

A Comprehensive Review on *Mentha piperita*: Botany, Phytochemistry, Pharmacology, Clinical Applications, and Safety

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Abstract

Mentha × piperita L. (peppermint) is one of the most widely used medicinal plants, valued both as a flavourant and for its therapeutic properties. This review consolidates current knowledge on the botany, phytochemistry, pharmacological activities, clinical efficacy, and safety of peppermint. A systematic literature search was performed using PubMed, Scopus, Web of Science, and Google Scholar (up to December 2025). More than 200 articles were screened, and 103 relevant studies were included. Peppermint essential oil is dominated by menthol (26–48%) and menthone (14–32%). Non-volatile polyphenols (flavonoids, phenolic acids) provide strong antioxidant activity. The oil exhibits broad-spectrum antimicrobial effects against multidrug-resistant bacteria, antifungal activity, and anti-inflammatory properties (inhibition of TNF- α , IL-6). Its spasmolytic action is mediated mainly via calcium-channel blockade. Enteric-coated peppermint oil is effective for irritable bowel syndrome (IBS) and functional dyspepsia. Toxicological data indicate a favourable safety profile at therapeutic doses.

Peppermint is an evidence-based herbal remedy with validated efficacy in functional gastrointestinal disorders. Further research should focus on standardised clinical trials and novel applications (anticancer, neuroprotection).

Keywords: *Mentha piperita*, peppermint, essential oil, menthol, irritable bowel syndrome, antimicrobial, antioxidant, phytochemistry

1. Introduction

The genus *Mentha* (family Lamiaceae) comprises approximately 25–30 species, many of which are used in traditional medicine, food, and cosmetics [1,2]. Among them, *Mentha × piperita* L. – commonly known as peppermint – is a sterile hybrid derived from *M.*

aquatica (water mint) and *M. spicata* (spearmint) [3,4]. It is native to Europe and the Middle East but is now cultivated worldwide, especially in the United States, India, China, and Mediterranean countries [5].

Historically, peppermint has been used for digestive complaints (flatulence, dyspepsia, colic), respiratory infections, fever, and oral inflammation [6,7]. Modern research has substantiated many of these uses, particularly in functional gastrointestinal disorders [8,9]. The plant's essential oil and polyphenolic extracts possess antimicrobial, antioxidant, anti-inflammatory, antispasmodic, and analgesic activities [10,11].

The present review provides a comprehensive update on the botany, phytochemistry, extraction methods, pharmacological properties, clinical evidence, and safety of *M. × piperita*. Special emphasis is placed on mechanistic insights and translational applications.



Fig. 01: Mentha Plant (Leaves)

2. Methodology

A literature search was conducted in PubMed, Scopus, Web of Science, and Google Scholar from inception to December 2025 using the keywords: “*Mentha piperita*”, “peppermint”, “essential oil”, “menthol”, “phytochemistry”, “antimicrobial”, “antioxidant”, “anti-inflammatory”, “irritable bowel syndrome”, “clinical trial”, and “safety”.

Table No. 01: Taxonomic classification of *Mentha piperita*

Rank	Name
Kingdom	Plantae
Clade	Angiosperms
Clade	Eudicots
Clade	Asterids
Order	Lamiales
Rank	Name
Family	Lamiaceae
Genus	<i>Mentha</i>
Species	<i>Mentha × piperita</i> L.

3. Botany and Taxonomy

3.1 Taxonomic classification

Peppermint is an allohexaploid ($2n = 6x = 72$) hybrid, which explains its sterility and the need for vegetative propagation (rhizomes) [3,12].

3.2 Morphological description

Peppermint is a perennial herb with creeping rhizomes. Stems are erect, 30–90 cm tall, glabrous to sparsely hairy. Leaves are opposite, petiolate, ovate-lanceolate, 3–8 cm long, with serrate margins and a characteristic pungent odour when crushed. Inflorescences are terminal spikes of small purple or violet flowers. Flowering occurs from mid-summer to early autumn [3,13].

3.3 Cultivation and geographical distribution

Peppermint thrives in moist, well-drained soils with partial shade to full sun. Major commercial producers are the USA (Oregon, Washington), India (Uttar Pradesh), China, France, and Italy [5,14]. Harvesting is typically done just before flowering, when the essential oil content is highest.

4. Phytochemistry

4.1 Essential oil composition

The essential oil yield from dried leaves is 0.5–4.0% (v/w), depending on genotype, agronomic conditions, and extraction method [15,16]. Gas chromatography-mass spectrometry (GC-MS) analyses consistently identify menthol and menthone as the major constituents. **Table 1** summarises representative compositions from different geographic origins.

Table No. 02 – Major compounds in peppermint essential oil from different regions

Origin	Menthol (%)	Menthone (%)	Menthofuran (%)	1,8-Cineole (%)	Reference
Turkey (fresh)	43.28	19.68	3.03	7.60	[17]
Iran (Kermanshah)	45.34	16.04	8.91	3.12	[18]
Mexico (Jalisco)	35.4	15.4	18.2	5.1	[19]
Morocco	46.32	21.05	6.47	4.22	[20]
Estonia	26.4–47.7	13.6–31.9	0.9–6.5	4.1–7.3	[21]
China (Guangxi)	38.5	22.3	9.1	4.6	[22]

Other volatile compounds include pulegone, isomenthone, limonene, β -caryophyllene, and germacrene D [23,24].

4.2 Non-volatile polyphenols

The methanolic extract contains high amounts of phenolic acids and flavonoids (Table 2). Rosmarinic acid is the dominant phenolic acid, followed by caffeic, chlorogenic, and ferulic acids [25,26]. Flavonoids include eriocitrin, luteolin-7-O-rutinoside, hesperidin, and quercetin derivatives [27,28].

Table No. 03– Major polyphenols in *M. × piperita* leaves (mg/g dry weight)

Compound	Concentration range	Reference
Rosmarinic acid	5.2 – 18.4	[26,29]
Eriocitrin	3.1 – 9.7	[27]
Luteolin-7-O-rutinoside	2.4 – 7.9	[28]
Hesperidin	1.9 – 6.2	[25]
Caffeic acid	0.5 – 2.1	[29]
Chlorogenic acid	0.3 – 1.4	[26]

4.3 Factors affecting chemical composition

The phytochemical profile is influenced by:

- **Genotype** (different chemotypes exist) [21]
- **Growth stage** (highest oil content at full flowering) [30]
- **Climate and soil** (temperature, water availability, nitrogen fertilization) [31]
- **Post-harvest processing** (drying temperature; air-drying preserves more menthol than oven-drying) [32]

5. Extraction Methods

5.1 Hydrodistillation (HD)

HD is the most common laboratory and industrial method. The yield is typically 0.2–0.5% (v/w). A comparison between HD and supercritical fluid extraction (SCFE) showed that HD gave higher yield (0.20% vs. 0.13%) but SCFE produced an oil with a more natural aroma [33,34].

5.2 Supercritical CO₂ extraction (SC-CO₂)

SC-CO₂ (pressure 100–300 bar, temperature 40–60°C) yields a terpene-rich extract without thermal degradation. The oil from SC-CO₂ has a higher proportion of oxygenated monoterpenes and lower hydrocarbon content than HD oil [33,35].

5.3 Solvent extraction (maceration, Soxhlet)

For polyphenol extraction, ethanol/water mixtures (50–70% ethanol) are optimal. Ultrasound-assisted extraction (UAE) and microwave-assisted extraction (MAE) increase yield and reduce time [36,37].

6. Pharmacological Activities

6.1 Antimicrobial activity

Peppermint essential oil (PEO) shows broad-spectrum activity against bacteria, fungi, and viruses.

6.1.1 Antibacterial effects

PEO is active against both Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*, *Listeria monocytogenes*) and Gram-negative (*Escherichia coli*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*) bacteria [20,38]. MIC values range from 0.03 to 2.5 $\mu\text{L/mL}$. Notably, PEO is effective against multidrug-resistant (MDR) clinical isolates, including MRSA and extended-spectrum β -lactamase (ESBL)-producing *E. coli* [20,39].

A synergistic effect with conventional antibiotics (vancomycin, gentamicin, ciprofloxacin) has been reported, with FICI values <0.5 [40].

6.1.2 Antifungal activity

PEO inhibits *Candida albicans* (MIC 0.5–2.0 $\mu\text{L/mL}$), *C. glabrata*, *Trichophyton rubrum*, and *Aspergillus niger* [41,42]. Combination with itraconazole or fluconazole produces synergistic fungicidal effects against azole-resistant *Candida* strains [43].

6.1.3 Antiviral activity

Limited studies show that peppermint extract reduces herpes simplex virus type 1 (HSV-1) plaque formation by 50–80% at non-cytotoxic concentrations [44].

6.2 Antioxidant activity

The antioxidant capacity of peppermint extracts has been measured by DPPH, ABTS, and FRAP assays. The IC_{50} for DPPH radical scavenging is 25–60 $\mu\text{g/mL}$, comparable to ascorbic acid [45,46]. This activity correlates strongly with total phenolic content ($R^2 = 0.91\text{--}0.96$) [29].

The main contributors are rosmarinic acid, eriocitrin, and luteolin derivatives [47]. In silico docking studies suggest that these compounds activate Nrf2 and inhibit Keap1 [48].

6.3 Anti-inflammatory activity

In vitro, PEO (0.01–0.1% v/v) reduces lipopolysaccharide (LPS)-induced TNF- α and IL-6 production in RAW 264.7 macrophages by 40–70% [49,50]. In vivo, carrageenan-induced rat paw oedema is significantly reduced by oral PEO (50–200 mg/kg) [51,52]. The effect is comparable to indomethacin (10 mg/kg). The mechanism involves inhibition of NF- κB translocation and downregulation of COX-2 and iNOS expression [53].

6.4 Antispasmodic and gastrointestinal effects

PEO and menthol relax intestinal smooth muscle via:

- **Voltage-dependent calcium channel blockade** (L-type) [54]
- **Activation of TRPM8 channels** (causing sensory desensitisation) [55]

- **Inhibition of muscarinic receptors** (non-competitive) [56]

In isolated rabbit jejunum, PEO (10–100 µg/mL) reduces acetylcholine-induced contractions by 80–95% [57]. This spasmolytic action underlies its efficacy in IBS.

6.5 Analgesic activity

The aqueous leaf extract (100–400 mg/kg, p.o.) significantly reduces acetic acid-induced writhing in mice (by 45–70%) and increases latency in the hot-plate test, indicating both peripheral and central analgesic effects [58,59]. Naloxone partially reverses the effect, suggesting opioid pathway involvement [59].

6.6 Neuropharmacological effects

Inhalation of PEO (1–5% v/v) improves attention, memory, and mood in healthy volunteers, as measured by the Cognitive Drug Research (CDR) battery [60,61]. The effect is attributed to menthol-induced stimulation of the olfactory-limbic system and modulation of GABAergic transmission [62].

6.7 Anticancer activity

PEO (0.01–0.1% v/v) induces dose-dependent cytotoxicity in human laryngeal carcinoma (HNO210) cells ($IC_{50} = 0.045\%$ v/v) and basal cell carcinoma cancer stem cells (BCC-CSCs) [63,64]. The mechanism includes apoptosis (caspase-3 activation), ROS generation, and cell cycle arrest at G2/M [65]. Importantly, PEO shows low toxicity to normal human fibroblasts ($IC_{50} > 0.5\%$ v/v) [63].

7. Mechanism of Action – Integrated Summary

Figure 1 (conceptual diagram, not reproduced here) summarises the main mechanisms:

- **Gut:** Calcium channel blockade → smooth muscle relaxation → reduced abdominal pain and spasms.
 - **Immune cells:** NF-κB inhibition → decreased TNF-α, IL-6, COX-2 → anti-inflammation.
 - **Nervous system:** TRPM8 activation → analgesic and cooling sensation; GABA modulation → cognitive enhancement.
 - **Microbes:** Membrane disruption, efflux pump inhibition, and biofilm disruption.
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8. Clinical Applications

8.1 Irritable Bowel Syndrome (IBS)

A 2022 meta-analysis of 12 RCTs ($n = 1,658$) found that enteric-coated peppermint oil capsules (180–360 mg/day for 4–8 weeks) significantly improved global IBS symptoms ($RR = 2.39$, 95% CI: 1.72–3.32) and reduced abdominal pain ($SMD = -0.68$, 95% CI: -0.94 to -0.42) compared to placebo [66,67]. The number needed to treat (NNT) is 3 [68].

In paediatric IBS (8–17 years), a recent double-blind RCT showed no significant difference between peppermint oil and placebo for the primary endpoint ($\geq 30\%$ pain reduction at 8 weeks: 48% vs. 45%, $p = 0.44$) [69]. This suggests age-dependent or formulation-dependent effects.

8.2 Functional dyspepsia

Peppermint oil (90 mg four times daily) accelerates gastric emptying (by 30–40%) and reduces postprandial distress symptoms compared to placebo [70,71]. A combination of peppermint oil and caraway oil (enteric-coated) is approved in Germany for functional dyspepsia [72].

8.3 Postoperative nausea and vomiting (PONV)

Aromatherapy with peppermint oil (2–3 drops on a gauze) reduces PONV severity at 5 minutes after treatment, but a Cochrane meta-analysis (4 RCTs, $n = 584$) found no significant difference in nausea scores compared to placebo (SMD = -0.18 , 95% CI: -0.86 to 0.49) [73]. However, patient satisfaction was higher with peppermint oil [74].

8.4 Endoscopic spasmolysis

Intraluminal application of peppermint oil solution (0.1–0.8%) during colonoscopy or upper endoscopy significantly reduces colonic spasm and improves mucosal visualisation, without serious adverse events [75,76].

9. Pharmacokinetics

After oral administration of enteric-coated capsules, menthol is absorbed in the small intestine ($T_{max} = 1\text{--}2$ h) and is rapidly glucuronidated in the liver. The main metabolite, menthol glucuronide, undergoes enterohepatic recirculation. The elimination half-life is 2–4 hours [77,78].

Peppermint oil inhibits CYP3A4 in vitro ($IC_{50} \approx 50 \mu\text{g/mL}$), which could theoretically increase the bioavailability of drugs metabolised by this enzyme (e.g., nifedipine, midazolam) [79]. Clinical significance is likely low with enteric-coated formulations at recommended doses.

10. Safety and Toxicology

10.1 Acute and subchronic toxicity

The oral LD_{50} of PEO in rats is >5 g/kg, indicating low acute toxicity [80]. In a 90-day rat study, no adverse effects were observed at 100 mg/kg/day, but at 400 mg/kg/day, cerebellar cystic lesions occurred (attributed to pulegone content) [81]. Human therapeutic doses are typically ≤ 180 mg/day, which is far below the no-observed-adverse-effect level (NOAEL).

10.2 Adverse events

In clinical trials, adverse events are mild and transient: heartburn (5–10%), perianal burning (2–5%), nausea (3%), and allergic reactions ($<1\%$) [66,82]. Enteric-coated formulations significantly reduce gastric irritation.

10.3 Contraindications and precautions

- **Gastroesophageal reflux disease (GERD):** May relax the lower oesophageal sphincter → worsening reflux [83].
- **Gallstones:** Peppermint oil stimulates bile flow; caution in biliary obstruction.
- **Pregnancy and lactation:** Insufficient data; avoid high doses.
- **Children under 4 years:** Risk of laryngospasm from menthol inhalation [84].

10.4 Regulatory status

- **EMA:** Peppermint oil is approved as a traditional herbal medicinal product for digestive symptoms (well-established use) [85].
- **FDA:** GRAS status for food use; marketed as a dietary supplement.
- **ESCOP:** Monographs for IBS and dyspepsia [86].

11. Discussion and Future Perspectives

The present review confirms that *Mentha × piperita* is a well-characterised medicinal plant with robust evidence for its traditional uses. The major strengths are the strong clinical data for IBS and the favourable safety profile. However, several gaps remain:

1. **Standardisation:** Essential oil composition varies widely between products. Pharmacopoeial standards (e.g., Ph. Eur., USP) require 30–55% menthol and 14–32% menthone, but many commercial products do not meet these criteria [87].
2. **Long-term safety:** No trials beyond 12 weeks have been published.
3. **Drug interactions:** In vivo studies on CYP3A4 inhibition are lacking.
4. **Novel applications:** Preliminary anticancer and neurocognitive effects require confirmatory RCTs.
5. **Formulation development:** Nanoparticle encapsulation could improve stability and targeted delivery [88].

Future research should prioritise multicentre, double-blind, placebo-controlled trials in functional dyspepsia (using Rome IV criteria), paediatric IBS, and COVID-19-related anosmia (menthol is a TRPM8 agonist that may promote olfactory recovery). Mechanistic studies using organoids and CRISPR-edited cell lines could elucidate the molecular targets of individual constituents.

12. Conclusions

Mentha × piperita L. is a valuable medicinal herb with a rich phytochemical profile dominated by menthol and menthone. Its essential oil and extracts exhibit scientifically validated antimicrobial, antioxidant, anti-inflammatory, antispasmodic, and analgesic activities. Clinical evidence strongly supports the use of enteric-coated peppermint oil for relieving symptoms of irritable bowel syndrome and functional dyspepsia, with a good safety profile. The plant represents a successful model of translating ethnopharmacology into evidence-based phytotherapy. Ongoing research into its anticancer, neurocognitive, and antiviral potential promises to expand its therapeutic applications.

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