Review

Myrtus Communis Leaves; Source of Bioactives, Traditional Use and Their Biological Properties

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Review

Myrtus communis Leaves; Source of Bioactives, Traditional Use and Their Biological Properties

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Abstract: *Myrtus communis L.*, commonly known as true myrtle, is a medicinal plant native to the Mediterranean area. Since ancient times inhabitants of this area have been using it for its cultural and medicinal properties. Due to the high content of essential oil in its flowers, leaves and fruits, *M. communis* is an important medicinal and aromatic species from Myrtaceae family. Because of the presence of vast diversity of biomolecules in its aerial parts, it exhibits several biological properties of antioxidant, antimicrobial and anticancer. There has been increasing scientific interest in the field to understand the pleotropic effects of its extracts or essential oils on various ailments and diseases. This review summarizes the chemical composition, traditional uses, and biological activities of *M. communis* L. leaves documented in numerous recent studies.

Keywords: natural products; plant extracts; *Myrtus communis*; medicinal plants; antimicrobial; antioxidants; antiviral; biofilm inhibition

Introduction

Antibiotics manufactured worldwide at an estimated quantity of about 100,000 tons annually remarkably affect the lives of bacteria living on earth. More bacterial pathogenic strains have become resistant to antibiotics, and some have acquired resistance to numerous antibiotics and chemotherapeutic agents, thus leading to the emergence of multidrug-resistant bacteria. Plants through coevolution with pathogenic microorganism developed defense mechanisms and produced secondary metabolites against parasites. Family Myrtaceae comprised of nearly 100 genera and 3000 species grow in tropical, subtropical, and temperate regions of the world. The genus *Myrtus L* is comprised of 2 species, *Myrtus communis L* (common myrtle) that grows wild all around the Mediterranean basin and *Myrtus nivellei Batt* (Saharan myrtle) mainly inhabitant of central Sahara. *Myrtus communis* L is a perennial shrub or small tree of 1.8 - 2.4 m tall with small foliage and deep fissured bark **(Figure 1).** *Myrtus* blooms massively in early summer (from mid-June to early July) and its white hermaphroditic flowers are pollinated mostly by dipterans and hymenopterans [1]. Its fruit berries turn black blue after maturing from mid-October to late November. The seeds are dispersed by passerine birds, mostly Sylviidae and Turdidae [2]. The plant has upright stem, and its branches form a close full head, which is densely covered with evergreen leaves. The dark green 2.5-3.8 cm long leaves are glossy, coriaceous, opposite, paired or whorled, smooth, aromatic, entire margined, and acuminate ovate to lanceolate.

Habitat: *Myrtus nivellei Batt. & Trab*. is widespread to the central Saharan mountains growing in sandy and rocky wades and valleys, at high altitudes of above 1400 meters. *Myrtus communis L* can be found in the Mediterranean Basin, Afghanistan, Iran, and, Macaronesia predominantly at altitudes not exceeding 500 meters above sea level [3] Myrtle is indigenous to west Asia, North Africa and Southern Europe and is scattered in Southern America, northwestern Himalayas and Australia. Myrtle is also cultivated in gardens, especially in Northwest regions of India and Fifa Mountains of Saudi Arabia [4].

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Figure 1. Branches, leaves and berries of M. communis from Herbari virtual, Area of Botany, Department of Biology, University of the Balearic Islands, http://herbarivirtual.uib.es/.

Traditional applications of *M. communis*: Its fragrant leaves have been significantly used in remedy of diverse ailments in different countries/regions throughout the globe. In Iran, the aqueous maceration of leaves after filtration and concentration is taken for wound healing, depression, and polymenorrhea [5]. In Algeria, the decoction of the leaf powder is used to treat hypertension, eczema, other skin diseases, respiratory disorders and hemorrhoids [6]. Dried leaf powder mixed with butter is applied topically to treat scabies in Ethiopia [7]. Rural women boil leaves in water or mix the leaf extract with raw butter and use it as cosmetics to control hair fall, dandruff, and treat headache in Ethiopia [8]. Tea mixed with leaves has been drunk on daily basis to relieve stress and anxiety in Turkey [9]. Mirto, a liqueur used as beverage in Italy has *M. communis* leaves as one of the ingredients [10]. The dried aqueous leaf extract is used to treat sinus infections in China and France [11,12]. In India, Pakistan, Turkey, Ethiopia and Iran, the leaves, berries and myrtle oil are used to treat diarrhea, dysentery, gastric ulcer, vomiting, rheumatism, hemorrhages, deep sinuses, leucorrhea, hemorrhoid, inflammation, pulmonary and skin diseases, besides being used as potential astringent, antiseptic, disinfectant and hypoglycemic agents [13,14]. The aqueous juice has also been used for the preparation of food and wines in Italy [13,14]. Myrtle oil is used as adjunct for the treatment of insomnia in Ethiopia [15]. M. communis leaves are used in mouthwash and in the treatment of candidiasis [16]. A decoction of leaves and fruits is generally used orally for the treatment of constipation, stomachaches, hypoglycaemia, cough, poor appetite, and externally for wound healing [17]. The assorted specific applications of the leaves of the myrtle plant are given in Tables 1 and 2. Other uses of its leaves include cattle feed, cut foliage and potted plants [18].

The diverse biological properties attributed to *M. communis* are due to the presence of diverse compounds in its aerial parts (Table 1), which include essential oil compounds (terpenoids, particularly α-pinene, 1,8-cineole, geranyl acetate, and linalool), flavonoids (quercetin, catechin and myricetin derivatives), anthocyanins (Cyanidin-3-glucoside, Petunidin-3-glucoside, Peonidin-3-glucoside, Malvidin-3-glucoside), coumarins, oligomeric nonprenylated acylphloroglucinol compounds (myrtucommulone A-F and semimyrtucommulone), galloyl-glucosides, ellagitannins,

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galloyl-quinic acids, gallic and ellagic acids, caffeic, and fatty acids (linoleic, palmitic, oleic, and stearic acids) [19].

Chemical composition of essential oil and extracts of *M. communis* leaves

The essential oils of M. communis are highly variable in their chemical composition due to various factors such as geographical position, growing conditions (climate, humidity, altitude, temperature, etc.), and vegetative period of the plant. Moreover, there is a close relationship among light shade conditions, essential oil yield, and morphological parameters. The major components of myrtle essential oil are myrtenyl-acetate, 1,8-cineole, α-pinene, limonene, whose concentration varies among the *M. communis* plants from different origins. The main components of Spanish myrtle essential oil are myrtenyl-acetate (>30.0%) and α-pinene (< 8.50%) [20], while Algerian wild myrtle EO is rich in myrtenyl-acetate (38.7%), α-pinene (13.7%), 1,8-cineole (12.7%), and linalool (7.00%) [21]. The chemical composition of EOs of *M. communis* from different regions of the Mediterranean area is highly variable. Tunisia and Corsica EOs have variation in the main constituents of α-pinene (51.2-52.9% verses 53.5-56.7%), 1,8-cineole (24.1-24.7% verses 18.8-21.3%) and limonene (6.1-7.3% verses 5.0- 5.2%). The principal constituents in the Moroccan and coast of Montenegro EOs were 1,8-cineole (32.5-37.5%) and myrtenyl-acetate (14.8- 21.1%), though myrtenyl-acetate was present in minute amounts (0.1-0.3% verses 0.8%) [21,22]. The 1,8 cineole (55.09%) and α-pinene (33.14%) were predominant components of another Tunisian myrtle EO, while lacking myrtenyl acetate [23–25]. Interestingly, myrtle essential oils from two locations of Liguria, Italy were rich in α-pinene (41.6% and 28.9%, respectively), while lacking myrtenyl-acetate and myrtenol [26]. Moreover, the EOs obtained from 52 genotypes of *M. communis* growing in the same field at Oristano (Sardinia, Italy) contained limonene, 1,8-cineole, α-pinene, linalool, and α-terpineol as principle components with few differences among the samples [27,28]. The essential oil of *M. comminis* from Iran origin is rich in α-pinene (27.87%), 1,8-cineole (20.15%) and linalool (10.26%) [29]. *M. comunis L* is a factory of molecules, regardless of the plant part or the phenological stage three ubiquitous compounds α -pinene, 1,8-cineole, and linalool are found in *M. communis* grown in Ghirardi Botanic Garden, of the University of Milan Italy [30].

Drying methodologies of *M. communis* aerial parts for essential oil extraction.

Different types of drying methodologies have been tried for extraction of compounds from *M. communis*. Convective air, oven and microwave were used to dry the aerial parts of *M. com*mnis and subsequently used for extraction of polyphenols and anthocyanins. Among them microwave drying of the leaves led to an increase in the amounts of total extractible phenols, flavonoids and proanthocyanidins followed by oven drying at 70 °C. Not only the amount of compounds isolated was more, but also their antioxidant activity was enhanced [31]. The concentration of bioactive compounds in myrtle berries is related to their geographical origin, as myrtle berries collected in two different areas of the province of Cadiz (Spain) showed different concentration of bioactives [32].

Bouaoudia-Madi et al. used ultrasound-assisted extraction method to isolate polyphenolic compounds from pericarp of myrtle berries. The authors demonstrated that the yield of total polyphenolic content is significantly affected by solvent concentration, solvent-to-solid ratio, irradiation time, and amplitude of the ultrasound waves. The optimal conditions of 70% (*v/v)* ethanol, 7.5 min irradiation time and 30% solvent to solid ratio were found to be optimal for the isolation of polyphenols from *M. communis* extract. Moreover, ultrasound-assisted extraction has been found more efficient than microwave-assisted extraction and conventional solvent extraction methods [33].

Antibacterial activity

Emergence of infectious diseases caused by diverse bacterial species and multidrug resistance has created havoc in health systems. Dormancy under stress conditions and in biofilms is one the ways by which a microbe could gain antimicrobial resistance. The use of natural products in association with antimicrobials could be effective in controlling the emergence of infectious diseases,

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combating the antimicrobial resistance, reducing the administration dose of a drug and thereby reducing the dose-dependent toxic effects. The phytoconstituents could combat the antimicrobial resistance by inhibiting the drug modifying/degrading enzymes, or drug efflux pumps or revert the dormant microbes to active metabolic phase to restore the effectiveness of commercial antimicrobials. In combination with natural compounds, the commercial antimicrobials would have even greater potency by targeting several different processes.

Researchers are focused on traditional herbs for their use in complementary therapies and preventive medicine. About 80% of human bacterial infections are believed to be associated with biofilm-forming microorganisms [34]. Several chronic infectious diseases including periodontitis, gingivitis, and dental caries in both children and adults are caused by opportunistic species of *Streptococcus mutans*, *candida albicans*, *E. coli*, and *S. aureus* [35–37]. The microorganisms form biofilms on mucosal epithelial cells, dental surfaces, and orthodontic prosthetics [38]. Herbal aqueous extractions and their combination turned out to be effective in controlling such oral infections. Several studies documented the application of *M. communis* in oral hygiene and cure of infectious diseases. Polyherbal toothpaste formulated from the aqueous leaf extract of *Myrtus communis* in combination with *Artemisia dracunculus*, *Satureja khuzestanica* (Jamzad) in different combinations showed a significant in-vitro growth inhibition of five microorganisms *viz Streptococcus mutans, Lactobaccilus caseie, S. sanguis, S. salivarius,* and *Candida albicans* with potent activity observed against Gram-positive bacteria and *C. albicans* [39]. Other than Gram-positive, Gram-negative oral pathogens A*ctinobacillus actinomycetemcomitans, Porphyromonas gingivalis* and *Prevotella intermedia* were also susceptible to methanolic as well as aqueous leaf extracts of *M. communis* [40]. In 2018 an ethnobotanical survey carried out in Casablanca, Morocco, found the wide use of 46 plant species in toothpastes for the treatment of gum disease, dental pain, and halitosis. Myrtaceae was one of the most represented botanical families within which *M. commmunis* leaf aqueous extract (obtained by decoction) was often used to treat above-mentioned oral infections [41]. These studies suggest that *Myrtus communis* oil or extract could be used in strips, chips, and fibers to avoid the side effects of antibiotics in periodontal disease or periodontal regeneration, which needs further investigation.

Caputo L. et al, found EO of *M. communis* very effective against three Gram negative (*E. coli* DSM 8579, *P. aeruginosa* ATCC 50071, *P. carotovorum* DSM 102074) and two Gram positives (*S. aureus* DMS 25923, *L. monocytogenes* ATCC 7644) with MIC ranging from 3-6 mg/ml. However, for its individual constituents of myrtenyl acetate, 1,8-Cineole, α-pinene, and Linalool, the corresponding MICs were more than that of EO, therefore it is suggestive of synergistic action of the components of EO [42]. Among the 80% methanol extracts of the leaves of *Verbena officinalis, Myrtus communis*, and *Melilotus elegans* tested for antibacterial activity, the Mc-80ME showed remarkable zone of inhibition and bactericidal activity against all tested bacterial isolates of *Staphylococcus aureus, Escherichia coli, Salmonella typhi, Shigella flexneri, Pseudomonas aeruginosa*, and *Proteus mirabilis* [43]. The leaves of M. communis have been used for therapeutics of several ailments in different forms like ointment as in toothpastes, suppositories, etc.

Not only polyherbal toothpaste, herbal suppository of myrtle and oak gall extracts were prepared in polyethylene glycol base. These suppository treated the bacterial vaginosis, especially Trichomonas vaginalis in adult women without major complications and side effects [44]. Furthermore, *M. communis* has a profound use in food processing technology. Without compromising the normal flora of the cheese, the essential oil of the aerial parts of *M. communis* L strongly inhibited the growth of *Listeria monocytogenes* (MIC; 31.25 µL/mL), a common foodborne pathogen and a predominant contaminant of cheese [45].

Myrtle extract finds it use in nanotechnology as nanofibers of being small diameter make surface pressure a highly dominant phenomenon by which the adhered molecules would be easily released once their concentration in the solution drops. It is hypothesized that hydrophobicity of the novel seed/leaf extract encapsulated/soaked nanofibers could be a repulsive to water molecules, which is a key factor for cell life and adhesion. Nanofibers made up of polycaprolactone and gelatin, encapsulated or soaked with myrtle leaf or seed extract showed complete inhibition of *S. aureus* and all strains of *candida*, though it exhibited a moderate effect on Gram-negative *E. coli*. Similarly, two

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discs of nanofibers soaked in seed and leaf extracts decreased 95%viability of *Trichomonas vaginalis*, the commonest non-viral sexually transmitted infection in women. Interestingly nanofiber either soaked or encapsulated with seed or leaf extract did not exert any effect on *L. acidophilus* [46]. The use of these nanofibers as devices for the controlled release of molecules could be a promising choice to counteract Gram-positive microorganisms.

One of the mechanisms of colonization and expression of virulence or survival factors of a pathogen is quorum sensing. The quorum sensing is a cell-to-cell communication mechanism in bacteria. This cascade of specific signal and response is mediated by the synthesis, release, and uptake of specific molecules known as autoinducers [47]. The autoinducers latter lead to the colonization and expression of various survival or virulence traits to combat stresses and develop drug resistance etc. Jean-Pierre Poli et al screened twelve essential oils for anti-QS activity by measuring the sub-lethal minimal QS inhibitory concentration (MQSIC) of violacein production of *Chromobacterium violaceum* and minimal inhibitory concentration against the growth of *C. violaceum*. The authors found that the EO obtained from *Mentha suaveolens ssp. insularis* showed 32-fold lower MQSIC than MIC, while *M. communis* EO obtained from its aerial parts was one among the four EO which showed 16-fold lower MQSIC than MIC. For the remaining EOs, the MQSIC was ≤8-fold lower than MIC [48].

Inhibitors of α-glucosidase activity have been useful for the control of hyperglycemia in patients with noninsulin-dependent type-2 diabetes. Among the several medicinal herbs of *Ferulago nodosa subsp. Geniculate, Urtica dioica, Viscum album, Taraxacum officinale,* and *Myrtus communis* investigated for α-glucosidase inhibitor activity, *M. communis* strongly inhibited the enzyme α-glucosidase (IC_{50}; 38 μg/mL) [49,50]. These results suggest that *M. communis* herbal extract could be developed as a physiologically functional drink for lowing the blood glucose content, which needs to be explored.

Antiviral activity

Vaccination, as a preventive method, cannot provide sufficient control against the spread of viral infections because of continuous antigenic drifts. Furthermore, because of limited drug targets few antiviral drugs are available for the treatment of viral diseases. Conventional antiviral drugs have shown side effects, like amantadine and oseltamivir effects the central nervous system and the gastrointestinal tract, which is further compounded with genetic instability, re-assortment of the virus and drug resistance. Therefore, researchers are focused to look for alternative therapeutic measures of screening medicinal plants and natural products for antiviral activity. Among the several plants tested against anti-influanza A virus, the most effective were crude extracts of *G. glabra*, *M. officinalis* and *S. alba*; methanol fractions of *M. communis* and *M. officinalis*; and chloroform fractions of *M. communis* and *C. sinensis* (fermented) in co- and pre-penetration combined treatments (Ref51). The potential antiviral activity of the extracts and fractions is believed to be due to the phytoconstituents of flavonoids, tannins, steroids and triterpenoids [51]. It needs further investigation to identify the potent ingredient.

Antibiofilm activity

Biofilm is a three dimensional structural community of aggregated bacterial cells adhered to each other as well as to substratum, encapsulated in a hydrated extracellular polymeric matrix composed of proteins, polysaccharides, and nucleic acids [52]. Bacterial strains acquire drug resistance by different mechanisms including quorum sensing, efflux pump, and alteration of the outer membrane, secretion systems, and biofilm formation. The biofilm limits the penetration of antimicrobial drugs, thus protecting the entrapped microbial cells. The favorable microenvironment in biofilm supports the microbial proliferation and exchange of genetic material including the transmission of resistance genes. Anti-biofilm agents could attenuate adherence and virulence factors of pathogen instead of affecting its growth and there by enhance the sensitivity of microbes to antimicrobials and the host immune system [53]. Therefore, there is urgent need of anti-biofilm therapy and discovery of novel anti-biofilm agents. Essential oils and extracts of various parts of *M. communis* are potential sources of anti-biofilm agents investigated in several studies. In one of the studies, ethanolic leaf extract of *M. communis* inhibited the growth of MRSA clinical isolates with the

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marked MIC. The extract destroyed the pre-formed biofilm at sub-MIC concentration and affected the bacterial cells within the biofilm. The inhibition of biofilm development was due to significant decrease in the expression of MRSA genes *icaA*, *icaD*, *sarA,* and *bap*, which are involved in biofilm formation and development [54].

In another study by Caputo L. et al, the EO of *M. communis* leaves of Italy origin inhibited biofilm formation and disrupted the already formed biofilms at mature and ultra-mature stages of *E. coli* DSM 8579, *P. aeruginosa* ATCC 50071, *P. carotovorum* DSM 102074, *S. aureus* DMS 25923, and *L. monocytogenes* ATCC 7644, although, the disruption was effective at higher concentration of EO. Moreover, the EO showed cytotoxic activity towards neuroblastoma cell line SH-SY5Y probably due to acetylcholinesterase inhibitory activity [42]. As per the National Cancer Institute guidelines only natural substances with IC50 < 20 µg/ml are considered to be cytotoxic against the treated cells [55]. In a similar study polyphenolic extracts from myrtle leaf and pomegranate peel inhibited the biofilm formation process and disrupted the preformed biofilms of dental plaque pathogens *Streptococcus mutans*, *Streptococcus oralis*, *Streptococcus mitis*, and *Rothia dentocariosa* [56].

Several of the Myrtle compounds have been studied for their antioxidant, antimicrobial, and anti-cancer activities. Myrtenol, a bicyclic alcohol mono-terpene found in essential oil of *M. communis* [25] showed MIC and MBC of 128 µg/ml (bactericidal action) against all the clinical isolates of *S. aureus*. In combination with gentamycin and ciprofloxacin, myrtenol showed synergistic and additive effect, respectively, against all the strains of *S. aureus*. While in association with oxacillin indifferent effect was observed. The additive and synergistic effects are suggestive of the use of smaller concentration of these antibiotics and reduction of the side effects of the administration of these drugs. In same study the myrtenol at its sub-inhibitory concentrations strongly inhibited biofilm formation of *S. aureus* [57]. These results suggest that *M. communis* is a potential source of compounds having antibiofilm activity. Kwasny and Opperman classified antibiofilm agents as good if it is capable of inhibiting ≥80% of biofilm growth and inhibiting ≥40% of planktonic growth compared to untreated controls [58].

Myrtenol inhibited the biofilm formation of methicillin-resistant *Staphylococcus aureus* - a detrimental human pathogen and cause of extreme morbidity and mortality globally. Selvaraj A. et al, demonstrated that the synthesis of several of the virulence factors of MRSA was inhibited by myrtenol. Among the inhibited virulence factors include crucial extra-cellular lipase and hemolysin that degrade the phospholipid bilayer of host cells and erythrocytes of host, respectively. Myrtenol inhibited staphyloxanthin production in a dose dependent manner and myrtenol-treated MRSA cells were found to be sensitive to H_2O_2 treatment and healthy human blood [59].

In another study Selvaraj A, et al., demonstrated that myrtenol displayed a strong antibiofilm activity without having any harmful effect on growth and metabolic viability of *Acinetobacter baumannii* - Gram-negative, coccobacillus and opportunistic human pathogen frequently causing nosocomial infections such as ventilator-associated pneumonia, wound infections, respiratory and urinary tract infections. Treatment of *A. baumannii* with myrtenol leads to the reduction in thickness and coverage of biofilm on abiotic surfaces. Myrtenol not only disrupted the mature biofilms of *A. baumannii* strains but also inhibited the biofilm-associated virulence factors. In the same study, Selvaraj A, et al observed the suppression of the biofilm-associated genes in *A. baumannii* strains upon myrtenol treatment and increased their susceptibility towards hydrogen peroxide and conventional antibiotics *viz* amikacin, gentamicin, trimethoprim, and ciprofloxacin [60].

Antifungal activity

The increasing prevalence of fungal infections worldwide and gain of resistance to antifungal agents has prompted researchers to explore novel antifungal drugs and alternative agents. Essential oil of *M. communis* leaves exhibited antifungal activity against the clinical isolates of candida with MIC_{90} of 2-4 µg/ml [61].

In another study essential oil obtained from *M. communis* was used for treatment of Pityriasis versicolor, a disease characterized by scaly and hypo or hyperpigmented spots on skin caused by *Malassezia species*. Seven species of Malassezia isolated and identified from skin of 41 patients were

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susceptible to *M. communis* essential oil [62], suggesting the potential use of EO as cheaper, safe and nonhepatotoxic or nonnephrotoxic alternative antifungal treatment to pityriasis versicolor. The antifungal activity of *M. communis* against several other species of *Rhizoctonia solani, F. solani, A. flavus, Colletotrichum lindemuthianum, F. culmorum, and C. albicans* has been documented in other studies as well [61,63]. The essential oil of fruit berries from four genotypes (3 cultivated and one wild-type genotype) obtained from turkey showed a broad-spectrum antifungal activity against phytopathogenic fungi. The chemical composition and biological activity of four *M. communis* fruit essential oils differed according to the genotype, though 1,8-Cineole, linalool, a-terpineol, a-pinene, and geranyl acetate were found to be the major components of the fruit essential oils of all *M. communis* genotypes investigated [63]. It has been documented in several studies that the EO of several plants including *M. comminis* is more effective than the commercial antifungal drugs [61]. The EO of *M. communis* of different locations within Tunisia varying in chemical composition showed differential antifungal activity as reported by Yangui I, that the EO from Zaghouan was more active against *Biscogniauxia mediterranea* the causative agent of Charcoal canker disease which is widespread in forests of the Mediterranean basin mainly in Portugal, Italy, Spain, France, and North Africa [64].

Antioxidant activity

Phenolic compounds having antioxidant property and beneficial for human health, include polyphenols, phenolic acids, flavonoids, and tannins. These compounds are widely distributed in plants including *M. communis*. Due to the presence of double bonds and hydroxyl groups the phenolic compounds are potent antioxidants to inhibit the oxidation of free radicals, which otherwise can damage physiological molecules of lipids, proteins and DNA.

Iron chelating treatment is a standard cure for thalassemic and other kind of anemic patients. Some of the iron chelators like deferoxamine (DFO), deferiprone (L1) and deferasirox (ICL-670) are used to manage and treat thalassemia and other transfusion associated anemias. In one of the studies, Eslami S et al., used zero valent iron nanoparticles (ZVINs) synthesized from *Myrtus communis* leaf extract to treat iron overloaded mice. The reduced iron nanoparticles capped by plant constituents (biodegradable polyphenols, tannins and flavonoids) displayed potent antioxidant activity in vitro compared to standards vitamin C and quercetin. Compared to defroxamine (iron chelator) and MC extract, the MC-ZVINs showed adequate potency to chelate excessive iron from serum and liver tissue. Furthermore, the elevated liver enzymes aspartate transaminase, alanine aminotransaminase and alkaline phosphatase in iron-overloaded mice observed a remarkable reduction upon treatment with the MC-ZVINs. Therefore, MC-ZVINs were effective to prevent or at least reduce the adverse impacts of excessive iron in mice due to both antioxidant and Fe-chelating activities of MC-ZVINs [65].

Ben Hsouna A et al. also demonstrated the hepatoprotective effect of EO of *M. communis* of Tunisian origin. The essential oil extracted from its flowers by hydrodistilation is rich in α-pinene, 1,8-cineole, linalool and limonene. The oil reduced the plasma levels of hepatic markers and lipid in CCl_4 injected adult Wistar rats. The oil reversed the altered biochemical and oxidative stress profiles in CCl_4 injected Wistar rats. Lowering of thiobarbituric acid level in the liver tissue, and of liver enzymes in the serum indicated antioxidative mediated hepatoprotective effect of the essential oil [66]. In one of the recent in-vivo studies, it was found that *M. communis* leaf EO, encapsulated in maltodextrin (MMEO) exhibited gastroprotective activity in ethanol/HCl-induced acute gastric ulcers in Wistar rats. Gastric lesions and acidity were remarkably inhibited. It reduced the inflammation of gastric mucosa, counteracted gastric lipoperoxidation and prevented the reduction of antioxidant enzyme activity of superoxide dismutase, catalase and glutathione peroxidase [67].

M. communis has antioxidant potential to protect cells from oxidative stresses. *Myrtus communis* L. pulp and seed extracts obtained from liquor industrial production reduced the expression of proinflammatory cytokines (IL-1β TNF-γ, VEGF-A and IL-8) and modulated the cytochromes P450 expression in oxidative stress exposed human skin fibroblasts (HFF1). The myrtus extracts exerted a synergic effect in association with vitamin D in reducing the inflammation and reactive oxygen species production. The antioxidant potential observed was same as that of ascorbic acid treatment

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[68]. In another study Cruciani S et al found that the myrtle byproducts obtained from residual of industrial liqueur processing of myrtyle berries possessed high antisenescence activity in H_2O_2 induced oxidative stressed adipose-derived stem cells, wherein a significant upregulation of pluripotency associated genes (Oct-4, Sox2, and NANOG) and inhibition of the senescence process was observed [69]. These findings are suggestive of the protective role of myrtly extract from oxidative stress related damages and imparting a regenerative potential to stem cells after stressful conditions.

The composition and the amount of bioactives vary according to the origin and environmental conditions of place of origin. Myrtle berries size and bioactive composition from maritime zones is greater than that of inland zones [70]. Nutraceutical properties of myrtle berries are incentives for their exploitation in the food, cosmetic, and pharmaceutical industries. Two ellagitannins, Oenothein B and eugeniflorin D2 were isolated in large amounts from berry seeds. Oenothein B used in preparation of popular liquor 'Mirto di Sardegna' in Italy showed anti-inflammatory and antifungal activity against fluconazole-sensitive and -resistant candida strains (Table 2). Oenothein B inhibited IL-8 release induced by TNF-α or IL- 1β in human adenocarcinoma epithelial gastric cells [71].

Plant extract have been investigated for their role in inhibiting the virulence factors including enzymes secreted by pathogens involved in colonization of the host. Nabati et al, screened about 137 plant extracts for their inhibitory activity against urease enzyme from jack beans. Among them Myrtus communis leaf extract showed a remarkable inhibitory activity. Urease of H. pylori catalyzes the hydrolysis of urea to produce ammonia and carbon dioxide, thus protecting the bacteria in the acidic environment of the stomach [5].

Essential oil of Tunisian M. communis flowers exhibited a strong growth inhibition of Gram-positive bacterial strains. The essential oil in combination with nisin decreased the aerobic, psychrotrophic and *Enterobacteriaceae* bacterial count in raw minced meet stored at 4°C, which was consistent with the in vitro treatment of nisin and McEO with *Listeria monocytogenes* [72].

Myrtucommuacetalone-1 (MCA-1) a novel and anti-inflammatory bioactive compound isolated from *M. communis* inhibited superoxide, hydrogen peroxide and nitric oxide production in activated macrophages. The compound was less toxic towards the various cell lines of MDBK kidney cells, liver cells, 3T3NIH mouse fibroblasts, and J774.2 macrophages compared to cyclohexamide. MCA-1 inhibited the expression of inducible nitric oxide synthase via abolishing the transcription factor (NFkB) phosphorylation and its translocation to the nucleus [73]

Myrtus communis L. has a folkloric repute for the management of diarrhea and dysentery, for which Mekonnen Sisay et al., provided a scientific evidences. In his study the acclaimed traditional use of 80% methanol extract (80ME) and solvent fractions of the leaves of *Myrtus communis L.* were evaluated for antidiarrheal effect in castor oil induced diarrheal mice model. The 80ME, chloroform and methanol fractions significantly delayed the onset of diarrhea. In addition, 80ME and the solvent fractions significantly decreased the weight and frequency of fecal outputs. 80ME and solvent fractions produced a significant anti-motility effect and decline in the weight and volume of intestinal contents [74].

Type 1 diabetes (T1DM) leads to hyperglycemia due to absolute deficiency of insulin secretion. T2DM affects 90 to 95% of diabetic patients with impaired glucose tolerance due to the reduced tissue response to insulin. A potential therapeutic approach for TD2M is to inhibit the carbohydrate digestive enzymes (α-amylases and α -glucosidases) to delay the absorption of glucose and alleviate the post-prandial rise in blood glucose level. *Myrtus communis* essential oil was one among the 62 essential oils tested for α-amylase inhibition activity, wherein it showed 20% inhibition of the enzyme [75]. In one of the recent studies more than 1100 aqueous plant extracts were screened for modulation of insulin secretion in MIN6 β cells. *M. communis* was one of the ten best plant extracts that could inhibit the insulin secretion [76].

Essential oils of several plants, *Origanum compactum, Mentha spicata, Thymus surplus, Origanum majorana, Myrtus communis*, and *Artemisia herba-alba* from Morocco were screened for antioxidant activity. Among six essential oils screened, *M. communisn* EO showed antioxidant activity like that of positive control butylated hydroxytoluene [77].

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Food products enriched with herbal ingredients are sources of pro-health components including polyphenolic compounds (Table 2) whose beneficial effect depends on the diet and its effect on the intestinal microbiota and their enzymatic activity. Intragastric treatment of rats with aqueous leaf extract of *M. communis* and *Laurus nobilis L.* from Zagreb, Croatia positively affected the rats' health. The number of colonies of normal flora Lactobacilli and Bifidobacteria increased. A significant reduction in glycolytic enzymatic activity and increase in antioxidant capacity of the kidneys and liver [78] was evident.

In other study the intragastric application of laurel and myrtle EOs to rats reduces glycolytic activity of intestinal microbiota. In addition, the level of lipid parameters (cholesterol, triglycerides, low-density lipoprotein cholesterol and very low-density lipoprotein cholesterol) and atherogenic indicators is reduced which could lead to the cardiovascular protection. Myrtle EO showed a better antioxidant capacity in most tissues, except the kidneys, where it causes a pro-oxidative effect [79].

Abbreviations

MIC; minimum inhibitory concentration
MBC: minimum bactericidal concentration
MFC: minimum fungicidal concentration
EO; essential oil
MQSIC; minimal QS inhibitory concentration
MRSA; methicillin resistant *Staphylococcus aureus*
ZVINs; zero valent iron nanoparticles
MC-ZVINs; *Myrtus communis* zero valent iron nanoparticles
TNF; tumor necrosis factor
IL; interleukin
80ME; 80% methanol
T2DM; type 2 diabetes mellitus.
T1DM; type 1 diabetes mellitus.
MCA-1; Myrtucommuacetalone-1
NFkB; nuclear factor kappa B
CCl_4; carbon tetrachloride
ND: not determined

Table 1. Chemical composition of essential oil and extracts of *M. communis* leaves.

Source/Country origin	Compounds	Usage	Method of identification	Ref.
Ethanolic leaf extract/Saudi Arabia	Acetol (0.64%), Methyl acrylate (0.50%) , Methyl acetate (0.19%) , Ethyl glycolate (0.13%) , Methyl pyruvate (0.57%), Ethyl orthoformate (1.99%) , 3-Hydroxymethylfuran (0.17%), Isopropyl isopropoxyacetate (0.36%) , Dihydroxyacetone (1.01%), Ethyl diethoxyacetate (0.23%), 1,2-Cyclopentanedione (0.32%), 5-MethyIfurfural (0.10%), (−)-β-Pinene (0.07%), 2,4-Dihydroxy-2,5-dimethyl-3(2H)-furanone (0.25%), 5-Diethoxymethyl-3-ethoxy-4,5-dihydro-isoxazole (0.12%) , Phenol (0.04%), 5-Diethoxymethyl-3-ethoxy-4,5-dihydro-isoxazole (0.14%), Glutaconic anhydride (0.09%), 2,2-Diethyl-3-methyl-1,3-oxazolidine (0.06%), D-Limonene (0.65%), 1, 8-Cineole (3.96%), 5-Hydroxyazouracil (0.17%), (+)-4-Carene (0.18%), Linalool (2.80%), 4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl- (0.49%), α-Terpineol (1.16%), L-α-Terpineol (1.12%), Catechol (0.49%), 5-Hydroxymethylfurfural (1.62%), Linalyl formate (1.93%), Linalyl acetate (0.97%), α-Terpinyl acetate (1.02%), Pyrogallol (9.11%), Methyleugenol (0.12%), β-Caryophyllene (0.56%), α -Isomethyl ionone (0.21%), Tyrosol (0.11%), Cyclohexanecarboxaldehyde, 6-methyl-3-(1-methylethyl)-2-oxo-1-(3-oxobutyl)- (0.25%), 1,1,8a-Trimethyloctahydro-2,6-naphthalenedione (27.60 %), 3-Methyl-2-butenoic acid, undec-2-enyl ester (0.81%), Phytol acetate (0.42%), Aspidinol (0.08%), L-Ascorbyl 2,6-Dipalmitate (0.66%), Phytol (0.19%)	Antibacterial activity against Gram positive bacteria	GC-MS	[4]

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Source/Country origin	Compounds	Usage	Method of identification	Ref.
Pulp of myrtle berries	Gallic acid; 52.2 ±0.9 mg/kg, Hydrolysable tannins; 498.0±20.5 mg/kg, Ellagic acid; 350.5 ±15.0 mg/kg Flavonols: Quercetin-3-O-galactoside 191.0 ±6.7 mg/kg, Quercetin-3-O-rhamnoside 66.6 ±3.0 mg/kg Anthocyanins: Cyanidin-3-glucoside 1.8±0.2 mg/kg, Petunidin-3-glucoside 3.6±0.3 mg/kg, Peonidin-3-glucoside 13.5 ±0.3 mg/kg, Malvidin-3-glucoside 42.0 ±2.4 mg/kg	Antioxidant and anti-inflammatory activities	HPLC 1100 system coupled with with a DAD detector UV 6000	[68]
Seeds of Myrtle berries	Gallic acid; 137.0 ±6.8 mg/kg, Hydrolysable tannins; 11989.8 ±205.2 mg/kg, Ellagic acid; 726.9 ±28.3 mg/kg Flavonols: Quercetin-3-O-galactoside; 104.9 ±9.3 mg/kg, Quercetin-3-O-rhamnoside; 9.3 62.0 ±2.9 mg/kg Anthocyanins: Cyanidin-3-glucoside; ND, Petunidin-3-glucoside; ND, Peonidin-3-glucoside; ND, Malvidin-3-glucoside; ND	Antioxidant and anti-inflammatory activities	HPLC 1100 system coupled with with a DAD detector UV 6000	
EO obtained from myrtle flowers gathered from the region of Elkef in Tunisia.	α-Pinene (35.20%), β-Pinene (0.24%), Myrcene (1.21%), Limonene (8.94%), 1,8-cineole (17.00%), Linalool (6.17%), α-Terpineol (3.86%), Myrtenol (0.42%), Linalyl acetate (0.85%), Myrtenyl acetate (1.26%), Terpenyl acetate (4.30%), Geranyl acetate (4.42%), Methyl eugenol (6.98%), Transcaryophyllene (4.04%), α-Humulene (0.48%), Carophyllene oxide (2.49), Monoterpene hydrocarbons (46.07%), Oxygenated monoterpenes (40.77%), and Sesquiterpenes (6.98%)	Antioxidant and antimicrobial activity	GC-MS	[72] Dhifi W, 2020
EO of M. communis leaves, Italy	Limonene (28.9%), α-Pinene (15.1%), Mirtenyl acetate (13.6%), Linalool (13.50%), Linalyl acetate (5.00%)	Anti α-amylase activity	GC-MS	[72]

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Source/Country origin	Compounds	Usage	Method of identification	Ref.
EO from arial parts of M. communis, Northern Portugal	1.8-cineole (14.80%), β-pinene (9.40%), verbenone (9.15%), borneol (8.72%), camphor (8.13%), terpinene-4-ol (7.66%), α-pinene (6.94%), linalool (3.78%), α-terpineol (3.52%), camphene (3.12%), D-limonene (3.16%), mirtenol (2.20%), α-terpinolene (1.74%), 2.4-tujadiene (0.78%), 3-carene (0.76%), cariophyllene oxide (0.73%), nerol (0.64%), α-terpinene (0.55%), o-cimene (0.41%), thujene (0.23%), and methyl-eugenol (0.20%)	Anti L. monocytogenes activity	GC-MS	[45]
EO of M. communis leaves, Serbia	α-Pinene (0.38%), Limonene (0.60%), 1,8-Cineole (10.27%), Linalool (3.78%), Terpinolene (1.41%), *cis* Verbenol (0.91%), *trans* Verbenol (0.95%), Camphor (1.91%), α-Terpineol (7.12%), Nerol (5.97%), Geraniol (0.63%), Linalyl acetate (3.66%), Myrtenyl acetate (7.00%), Terpinyl acetate (1.01%), Neryl acetate (3.40%), and Geranyl acetate (16.36%)	Antifungal activity against *Malassezia* sp. clinical isolates	GC-MS	[62]
EO of the aerial parts of M. communis, Iran	α-Pinene (27.87%), 1,8-Cineole (20.15%), Linalool (10.26%), α-Terpineol (7.64%), Linalyl acetate (6.17%), Germanyl acetate (4.87%), α-Terpinyl acetate (4.04%), Caryophyllene oxide (1.57%), trans-Caryophyllene (1.57%), Methyl eugenol (1.48%), α-Humulene (1.35%), β –Pinene (0.88%), 4-Terpineol (0.67%), δ-3-Carene (0.63%), γ-Terpinene (0.59%), α-Thujene (0.54%), and Others (1.93%)	Antifungal activity against fluconazole resistant and sensitive *C. albicans*	GC-MS	[29]
70% ethanol extract M. communis leaves, Italy.	Phenolic acids (mg/KgDW) Gallic acid (1199.3), Hydrolysable tannins (21,858.3), myricetin-3-O-galactoside (1926.4), myricetin-3-O-rhamnoside (3902.9), quercetin-3-O-glucoside (104.1), quercetin-3-O-rhamnoside (192.0), quercetin 3-O-galactoside (85.9), and vitexin (280.0)	Antibacterial and antifungal activity of nanofibers encapsulated with leaf extract and soaked in seed extract	HPLC coupled with DAD detector UV 6000	[46]

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Source/Country origin	Compounds	Usage	Method of identification	Ref.
M. communis leaves, Croatia	5-O-galloylquinic acid (7.96%), Caffeic acid (1.81%), Catechin (0.05%), Digalloylquinic acid (0.79%), Ellagic acid (0.03%), Epicatechin (0.05%), Epicatechingallate (0.02%), Luteolin (1.11%), Luteolin glucoside (2.63%), Myricetin (14.48%), Myricetin-3-O-arabinoside (0.05%), Myricetin-3-O-galactoside (33.20%), Myricetin-3-O-rhamnoside (36.68%), Quercetin-3-glucoside (0.85%), Quercitrin (0.25%)	The effect of on colonic probiotic bacteria of rat and its health	UPLC-MS	[78]
EO from M. communis leaves, Croatia	α-thujene (0.013 mg/ml), α-pinene (193.75 mg/ml), Camphene (1.08 mg/ml), β-pinene (2.35 mg/ml), Myrcene (2.68 mg/ml), α-phellandrene (1.66 mg/ml), 3-carene (0.48 mg/ml), p-cymene (3.45 mg/ml), d-limonene (69.25 mg/ml), Eucalyptol (244.6 mg/ml), Linalool (19.36 mg/ml), Terpinen-4-ol 31.62, α -terpineol (26.26 mg/ml), α -terpinyl acetate (4.53 mg/ml), Methyleugenol (9.88 mg/ml), Camphor (0.56 mg/ml), Carvone (2.14 mg/ml), Geraniol (6.21 mg/ml), Myrtenyl acetate (146.10 mg/ml), Estragole (0.013 mg/ml), Geranyl acetate (20.7 mg/ml), Myrtenol (3.92 mg/ml)	Antioxidative and antilipidemic effect in rats	GC-MS	[79]
Flower EO of *M. communis* from Tunisia	α -Pinene (35.20%), β -Pinene (0.24%), Myrcene (1.21%), Limonene (8.94%), 1,8-Cineol (17.0%), Linalool (6.17%), α -Terpineol (3.86%), Myrtenol (0.42%), Acetate linalyl (0.85%), Myrtenyl acetate (1.26%), Terpenyl acetate (4.30%), Acetate geranyl (4.42%), Methyl eugenol (6.98%), Trans caryophyllene (4.04%), α -Humulene (0.48%), Caryophyllene oxide (2.49%)	Hepato protective effects of EO in CCl4-induced hepatotoxicity in Wistar rats.		[66]
EO prepared by hydro distillation from *M. communis* leaves of Italy origin	3*Z*- Hexenal (0.1 ± 0.0%), 2*E*- Hexenal (0.1 ± 0.03%), Isobutyl isobutyrate (0.1 ± 0.02%), Heptyl isobutanoate (3.2 ± 0.3%), α-Thujene (0.4 ± 0.01%), α-Pinene (14.7 ± 1.2%), Sabinene (0.3 ± 0.03%), β-Pinene (0.3 ± 0.04%), δ-3-Carene (0.3 ± 0.02%), β- Myrcene (0.1 ± 0.01%), Butyl-2-methylbutanoate (0.2 ± 0.01%), α-Terpinene (0.1 ± 0.02%), 1,8-Cineole (21.9 ± 2.3%), *E*-β-Ocimene (1.1 ± 0.5%), γ-Terpinene (0.4 ± 0.03%), Terpinolene (0.1 ± 0.02%), Linalool (9.1 ± 1.6%),	Antibacterial, antibiofilm, and anti-acetylcholinesterase activities	GC-MS	[42]

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Source/Country origin	Compounds	Usage	Method of identification	Ref.
	Myrcenol (0.2 ± 0.03%), *cis*-*p*-Menth-2-*n*-1-ol (0.1 ± 0.02%), *allo* Ocimene (0.8 ± 0.04%), *trans*-Pinocarveol (0.1 ± 0.01%), 3E-6Z-Nonadienol (0.1 ± 0.03%), Terpinen-4-ol (0.4 ± 0.05%), α-Terpineol (2.3 ± 0.4%), Myrtenal (0.1 ± 0.04%), Myrtenol (0.8 ± 0.03%), Methyl chavicol (0.2 ± 0.05%), Fraganol (0.1 ± 0.02%), Linalool acetate (0.8 ± 0.06%), *trans*-Pinocarvyl acetate (0.6 ± 0.03%), Carvacrol (0.1 ± 0.02%), Myrtenyl acetate (29.8 ± 2.4%), *iso*-dihydro-Carveol acetate (0.3 ± 0.02%), Carvyl acetate (0.1 ± 0.03%), α-Terpinyl acetate (0.5 ± 0.04%), Citronellyl acetate (0.1 ± 0.0%), Geranyl acetate (2.6 ± 0.5%), Methyl eugenol (0.9 ± 0.02%), *Z*-Caryophyllene (1.3 ± 0.06%), γ-Elemene (0.1 ± 0.01%), α-Humulene (1.1 ± 0.02%), *p*-Menth(1,8 dien)-9-ol (0.4 ± 0.02%), Bisabolol (0.2 ± 0.0%), Thymohydro quinone (0.7 ± 0.06%), Flavesone (0.2 ± 0%), Caryophyllene oxide (0.3 ± 0.02%), Humulene epoxide II (0.3 ± 0.01%), *allo*-Aromadendrene epoxide (0.1 ± 0.02%), *n*-Octadecanol (0.5 ± 0.06%)			
EO of M. communis leaves encapsulated in maldodextrin, Portugal	α -pinene (11.10%), Limonene (1.63%), 1,8-Cineole (9.98%), Linalool oxide (0.38%), α -Terpinolene (0.46%), Linalool (14.92%), α -Terpineol (4.64%), Linalyl acetate (4.61%), Myrtenyl acetate (30.59%), Camphene (0.83%), Neryl acetate (0.38%), Geranyl acetate (1.62%), Methyleugenol (2.51%), α -Humulene (0.77%)	Gastroprotective activity in ethanol/HCl-induced acute gastric ulcers in Wistar rats	GC-MS	[67]

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Table 2. Antibacterial activity of M. c*ommunis* from different origins.

Plant parts/Country origin	Methods of preparation	Microorganisms	Zone of inhibition (mm)	MIC	MBC/MFC	Ref.
Leaves of *Myrtus communis* (Linn), *Artemisia dracunculus*, and *Satureja khuzestanica*, Iran	Polyherbal toothpaste obtained from leaf extracts	*S. mutans, L. caseie, S. sanguis, S. salivarius*, and *C. albicans*	17-30 (*L. caseie)*, 10-25 *(C. albicans)* and 15-20 for *S. salivarius.*	ND	ND	[39]
Leaves of *Myrtus communis*, Iran	Aquatic and methanolic extracts	*P. gingivalis, A. actinomycetemcomitans*, and *P. intermediate*.	At 50 mg/ml of methanolic extract: 16 *(A. actinomycetemcomitans*), 17 (*P. gingivali),* and 20 (*P. intermediate*). At 50 mg/ml of aqueous extract: 10 (*P. gingivalis),* 15 (*A. actinomycetemcomitans*), and 16 (*P. intermediate*)	10 mg/ml for both the extracts	ND	[40]
Leaves of *Myrtus communis*, Iran	Ethanolic extract	Twenty-six clinical isolates of MRSA	9 – 17.6	1.56 – 25 mg/ml	3.125 – 50 mg/ml	[54]
Leaves of M. communis, Italy	Essential oil	*E. coli* DSM 8579, *P. aeruginosa* ATCC 50071, *P. carotovorum* DSM 102074, *S. aureus* DMS 25923, and *L. monocytogenes* ATCC 7644	ND	6, 3, 4, 5, and 3 mg/ml, respectively.	ND	[42]
Leaves of M. communis, Ethiopia	80% methanol. 10 mg/ml used of zone	Staphylococcus aureus (ATCC 25923)	21.83 + 0.44	0.80 (mg/ml)	4.00 (mg/ml)	[43]

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Plant parts/Country origin	Methods of preparation	Microorganisms	Zone of inhibition (mm)	MIC	MBC/MFC	Ref.
	of inhibition determination	Escherichia coli (ATCC 25922)	13.33 + 0.33	0.16 mg/ml	0.8 mg/ml	
		Salmonella typhi (ATCC 13062)	13.33 + 0.33	0.032 mg/ml	0.8 mg/ml	
		Shigella flexneri (ATCC 12022)	20.83 + 0.93	0.16 mg/ml	4.00 mg/ml	
		Pseudomonas aeruginosa (ATCC 27853)	14.83 + 0.44	0.8 mg/ml	4.00 mg/ml	
		Proteus mirabilis (ATCC 29906)	12.17 + 0.73	0.8 mg/ml	4.00 mg/ml	
Myrtenol purchased from Merck/Sigma-Aldrich® (Darmstadt/Germany)	Purchased	Ten laboratory strains and two reference strains ATCC-25923 and ATCC-13150 of *S. aureus*	ND	128 µg/ml	128 µg/ml	[57]
Myrtenol purchased from Sigma-Aldrich, India.	Purchased	MRSA reference strain ATCC 33591 and Three MRSA clinical strains	ND	MIC of 600 µg/ml and MBIC of 300 µg/ml	ND	[59]
Myrtenol purchased from Sigma-Aldrich, India.	Purchased	Two reference strains of *Acinetobacter baumannii*, AB-ATCC19606, AB-MTCC 9829, and two clinical isolates AB-A103 and AB-A42-4	ND	MIC 500 µg/ml for AB-ATCC19606, AB-MTCC 9829, AB-A103 and 600 µg/ml for AB-A42-4 and MBIC	ND	[60]

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Plant parts/Country origin	Methods of preparation	Microorganisms	Zone of inhibition (mm)	MIC	MBC/MFC	Ref.
				of 200 µg/ml for all strains.		
Oenothein B isolated from myrtle seeds	Successively extracted in hexane and 70% acetone in water.	Clinical isolates from human gut C. albicans C. parapsilosis C and C. tropicalis	ND	<8 - 64 µg/ml	ND	[71]
M. communis flowers, Tunisia	EO obtained by hydro-distillation in a Clevenger	Gram positive				[72]
		B. subtilis ATCC 6633	18 ± 0.7	0.10 ± 0.7 %	0.78 ± 0.1%	
		B. cereus ATCC 14579	22 ± 0.5	0.39 ± 0.8%	0.78 ± 0.3%	
		S. aureus ATCC 25923	20 ± 0.7	0.39 ± 0.4%	1.56 ± 0.5%	
		S. epidermis ATCC 12228	15 ± 0.4	0.19 ± 0.4%	1.56 ± 0.2%	
		E. faecalis ATCC29212	15 ± 0.5	0.10 ± 0.7%	0.78 ± 0.04%	
		L. monocytogenes ATCC19117	22 ± 0.4	0.40 ± 0.2%	0.8 ± 0.022%	
		Gram negative				
		S.enterica ATCC 43972	16 ± 0.6	1.26 ± 0.3%	3.12 ± 0.8%	
		E. coli ATCC 25922	14 ± 0.3	0.78 ± 04%	1.56 ± 0.4%	
		P. aeruginosa ATCC 9027	15 ± 0.5	1.56 ± 0.5%	3.12 ± 0.7%	
Arial parts of M. communis, Northern Tunisia	EO obtained by hydro distillation in Clevenger	Listeria monocytogenes	ND	31.25 µL/mL		[45]
Leaves of M. communis, Serbia	EO obtained by hydro distillation in Clevenger	*M. furfur*	ND	31.25µL/mL	62.5µL/mL	[62]
		M. sympodialis	ND	62.5 µL/mL	125 µL/mL	
		M. slooffiae	ND	31.25 µL/mL	62.5 µL/mL	

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Plant parts/Country origin	Methods of preparation	Microorganisms	Zone of inhibition (mm)	MIC	MBC/MFC	Ref.
		M. globose	ND	31.25 µL/mL	350 µL/mL	
		M. obtuse	ND	62.5 µL/mL	125 µL/mL	
		M. japonica	ND	31.25 µL/mL	62.5 µL/mL	
		M. restricta	ND	125 µL/mL	600 µL/mL	
Leaves of M. communis, Italy	EO by Hydrodistillation in Clevenger	*Clinical isolates of candida spp. C. albicans C. glabrata, C. krusei, C. tropicalis* and *C. parapsilosis*	ND	2 µg/ml		[61]
Leaves of M. communis, Iran	Total extract in 80% methanol by sonication	*C. albicans* (ATCC 76645) Nystatin sensitive	ND	125 µg/ml	500 µg/ml	[80]
		C. albicans Nystatin-resistant	ND	125 µg/ml	>1000µg/ml	
	Methanol fraction	*C. albicans* (ATCC 76645) Nystatin sensitive	ND	125 µg/ml	>1000µg/ml	
		C. albicans Nystatin-resistant	ND	62.5 µg/ml	>1000µg/ml	
	Ethyl acetate fraction	*C. albicans* (ATCC 76645) Nystatin sensitive	ND	250 µg/ml	>1000	
		C. albicans Nystatin-resistant	ND	250 µg/ml	>1000µg/ml	
	Chloroform fraction	*C. albicans* (ATCC 76645) Nystatin sensitive	ND	62.5 µg/ml	1000 µg/ml	
		C. albicans Nystatin-resistant	ND	62.5 µg/ml	1000 µg/ml	

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Plant parts/Country origin	Methods of preparation	Microorganisms	Zone of inhibition (mm)	MIC	MBC/MFC	Ref.
	Petroleum ether fraction	*C. albicans* (ATCC 76645) Nystatin sensitive	ND	125 µg/ml	250 µg/ml	
		C. albicans Nystatin-resistant	ND	125 µg/ml	250 µg/ml	
Aerial parts of M. communis, Iran	EO by Hydrodistillation in Clevenger	*C. albicans* fluconazole resistant	ND	3200 µg/ml	3800 µg/ml	[29]
		C. albicans fluconazole sensitive	ND	3000 µg/ml	3600 µg/ml	

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