Review Article

Clinical Applications of *Myrtus communis* L. in Traditional and Modern Medicine: A Scoping Review

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ABSTRACT

Background: *Myrtus communis* L. (MC), or common myrtle, is a member of the Myrtaceae family and has been widely used in herbal medicine, including Persian medicine (PM), the Unani system, and modern medical research.

Objectives: This review aimed to explore MC berries, leaves, seeds, and essential oils' therapeutic and biochemical properties in PM and contemporary scientific studies.

Methods: Modern research was sourced from databases, such as ScienceDirect, Scopus, Embase, and PubMed. PM sources included key traditional textbooks, such as 'the canon of medicine,' 'Makhzan al-Adviyah,' and others. The search was based on the keywords *Myrtus communis* or myrtle in new sources and Mord or Habb-ul-Aas in traditional medicine sources.

Results: In PM, MC has been used for neurological (headaches, epilepsy), ophthalmic (conjunctivitis), head and neck (toothache, earache, gingivitis), respiratory (cough, tuberculosis), gastrointestinal reflux disease (GERD, diarrhea), urogenital (bladder stones, dysuria), and skin conditions (warts, burns, acne). Modern studies have confirmed its efficacy in treating urogenital infections (vaginitis, human papillomavirus [HPV]), skin issues (acne and warts), GERD, and head and neck conditions (aphthous stomatitis). In vivo and in vitro studies have shown antiparasitic, cardiovascular, antibacterial, antiviral, anticancer, and neuroprotective effects (Alzheimer's and insomnia).

Conclusion: Modern research has validated many traditional uses of MC; however, further studies are required to confirm its medical benefits comprehensively.

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Introduction

Myrtus communis L. (MC), commonly known as myrtle, belongs to the Myrtaceae family. It grows spontaneously as an evergreen bush or small tree, native to the coastal areas of the Mediterranean regions, North Africa, and Southern Europe. The plant has also spread to South America, Australia, and Iran [1]. In Persian medicine (PM), the plant is referred to as Mord or Habb-ul-Aas. According to the morphology in the book "matching the old medicinal plant name with scientific terminology" by two Iranian botanists, these names correspond to MC [2, 3]. MC has been widely used to treat various conditions, including gastroesophageal reflux disease (GERD), cough, palpitation, dysuria, stress incontinence, anogenital and common warts, acne, and homeostasis, such as epistaxis, hemoptysis, uterine bleeding, hemorrhoids, and ulcers in PM. Similar to Unani medicine, PM is a traditional medical system based on humoral medicine, with rich literature on medicinal plants properties and their therapeutic applications. In PM, everything is believed to have a temperament based on four elementary properties (warmth, moisture, dryness, and coldness) [4, 5]. Plants also have temperaments. Temperaments are determined by the plant's actions, smell, taste, and color. PM scholars attribute a cold and dry nature to MC, making it widely used in illnesses with warm dystemperament [4].

In modern medicine, MC has been reported to possess hemostatic, anti-inflammatory, analgesic, antioxidant, antiviral, antibacterial, and cytotoxic activities [6-8]. The essential oil of MC from Benslimane region contains high percentages of geranyl acetate (11.64%), α-terpineol (15.5%), and methyl eugenol (18.7%) in gas chromatography–mass spectrometry analyses from Benslimane region [9] The plant has also been revealed to contain anthraquinones, phenolics, flavonoids, tannins, saponosides, coumarins, quinones, and alkaloids [10].

This review aimed to assess the pharmacological properties, adverse events, toxicity, and clinical applications of MC based on both modern research and PM, and beneficial clinical applications may be provided for future clinical trials.

Materials and Methods

In this review, the clinical and medicinal properties of MC were extracted from Iranian PhD students' PM textbooks. Famous pharmaceutical and medical textbooks taught at schools of traditional medicine in Iran, including 'the canon of medicine' and 'makhzan al-adviyah', were consulted for PM [4, 5]. In the references, sections relating to the therapeutic, appearance, habitat properties, and pharmaceutical products of common myrtle (Mord or Habb-ul-Aas) were assessed, and associated data were included and classified.

For modern medicine, the search was conducted through scientific databases, including ScienceDirect, Scopus, Embase, and PubMed, using 'common myrtle', '*Myrtus communis*', and '*Myrtus communis* L.' as keywords among abstracts, titles, and keywords parts of databases. All associated clinical trials, in vivo, and in vitro studies that may have clinical applications from the beginning to June 2024 were included. Whole letters, conference articles, and articles related to the genetics and agriculture of common myrtle were excluded. Figure 1 illustrates this selection process.

Results

Properties of plants

MC, commonly known as myrtle, is an evergreen shrub, occasionally a small tree, native to the Mediterranean region. It reaches 2.4-3 m in height with branches forming a close full head [11]. The leaves are simple, opposite, and from ovate to lanceolate, measuring 2.5-3.8 cm long. They are dark green, shiny, glabrous, coriaceous, and aromatic. Leaf margins are whole, and leaves are opposite or verticillate. Flowers are solitary in the axil, on filiform peduncles. They are white with a diameter of approximately 2 cm, and others are yellow. The petals are glandular and pure white, with somewhat tomentose margins, covered with small hairs. A sweet fragrant smell comes from the flowers. The fruit is a small berry, pea-sized (0.7-1.2 cm), shaped orbicular or ovoid-ellipsoid. When ripened, it is blue-black or white. The berry is glabrous, of a rounded (vase-like) shape with the central part swollen and having remnants of persistent 4-5 partite calyx at the outer part. It is pale green at first, deep red after, and dark indigo when fully mature. They are bitter when unripe and sweet when ripe. Leaves and berries, which are widely used in traditional medicine, were collected. Figure 2 illustrates a visual representation of the plant [2].

Phytochemical compositions

The phytochemical compositions are presented in Table 1. Table 1 summarizes detailed components.

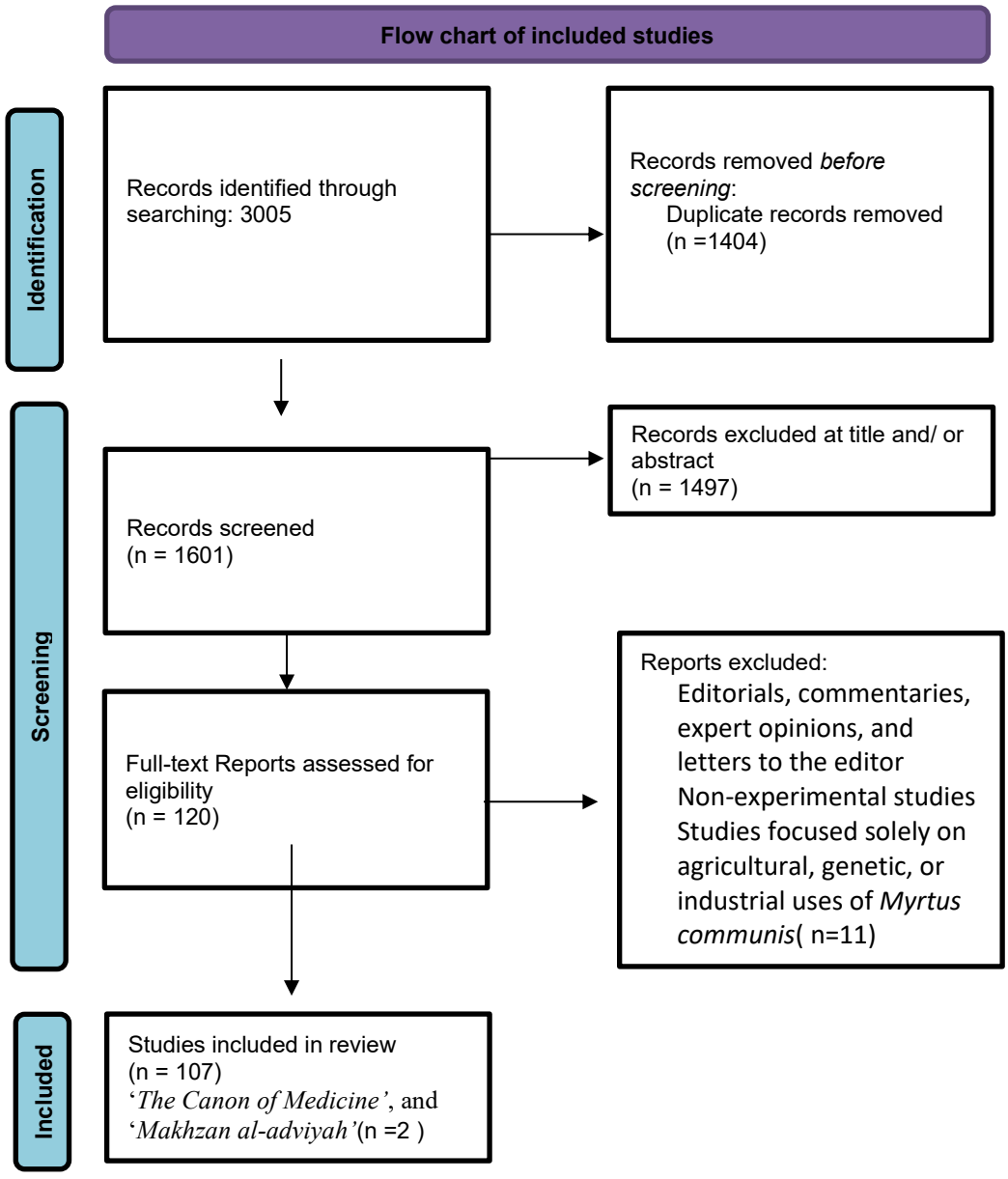

Figure 1. Flowchart of included studies

Clinical applications from PM

Nature of MC in PM

PM physicians believed that the nature of MC is cold and dry because of two elements, water and soil. Coldness and astringency in the seeds, roots, and leaves are more pronounce than in other plant sections [4].

The history of MC

The use of myrtle to treat various diseases dates back thousands of years. The oldest known book on medicinal plants is "Materia Medica" (known as "Hashayesh" in Arabic), written by Pedanius Dioscorides (40 – 90 AD), a Greek physician and pharmacologist renowned as the father of botany. This work is considered the world's first pharmacopeia and serves as an encyclopedia of herbal medicines. The name MC can be found in the Materia Medica [25].

Following Pedanius Dioscorides, eminent scientists such as Rhazes, and Avicenna. emerged from medical schools. These scholars expanded upon the knowledge of herbs, including MC, detailing their properties, such as temperament, habitat, indications, contraindications, duration of action, effectiveness, toxicity, dosage, types of preparations, and side effects [4].

Figure 2. Myrtus communis (MC)

Mode of application in PM

Neurological effects

Inhaling the aroma of myrtle leaves is recommended to treat headaches, dizziness, sinusitis, and epilepsy [4, 5].

Ophthalmic effects

A poultice prepared from barley and myrtle leaf extract is beneficial for treating pterygium, preventing tearing, and alleviating conjunctivitis [4, 5].

Ear, nose, and throat (ENT) and oral effects

MC is prescribed for toothache, earache, halitosis, oral lesions, mouth sores, epistaxis, hemoptysis, loose teeth, gingivitis, and tonsillitis. Applying the leaf extract inside the nose or ear is effective for epistaxis, ear pain, and ear discharge. Gargling with myrtle extract is beneficial for gingivitis, toothache, stuttering, and strengthening the gums [4].

Pulmonary effects

Myrtle syrup is beneficial for cough, hemoptysis, and tuberculosis [4, 5].

Gastrointestinal effect

MC extract acts as a tonic for the stomach and reduces nausea and vomiting. Myrtle syrup is effective for stomachache, heartburn, reflux, diarrhea, intestinal ulcers, mouth ulcers, and aphthous ulcers. Myrtle suppositories and sitting in a bath of boiled myrtle leaves are beneficial for anal prolapse, hemorrhoids, and intestinal worm infections. The smoke from burning myrtle leaves treats hemorrhoids [4].

Urogenital effects

MC syrup and suppositories are prescribed for heavy menstrual bleeding, uterine ulcers, warts, kidney stones, frequency, genital warts, and dysuria [4].

Table 1. Components of myrtle plant parts

Plant Part	Components	Ref.
Essential oil	Limonene, α-terpineol, linalool, eucalyptol, p-cymol, β-pinene, geraniol, camphene, butyl butyrate, myrtenol, 1,8-cineole, α-pinene, methyl eugenol, terpineole, trans-carveole, cis-carveole, methyl geranate, α-terpinyl acetate, neryl acetate, β-caryophyllene, myrcene, sabinene, p-cymene, c-terpinene, linalyl acetate, car-3-ene, phellandrene, methyl butyrate, methyl benzoate, benzyl alcohol, isobutyl butyrate, myrtenylacetate	[12-15]
Berries	Sugar, flavonoids, anthocyanin arabinosides, anthocyanin glucosides, kaempferol, quercetin, myricetin 3-o-glucoside, myricetin 3,3-di-o-galactoside, myricetin 3 rutinoside, aesculin, scopoletin, caffeic acid, myricetin 3-o-rhamnoside (myricitrin), esculetin-6-o-glucoside (esculin), hesperetin 7-o-rhamnoglucoside (hesperidin), hesperetin-2-o-methyl-chalcone-4-o-rhamnoglucoside, citric acid, malic acid, resin, tannin, fixed oil	[13, 16-19]
Leaves	Galloyl-glucosides, ellagitannins, galloyl-quinic acids, caffeic acid, gallic acid, ellagic acid, tannins, flavonoids, coumarins, myrtucommulone A & B, semimyrtucommulone	[13, 20-22]
Seeds	Oenothein B, eugeniflorin D2	[23, 24]

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Dermatologic effects

Myrtle oil is useful for hair loss, dandruff, and acne. MC is used in various types of wounds and skin diseases in PM, such as deep, Purulent, chronic, and progressive wounds, burns, erysipelas, progressive blisters, pruritus, urticaria, and head and face skin lesions.

Body massaging with leaf powder in the bath strengthens the skin. Rubbing the leaves on the skin of warts causes them to disappear. Utilizing a dry leaf poultice on the armpits and groin areas eliminates unpleasant body sweat odor. Locally, myrtle leaves are used to removes dark spots on the face and bruises caused by trauma. An ointment from myrtle leaves and olive oil effectively treats burns [4].

Clinical applications from modern medicine

Dermatologic effects

The efficacy of the topical use of mixed 1x MC leaves processed with 2x water and oral 4.5 g *Descurainia Sophia* L. was nearly twice than the salicylic acid (16.5%) group, the MC alone group, and the combined salicylic acid and *D. Sophia* group in terms of wart size and number reduction on days 40 and 90. No wart relapse was reported in any group. The combined MC and *D. Sophia* group had fewer side effects than the salicylic acid group [26].

A dermo-cosmetic cream containing azelaic acid and MC leaves reduced acne relapse by 18% compared to a light moisturizing cream at week 16. However, it was not statistically significant, probably due to the small sample size [27]. The use of topically applied myrtle leaves significantly decreased comedones, acne severity index, and total lesion count compared to the clindamycin group. The myrtle and clindamycin groups showed similar reductions in inflammatory lesions [28]. In a clinical trial, MC leaf cream was administered to 100 nulliparous women after episiotomy for wound healing evaluation. The Reeda score (edema, erythema, exudation, and bruising) was significantly reduced on days 5 and 10 in the MC leaves cream group compared to the placebo group [29].

MC leaves solution was as effective as ketoconazole shampoo for dandruff treatment. While the difference between the two groups was not statistically significant, both treatments significantly reduced excoriation pruritus grading, adherent scalp flaking score, redness of scalp skin, and grading of scalp skin involvement [30]. Itching and erythema were reported as adverse effects of 2% ketoconazole shampoo [31]. No side effects have been reported for myrtle. Therefore, myrtle may be more effective than ketoconazole shampoo for dandruff treatment.

Gastrointestinal effect

It was demonstrated that the essential oil from myrtle leaves in the ointment could significantly decrease anal itching compared to the anti-hemorrhoid drug group in postpartum women with grade I and II internal hemorrhoids at week 8. Pain, itching, swelling, bleeding, and discomfort in the anus were reduced within both myrtle and anti-hemorrhoid drug groups, similar to each other [32]. The effects of the MC freeze-dried aqueous extract capsule, omeprazole, and a combination of omeprazole and the MC capsule were evaluated in adults with GERD at 6 weeks. All three interventions were effective on acid reflux-related symptoms (RS), dysmotility-like symptoms (DS), and scores of frequency scale for the symptoms of gastroesophageal reflux disease (GERD) within group comparisons. Between-group comparisons showed similar efficacy. Although all interventions were significant, the FSSG and reflux-related symptoms (RS) mean differences of the omeprazole group were reported to be the highest, while the dysmotility-like symptoms (DS) mean difference of the omeprazole and MC

capsule combination was shown to be the largest [33]. A clinical trial on children showed no differences in GERD symptom questionnaire scores for young children between the combination of MC fruit syrup and omeprazole and omeprazole alone in weeks 8 and 12. However, children in the myrtle group experienced a significant increase in appetite [34]. An in vivo study demonstrated that a-tocopherol and flavonoids protect against mucosal damage in rats with GERD via antioxidative activities. Notably, flavonoids are found in myrtle [13, 35].

Urogenital effects

The efficacy of MC and oak gall vaginal suppositories (MOGS) compared to the placebo and metronidazole groups in women with vaginitis was assessed. Metronidazole was more effective in reducing malodor discharge, malodor discharge after intercourse, dyspareunia, vaginal irritation, dysuria, lower abdominal pain, Whiff test-positivity, clue cells-presence, *Candida albicans*-presence, *Gardnerella*-presence, Trichomonas-presence than the MOGS and placebo groups. However, MOGS was more effective in relieving itching than other groups. In both trichomoniasis vaginosis (TV) and bacterial vaginosis (BV) patients, MOGS treatment resulted in a greater mean difference in discharge, although not statistically significant. The Nugent score and trichomoniasis vaginosis (TV) significantly decreased in both MOGS and metronidazole groups, while BV was reduced considerably only in the metronidazole group [36]. In another clinical trial, BV was assessed among women with BV on day 7. Metronidazole alone was more effective against BV than MC in a metronidazole base and *Berberis vulgaris* in a metronidazole base, although relapse was reported as zero in the MC and *B. vulgaris* groups as opposed to the metronidazole group [37].

The efficacy of 15 mL of MC fruit syrup was evaluated in women with excessive uterine bleeding. In month 3, the results reported a marked reduction in the mean pad number, mean bleeding days, and MQ score [38]. Another study administering 750 mg MC fruit capsules to women with menorrhagia for 10 days in two cycles demonstrated a significant reduction in pictorial blood loss assessment chart (PBAC) scores and a considerable increase in quality of life and hemoglobin percentage after the second cycle of treatment compared to the control group [39].

A 3-month study was conducted to evaluate human papillomavirus (HPV) test circumstances in women with cervicovaginal HPV infection. Vaginal suppositories containing 0.5% MC leaf essential oil, and 10% MC leaf aqueous extract and placebos were administered. The HPV test was significantly negative in the MC group compared to the placebo group, and as a result, the cervical lesion size decreased considerably [40].

In women with vulvovaginal candidiasis, Ward preparation (containing *Quercus infectoria*, *Rosa damascena*, *Nardostachys jatamansi*, MC, and *Punica granatum*) markedly decreased symptoms, including itching, vaginal edema, dyspareunia, vaginal discharge, and vaginal redness compared to the placebo group after five weeks of treatment [41].

A study on nulliparous women after an episiotomy procedure showed that MC cream considerably reduced pain severity at 5- and 10-hours post-procedure compared to the placebo group [29].

ENT and oral effects

A before-and-after clinical trial was conducted on patients with epistaxis, nasal erosion, and mucosal dryness administering an intranasal spray mixture containing anthocyanin, fucoidan, hyaluronic acid, and MC. At week 8, endoscopic examination showed a remarkable reduction in epistaxis, nasal erosion, and mucosal dryness, compared to baseline [42].

The efficacy of MC oral paste in patients with recurrent aphthous stomatitis (RAS) demonstrated significant reductions in ulcer size, pain sensitivity, erythema, and exudation [43].

A clustered clinical trial assessed the efficacy of 4 essential oil mixtures vaporization, containing *Citrus aurantifolia*, *Citrus limon*, *Osmanthus fragrance*, *Citrus sinensis*; forest walk (FW): Containing MC, *Pinus cembra*, *A. sibirica*, *A. grandis*, *Vetiveria zizanoides*, *Citrus paradisi*, *Abies alba*, *Pseudotsuga menziesii*; Swiss pine (SP): Containing *P. cembra* compared to the control group on acute anxiety. Acute anxiety, as measured by the state-trait-anxiety inventory (STAI-T), was significantly reduced in all intervention groups compared to the control group, particularly in women [44].

Table 2 summarizes the characteristics of the 17 included clinical trials. Table 3 presents the potential in vivo and in vitro applications.

Potential clinical applications from in vivo and in vitro studies

Due to the myrtle's various yet unexplored medical applications, we have summarized in vivo and in vitro studies regarding myrtle in Table 3. These findings may inform future clinical trials.

Table 2. Characteristics of included clinical trials (17 items)

Ref.	Target	Intervention	Comparator	Treatment/ Duration/ Dosage	Study Design	Outcome
[36]	Women with BV, trichomoniasis or vaginitis	MC and oak gall powder	Placebo, metronidazole	A vaginal suppository/a day/ for a week	Parallel RCT, DB	↓Bacterial vaginosis, ↓vaginal discharge, ↓vaginitis, ↓trichomoniasis
[43]	Patients with RAS history or ulcers	MC oral paste	Placebo	Q6h/ day/6 days	RCT, DB, multicenter	↓Ulcer size, ↓pain sensitivity, ↓erythema level, ↓exudation level, ↑oral health impact profile
[27]	Adult women with acne	TP (with MC)	LCM	16 weeks	RCT, DB, multicenter	↓Acne relapse, ↓acne severity
[44]	Dental offices patients	FW (with MC)	GM, CS, SP and placebo	4-6 drops three times a day/5 weekly cycles	Cluster-RCT, SD	↓Dental anxiety, ↓acute anxiety, ↓pain perception
[41]	Women with vulvovaginal candidiasis	Ward (with MC)	Placebo	a 200 mg vaginal tablet/ day/week	Parallel RCT, DB	↓Vulvovaginal candidiasis, ↓itching, ↓irritation, ↓vaginal discharge
[32]	Postpartum women with hemorrhoid	MC ointment	Anti hemorrhoid drug	60 mg ointment BID/day/4 weeks	RCT, TB	↓Anal itching, ↑satisfaction from treatment
[34]	Children with GERD	MC fruit syrup and omeprazole	Omeprazole	1 mg/kg/day/8 weeks	RCT, DB	↓Symptom of drug consumption refusal, ↑appetite
[38]	Women with menometrorrhagia	MC fruit syrup	Placebo	15 mL syrup TID/ day/3 weeks	RCT, DB	↓Uterine bleeding
[39]	Women with menorrhagia	MC fruit capsule	Placebo	750 mg /10 days	RCT, SD	↑HB%, ↑quality of life, ↓heavy menstrual bleeding
[33]	Adults with GERD	MC capsule	Omeprazole	1000 mg capsule/ day/6 weeks	RCT, DB	↓GERD, ↓dyspepsia
[40]	Women with cervicovaginal human papilloma infection	MC suppository	Placebo	12 weeks	RCT, DB	↓HPV, ↓cervical lesion size
[26]	Patients with warts (less than 20)	Topical MC use	Salicylic acid, DS	BID/ day/40 days	RCT, SB	↓Warts number, ↓warts size, ↓wart relapse
[37]	Women with BV	MC gel	*B. vulgaris*, metronidazole	A vaginal gel/day /5 days	RCT, SB	↓BV, ↓vaginitis, ↓vaginitis relapse
[29]	Nulliparous women	MC cream	Placebo	BID/10 days	RCT, DB	↑Wound healing, ↓episiotomy pain
[30]	Patients with dandruff	MC solution	Ketoconazole shampoo	8 times/ month	RCT, DB	↓Dandruff, ↓redness of scalp skin, ↓grading of scalp skin involvement, ↓pruritus grading, ↓scalp flaking
[28]	Patients with acne vulgaris	Topical MC solution	Clindamycin	Topical MC solution/ twice a week/12 weeks	Clinical trial,TB	↓Comedones, ↓acne severity, ↓acne lesion number, ↓inflammatory lesions
[42]	Patients with hemorrhage, nasal erosion and mucosal dryness	Intranasal MC		Intranasal MC spray/BID/6-8 weeks	Clinical trial	↓Epistaxis, ↓nasal erosion, ↓mucosal dryness

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Abbreviations: MC: *Myrtus communis* L.; RCT: Randomized controlled trial; DB: Double-blind; BV: Bacterial vaginosis; RAS: Recurrent aphthous stomatitis; LCM: Light moisturizing cream; TP: Test product (containing *M. communis* extract and azelaic acid); SD: Single-blind; SP: Swiss pine (containing *P. cembra*); CS: Citrus sinensis; GM: Good mood (containing *C. aurantifolia*: *C. limon*: *O. fragrance*: Citrus sinensis); FW: Forest walk (containing MC, *P. cembra*, *A. sibirica*, *A. grandis*, *V. zizanoides*, *C. paradisi*, *A. alba*, *P. menziesii*); Ward: Containing *Querqus infectoria*: Rosa damascene, *N. jatamansi*, MC and *P. granatum*; TB: Triple-blind; GERD: Gastroesophageal reflux disease; HB: Hemoglobin; HPV: Human papillomavirus virus.

Table 3. Characteristics of in vivo, in vitro, and review studies

Potential Clinical Applications	Intervention	Study Design	Outcome	Ref.
Neurology system	MC extract	In vivo	↑Cognition in hypertension	[47]
	MC leaves extract, MC extract	In vivo	↓Alzheimer's disease, ↑hypnosis, ↑anxiolysis, ↑muscle relaxation, ↓neurodegenerative diseases, ↑neuronal functions, ↑cognition	[48-53]
	MC EO, *Rosmarinus officinalis* EO	In vivo	↓Meningitis, ↑anti-bacterial (against *Listeria monocytogenes*)	[54]
Urology system (urinary and genital system)	MC leaves extract	In vivo	↓Urine calcium, ↓urine citrate, ↓urine creatinine, ↑urine oxalate, ↓kidney stone formation, ↓renal cell damage, ↓oxidative stress, ↓nephrolithiasis	[55]
	MC leaves extract	In vivo	HFD-induced testicular injury	[56]
	MC leaves EO	In vitro	↓Prostate cancer, ↓bladder cancer	[57, 58]
	MC flowers EO	In vitro	↑Anti-bacterial (*Escherichia coli*, *Klebsiella oxytoca* and *Serratia marcescens*), ↓urinary infection	[59]
Cardiovascular system	MC leaves EO	In vivo	↑Anti-atherogenic activities, ↑cardiovascular protection	[60]
Hematology system	MC leaves EO	In vivo, in vitro	↓Bleeding time, ↓bleeding; ↑hemostasis, ↑platelet aggregation	[61]
Skin system (dermatology system)	MC leaves extract	In vivo	↑Wound healing, ↑anti-inflammatory, ↑anti-microbial, ↓bacterial growth	[7]
	MC leaves extract, etc.	In vitro	↓Cutibacterium acnes, ↑anti-bacterial, ↓acne	[62, 63]
	MC	Systematic review	↓Diabetic foot ulcer	[64]
	MC extract	In vivo, in vivo	↑Wound healing in diabetes	[65, 66]
	MC extract	In vitro, systematic review	↓Burn-induced skin damage, ↓UV-induced skin damage, ↓molluscum contagiosum, ↓warts	[67-69]
	MC extracts, etc.	In vitro	↑Anti-bacterial (against *Staphylococcus aureus*, methicillin-resistant *S. aureus*, *Staphylococcus epidermidis*, *Enterococcus faecalis*)	[70, 71]
Endocrine system	MC extract	In vivo	↓Diabetes mellitus type 1	[65, 66]
	MC berries and seeds	In vivo	↓Dyslipidemia, ↓metabolic syndrome	[72, 73]
Respiratory system	MC	Review	↓Lung disorder	[74]
	MC	Review	↓Rhinitis, ↓rhinosinusitis	[75]
	MC	Review	↓COVID-19 (coronavirus disease, SARS-CoV-2)	[76]
	MC extract	In vivo	↑Anti-influenza A virus, ↑anti-viral effect	[77]
	MC oil	In vivo	↓Allergic rhinitis	[78]
	MC EO	Review	↓Viral respiratory infections	[79]
	MC	In vivo	↓Allergic asthma	[80]
	MC extract	In vivo	↓Pulmonary fibrosis	[81]
	MC flowers, MC leaves extract	In vitro	↑Anti-bacterial (*S. marcescens*), ↓pneumonia, ↓pneumonitis, ↓gram-positive bacterial infections	[59, 82]

Potential Clinical Applications	Intervention	Study Design	Outcome	Ref.
Gastrointestinal system	MC leaves extract	In vivo	↓HFD-induced pancreatic injury	[83]
	MC	In vivo	↓Colon cancer	[84]
	MC EO	In vivo	↑Gastroprotection	[85]
	MC beery seeds, MC EO	In vitro	↓Helminthiasis, ↓hydatid cyst	[86, 87]
	MC EO, MC extract, etc.	In vivo	↓Oral pathogens (against *S. mutans*, *Rothia dentocariosa*, *Porphyromonas gingivalis*), ↓gingivitis	[88, 89]
	MC extract	In vitro	↓Nystatin-resistant *C. albicans*	[90]
	MC leaves extract, MC flowers EO	In vitro, in vivo	↓Hepatotoxicity, ↑ehepatoprotection	[91, 92]
	MC leaves extract	In vivo	↓Acute pancreatitis	[93]
	MC	In vivo	↑Oral ulcer healing	[94]
	MC leaves extract, MC berries	In vivo	↓Diarrhea, ↓intestinal motility	[95, 96]
	MC extract	In vivo	↓Bile ductal obstruction, ↓hepatic fibrosis	[97]
	MC EO, MC	In vivo, in vitro	↓Helicobacter pylori, ↓peptic ulcer, ↓gastric cancer	[98, 99]
	MC flowers	In vitro	↑Anti-bacterial (*E. coli*)	[59]
Musculoskeletal system	MC	In vivo	↑Muscle relaxation	[48-53]
Oncology	MC leaves	In vitro	↑Antioxidant activity	[100]
	MC leaves EO	In vitro	↓Prostate cancer, ↓bladder cancer	[57, 58]
	MC	In vivo	↓Colon cancer	[84]
	MC EO, MC	In vivo, in vitro	↓Gastric cancer	[98, 99]
Immunology system	MC leaves extract	In vivo	↑Wound healing, ↑anti-inflammatory, ↑anti-microbial, ↓bacterial growth	[7]
	MC leaves extract, MC EO	In vivo, in vitro	↓Inflammation	[101-103]
Infectious disease	MC leaves extract, MC extract	In vitro	↑Destruction of resistant gram-negative bacteria, ↓gram-positive bacterial infections	[82, 104]
	MC EO	In vivo	↑Antibacterial (against *E. coli*, *Escherichia pseudocoloides* and *Escherichia vekanda*)	[105]
	MC leaves extract, etc.	In vitro	↓Cutibacterium acnes, ↑anti-bacterial	[62, 63]
	MC EO, *R. officinalis* EO	In vivo	↑Anti-bacterial (against *L. monocytogenes*)	[54]
	MC extracts, etc.	In vitro	↑Anti-bacterial (against *S. aureus*, methicillin-resistant *S. aureus*, *S. epidermidis* and *E. Faecalis*)	[70, 71]
	MC flowers EO	In vitro	↑Anti-bacterial (*E. coli*, *K. oxytoca* and *S. marcescens*)	[59]
	MC EO	In vitro	↑Anti-bacterial (against *L. monocytogenes*)	[106]
	MC extract	In vivo, in vitro	↑*anti-parasite (against Salmonella typhimurium* and *Leishmania major*)	[107, 108]
	MC EO, MC extract, etc.	In vivo	↓Oral pathogens (against *Streptococcus mutans* and *R.dentocariosa*, *P. gingivalis*), ↓gingivitis	[88, 89]
	MC leaves EO	In vitro	↑Anti-fungal activity	[109]

PBR

Abbreviations: HFD: High-fat diet; EO: Essential oil; MC, *Myrtus communis*.

Side effects and toxicity

The efficacy of a 4% myrtle leaves diet on sheep was evaluated. The study showed a considerable decrease in triglyceride and blood sugar. While this effect has not been reported in humans, it suggests the potential for similar outcomes in human subjects [45]. Additionally, the LD_{50} values (median lethal dose) of aqueous and ethanolic myrtle extracts were reported as 0.473 and 0.79 g/kg, respectively [46]. High cineole content in MC can cause hypotension and respiratory failure [2].

Discussion

In this review article, for the first time, the myrtle plant has been evaluated from the perspective of temperament and humoral medicine. The properties of this plant have been explained based on its temperament in the oldest books of traditional Persian and Greek medicine, such as "Materia Medica" (known as "Hashayesh" in Arabic), by Pedanius Dioscorides and The Canon of Medicine by Avicenna.

Alipour et al. (2014) examined the mechanisms of various activities of this plant [6], and Hennia et al. in 2018 examined its antioxidant activity [13].

This article reviewed for the first time the therapeutic applications and methods of oral and topical use of myrtle plants in traditional medicine books and compared them with the results of modern clinical studies. However, other review articles have only mentioned the therapeutic effects of myrtle in scientific studies, along with the plant's pharmacology and mechanism of action [6, 10, 13].

One of our article's strengths is the review of the therapeutic uses of myrtle in traditional medicine books from thousands of years ago to the present, based on human, animal, and laboratory studies. One of our article's weaknesses is the less thorough review of the mechanism of myrtle's pharmacological effects.

Conclusion

Herbal medicines have been extensively used in PM. Some MC applications in PM have been proven by modern medicine, while others remain unproven. Many potential uses were conducted in in vivo and in vitro studies; therefore, they have the potential to be conducted in future clinical trials. MC contains crucial bioactive components, including anthraquinones, phenolics, flavonoids, tannins, saponosides, coumarins, quinones, and alkaloids. These compounds suggest potential applications in treating neurological, urogenital, gastrointestinal, dermatological, and otorhinolaryngological diseases.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors' contributions

Conceptualization: Mohsen Rezaee and Ali Rezaee; Methodology: All authors; Writing the original draft: Ali Rezaee; Review and editing: Zohre Feyzabadi and Mohammad M. Zarshenas.

Conflict of interest

The authors declared no conflict of interest.

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