

Phytochemistry and pharmacological properties of *Myrtus communis* L.

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Myrtus communis L. (Myrtaceae) is known as True Myrtle. *M. communis* extracts and essential oil are important in drug development with some pharmacological activities in the Middle East especially in Iran. For a long time *M. communis* has been used in traditional medicines for the treatment of lung disorders and as an antiseptic, anti-inflammatory, mucolytic, carminative and astringent remedy. *M. communis* has recently been shown to have antioxidant, analgesic, antibacterial and antifungal activities and larvicide, insecticide and repellency effects. Myrtucommulone A & B and semi-myrtucommulone are oligomeric, nonprenylatedacylphloroglucinols which are reported from leaves of myrtle. α -pinene, 1,8-cineol, limonene and linalool were identified as the major constituents in *M. communis* essential oil. Due to the easy collection of the plant and being widespread and also the remarkable biological activities, this plant has been regarded as an important medicinal plant in Iran. This article presents comprehensive analyzed information on the Botanical, phytochemical and pharmacological aspects of *M. communis*.

Keywords: *Myrtus communis*, Myrtaceae, Essential oil, Pharmacology

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Myrtus communis commonly known as “True Myrtle” is a flowering shrub and native to Mediterranean regions and Middle East especially in Iran. It belongs to Myrtaceae family in the order of Myrtales that contains about 140 genera and more than 4000 species¹.

Myrtus species probably originates from the Middle East, somewhere South of Caucasian, but has spread as an ornamental plant up to southern Europe and North of Africa. *Myrtus* genus has 24 fossile species of which two are still alive. *M. communis* has been known as *Moord* in Iran and distributed in the northern parts of Iran and South parts such as Fars, Kerman, Yazd and Hormozgan Provinces. Myrtle is an evergreen shrub or small tree, growing to 5 m tall. The leaf is entire, 3–5 cm long, with a fragrant essential oil. The star-like flower has 5 petals and sepals, and numerous stamens. Petals usually are white. The fruit is a round blue-black berry containing several seeds. The flower is pollinated by insects, and the seeds are dispersed by birds that eat the berries. *M. communis* L. (Myrtaceae) has been used since ancient times for medicinal and food and purposes.

The essential oil obtained from the leaves by steam distillation is also important in perfumery, liqueur and cosmetic industries. For a long time, *M. communis* has been used as a folk medicine for treatment of various conditions such as lung disorders and as an antiseptic, anti-inflammatory, mucolytic, carminative and astringent remedy¹. The fruit decoction was used to bath new borns with reddened skin, while the decoction of leaves and fruits was useful for sore washing. The decoction of the leaves is still used for vaginal lavage, enemas and against respiratory diseases. The extract of the myrtle herb is used to make the hair grow longer in a short period of time. The fresh, clear aroma of this oil is excellent at clearing the airway and as is considered safe for young and old alike. In addition a recent systematic review of herbal medicines, have proven a positive effect for myrtle compounds in the treatment of rhino sinusitis^{2,3}.

M. communis possess several pharmacologic, biologic and medical activities such as antibacterial, antiviral, antifungal, anti-inflammatory, analgesic, antioxidant, antimutagenic, anti-hemorrhagic, hepatoprotective, wound healing and anti-hyperglycemic activities⁴⁻⁷.

A number of chemical constituents such as volatile substances, terpenoids, triterpene, flavonoids,

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tannins, fatty acids have been isolated from different parts of the plant¹.

Although review and systemic analysis of chemistry, pharmacology and clinical properties of *M. communis* have been reported, we provided an overview on traditional and local knowledge, ethnobiological and ethnomedicinal issues, identification of pharmacologically important molecules and pharmacological studies on this useful plant.

The aim of this article is to introduce *M. communis* as a potent medicinal plant by highlighting its traditional applications as well as the recent findings for its pharmacological and clinical applications.

Chemical composition

The commonly known phytochemical compounds from *M. communis* are volatile substances, terpenoids, triterpenes, flavonoids, phenolics, tannins and fatty acids¹. α -pinene (37.8%), 1,8-cineol (23.1%), limonene (17.1%) and linalool (10.1%) were identified as the major constituents of the *M. communis* leaves essential oil from Iran¹. The leaves are rich in flavonoids such as quercetin, catechin and myricetin derivatives. The fruits of *M. communis* are mostly composed of volatile oils, tannins, sugars, flavonoids and organic acids such as citric and malic acids.

M. communis flowers growing wild in Morocco have been reported to contain 1.75% of essential oil. The most abundant components found in the flower oil were α -pinene (48.54%) followed by 1,2-cineole (14.75%), myrtenal (5.01%), myrtenol (4.01%), myrtenyl acetate (3.45%), myrcene (2.09%), linalool (2.01%) and geraniol (1.67%)⁸.

Myrtucommulone A, myrtucommulone B and semi-myrtucommulone which are oligomeric, nonprenylatedacylphloroglucinols have been reported in *M. communis* leaves⁹. Galloylatedalkylphloroglucinol glycosides such as gallomyrtucommulone A, gallomyrtucommulone B, gallomyrtucommulone C and gallomyrtucommulone D were also isolated from the leaves¹⁰.

M. communis fruits are rich in oleic acid (67.07%), palmitic acid (10.24%), and stearic acid (8.19%)¹⁰.

Potential of *M. communis* in phytotherapies

M. communis is used in traditional Iranian medicine to treat various infectious and inflammatory diseases such as lung disorders, fungal infections and urinary disorders^{1,11}. It has been used since ancient times for medicinal, food and spices purposes (Akin *et al.*, 2010). Although the antioxidant, antibacterial,

antifungal and analgesic effects of *M. communis* extracts have been well documented^{8,9,12-14}, so far the therapeutic potential has not been exploited by the western countries. In recent years, accumulating evidence indicated that not only is *M. communis* important in treating inflammation and pain, but that it also contains antihyperglycemic, antibacterial, antiviral, antifungal, antioxidant, antimutagenic, anti-hemorrhagic, hepatoprotective, wound healing and insecticidal activities^{4-7,15}.

Analgesic properties

The leaves of *M. communis* have been functionally used as a traditional crude drug as a pain killer. Results suggest an anti-inflammatory potential for myrtle leaves are an open door for new and effective compounds¹⁴. This suggestion is based on the observation that the nonprenylatedacylphloroglucinol constituents, myrtucommulone and semi-myrtucommulone (Fig. 1), suppress various functional cellular leukocyte responses, including the biosynthesis of PGs and LTs, the release of leukocyte elastase, and the formation of peroxides that are of relevance for initiation and maintenance of inflammatory processes.

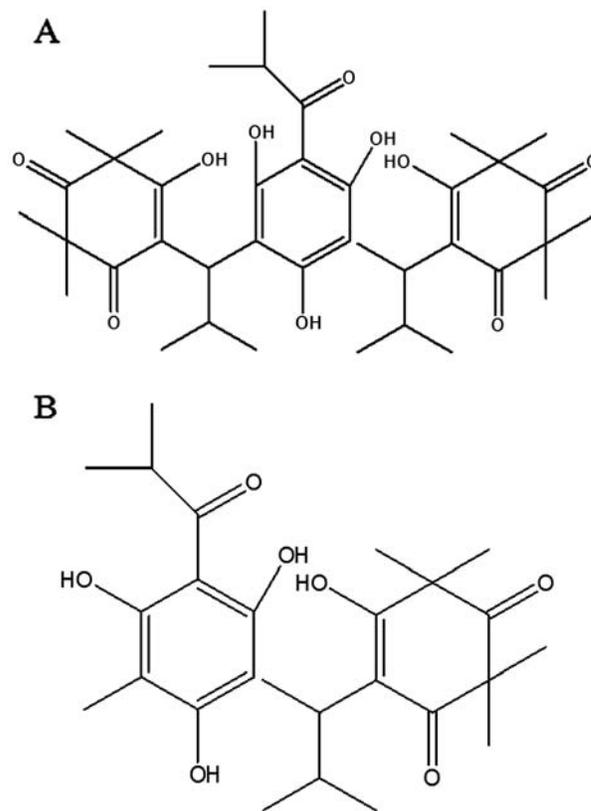


Fig. 1—Structures of A= Myrtucommulone; B= Semi-Myrtucommulone from *M. communis*

Myrtucommulone and semi-myrtucommulone were identified as direct inhibitors of 5-LO and COX-1 and were able to suppress the biosynthesis of PGs and LTs in vitro and *in vivo*. In addition, these compounds inhibited the release of elastase and the formation of ROS, apparently by their ability to block receptor-coupled Ca²⁺ mobilization^{9,14}.

Tests involving thermal stimuli which tend to detect only narcotic analgesics have also shown that the aqueous extract of *M. communis* leaves with dose of 150 mg/kg (i.p) has narcotic analgesic properties. However, animal testing methods have a number of limitations because perception of pain in human is a complex psychophysiological process¹⁶.

Antioxidant activity

An antioxidant is defined as 'any substance that, when present at low concentrations compared to those of an oxidizable substrate, significantly delays or prevents oxidation of that substrate. Antioxidants are of interest to biologists and clinicians because they help to protect the human body against damages induced by reactive free radicals generated in atherosclerosis, ischemic heart disease, cancer, Alzheimer's disease, Parkinson's disease and even in aging process. There are many evidences that natural products and their derivatives have efficient anti-oxidative characteristics, consequently linked to anti-cancer, hypolipidemic, anti-aging and anti-inflammatory activities.

Anti-oxidative capacities of *M. communis* different parts were evaluated by determining DPPH radical scavenging capacity. Radical scavenging activity (% inhibition) of the essential oil of myrtle flowers was the highest (89.15 ± 2.01%) at the concentration of 200 µg/ml. It was clear that the concentration of 200 ppm of *M. communis* essential oil gave a percentage inhibition of DPPH (89.15 ± 2.01%) nearly of the same concentration of vitamin C which was 94.03 ± 1.01. The essential oil was able to neutralized or reduce the oxidation of DPPH with IC₅₀ of 72.16 µL/ml. The essential oil contained mainly monoterpene hydrocarbons and these compounds are known to possess good antioxidant activity⁸. The essential oil of *M. communis* leaves was also able to reduce the stable radical DPPH to the yellow-colored DPPH-H reaching 50% of reduction with an IC₅₀ of 5.99 µL/ml⁵.

The methanol extract of the fruits of *M. communis* from the Mediterranean region of Turkey was evaluated for its antioxidant activities. The extract

exhibited a high level (82.5%) of free radical scavenging activity¹⁰.

Both semi-myrtucommulone and myrtucommulone have showed powerful antioxidant properties, protecting linoleic acid against free radical attack and inhibiting its autoxidation and its FeCl₃- and EDTA-mediated oxidation. Semi-myrtucommulone was found to be more powerful than myrtucommulone and was further evaluated in rat liver homogenates for activity against lipid peroxidation induced by ferric-nitrosyltriacetate, and in cell cultures for cytotoxicity and the inhibition of TBH- or FeCl₃-induced oxidation. It is established that semi-myrtucommulone could serve as a novel dietary antioxidant lead⁹.

Antibacterial properties

Isolation of microbial agents less susceptible to regular antibiotics and recovery of increasing resistant isolates during antibacterial therapy is rising throughout the world which highlights the need for new principles. It is reported that the essential oil of *M. communis* leaves have significant antimicrobial activity against *S. aureus*, *S. epidermidis*, *E. coli*, *B. subtilis* and *Serratiamarcescens*¹². The antibacterial activity of *M. communis* essential oil against *E. coli*, *S. aureus* and *Candida albicans* also demonstrated and it is shown that the large amounts of α-pinene (37.8%), 1,8-cineol (23.1%), limonene (17.1%) and linalool (10.1%) in *M. communis* could be responsible for the activity observed¹³.

The antimicrobial activity of topical formulation of 1% *Eugenia caryophyllus* and 4% *M. communis* essential oils have shown significantly high antimicrobial activity against: *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Aspergillus niger*, *Aspergillus flavus*, *Trachophyton mentagraphyte*, *Trachophyton vericusom*, *Microsporum cannis*, *Candida albicans* and *Cryptococcus neoformans* than commonly used drugs¹⁷.

Repellency and insecticidal effects

Insect repellents are used to prevent nuisance bites from mosquitoes as well as other blood feeding arthropods and may aid in lowering disease transmission. Since the plant-based repellents are safer than DEET (N, N-diethyl-toluamide) which is a broad-spectrum repellent with longer-lasting protection against many species of biting arthropods including mosquito³¹, the effect of essential oil of myrtle as a botanical repellent was compared with it¹⁹. The myrtle essential oil is suggested to be useful and

safe in preventing mosquito bites and have potential use as a botanical repellent. This suggestion is based on that the mean of protection time of 50% myrtle essential oil showed considerable repellency on human subjects and provided 4.36 hours protection¹⁹.

The major components of the essential oil responsible for the repellency activity are monoterpenes, primarily 1, 8-cineole which was detected in moderate percentages (18-23%) in the essential oil of *M. communis*¹⁹. The insecticidal effect of myrtle at 1.6 mg/cm² was reported 62.2% against lab-bred *Plasmodium papatasi* on animal model²⁰.

It is shown that the myrtle oil has insecticidal activity against adults of *E. kuehniella*, *P. interpunctella* and *A. obtectus*. Due to the linalool and 1,8-cineole constituents of the myrtle oil, this plant could also be used effectively against *S. oryzae* and *R. dominica* maghale¹⁵.

Hepatoprotective properties

The aqueous extract of *M. communis* leaves was screened for hepatoprotective activity in paracetamol induced hepatotoxicity in albino rats. The degree of hepatoprotection of the aqueous extract of *M. communis* leaves was measured by estimating biochemical parameters like serum glutamate-pyruvate transaminase, Serum glutamate oxaloacetate- transaminase, serum alkaline- phosphatase , total protein and level of serum bilirubin (both total and direct). Hepatoprotective activity of the extract at a dose of 200 mg/kg and 400 mg/kg body weight, orally, exhibited significant reduction in serum hepatic enzymes. Furthermore, in histopathological studies, the rats treated with extract along with toxicant (carbon tetrachloride and acetaminophen) showed sign of protection against the toxicants²¹.

Antidiabetic effects

Anti-hyperglycemic effect of *M. communis* leaves extract in streptozotocin induced diabetic mice had been reported³⁵. Recently, it was found that phenolic compounds are responsible for this activity. Phenolics extracted from the leaves of *M. communis* have shown statistically significant anti-hyperglycemic effect²². Histopathological studies have revealed no appreciable gross lesions in pancreas, liver and kidney²².

No pathological reports are available on efficacy of *M. communis* in diabetic rats. The findings also revealed that myrtle phenolics exhibit marked antidiabetic effect when administered at 800 mg/ kg body weight and moderate antidiabetic response at

400 mg/kg in non diabetic rats as evidenced by regenerative changes in islet cells of the pancreas. The study also revealed that the phenolic compounds alone do not exhibit any toxic effects as evidenced by absence of histological changes in the liver and kidney in non-diabetic control rats²².

Antigenotoxicity and antimutagenic effects

The effect of extracts from leaves of Myrtle on the SOS reponse induced by aflatoxin B1 (AFB1) and nifuroxazide was investigated in a bacterial assay system, i.e. the SOS chromotest with *Escherichia coli* PQ37. Aqueous extract, the total flavonoids oligomer fraction (TOF), hexane, chloroform, ethyl acetate and methanol extracts and essential oil obtained from *M. communis* significantly decreased the SOS response induced by AFB1 (10 µg/assay) and nifuroxazide (20 µg/assay). Ethyl acetate and methanol extracts showed the strongest inhibition of the induction of the SOS response by the indirectly genotoxic AFB1. The methanol and aqueous extracts exhibited the highest level of protection towards the SOS-induced response by the directly genotoxic nifuroxazide. In addition to anti-genotoxic activity, the aqueous extract, the TOF, and the ethyl acetate and methanol extracts showed an important free-radical scavenging activity towards the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical. These results suggest the future utilization of these extracts as additives in chemoprevention studies²³.

Also, the different extracts from *M. communis* have shown no mutagenicity when tested with *Salmonella typhimurium* strains TA98 and TA100 either with or without metabolic system (S9). On the other hand, each of the tested extracts exhibited a significant protective effect against the mutagenicity induced by aflatoxin B1 (AFB1) in *Salmonella typhimurium* TA100 and TA98 assay systems, and against the mutagenicity induced by sodium azide in TA100 and TA1535 assay system²⁴.

Cytotoxic activity

As mentioned above, myrtucommulone is a unique, nonprenylated acylphloroglucinol contained in the leaves of *M. communis*¹⁴. This compound potently induced cell death of different cancer cell lines (EC₅₀= 3-8 µM) with characteristics of apoptosis, visualized by the activation of caspase-3, -8 and -9, cleavage of poly ADP-ribose polymerase (PARP), release of nucleosomes into the cytosol, and DNA fragmentation. It was much less cytotoxic for non-transformed human peripheral blood mononuclear

cells (PBMC) or foreskin fibroblasts (EC_{50} cell death = 20-50 μ M), and MC up to 30 μ M hardly caused processing of PARP, caspase-3, -8 and -9 in human PBMC. Myrtucommulone -induced apoptosis was mediated by the intrinsic rather than the extrinsic death pathway. Thus, MC caused loss of the mitochondrial membrane potential in MM6 cells and evoked release of cytochrome C from mitochondria. Interestingly, *Jurkat* cells deficient in caspase-9 were resistant to myrtucommulone-induced cell death and no processing of PARP or caspase-8 was evident. Conclusively, myrtucommulone induces apoptosis in cancer cell lines, with marginal cytotoxicity for non-transformed cells, via the mitochondrial cytochrome c/Apaf-1/caspase-9 pathway²⁵.

Conclusion

The objective of this article has been to show the recent advances in the exploration of *M. communis* in phytotherapy and to illustrate its potential as a therapeutic agent. With the current information, it is evident that *M. communis* has pharmacological functions including anti-inflammatory, analgesic, antidiabetic, antibacterial, antifungal and antioxidant activities, among others. As the current information shows, it is also possible that monoterpenoids from the essential oil and nonprenylatedacyl phloroglucinols isolated from the leaves might be useful in the development of new drugs to treat various diseases. However, the present results suggest a possibility that non-prenylated acylphloroglucinols can be further developed as a potential disease-curing remedy. It must be kept in mind that clinicians should remain cautious until more definitive studies demonstrate the safety, quality and efficacy of *M. communis*. For these reasons, extensive pharmacological and chemical experiments, together with human metabolism will be a focus for future studies. Last but not the least, this article emphasizes the potential of *M. communis* to be employed in new therapeutic drugs and provide the basis for future research on the application of transitional medicinal plants.

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