

Ethnobotanical, Ethnopharmacological, and Phytochemical Studies of *Myrtus communis* Linn: A Popular Herb in Unani System of Medicine

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Abstract

Myrtus communis L (Myrtaceae) is one of the popular drugs being used in the Unani system of phytomedicine since ancient Greece period. From time immemorial, different parts of this plant and essential oil have been used for a variety of purposes such as cosmetics (hair fall control), flavoring of food and drinks as well as extensive therapeutic purposes. Ethnobotanical information revealed that *M communis* L has been a folkloric reputed for the treatment of several diseases like gastric ulcer, diarrhea, dysentery, cancer, rheumatism, hemorrhage, deep sinuses, leucorrhoea, hemorrhoid, inflammation, dyspepsia, anxiety, insomnia, diabetes, hypertension, pulmonary disorders, and skin diseases. Moreover, ethnopharmacological studies revealed that the plant is endowed with extensive pharmacological activities, including antimicrobial, antidiarrheal, antidiabetic, antispasmodic, vasodilator, antiulcer, antioxidant, anticancer, anxiolytic, sedative-hypnotic, and anti-inflammatory activities, among others. The plant has been known to contain phenolic acids, tannins, flavonoids, glycosides, and terpenes. The myrtle oil was also found to be rich in a variety of bioactive monoterpenes and sesquiterpenes with their derivatives. Most of these studies validate the aforementioned traditional claims of this medicinal plant. Further studies are needed to unravel other pharmacological activities of this plant in the long run.

Keywords

Myrtus communis L, ethnobotanical uses, ethnopharmacological studies, phytochemical studies

Received March 15, 2017. Accepted for publication June 5, 2017.

Botanical Source and Characteristics

Family Myrtaceae includes approximately 100 genera and 3000 species growing in temperate, tropical, and subtropical regions of the world. *Myrtus* is a small genus belonging to this family¹ (Table 1). The genus *Myrtus* L comprises 2 species, *Myrtus communis* L (common myrtle) growing wild all around the Mediterranean basin and *Myrtus nivellei* Batt (Saharan myrtle) found in central Sahara. It is an aromatic evergreen perennial shrub² (Figure 1).

Methods

Data were collected from several legitimate data bases and services such as PubMed, Medline, Scopus, and other database sources like Google Scholar using key terms “*Myrtus communis* L”, “ethnobotanical uses”, “ethnopharmacological studies”, “phytochemical studies” in each database. Relevant and related data were filtered properly if it was found appropriate to the topic of interest. Time frame was also adjusted to obtain up-to-date information

regarding *M communis* L and its role in Unani system of medicine, ethnobotanical, ethnopharmacological, and phytochemical aspects of it by emphasizing on original researches conducted and published from 2010 to 2017. Excluding the background information, around 73 references were included in this scientific review. The study was conducted from September 2016 to January 2017.

Ethnobotanical Uses

The common myrtle is one of the most important drugs being used in Unani system of medicine, which originated in Greece

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Table 1. Ethnobotanical Sources and Characteristics of *Myrtus communis* Linn.

Botanical Sources and Other Characteristics	General Description About This Plant	References
Botanical origin	Family: Myrtaceae Genus: -Myrtus Species name: <i>Myrtus communis</i> Linn (from Greece) Vernacular names (in Ethiopia): Ades (Amharic, Guragegna Tigregna), Addisaa, Coddoo (Affan Oromo); Wobattaa (Welaitigna)	1-4
Geographical origin	Only species of the genus found in the Northern Hemisphere, Southern Europe, North Africa, and West Asia Widespread in the Mediterranean region and others areas It is highly drought tolerant and needs only little to moderate water. It can grow in damp places, shades as well as full sun up to 800 m altitudes	1, 5, 6
Morphological characteristics of organized parts	Stem: Upright, 2.4-3 m tall, branched, thickly covered with evergreen leaves Leaves arrangement: Opposite, paired or whorled Leaves margin and size: Ovate to lanceolate with stiff structure, entire margined, acuminate, 2.5-3.8 cm long Flowers: Slender peduncles, medium size (2 cm diameter), stiff, has anthers Berries: Pea sized, orbicular	1, 5, 6
Organoleptic properties	Leaves: Dark green, glossy, glabrous, coriaceous Flowers: White, yellow anthers, fragrant smelling Berries: Blue black Fruits: Bitter when unripe, sweet when ripe Essential oil: Myrtle oil (very fragrant aromatic oil of this plant)	1, 2, 5, 6

and expanded by Arabs into an elaborate medical science based on the framework of the teaching of Hippocrates and Galen. It is a well-known shrub for its therapeutic, cosmetic, and food uses (Table 2). The name and use of *M communis* have been associated with myth and rituals in many societies.^{6,7}

Ethnopharmacological Studies

Extensive ethnopharmacological studies demonstrated that *M communis* L is endowed with promising pharmacological

**Figure 1.** *Myrtus communis* Linn.

activities, including antimicrobial, anticancer, antidiabetic, antiulcer, antidiarrheal, and anti-inflammatory activities.

Antimicrobial Effects

The leaves of *M communis* L revealed promising antimicrobial activities in the aqueous and ethanolic crude extracts,²⁵ fractionated constituents,^{26,27} a polar glycoside fraction, gallomyrtucommulone, isolated from the leaves,²⁸ in the biosynthesized silver nanoparticles.²⁹ The alcoholic extract of *M communis* was also found to be effective against selected extended-spectrum β -lactamase producing *Escherichia coli* isolates.³⁰ Also, the myrtle oil showed potent antimicrobial activities against *Helicobacter pylori*³¹ and clinical strains of *Mycobacterium tuberculosis*.³² It was further supported by the fact that α -pinene, 1,8 cineole, β -pinene, and limonene were found to be the highest contributors in antimicrobial properties of myrtle oil.³³ In situ results showed that the microbial population, except for *Pseudomonas* spp, decreased significantly in ground meat with added 5% of freeze-dried myrtle extract. The finding demonstrated the effectiveness of myrtle extract to control the proliferation of meat spoilage bacteria.³⁴ In a comparative study, patients treated with both *M communis* L and metronidazole base did not show any relapse; however, from those who were treated with metronidazole alone, 30% of them experienced relapsed during the follow-up period. From this it can be concluded that vaginal gel containing both the extract and the base is a more effective antibacterial than the base alone.³⁵ Besides, the isolated constituent, myrtacine, showed promising antibacterial activity against *Propionibacterium acnes* either alone or in combination with antibiotics and can be used for acne vulgaris treatment.³⁶

The ethnopharmacological studies of common myrtle extend to other microbial agents such as fungi and protozoa. All of the crude extracts of *M communis* have showed promising antifungal activity on *Candida albicans*.³⁷ What is more, myrtle oil was effective against all isolates of *Aspergillus* species.^{38,39} Another study revealed that the oil was also more active against *Cryptococcus neoformans* (yeast) and *Epidermophyton floccosum*, *Microsporum canis*, *Trichophyton rubrum* (dermatophytes).¹¹ Moreover, the oil inhibited growth of *Rhizoctonia solani* by 60% at the dose of 1600 ppm *in vitro*. Apart

Table 2. Ethnobotanical Uses of *Myrtus communis* Linn.

Parts Used	Description of Preparation	Application	Country (Used)	References
Leaves alone	Leaves have been used as an input for preparing liqueur called Mirto	Beverage	Italy	1, 4
	One gram of tea mixed with leaves has been drunk on daily basis	Stress and anxiety	Turkey	8
	Aqueous maceration of leaves can be taken after filtration and concentration	Depression, polymenorrhea, and wound	Iran	9
	The decoction of the leaf powder	Hypertension, eczema and other skin diseases	Algeria	10
	Not specified	Respiratory disorders and hemorrhoids		11
	Leaves are boiled and the stock is drunk (Turkey)	Abdominal pain and diarrhea	Pakistan, India, Turkey, Iran, Ethiopia	8, 11-14
	Juice of leaf is taken orally in the morning (Ethiopia), others unspecified			
	Rural women mix the leaf extract with raw butter and apply it to their hair	Cosmetics (hair fall control)	Ethiopia	4, 15
	Bathing with crushed fresh leaves	Dandruff	Ethiopia	14
	Dried leaf powder mixed with butter is applied topically	Scabies	Ethiopia	16
	The leaves are crushed, boiled with water, and are then drunk	Headache	Ethiopia	17
	The dried aqueous extract (leaf powder)	Sinus infections	China, France	18, 19
	Dried leaf powder	Tinea capitis ("buha ras") and as antipyretic and sedative agent	Ethiopia	20
Leaves, berries and myrtle oil	Depending on the nature of the disease states and parts of the plants used (remains unspecified)	Diarrhea, dysentery, gastric ulcer, vomiting, rheumatism, hemorrhages, deep sinuses, leucorrhea	India, Pakistan, Turkey, Ethiopia, Iran	6, 21, 22
		Hemorrhoid, inflammation, pulmonary and skin diseases		
		An astringent, antiseptic, disinfectant and hypoglycemic agent		
	The aqueous juice has also been used for the preparation of food and wines	Food and drinks	Europe (Italy)	6, 21
Leaves and fruits	Myrtle oil	Adjunct for the treatment of insomnia	Ethiopia	23
	Unspecified	Vulnerary, cough suppressant, and digestant effects	India, Pakistan	24

from this, both essential oil and methanolic extract of *M. communis* leaf showed promising antileishmanial effect on *Leishmania tropica* in an *in vitro* model.⁴⁰ Myrtle oil also revealed antimalarial activity against *Plasmodium falciparum* *in vitro*.⁴¹

Anticancer Properties

Alwan et al⁴² showed that ethanolic extract of *M. communis* leaves inhibited aryl hydrocarbon hydroxylase activity and 3H-benzo(a)pyrene binding to microsomal protein of rat liver, effectively. In the same study, no inhibitory effect was observed with aqueous extract.⁴² By the same authors of *in vitro* study, *M. communis* showed significant inhibitory effect when *n*-butanol extract was used. The *n*-butanol extract was more effective than chloroform and petroleum ether extract. However, aqueous extract showed any inhibitory effects on both aryl hydrocarbon hydroxylase activity and 3H-benzo(a)pyrene binding to DNA *in vitro* unlike the *in vivo* study.⁴³ Myrtle oil also showed significant inhibition in cancer cell lines. At 200 µg/mL concentration, the inhibition was 67% and

95.2% for prostate and breast cancer cell lines, respectively. Probably the most exciting and hopeful result of this finding is that the inhibition value of essential oil of *M. communis* on 3T3 fibroblast cell line is 3.7% and 6.5% for the dosages of 100 µg/mL and 200 µg/mL, respectively.⁴⁴ These results are so important and exciting since all of the aforementioned findings look like that sound of footsteps of the pioneer of an ideal and selective anticancer drug in the near future.⁴⁵

The cytotoxicity of myrtucommulone-A (MC-A) and its potential to induce apoptosis in cancer cells was demonstrated. MC-A showed an antiproliferative and strong inhibitor of migration of cancer cell. About 84 apoptotic pathway genes were screened to evaluate the effect of it on cancer cells. MC-A also mediated upregulation of apoptotic genes, including Fas, FasL, Gadd45a, Tnf, Tnfsf12, Trp53, and caspases through induction of both intrinsic and extrinsic apoptotic pathways.^{46,47} It can also induce apoptosis via activation of caspases (3, 8, and 9), cleavage of poly(ADP-ribose) polymerase (PARP), release of nucleosomes, and fragmentation of DNA. Moreover, it caused loss of the mitochondrial membrane

potential in MM6 cells and brought release of cytochrome *c* from mitochondria.⁴⁸ The activity of the myrtle oil was evaluated against spontaneous and t-BOOH (*t*-butyl hydroperoxide)-induced mutagenesis in *E coli* oxyR mutant IC202, a bacterial strain deficient in removing reactive oxygen species. When the oxidative mutagen was used, the oil expressed higher reduction of mutagenesis in a concentration-dependent manner.⁴⁹ Antimutagenic activity of myricetin-3-O-galactoside and myricetin-3-O-rhamnoside, isolated from the leaves of *M communis* L was assessed using the SOS chromotest and the Comet assay and they were found effective.⁵⁰

Antidiabetic Activity

The common myrtle demonstrated significant antihyperglycemic activity on its crude extracts against streptozotocin-induced diabetic mice.⁵¹ By the same token, the aqueous and methanolic extracts of *M communis* have significantly lowered blood glucose level in alloxan-induced diabetic mice. The aqueous extract has shown higher activity at relatively lower dose (500 mg/kg) than the methanolic extract at 1000 mg/kg dose. This indicates the aqueous extract is endowed with better efficacy compared with the methanolic extract as antidiabetic agent.⁵² A year later, another contradictory result, regarding aqueous and hydroalcoholic extracts, was also reported. Ethanol extract of the leaves (2 g/kg) had a better hypoglycemic effect in diabetic rats compared with the aqueous extract ($P < .05$). Oral administration of the ethanol extract (2 g/kg) had shown an additive effect on the hypoglycemic action of glibenclamide in rats.⁵³ Furthermore, data suggested that myrtle oil treatment reduces intestinal absorption of glucose, possibly via inhibiting α -glycosidase enzyme on alloxan-induced diabetic rabbits and on orally glucose loaded group.⁵⁴

Antilulcer Activity

Both methanol and aqueous crude extracts of the dried berries of myrtle revealed antiulcer activities against ethanol, indomethacin and pyloric ligation induced models in Wistar rats.⁵⁵ (–)-Myrtenol, isolated from the leaves of *M communis* L showed a significant reduction in the severity of ethanol-induced gastric lesions at all tested doses. The results provided an evidence for the gastroprotective effect of (–)-myrtenol that could be related to GABA_A-receptor activation and antioxidant activity.⁵⁶ A double-blind randomized controlled clinical trial revealed that *M communis* L freeze-dried aqueous extract showed comparable effect with omeprazole in gastrointestinal reflux disease.⁵⁷

Antidiarrheal Activity

In vitro studies on isolated tissue preparations demonstrated that hydroalcoholic (70% methanol) extract of *M communis* L possesses spasmolytic, bronchodilator, and vasodilator activities possibly due to blockade of voltage-dependent calcium channels and anticholinergic activity.⁵⁸ Furthermore, the

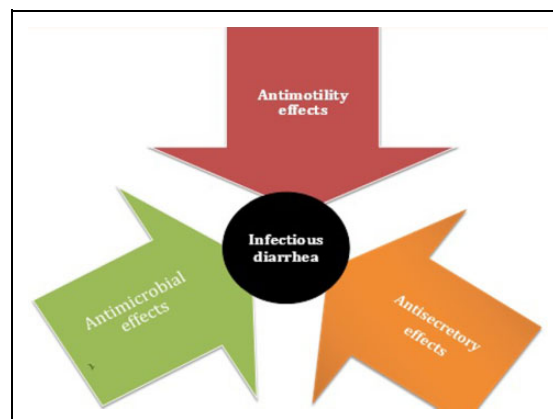


Figure 2. *Myrtus communis* L. as a candidate for the treatment of infectious diarrhea.

essential oil of the leaves of *M communis* possesses significant antidiarrheal and antispasmodic activity both *in vivo* and *in vitro*. The antidiarrheal activity produced by the oil was proved to be highly potent inhibitor of gastrointestinal motility and fluid secretion in mice and rat model of diarrhea, respectively. The oil also possesses antispasmodic activity in *ex vivo* model using isolated guinea pig ileum.⁵⁹ Similarly, an *in vivo* study found that myrtle berry seed aqueous extract administration induced a significant dose-dependent protection against diarrhea and intestinal fluid accumulation. The study revealed that myrtle berry seed aqueous extract had a potent protective effect against castor oil-induced acute diarrhea due in part to its antioxidant and antimicrobial properties.⁶⁰ Sisay et al⁶¹ also investigated the antidiarrheal activity of 80% methanol extract and solvent fraction of the leaves of *M communis* L in mice model of diarrhea *in vivo*. Therefore, it can be concluded that *M communis* L can be used for the treatment of diarrheas of diverse etiologies, including those with infectious component (Figure 2).

Antinflammatory Activity

The 80% ethanol extract of *M communis* L leaf possessed anti-inflammatory activity on rats by measuring the suppression of carrageenan-induced paw edema using aspirin as the standard drug.⁶² It is further supported by isolated constituents (myrtucommulone, semimyrtucommulone, and nonprenylated acylphloroglucinols) that have also shown a promising anti-inflammatory activities.⁶³ MC-A isolated from myrtle showed the same pharmacological activity for inhibition of inflammation compared with the synthetic counterpart.⁴⁷ Treatment with *M communis* L ethanol extract reversed all the biochemical indices as well as histopathological alterations induced by acetic acid with the protective effects being similar to that of sulfasalazine treatment. The study showed that *M communis* L extract could alleviate colitis in rats and can be considered an alternative therapeutic approach for management of inflammatory bowel diseases.²¹ The anti-inflammatory potential of myrtle oil was also evaluated using an *in vitro* model of

Table 3. *Myrtus communis* L With Potential Antioxidant Activities.

Extracts	Methods Used	Result	Reference
Fruit crude extracts	1. DPPH and β -carotene-linoleic acid assays 2. Gas chromatography for fatty acid assay	High free radical scavenging activity in methanolic fruit extract	64
Chloroform, ethyl acetate, methanol, and aqueous extracts	1. DPPH assay 2. β -carotene bleaching assay 3. Ferric thiocyanate method 4. Thiobarbituric acid method	1. Ethyl acetate extract has the highest free radical scavenging power and reducing capability for DPPH and hydroxyl radical 2. Methanol extract exhibited higher chelating activity than ethyl acetate 3. Chloroform extract was strong inhibitor of lipid peroxidation in all assays	65
Leaves and berries Ethanol, methanol, water and ethyl acetate extracts of	1. Folin-Ciocalteu assay (total phenolic measurements) 2. Colorimetric method (total flavonoid measurements) 3. ABTS ⁺	1. Methanol and water extracts have significant antioxidant activities 2. Methanol > water > ethanol > ethyl acetate in both extracts (leaf and fruit) 3. Generally, the leaves have higher antioxidant activity than berries in phenolic and flavonoid content as well as activity	66
Berry extracts	1. HPLC coupled with electrospray mass spectrometry 2. Ultraviolet/visible detection 3. TEAC assay	Free radical scavenging activity. Antioxidant activity was preserved in 3 months	67
Myrtle oil	DPPH assay	The oil has moderate free radical scavenging activity	49
MBSAE extract	In isolated rat esophagus ER-induced damage	Potential protective and antioxidant effect	60

Abbreviations: DPPH, 2,2-diphenyl-1-picrylhydrazyl; ABTS⁺, 2,2'-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt; TEAC, trolox equivalent antioxidant capacity; ER, esophageal reflux; HPLC, high-performance liquid chromatography; MBSAE, myrtle berries seed aqueous extract.

lipopolysaccharide-stimulated macrophages. Assessment of cell viability was made through the MTT assay. The oil was able to significantly inhibit NO production, without affecting cell viability.¹¹

Antioxidant Activity

The antioxidant activity of various extracts of *M communis* L was investigated in extensive *in vitro* experimental methods as shown in Table 3.

Sedative-Hypnotic Activity

The essential oil of common myrtle revealed sedative-hypnotics.⁶⁸ Two years later, another controversial finding revealed that there was no induction of hypnosis. However, the myrtle oil prolonged pentobarbital-induced sleeping time and there was also half (50%) negative response on the chimney and traction test in a dose-dependent manner. The myrtle oil did not produce a hypnotic effect; however, it potentiated a hypnotic effect with significant central nervous system depressant activity.²³

Anxiolytic and Narcotic Analgesic Activity

Anxiolytic effect of 80% ethanolic extract of the leaves was investigated in rodent model. The data showed muscle relaxant

and anxiolytic effects of the extract with negligible anticonvulsant activity. The anxiolytic, myorelaxant, and hypnotic effects without effect on seizure threshold are in line with the effect of an $\alpha 2$ GABA receptor agonist.⁶⁹ The anxiolytic potential of myrtle oil was also investigated in rodent model.⁷⁰ These data were further supported by another finding in which a monoterpene alcohol, (–)myrtenol isolated from oil of myrtle presented anxiolytic-like activity that can be mediated by GABAergic transmission.⁷¹ Besides, its different crude extracts and isolated constituents showed narcotic analgesic properties.⁷²

Anthelmintic Activity

Findings of the study demonstrated that the myrtle oil at the concentration of 100 μ L/mL after 5 minutes of exposure killed 100% protoscoleces. Similarly, the mean mortality rate of protoscoleces after 10 minutes of exposure to concentration of 50 μ L/mL was 100%. The results showed potent scolicidal activity of *M communis* with no significant toxicity, which might be used as a natural scolicidal agent in hydatid cyst surgery.¹⁸

Antilipidemics and Antithrombotic Activity

The aqueous extract of *M communis* L leaves revealed antilipidemic and antithrombotic activities.⁷³

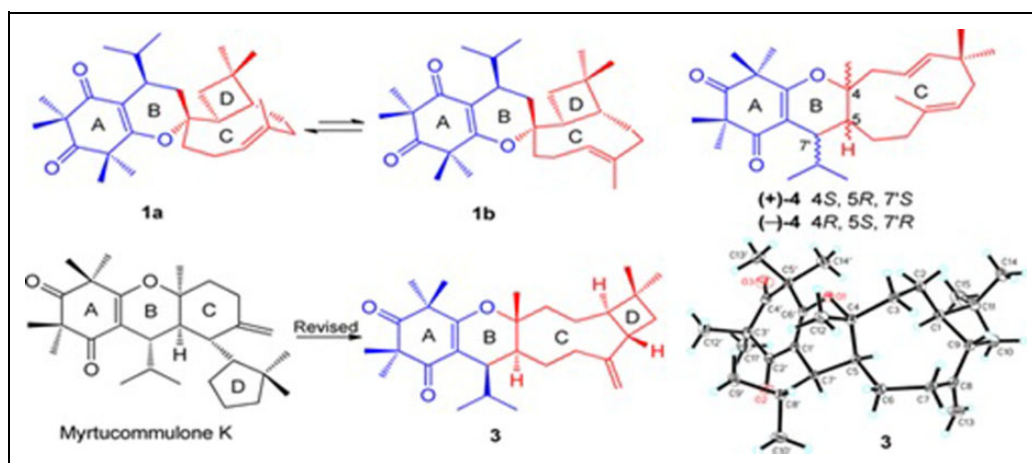


Figure 3. Five sesquiterpene-based meroterpenoids with 3 kinds of new skeletons [1, 2, 3, (+)-4, and (–)-4].

Pesticides

Myrtle oil has insect repellency effect, even with lower (10%) concentration.⁷⁴ Another finding suggested that the myrtle oil might have potential to be used as natural herbicides as well as fungicides.⁷⁵

Phytochemical Studies

The leaves of *M communis* were investigated to contain small amounts of phenolic acids (caffeic, ellagic, and gallic acids), and a flavonoid, quercetin derivatives (quercetin 3-O-galactoside and quercetin 3-O-rhamnoside). On the other hand, flavonoids such as galloyl derivatives of catechin and gallocatechin as well as myricetin derivatives are present in large amounts.⁷⁶ Similarly, 4 hydrolyzable tannins, 2 related polyphenolic compounds, and 4 myricetin glycosides were isolated from the leaves of *M communis* in another study.⁷⁷ The major terpenoids and their derivatives found in the essential oils of *M communis* L leaves were α -pinene, α -terpineol, linalool, 1,8-cineole, geranyl butyrate, geraniol, caryophyllene oxide, and neryl acetate.⁷⁸ Five sesquiterpene-based meroterpenoids with 3 kinds of new skeletons [1, 2, 3, (+)-4, and (–)-4] were isolated from the leaves of *M communis*⁷⁹ (Figure 3). It was further supported by both qualitative and quantitative studies. The chemical composition of 2 myrtle oil samples, taken from different localities, was investigated by gas chromatography–flame ionization detector, gas chromatography–mass spectrometry, and C^{13} nuclear magnetic resonance spectroscopy. Monoterpene derivatives were found to be the main compounds: α -pinene (50.8% and 33.6%), 1,8-cineole (21.9% and 13.3%), linalool (2.7% and 14.8%), and linalyl acetate (0.5% and 9.5%).¹¹ Chemical analysis of ethyl acetate extract revealed the presence of myrecitin-3-O- α -rhamnoside. Ethyl acetate extract was found to have the highest total phenolic and total flavonoid contents with the values of 435.37 mg gallic acid equivalents/g dried weight and 130.75 mg quercetin equivalent/g dried weight, respectively.¹¹

Conclusion

The overall ethnobotanical, ethnopharmacological, and phytochemical studies of *M communis* L were well emphasized in this review article. Since time immemorial, this medicinal plant has played a significant role in the area of medicine and pharmacy as well as food and cosmetics applications. Majority of the folkloric reputes were validated by experimental studies, including antimicrobial, antidiarrheal, anticancer, antioxidant, antiulcer anti-inflammatory, and antidiabetic activities. Regarding the phytochemical analysis, sesquiterpene-based meroterpenoids were currently investigated in this plant and have shown to be associated with a multitude of biological activities.

Author Contributions

MS collected the literature, reviewed the literature critically, prepared the manuscript for publication, and read and approved the final version of the manuscript. TG edited the literature review and read and approved the final version of the manuscript.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

This article is a review study; therefore, no ethical approval is needed.

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