et al., 2018). Several bioactive components such as luteolin, gallocatechin, epigallocatechin gallate, rosmarinic acid, caffeic acid, catechins, menthone, isomenthone, and hexadecanoic acid present in *Mentha* spp. are possibly responsible for their antimicrobial effects. A recent study exhibited a pronounced antibacterial trait of *M. piperita* against fermented food-associated coagulase-negative staphylococci with a high zone of inhibition (Khusro et al., 2020). In another study, *M. piperita* was used to provide mild stress to *Staphylococcus hominis* for synthesizing anti-tubercular protein (Khusro et al., 2020). Antibacterial activities of varied *Mentha* spp. are shown in Table 2.

The wide prevalence as well as the presence of microbial resistance has turned fungal diseases into emerging health problems globally (Portillo et al., 2001, Fortes et al., 2008). *Mentha* spp. were screened for their antifungal activities too (Saba and Anwar, 2018), as illustrated in Table 2. *M. spicata* essential oil inhibited the growth of mycelium of *Fusarium oxysporum* at varied concentrations (Nosrati et al., 2011). *M. piperita* and *M. spicata* essential oils exhibited antifungal

**Table 2** Antimicrobial traits of common *Mentha* spp.

| *Mentha* spp. | Indicator pathogens | References |
|---|---|---|
| *M. piperita* | *E. coli*, *K. pneumoniae*, *P. mirabilis*, *P. vulgaris*, *P. aeruginosa*, *S. enteritidis*, *S. paratyphi* A and B, *S. pullorum*, *S. typhi*, *S. typhimurium*, *Shigella dysenteriae*, *Yersinia enterocolitica*, *B. cereus*, *B. subtilis*, *Listeria monocytogenes*, *S. aureus*, *S. hominis*, *Streptococcus pyogenes*, *A. niger*, Herpes simplex virus, and HIV | Yamasaki et al., 1998, Tassou et al., 2000, İşcan et al., 2002, Schuhmacher et al., 2003, Saeed and Tariq, 2005, Bupesh et al., 2007, Rodriguez-Fragoso et al., 2008, Chauret, 2011, Sujana et al., 2013, Moghtader, 2013, Singh et al., 2015, Patil et al., 2016, Khusro et al., 2020 |
| *M. spicata* | *E. coli*, *K. pneumoniae*, *P. mirabilis*, *P. aeruginosa*, *S. typhimurium*, *Vibrio* spp., *B. cereus*, *B. subtilis*, *L. monocytogenes*, *S. aureus*, *F. oxysporum*, *A. niger*, *R. solani*, *B. theobromae*, *M. mucedo*, and *F. solani* | Hussain et al., 2010b, Nosrati et al., 2011, Aliakbarlu et al., 2013, Snoussi et al., 2015, Shahbazi, 2015 |
| *M. suaveolens* | *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *P. mirabilis*, *B. anthracis*, and *S. aureus* | Oumzil et al., 2002 |
| *M. rotundifolia* | *E. coli*, *S. typhimurium*, *B. cereus*, and *S. aureus* | Riahi et al., 2013 |
| *M. arvensis* | *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *Shigellaflexneri*, and *S. aureus* | do Nascimento et al., 2009 |
| *M. longifolia* | *E. coli*, *P. aeruginosa*, *S. typhimurium*, *B. cereus*, *L. monocytogenes*, *S. aureus*, *S. pyogenes*, *P. ochrochloron*, *C. fulvum*, and *C. cladosporioides* | Al-Bayati, 2009, Džamić et al., 2010, Aliakbarlu et al., 2013 |
| *M. pulegium* | *E. coli*, *P. aeruginosa*, *S. typhimurium*, *B. cereus*, and *S. aureus* | Aires et al., 2016 |

activities against seventeen micromycetal food poisoning and human pathogens (Soković et al., 2009). In another study, the antifungal effects of *Mentha* spp. (*M. piperita*, *M. arvensis*, *M. spicata*, and *M. longifolia*) were tested. Results showed maximum antifungal activity with low minimum inhibitory concentration value of *M. arvensis* (Hussain et al., 2010b, Hussain et al., 2010a). The growth of pathogenic molds of *Aspergillus niger*, *Rhizopus solani*, *Botryodiplodia theobromae*, *Mucor mucedo*, and *Fusarium solani* was inhibited by the essential oil of *M. spicata* (Hussain et al., 2010b, Hussain et al., 2010a). *Penicillium ochrochloron*, *Cladosporium fulvum*, and *Cladosporium cladosporioides* were observed to be the most sensitive to *M. longifolia* extract (Džamić et al., 2010). Also, the essential oils of *M. piperita* showed promising growth inhibitory effects against *A. niger* in comparison with gentamycin as the standard antibiotic (Moghtader, 2013). High concentrations of oxygenated monoterpenes found in *M. piperita* essential oil have been attributed to its antifungal activities. The presence of menthone, menthol, carvone, and piperitenone in *Mentha* spp. essential oils were observed which could be attributed to their antifungal effects against several fungi (Hussain et al., 2010b, Hussain et al., 2010a). Moreover, it has been shown that the incorporation of *Mentha* spp. extracts with chitosan nanoparticles have enhanced their antifungal effect against mycelium growth (Abd El-Aziz et al., 2018).

*Mentha* spp. are considered important antiviral agents (Table 2). Varied phenolic components of *M. spicata* revealed antiviral activities (Mahady et al., 2005, Mckay and Blumberg, 2006). Yamasaki et al. (1998) depicted antiviral activity of aqueous extract of *M. piperita* against human immunodeficiency virus (HIV) (Yamasaki et al., 1998). In another study, the essential oil of *M. piperita* demonstrated antiviral attributes against Herpes simplex virus (Schuhmacher et al., 2003). In general, menthol, luteolin, rosmarinic acid, and phytol of *Mentha* spp. are pivotal antiviral agents.

### 3.5. Other activities

Bioactive components of *Mentha* spp., particularly essential oils are known to reveal insecticidal properties against several insects (Kumar et al., 2009). Essential oils of *M. spicata*, *M. pulegium*, and *M. rotundifolia* exhibited activities against *Rhyzoper thadominica* (Benayad et al., 2012). *M. arvensis* and *M. microphylla*oils showed insecticidal properties against *Sitophilus oryzae* (Lee et al., 2001, Mohamed and Abdelgaleil, 2008). In another investigation, the ethanol extract of *M. longifolia* revealed toxicity against *Sitophilus oryzae* (Kumar et al., 2009). Essential oils of *M. pulegium* and *M. longifolia* revealed insecticidal traits against *Sitophilus granaries* (Abdelli et al., 2016) and *Sitophilus zeamais* (Mikaili et al., 2013). *Tribolium castaneum* was completely inhibited using *M. arvensis* essential oil (Varma and Dubey, 2001). Pulegone and menthone of *M. rotundifolia* essential oil revealed promising toxicity against *T. castaneum* (Kasrati et al., 2015). The essential oil of *M. pulegium* showed pronounced toxicity towards *Mayetiola destruc-*


**Fig. 3** Some of *Mentha* based therapeutic products available in market.

*tor* (Lamiri et al., 2001), *Lycoriella ingénue* (Kunnumakkara et al., 2009), and *Callosobruchus maculates* (El Nagar et al., 2012). In another study, *M. pulegium* and *M. suaveolens* hydrosol depicted potential insecticidal traits against *Toxoptera aurantii* (Zekri et al., 2016).

*Mentha* sp. is known for exhibiting anti-spasmodic property too. *M. piperita* essential oil reduces calcium influx in the large intestine and jejunum, thereby relaxes the smooth muscles of the gastrointestinal tract (Sadraei et al., 2016). Likewise, *in vivo* study demonstrated that menthol of *M. piperita* essential oil blocked the calcium channel (Harris, 2016). *Mentha* sp. exhibited anti-emetic trait by inhibiting potassium depolarization in the ileum as well as showing its effect on histamine, serotonin, and cholinergic receptors in the gastrointestinal tract (Sagduyu, 2002). Besides, *M. piperita* and its derivatives are potent anti-headache agents too (Maliakal and Wanwimolruk, 2001).

Menthol, luteolin-7-o-rutinoside, and α-humulene of *Mentha* spp. are considered promising non-toxic anti-allergic agents in terms of suppressing the release of distinct inflammatory agents viz. histamine (Inoue et al., 2002), interleukin, prostaglandin E2, and leukotriene B4 (Juergens et al., 1998). In another report, monocyclic sesquiterpene and α-humulene of *Mentha* sp. revealed enhanced production of interleukin-8 (Satsu et al., 2004).

Currently, several *Mentha*-based therapeutic products are available in the market, as shown in Fig. 3. Despite the paramount medicinal attributes, *Mentha* spp. are also known to show adverse effects. The minor and major side effects include cyst-like formation in the white matter of the cerebellum, hypersensitivity, heartburn, bradycardia, dermatitis, muscle tremor, abdominal pain, perianal burning, reduced creatinine level in the blood, weight loss, atonia, and hepatocellular variations (Fig. 4).

## 4. *In silico* studies

The impact of antioxidant compounds on different human tissues has been investigated during drug discovery. Plant-derived essential oils encompass several biologically active constituents exhibiting potential antioxidant effects (Hussain et al., 2008, Gull et al., 2015, Abbas et al., 2017, Mushtaq et al., 2017, Qadir et al., 2019). However, the applications of conventional methods are time-consuming, expensive, and are unable to identify antagonism and/or synergistic effects of the bioactive components. Computational approaches that are more efficient in predicting drug effects have created huge attention. Effective drug development needs multi-objective optimization that can support developing novel drugs (Abbasi et al., 2018). Chemo-informatics techniques with chromatographic assays have been integrated to understand the antioxidant function of biologically active components derived from *Mentha* spp. The quantitative chemical component antioxidant activity relationship model was utilized to develop a new drug. Multi-objective feature selection algorithms dependent on an artificial neural network were implemented to generate new antioxidants. Novel synergistic effects of some non-phenolic components were identified via this technique too. Gas chromatography-mass spectrometry (GC–MS) was implied for analyzing the presence of varied volatile components in *Mentha* essential oil. Computational results were often found in close agreement with *in vitro* techniques. Computa-

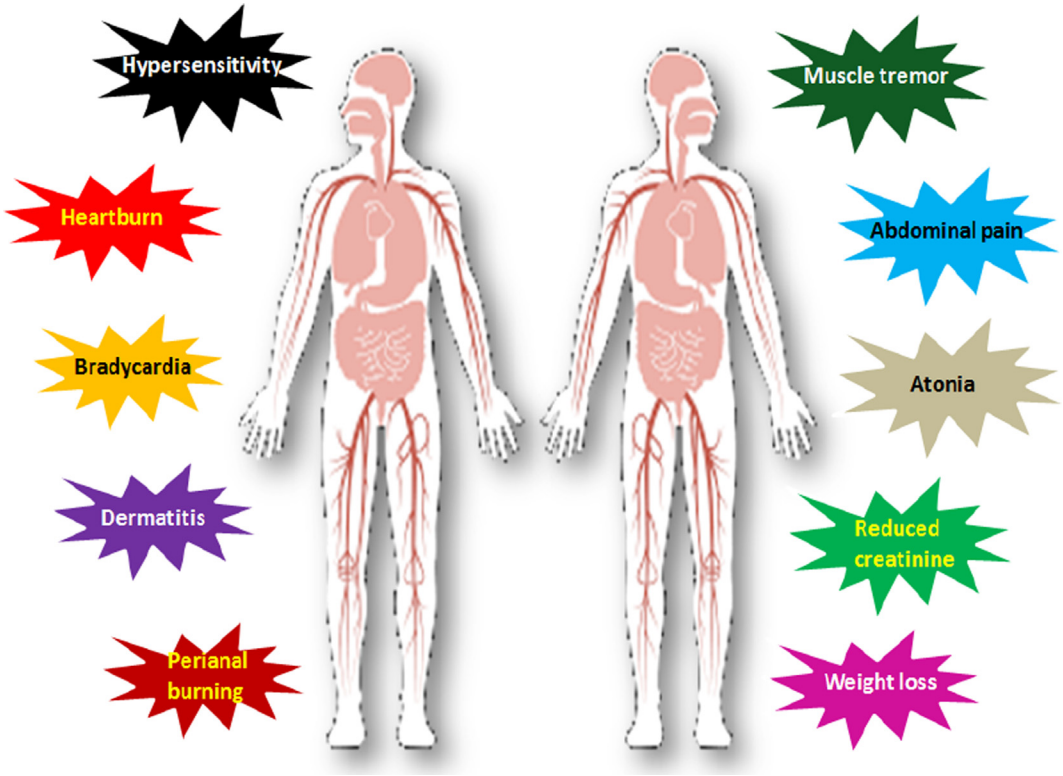


**Fig. 4** Minor and major side effects of *Mentha* spp.

tional chemistry and geometric optimization were used in another study (Gende et al., 2014). GC–MS was utilized to analyze the composition of *M. rotundifolia* and *M. arvensis* essential oils. Results indicated that the antimicrobial effects of these oils were mainly due to menthofuran, menthone, menthol, and piperitone oxide. The quantitative structure–activity relationship method was developed too for terpenoids which provided comprehensive data of the active components found in these terpenoids. The compound 3,7,11,15-tetramethyl-2-h exadecen-1-ol of *M. arvensis* showed a maximum binding affinity with dengue and poliovirus and suggested its pivotal role in the designing future drugs (Sen et al., 2019).

## 5. Conclusion and prospects

*Mentha* spp., its extracts, and essential oils are promising agents in terms of traditional medicine. The widespread effects of this plant have shown effective therapeutic options against several human diseases. Different components such as volatile oils, flavonoids, and tannins present in these plants have been attributed to their medicinal significance. Menthol, carvone, menthofuran, piperitenone, α-pinene, piperitone, linalool, menthone, and pulegone are a volatile bioactive component of *Mentha* spp. associated essential oils that exhibit anti-inflammatory and anticoagulant effects. However, there is desperate essentiality to explore the bioactivities of several unexplored *Mentha* spp. Also, it is imperative to determine the mechanisms of action of *Mentha* spp. associated bioactive components using *in vivo* studies for developing novel and ideal therapeutic drugs in the future.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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