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Revisión / Review

Myrtus communis leaves: source of bio-actives, traditional use, their biological properties, and prospects.

[Hojas de *Myrtus communis*: fuente de bioactivos, uso tradicional, sus propiedades biológicas y perspectivas]

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Section Review

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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, the inhabitants of this area have been using it for its cultural and medicinal properties. Because of the vast diversity of biomolecules in its aerial parts, it exhibits several biological properties, including antioxidant, antimicrobial, and anticancer properties. This review retrospect the research on the source, biological activities with empirical evidence, chemical composition, applications, and cellular targets of extracts and essential oils obtained from *M. communis* leaves, which provides a perspective for further studies on the applications and formulations of extract and EO of *M. communis* leaves. The efficacy of constituents' individually, in association with other bioactive constituents, or in combination with available commercial drugs would provide insights into the development of these bio-actives as future drugs and their evolving future potential applications in the pharmaceutical, food, and aroma industries.

Keywords: *Myrtus communis*; Cellular targets; Antimicrobial; Antioxidants; Anticancer

Resumen: *Myrtus communis* L., comúnmente conocido como arrayán verdadero, es una planta medicinal originaria de la zona mediterránea. Desde la antigüedad, los habitantes de esta zona lo utilizan por sus propiedades culturales y medicinales. Debido a la gran diversidad de biomoléculas en sus partes aéreas, exhibe varias propiedades biológicas, incluidas propiedades antioxidantes, antimicrobianas y anticancerígenas. Esta revisión retrospectiva de la investigación sobre la fuente, las actividades biológicas con evidencia empírica, la composición química, las aplicaciones y los objetivos celulares de los extractos y aceites esenciales obtenidos de las hojas de *M. communis*, lo que brinda una perspectiva para futuros estudios sobre las aplicaciones y formulaciones de los extractos y EO de *M. communis*. La eficacia de los componentes individualmente, en asociación con otros componentes bioactivos o en combinación con medicamentos comerciales disponibles proporcionaría información sobre el desarrollo de estos bioactivos como medicamentos futuros y sus futuras aplicaciones potenciales en las industrias farmacéutica, alimentaria y aromática.

Palabras clave: *Myrtus communis*; Objetivos celulares; Antimicrobiano; Antioxidantes; Anticancerígeno

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

INTRODUCTION

Antibiotics manufactured worldwide in an estimated quantity of about 100,000 tons annually remarkably affect the lives of bacteria living on earth. The number of bacterial strains that are resistant to antibiotics is increasing, with some strains becoming resistant 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. The family Myrtaceae, compised of nearly 100 genera and 3000 species, grows in tropical, subtropical, and temperate regions of the world. There are two species in the genus *Myrtus* L*:* the common myrtle *Myrtus communis* L, found in the wild throughout the Mediterranean basin, and the Saharan myrtle *Myrtus nivellei* Batt, mostly found in the central Sahara. *Myrtus communis* L is a perennial shrub or small tree of 1.8−2.4 meters tall with small foliage and deep fissured bark **(Figure No. 1).** *Myrtus* blooms profusely from mid-June to early July. Dipterans and hymenopterans are primarily responsible for pollinating its white hermaphrodite flowers (González-Varo *et al*., 2009). Its fruit berries turn blue-black after maturing from mid-October to late November. Passerine birds, primarily Sylviidae and Turdidae, disperse the seeds (González-Varo *et al*., 2010). The plant has an upright stem, and its branches form a close, full head that 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.

Figure No. 1
Branches,leaves, ande berries of M. communis from Herbarivirtual, Area of Botany, Department of Biology, University of Balearic Island. http://herbarivirtual.uib.es

Habitat

Widespread throughout the central Saharan mountains, *Myrtus nivellei* Batt. & Trab. grows 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 (Migliore *et al*., 2012). Myrtle is indigenous to west Asia, North Africa, and southern Europe and is scattered in southern America, the northwestern Himalayas, and Australia. Myrtle is also cultivated in gardens, especially in the Northwest regions of India and the Fifa Mountains of Saudi Arabia (Mir *et al*., 2020).

For this review, the articles published on *Myrtus communis* were searched using key words *Myrtus communis*, leaves, extract, essential oil, and traditional medicine in the PMC database using the National Library of Medicine, the National Center for Biotechnology Information (**https://www.ncbi.nlm.nih.gov**), and Google Scholar (**https://scholar.google.com**). 328 articles surfaced in these databases. The articles were screened for indexing in the Web of Science, and 68 non-indexed articles were excluded from the list. If it was deemed appropriate to the subject of interest and relevance, the related data was correctly filtered. From the remaining 260 articles, 173 were excluded from the list due to the following reasons: i) the article wherein *M. communis* is simply referred to once and the referred article dates to 2017 or prior ii) The article is about physiochemical changes responsible for the adaptation of *M. communis* to various environmental conditions. Out of the remaining 87 articles, 27 were accessible only by abstracts, while the complete pdfs of 60 articles were retrieved using the Saudi Digital Library (**https://sld.edu.sa/SLDPotal/en/Publishers.aspx**). The main goal of this review was to evaluate the use of leaves in traditional medicine and their evolving future potential use in the pharmaceutical, food, and aroma industries.

Traditional applications of M. communis

Fragrant leaves of *M. communis* are being significantly used in the remedy of diverse ailments in different countries and regions of the world. In Iran, the aqueous maceration of leaves after filtration and concentration is taken for wound healing, depression, and polymenorrhea (Nabati *et al*., 2012). In Algeria, the decoction of the leaf powder is used to treat hypertension, eczema, other skin diseases, respiratory disorders, and hemorrhoids (Bouzabata *et al*., 2015). Dried leaf powder mixed with butter is applied topically to treat scabies in Ethiopia (Amsalu *et al*., 2018). 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 (Seyoum & Zerihun, 2014). Tea mixed with leaves has been drunk on daily basis to relieve stress and anxiety in Turkey (Akaydin *et al*., 2013). Mirto, a liqueur used as a beverage in Italy, has *M. communis* leaves as one of the ingredients (Franco *et al*., 2019). The dried aqueous leaf extract is used to treat sinus infections in China and France (Jabri *et al*., 2016; Mahmoudvand *et al*., 2016). 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 (Alipour *et al*., 2014; Sen *et al*., 2017). The aqueous juice has also been used for the preparation of food and wines in Italy (Alipour *et al*., 2014; Sen *et al*., 2017). Myrtle oil is used as an adjunct for the treatment of insomnia in Ethiopia (Birhanie *et al*., 2016). *M. communis* leaves are used in mouthwash and in the treatment of candidiasis (Gortzi *et al*., 2008). A decoction of leaves and fruits is generally used orally for the treatment of constipation, stomachaches, hypoglycemia, cough, and poor appetite, and externally for wound healing (Serce *et al*., 2010). Other uses of its leaves include cattle feed, cut foliage, and potted plants (Bruna *et al*., 2007). The assorted specific applications of the leaves of the myrtle plant are given in Table No. 1 and Table No. 2.

Table No. 1
Chemical composition of essential oil and extracts of *M. communis* leaves

Source/Country origin	Compounds	Usage	Method of identification	Reference
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%), 1,1,8a-Trimethyloctahydro-2,6-naphthalenedione (27.60 %),	Antibacterial activity against Gram positive bacteria	GC-MS	Mir *et al*., 2020

	3-Methyl-2-butenoic acid, undec-2-enyl ester (0.81%), Phytol acetate (0.42%), Cyclohexanecarboxaldehyde, 6-methyl-3-(1-methylethyl)-2-oxo-1-(3-oxobutyl)- (0.25%), Aspidinol (0.08%), L-Ascorbyl 2,6-Dipalmitate (0.66%), Phytol (0.19%)			
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	Cruciani *et al*., 2019
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-rhamnoside; 9.3 62.0 ± 2.9 mg/kg, Quercetin-3-O-galactoside; 104.9 ± 9.3 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	Antioxidant and antimicrobial activity	GC-MS	Dhifi *et al*., 2020

	acetate (1.26%), Terpenyl acetate (4.30%), Geranyl acetate (4.42%), Monoterpene hydrocarbons (46.07%), Oxygenated monoterpenes (40.77%), Methyl eugenol (6.98%), Transcaryophyllene (4.04%), α-Humulene (0.48%), Carophyllene oxide (2.49), and Sesquiterpenes (6.98%)			
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	Dhifi *et al.*, 2020
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	Saraiva *et al.*, 2021
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	Barac *et al.*, 2018
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	Antifungal activity against fluconazole resistant and sensitive *C. albicans*	GC-MS	Sharifzadeh & Shokri, 2016

	(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%)			
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	Bellu *et al*., 2022
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	Berendika *et al*., 2022
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-	Antioxidative and antilipidemic effect in rats	GC-MS	Odeh *et al*., 2022

	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)			
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.		Ben Hsouna *et al*., 2019
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%), 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 ±	Antibacterial, antibiofilm, and anti-acetylcholinesterase activities	GC-MS	Caputo *et al*., 2022

	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	Mansour *et al*., 2022

EO from *M. communis* leaves, Iran	2e-hexenal 0.19, Propyl butanoate (= propyl butyrate) 0.53, α-pinene 22.95, β-pinene 0.21, Myrcene 0.23, Dehydroxy-trans linalool oxide 0.21, Dehydroxy-cis linalool oxide 0.38, Para cymene 0.26, Limonene 3.63, β-phellandrene 4.26, 1,8-cineole 31.19, Trans linalool oxide (furanoid) 0.28, Cis linalool oxide (furanoid) 0.31, Linalool 12.14, Trans pinocarveol 0.35, Terpinen-4-ol 0.18, Alpha terpineol 5.06, Trans carveol 0.22, Nerol 0.16, Linalyl acetate 4.41,Carvacrol 0.20, α-terpinyl acetate 1.49, Neryl acetate 0.35, Geranyl acetate 2.74, Methyl eugenol 0.35, E-caryophyllene 0.16, humulene 0.21, Humulene epoxide II 0.16, Octadecane 2.28, Nonadecane 4.91	Antibacterial activity *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Serratia marcescens*, and *Bacillus subtilis*	GC-MS	Raeiszadeh *et al*., 2018

Table No. 2
Antibacterial activity of *M. communis* 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	Sadeghi-Nejad *et al*., 2018
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.*	10 mg/mL for both the extracts	ND	Rahimvand *et al*., 2018

			actinomycetemcomitans), and 16 (*P. intermediate*)			
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	Khaleghi & Khorrami, 2021
Leaves of *M. communis*, Italy	Essential oil	*S. aureus* DMS 25923, *P. aeruginosa* ATCC 50071, *P. carotovorum* DSM 102074, and *L. monocytogenes* ATCC 7644, *E. coli* DSM 8579	ND	6, 3, 4, 5, and 3 mg/mL, respectively.	ND	Caputo *et al*., 2022
Leaves of *M. communis*, Ethiopia	80% methanol. 10 mg/ml used of zone of inhibition determination	Staphylococcus aureus (ATCC 25923)	21.83 + 0.44	0.80 (mg/mL)	4.00 (mg/mL)	Sisay *et al*., 2019
		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	Cordeiro *et al*., 2020
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	Selvaraj *et al*., 2019
Myrtenol purchased from Sigma-Aldrich, India.	Purchased	Two reference strains of *Acinetobacter baumannii*, AB-ATCC19606, AB-MTCC 9829, and two clinical isolates AB-A103	ND	MIC 500 µg/mL for AB-ATCC19606, AB-MTCC 9829, AB-A103 and 600 µg/mL for AB-A42-	ND	Selvaraj *et al*., 2020

		and AB-A42-4		4 and MBIC 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	Franco *et al*., 2019
M. communis flowers, Tunisia	EO obtained by hydro-distillation in a Clevenger	**Gram positive**				Dhifi *et al*., 2020
		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		Saraiva *et al*., 2021
Leaves of *M. communis*, Serbia	EO obtained by hydro distillation in Clevenger	*M. furfur*	ND	31.25µL/mL	62.5µL/mL	Barac *et al*., 2018
		M. sympodialis	ND	62.5 µL/mL	125 µL/mL	
		M. slooffiae	ND	31.25 µL/mL	62.5 µL/mL	
		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 Hydrodisti-llation in Clevenger	*Clinical isolates of candida* spp, *C. albicans*, *C. glabrata*, *C. krusei*, *C.*	ND	2 µg/mL		Cannas *et al*., 2013

		tropicalis and *C. parapsilosis*				
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	Torabi *et al*., 2022
		C. albicans Nystatin-resistant	ND	125 µg/mL	>1000 µg/mL	
	Methanol fraction	*C. albicans* (ATCC 76645) Nystatin sensitive	ND	125 µg/mL	>1000 µg/mL	
		C. albicans Nystatin-resistant	ND	62.5 µg/mL	>1000 µg/mL	
	Ethyl acetate fraction	*C. albicans* (ATCC 76645) Nystatin sensitive	ND	250 µg/mL	>1000	
		C. albicans Nystatin-resistant	ND	250 µg/mL	>1000 µg/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	
	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	Sharif-zadeh & Shokri, 2016
		C. albicans fluconazole sensitive	ND	3000 µg/ml	3600 µg/mL	

The diverse biological properties attributed to *M. communis* are due to the presence of diverse compounds in its aerial parts (Table No. 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, galloyl-quinic acids, gallic and ellagic acids, caffeic, and fatty acids (linoleic, palmitic, oleic, and stearic acids) (Nicoletti *et al*., 2018).

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, and 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%) (Boelens & Jimenez, 1992), 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%) (Touaibia, 2017). 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%) (Chalchat *et al*., 1998; Touaibia, 2017). 1,8 cineole (55.09%) and α-pinene (33.14%) were predominant components of another Tunisian myrtle EO, while lacking myrtenyl acetate (Mimica-Dukić *et al*., 2010; Mulas & Melis, 2011; Bekhechi *et al*., 2019). 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 (Flamini *et al*., 2004). 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 principal components, with few differences among the samples (Tuberoso *et al*., 2006; Usai *et al*., 2020). The essential oil of *M. comminis* from Iran is rich in α-pinene (27.87%), 1,8-cineole (20.15%), and linalool (10.26%) (Sharifzadeh & Shokri, 2016). *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 (Giuliani *et al*., 2022). The chemical composition of the extract, or EO, varies according to the season, growing condition, and part of the plant used in the process of obtaining the extract, or EO. Compared to crude extract, a new dibenzofuran-type phloroglucinol compound named 1,1'-(1,3,7,9-tetrahydroxydibenzo[b,d]furan-2,8-diyl)bis(ethan-1-one) isolated from the leave of *M. communis* native to Pakistan showed higher antibacterial activity in a dose-dependent manner against *S. aureus* and *E. coli* (Khan *et al*., 2020).

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

Different types of drying methodologies have been tried for the extraction of compounds from *M. communis*. Convective air, an oven, and microwave were used to dry the aerial parts of *M. communis* and were subsequently used for the 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 was the quantity of compounds isolated higher, but their antioxidant activity was also enhanced (Snoussi *et al*., 2021). 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 concentrations of bioactives (V González de Peredo *et al*., 2018). Bouaoudia-Madi *et al*. (2019), used the ultrasound-assisted extraction method to isolate polyphenolic compounds from the 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 the amplitude of the ultrasound waves. The optimal conditions of 70% (*v/v)* ethanol, 7.5 min irradiation time, and a solvent-to-solid ratio of 30% were found to be optimal for the isolation of polyphenols from *M. communis* extract. Moreover, ultrasound-assisted extraction has been found to be more efficient than microwave-assisted extraction and conventional solvent extraction methods (Bouaoudia-Madi *et al*., 2019).

Scientific validations for traditional use

To validate the traditional usage of *M. communis* leaves, dose dependence of a biological property associated with a medicinal plant is of paramount importance. The scientific observations that validate the biological property *in-vivo* and *in-vitro* in a dose-dependent manner serve as a proof-of-concept for the traditional use of medicinal plants. The second important property besides dose dependence of a biological property attributed to a medicinal plant is the effectiveness of the biological property, which is

determined by several factors including bioavailability, stability, cytotoxicity, and the slow and steady release of the compound within the host.

Topical application of EO of *M. communis* leaves of Italian origin induced a dose-dependent significant reduction in ear edema and myeloperoxidase activity in croton oil-induced ear edema in mice and a dose-dependent reduction in granuloma formation in a cotton pellet-induced granuloma model (Maxia *et al*., 2011). In another study, a polyphenol-enriched fraction of the *M. communis* leaves of Moroccan origin showed dose-dependent cytotoxicity against HL60 (IC_{50}=19.87 μM) and K562 (C_{50}=29.64 μM) leukemia cell lines with the highest activity at 100 mg/kg body weight of mice. The dosage was safe for the noncancerous Vero cell line and the mice. These fractions reduced the inflammation of the paws of rats better than that of diclofenac (10 mg/kg) in a time-dependent manner in the carrageenan-induced inflammatory edema model. In the same study, the authors found that the topical application of 0.1% polyphenol-enriched fractions significantly reduced the wound surface area, like that of 1% madecassol ointment. Moreover, the biochemical tests suggested that polyphenol-enriched fraction was safe as it did not show any effect on the weight or function of the kidney and liver (Mechchate *et al*., 2022). Few more *in-vivo* studies validated the safe use of essential oils or extracts. One of the studies from Iran evaluated *M. communis* EO against chronic toxoplasmosis induced by *Toxoplasma gondii* in mice. The oral administration of EO significantly decreased the mean number and diameter of *T. gondii* brain tissue cysts in a dose-dependent manner, with the highest being at 200 and 300 mg/kg/day. It was confirmed by the induction of innate immunity due to increased production of INF-© and IL-12 at the above-mentioned dosage (Shaapan *et al*., 2021). In another study, the anti-inflammatory role of the aqueous and ethanolic extracts was validated *in vivo*. The extracts exhibited significant activity against acute inflammation in a dose-dependent manner and antinociceptive activity against acetic acid-induced writhing in mice. The ethanolic (0.05 g/kg) and aqueous extracts (0.005, 0.015, and 0.03 g/kg) demonstrated anti-inflammatory effects against chronic inflammation, with the percentage of swelling inhibition in the ear of the experimental animal by the aqueous extract (0.2 g/kg body weight) being 66% compared to 83% by diclofenac (15 mg/kg). The percent inhibition of granuloma formation by the aqueous extract was 57.9%, compared to 64.4% by diclofenac, though the lethal dose value (LD_{50}) of intraperitoneal injection of the aqueous and ethanolic extracts was much higher of 0.473 g/kg body weight of mice (Hosseinzadeh *et al*., 2011). The folkloric use of *Myrtus communis* L. for the treatment of diarrhea and dysentery has been empirically supported by the study of Sisay *et al*. (2017). In his study, the acclaimed traditional use of 80ME and solvent fractions of *Myrtus communis* L. leaves was assessed for their ability to treat diarrhea in a model using castor oil-induced diarrheal mice. 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 a decline in the weight and volume of intestinal contents (Sisay *et al*., 2017). Type 1 diabetes (T1DM) leads to hyperglycemia due to an absolute deficiency of insulin secretion. Because of the diminished tissue response to insulin, T2DM impairs glucose tolerance in 90-95% of diabetic patients. Inhibiting the carbohydrate-digesting enzymes (α-amylases and α-glucosidases) could be used as a treatment for TD2M to delay glucose absorption and reduce the postprandial rise in blood sugar levels. *Myrtus communis* essential oil was one of the 62 essential oils tested for α-amylase inhibition activity, wherein it showed 20% inhibition of the enzyme (Capetti *et al*., 2020). 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 insulin secretion (Hager *et al*., 2021). Further research work is required to evaluate the role of *M. communis* EO in treating T1DM *in vivo* models.

The traditional use of the EO or extract is not only in its crude form but has also been substantiated by the compounds of *M. communis*. Linalool, one of the major bioactive components of *M. communis* leaves, significantly inhibited the biofilm formation of *P. aeruginosa*, *E. coli*, *A. bambini*, and *S. marcescens.* Linalool also inhibited the production of QS-regulated violacein pigment in *C. violaceum* 12472 in a dose-dependent manner, with 69% inhibition at 50 mg/ml (Alyousef *et al*., 2021).

Furthermore, two compounds, myricetin-3-*o*-galactoside and myricetin-3-*o*-rhamnoside, exhibited antioxidant activity by scavenging the free radical 1,1-diphenyl-2-picrylhydrazyl, inhibiting the lipid peroxidation, and inhibiting xanthine oxidase (Hayder *et al*., 2008). Both compounds inhibited the xanthine oxidase (57% and 59%, respectively, at 100 µg/ml concentration) and modulated the expression of genes involved in oxidative stress. These observations are the empirical proof for the attributed antioxidant activity of *M. communis*.

Formulations

The constituents of EO are volatile, unstable, and easily degradable if not protected from oxidation, heat, and light. For effective pharmacokinetic and therapeutic effects of *M. communis* bioactives, several delivery systems of nanogels, liposomes, niosomes, micelles, and others, can be explored and tested (Figure No. 2). *M. communis*, owning its diverse biological properties and being in traditional use since ancient times in human history, demands future research in stabilization, prolonged release, targeted delivery, and maintenance of the activity of its constituents in the human host. A few formulations have been tested (Figure No. 3) for the safe use of *M. communis* bioactives in vivo. Liposomes and niosomes would be the most promising carriers for the stable and steady release of the EO components. Niosomes (nonionic surfactant vesicles), being osmotically active, chemically stable, and less toxic, are promising nanocarriers for target delivery of natural compounds, or EOs. Encapsulation, to maintain the physiochemical and biological characteristics of the EOs, extracts, and purified compounds, would allow *M. communis* to be used in various commercial sectors of the food, textile, pharmaceutical, cosmetics, and environmental industries. Nanoemulsions one of the methods of nanoencapsulation to increase the stability and solubility of *M. communis* EO without affecting their biological properties, have been reported for several other EOs of *Aniba canelilla*, peppermint pennyroyal *(Mentha pulegium)*, and thyme *(T. vulgaris)* (Ghodrati *et al*., 2019; Khezri *et al*., 2020; Kreutz *et al*., 2021; Moazeni *et al*., 2021). Several materials, including chitosan, sodium alginate, and poly(ε-caprolactone) are at disposal for the preparation of nanoemulsions or nanogels of *M. communis* EOs in the future. More importantly, the validation of the antimicrobial, antioxidant, anti-inflammatory, and anticancer properties of these nanoemulsions or nanogels *in vivo* would be imperative to broaden their application in cosmetics, food processing, and environmental safety against insecticides and pesticides that would otherwise pollute not just the environment but also food.

One study already documented the niosomal formulation of M. communis leaf EO using non-ionic surfactants and cholesterol, wherein the authors found increased stability and bioavailability of EO's constituents. More interestingly, this formulation not only retained but increased the EO's efficacy, as evidenced by enhanced antimicrobial activity against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Serratia marcescens*, and *Bacillus subtilis* (Raeiszadeh *et al*., 2018). The *M. communis* leaves have been used in different forms, like toothpaste, suppositories, etc. Polyherbal toothpaste, herbal suppository of myrtle, and oak gall extracts were prepared in a polyethylene glycol base. The suppositories treated the bacterial vaginosis, especially *Trichomonas vaginalis*, in adult women without major complications or side effects (Askari *et al*., 2020). Without compromising the normal flora of the cheese, the essential oil 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 (Saraiva *et al*., 2021), thus finding its use in food processing technology. Myrtle extract finds use in nanotechnology as nanofibers of small diameter make surface pressure a highly dominant phenomenon by which the adhered molecules are released once their concentration in the solution drops. It is hypothesized that the hydrophobicity of the novel seed or leaf extract encapsulated, or soaked nanofibers could be 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 they exhibited a moderate effect on Gram-negative *E. coli*. Similarly, two discs of nanofibers soaked in seed and leaf extracts decreased the 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*

(Bellu *et al*., 2022). The use of these nanofibers as devices for the controlled release of molecules could be a promising choice to counteract Gram-positive microorganisms. More *in-vivo* studies are required to validate the bioavailability and stability of the formulation of extracts, EOs, and purified compounds. The *M. communis* leaves exhibit diverse biological properties by targeting several cellular processes.

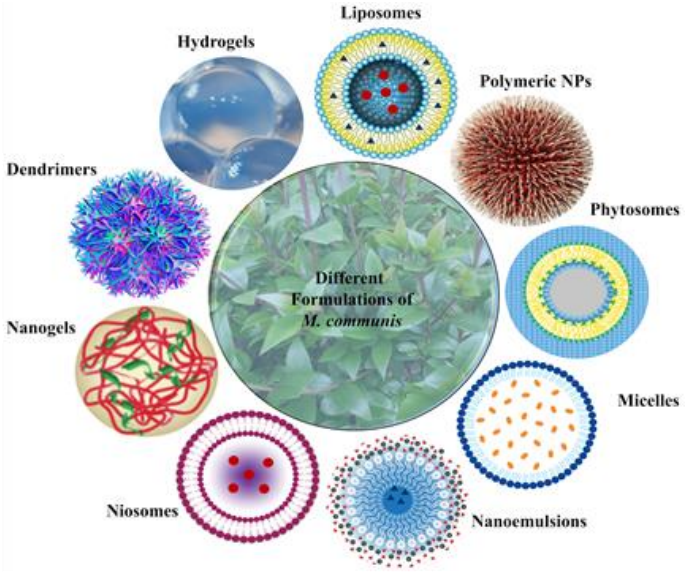

Figure No. 2
Proposed delivery systems for EOs or extract or purified compounds of *M. communis*

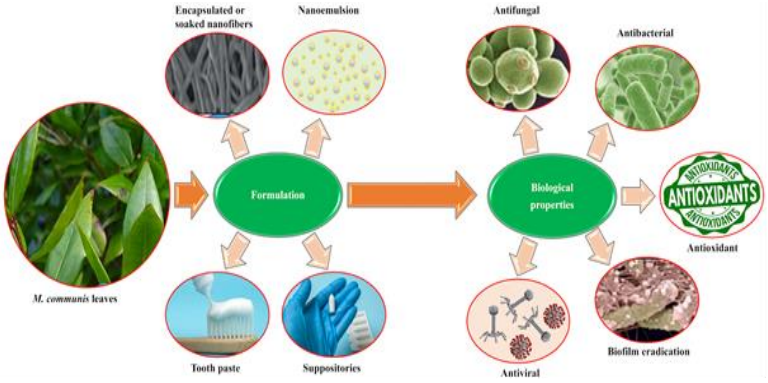

Figure No. 3
Biological properties and formulations of *M. comunis* leaf extract and its essential oils

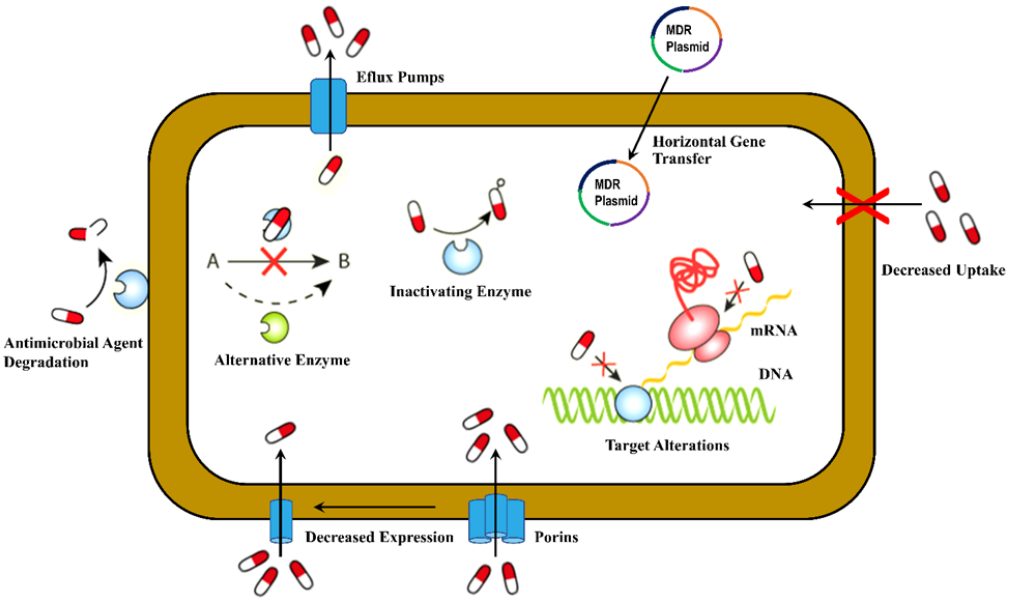

Figure No. 4
Antimicrobial resistance mechanisms

Figure No. 5
Cellular targets of *M. communis* bioactives

Biological properties

Antibacterial activity

Emergence of infectious diseases caused by diverse bacterial species and multidrug resistance has created havoc in health systems. Bacteria have evolved many antibiotic resistance mechanisms to withstand the actions of antibiotics. Antimicrobial resistance is achieved either by stopping the access of drug to its target or modifying or bypassing the target of the drug (Figure No. 4). Efflux pump expression, membrane impermeability, destruction/modification of the drugs would be the strategies used by microbes to restrict the access of drug to its target. Mutation in drug target and expression of alternative proteins would be the other strategies used by pathogens to modify/bypass the action of drug. Other strategies to gain antimicrobial resistance could be dormancy under stress conditions and the formation of biofilms. Therefore, there is a need of new antimicrobials to combat the antimicrobial resistance. The phytoconstituents can effectively combat the antimicrobial resistance by inhibiting the drug modifying/degrading enzymes, reducing the expression of efflux pumps, targeting the alternative or mutated proteins, and reverting the dormant microbes to active metabolic phase of growth. Furthermore, in association with antimicrobials, natural products could be effective in controlling the emergence of infectious diseases, combating antimicrobial resistance, reducing the administration dose of a drug, and thereby reducing the dose-dependent toxic effects. About 80% of human bacterial infections are believed to be associated with biofilm-forming microorganisms (Wenzel, 2007). 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* (Nishikawara *et al*., 2007; Nomura *et al*., 2020; Patel, 2022). These microorganisms form biofilms on mucosal epithelial cells, dental surfaces, and orthodontic prosthetics (Marsh, 2004). 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* (Sadeghi-Nejad *et al*., 2018). 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* (Rahimvand *et al*., 2018). 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 the above-mentioned oral infections (Zougagh *et al*., 2019). 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 *et al* (2022), found the EO of *M. communis* very effective against three Gram negative (*E. coli* DSM 8579, *P. aeruginosa* ATCC 50071, and *P. carotovorum* DSM 102074) and two Gram positives (*S. aureus* DMS 25923 and *L. monocytogenes* ATCC 7644), with MIC ranging from 3-6 mg/mL. However, for its individual constituents, myrtenyl acetate, 1,8-Cineole, α-pinene, and Linalool, the corresponding MICs were higher than that of EO; therefore, it is suggestive of synergistic action of the components of EO (Caputo *et al*., 2022). Myrtenol, a bicyclic alcohol mono-terpene found in the essential oil of *M. communis* (Mimica-Dukić *et al*., 2010), 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 effects, respectively, against all the strains of *S. aureus*. While in association with oxacillin, an indifferent effect was observed. The additive and synergistic effects are suggestive of the use of smaller concentrations of these antibiotics and a reduction of the side effects of the administration of these drugs (Cordeiro *et al*., 2020). Myrtenol not only inhibited the synthesis of the virulence factor of MRSA and *A. baumannii* but also made the cells sensitive to H_2O_2,

healthy human blood, and conventional antibiotics (Selvaraj *et al*., 2019; Selvaraj *et al*., 2020). Among the methanolic leaf extracts of *Verbena officinalis*, *Myrtus communis*, and *Melilotus elegans* tested for antibacterial activity, the *M. communis* methanolic extract showed remarkable zones of inhibition and bactericidal activity against all bacterial isolates of *Staphylococcus aureus, Escherichia coli, Salmonella typhi, Shigella flexneri, Pseudomonas aeruginosa*, and *Proteus mirabilis* (Sisay *et al*., 2019).

One of the mechanisms of colonization and expression of the virulence or survival factors of a pathogen is quorum sensing. Quorum sensing is a cell-to-cell communication mechanism in bacteria. This cascade of specific signals and responses is mediated by the synthesis, release, and uptake of specific molecules known as autoinducers (Waters & Bassler, 2005). The autoinducers latter lead to the colonization and expression of various survival or virulence traits to combat stresses and develop drug resistance, etc. Poli *et al.* (2018), screened twelve essential oils for anti-QS activity by measuring the sub-lethal minimal QS inhibitory concentration (MQSIC) of violacein production in *Chromobacterium violaceum* and the minimal inhibitory concentration against the growth of *C. violaceum*. The authors found that the EO obtained from *Mentha suaveolens* ssp. *insularis* showed a 32-fold lower MQSIC than MIC, while the *M. communis* EO obtained from its aerial parts was one of the four EOs that showed a 16-fold lower MQSIC than MIC. For the remaining EOs, the MQSIC was ≤ 8-fold lower than the MIC (Poli *et al*., 2018).

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 (Aparna & Yadav, 2008). The biofilm protects the entrapped bacteria cells by restricting the entry of antimicrobial drugs. The biofilm's favorable milieu promotes microbial growth and genetic material exchange, including the spread of resistance genes. Instead of impacting a pathogen's growth, anti-biofilm treatments may reduce its adhesion and pathogenicity and there by enhance the sensitivity of microbes to antimicrobials and the host immune system (Koo *et al*., 2017). Therefore, there is an urgent need of anti-biofilm therapy and the 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 marked MIC. The extract destroyed the pre-formed biofilm at sub-MIC concentration and affected the bacterial cells within the biofilm. The MRSA genes *icaA, icaD, sarA,* and *bap,* which are involved in biofilm formation and development, were significantly repressed, thus inhibiting biofilm development (Khaleghi & Khorrami, 2021). Biofilm inhibition and suppression of biofilm genes in MRSA and *Acinetobacter baumannii* (Selvaraj *et al*., 2020) by *myrtenol* substantiates the anti-biofilm property of *M. communis*.

In another study, Caputo *et al.* (2022), found that the EO of *M. communis* leaves of Italian origin inhibited biofilm formation and disrupted the already-formed mature and ultra-mature biofilms of *E. coli* DSM 8579, *P. aeruginosa* ATCC 50071, *P. carotovorum* DSM 102074, *S. aureus* DMS 25923, and *L. monocytogenes* ATCC 7644. In a similar study, polyphenolic extracts from myrtle leaf inhibited biofilm formation and disrupted the preformed biofilms of dental plaque pathogens *Streptococcus mutans*, *Streptococcus oralis*, *Streptococcus mitis*, and *Rothia dentocariosa* (Sateriale *et al*., 2020).

Myrtenol, a component of *M. communis* EO, at its sub-inhibitory concentrations strongly inhibited the biofilm formation of *S. aureus* (Cordeiro *et al*., 2020). These results suggest that *M. communis* is a potential source of compounds with antibiofilm activity. According to Kwasny & Opperman (2010), antibiofilm treatments are considered effective if they can prevent 80% of biofilm growth and ≥ 40% of planktonic growth when compared to untreated controls (Kwasny & Opperman, 2010).

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. For example, amantadine and oseltamivir effect the central nervous system and the

gastrointestinal tract, which is further compounded by genetic instability, re-assortment of the virus, and drug resistance. Therefore, researchers are focused on looking for alternative therapeutic measures for screening medicinal plants and natural products for antiviral activity. Among the several plants tested against the anti-influanza A virus, the most effective were crude extracts of *G. glabra*, *M. officinalis,* and *S. alba;* the methanol fractions of *M. communis* and *M. officinalis*; and the chloroform fractions of *M. communis* and *C. sinensis* (fermented) in co- and pre-penetration combined treatments. The potential antiviral activity of the extracts and fractions is believed to be due to the phytoconstituents of flavonoids, tannins, steroids, and triterpenoids (Mehrbod *et al*., 2021).

Antifungal activity

The increasing prevalence of fungal infections worldwide and the gain of resistance to antifungal agents have prompted researchers to explore novel antifungal drugs and alternative agents. The essential oil of *M. communis* leaves exhibited antifungal activity against the clinical isolates of candida with MIC_{90} of 2-4 μg/mL (Cannas *et al*., 2013). In one of the studies, essential oil obtained from *M. communis* was used for the treatment of pityriasis versicolor, a disease characterized by scaly and hypopigmented or hyperpigmented spots on the skin caused by *Malassezia species*. Seven species of Malassezia isolated and identified from the skin of 41 patients were susceptible to *M. communis* essential oil (Barac *et al*., 2018), suggesting the potential use of EO as a 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 (Cannas *et al*., 2013; Kordali *et al*., 2016). It has been documented in several studies that the EO of several plants, including *M. comminis,* is more effective than the commercial antifungal drugs (Cannas *et al*., 2013). The EO of *M. communis* from different locations within Tunisia, varying in chemical composition, showed differential antifungal activity, as reported by Yangui *et al*. (2017). The EO from Zaghouan was more active against *Biscogniauxia mediterranea,* the causative agent of charcoal canker disease, which is common in Mediterranean forests, especially in Portugal, Italy, Spain, France, and North Africa (Yangui *et al*., 2017). The methanolic leaf extract of *M. communis* from Saudi Arabia inhibited the growth of candida strains by damaging the cell wall, as evidenced by scanning electron microscopy and leakage of cell contents into the culture supernatant (Alyousef, 2021). The EO from *M. comminis,* rich in 1.8 Cineol (41.24 %), D-Limonene (15.37 %), α-pinene (15.22 %), and myrtenyl acetate (14.35 %), showed strong antifungal power against *Penicillium digitatum* and *Aspergillus Niger* (Brahmi *et al*., 2023).

Antioxidant activity

Phenolic compounds having antioxidant properties and being 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 that inhibit the oxidation of free radicals, which otherwise can damage physiological molecules of lipids, proteins, and DNA. *M. communis* extracts and/or EOs exhibited *in-vivo* antioxidant activities in various mouse and rat models. Thalassemia and other transfusion-associated anemias are managed and treated with several iron chelators, such as deferoxamine (DFO), deferiprone (L1), and deferasirox (ICL-670). In one of the studies, Eslami *et al*. (2018), 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 standard vitamin C and quercetin. Compared to defroxamine (an iron chelator) and *M. communis* 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 in preventing or at least reducing the adverse impacts of excessive iron in mice due to the antioxidant and Fe-chelating activities of MC-ZVINs (Eslami *et al*., 2018).

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 by remarkable inhibition of gastric lesions and acidity. It reduced the inflammation of gastric mucosa, counteracted gastric lipoperoxidation, and prevented the reduction of antioxidant enzyme activity of glutathione peroxidase, catalase, and superoxide dismutase (Mansour *et al*., 2022).

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 the six essential oils screened, *M. communisn* EO showed antioxidant activity like that of the positive control butylated hydroxytoluene (Ouedrhiri *et al*., 2021).

M. communis extracts and EOs not only showed antioxidant activities but inhibited the vital enzymes of the human pathogens. Plant extracts have been investigated for their role in inhibiting virulence factors, including pathogen's enzymes involved in colonization of the host. Nabati *et al*. (2012), screened about 137 plant extracts for their inhibitory activity against the urease enzyme from jack beans. Among them, *Myrtus communis* leaf extract showed remarkable inhibitory activity. Actually, *H. pylori* utilizes urease to catalyze the hydrolysis of urea to produce ammonia and carbon dioxide, thus protecting the bacteria in the stomach's acidic environment (Nabati *et al*., 2012).

The biological activities of the *M. communis* extract and EOs are attributed very well to their constituent compounds. Myrtucommuacetalone-1 (MCA-1) is a novel and anti-inflammatory bioactive compound isolated from *M. communis* that inhibits superoxide, hydrogen peroxide, and nitric oxide production in activated macrophages. The compound was less toxic to the various cell lines of MDBK kidney cells, liver cells, 3T3NIH mouse fibroblasts, and J774.2 macrophages in comparison to cyclohexamide. By abolishing the phosphorylation of the transcription factor (NFkB) and its nuclear translocation, MCA-1 inhibited the expression of iNOS (inducible nitric oxide synthase) (Soomro *et al*., 2019)

Food products enriched with herbal ingredients are sources of pro-health components, including polyphenolic compounds (Table No. 2), whose health benefits depend on diet, how it affects the gut flora, and how it affects their enzymatic activity. Intragastric treatment of rats with aqueous leaf extracts of *M. communis* and *Laurus nobilis L*. from Zagreb, Croatia, positively affected the rats' health and increased the number of colonies of the normal flora *Lactobacilli* and *Bifidobacteria*. It was clear that the kidneys and liver had significantly less glycolytic enzymatic activity and had more antioxidant capability (Berendika *et al.*, 2022). In other studies, laurel and myrtle EOs administered intragastrically to rats caused a decrease in the intestinal microbiota's ability to cause glycolysis. Additionally, lipid markers such as cholesterol, triglycerides, low-density lipoprotein cholesterol, and very low-density lipoprotein cholesterol were lowered, which may result in cardiovascular protection. With the exception of the kidneys, where it has a pro-oxidative effect, myrtle EO exhibited greater antioxidant capacity in most tissues (Odeh *et al*., 2022). *M. communis* leaf extract increased malondialdehyde (MDA) and glutathione (GSH) levels, glutathinone-S-transferase (GST), superoxide dismutase (SOD), and catalase (CAT) production in thermal injury to avoid burn-induced oxidative damage to internal organs (Ozcan *et al*., 2019; Ozcan *et al*., 2020). *M. communis* extract significantly reduced parenchymal inflammation and fibrotic changes in bleomycin (BLM)-induced pulmonary fibrosis in an animal model with a decrease in lipid peroxidation and hydroxyproline content and a subsequent increase in catalase activity (Samareh Fekri *et al*., 2018). 3,5-*O*-di-galloylquinic acid (DGQA) purified from the leaves of *Myrtus communis* showed antioxidative, antiproliferative, and antigenotoxic activities by increasing the activity of antioxidant enzymes and DNA repair enzymes in the H_2O_2-stressed chronic myelogenous leukemia cell line K562 (Skandrani *et al*., 2012).

Anti-inflammatory activity

Inflammation is the primary response against infection, injury, and irritation. If it is not cured, inflammation will lead to autoimmune diseases, neurodegeneration, or cancer. The *M. communis* EO decreased the expression level of pro-inflammatory cytokines IL-6, IL-10, and NFkB in 1L-1 inflammatory-induced cell lines (Gülbol Duran & Terzi, 2021). The antiparasitic (toxoplasmosis) effects of *M. communis* EO obtained from its leaves were believed to be due to the expression of

immunomodulators IL-12 and INF-γ in innate immunity (Shaapan *et al*., 2021). *M. cumminus* has protective effects against acute pancreatitis by decreasing pro-inflammatory cytokines IL-1β, IL-6, and MDA and increasing the anti-inflammatory markers IL-10 and GSH (Ozbeyli *et al*., 2020). The EO of *M. communis* leaves induced a significant reduction in ear inflammation and myeloperoxidase activity in croton oil-induced ear edema in mice and TNF-α and IL-6 production in cotton pellet-induced granuloma model (Maxia *et al*., 2011). The polyphenol fraction of the *M. communis* leaves reduced inflammation of paws of rats better than that of diclofenac in a carrageenan-induced inflammatory edema model without having any effect on kidney or liver function (Mechchate *et al*., 2022). Induction of anti-inflammatory cytokines INF-γ and IL-12 in *Toxoplasma gondii*-induced toxoplasmosis in mice reduced the mean number and size of *T. gondii* brain tissue cysts (Shaapan *et al*., 2021). The anti-inflammatory response was observed in the aqueous and ethanolic extracts towards acute inflammation and antinociceptive activity in acetic acid-induced writhing in mice (Hosseinzadeh *et al*., 2011). The ways by which the *M. communis* extract or oil could mediate these biological properties are depicted in Figure No. 5. *M. communis* could target several macromolecules to compromise cell wall or cell membrane integrity, pro-inflammatory and anti-inflammatory responses, DNA and enzyme structure or function, and gene expression. 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) (Onal *et al*., 2005; Badalamenti *et al*., 2020). These results suggest that *M. communis* herbal extract could be developed as a physiologically functional drink for lowering the blood glucose content, which needs to be explored further.

CONCLUSION

The diverse chemical composition of *M. communis* leaves broadens their use in the industries of pharmaceuticals, aroma, food, and agriculture. In recent years, there has been significant progress in validating the traditional use of its constituents, EO, and extracts by exploring their associated biological properties, including antimicrobial, anticancer, antioxidant, anti-inflammatory, etc.

PROSPECTS

Though significant progress has been made in validating the biological properties of *M. communis* leaves in vitro, there is a need for in-depth study to identify the cellular targets of its bioactives, their bioavailability, toxicity, and mechanism of action. Furthermore, the efficacy of bioactives individually and in combinations with other bioactive constituents and/or commercial drugs would provide insights into the development of these bioactives as future drugs.

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REFERENCES

Akaydin G, ŞiMşek I, Arituluk ZC, YeşiLada E. 2013. An ethnobotanical survey in selected towns of the Mediterranean subregion (Turkey). **Turk J Biol** 37: 230 - 247. **https://doi.org/10.3906/biy-1010-139**

Alipour G, Dashti S, Hosseinzadeh H. 2014. Review of pharmacological effects of *Myrtus communis* L. and its active constituents: *Myrtus communis* L. **Phytother Res** 28: 1125 - 1136. **https://doi.org/10.1002/ptr.5122**

Alyousef AA. 2021. Antifungal activity and mechanism of action of different parts of *Myrtus communis* growing in Saudi Arabia against *Candida* spp. **J Nanomater** 2021: 1 - 10. **https://doi.org/10.1155/2021/3484125**

Alyousef AA, Husain FM, Arshad M, Ahamad SR, Khan MS, Qais FA, Khan A, Alqasim A, Almutairi N, Ahmad I, Albalawi T, Alam P, Khan S. 2021. *Myrtus communis* and its bioactive phytoconstituent, linalool, interferes with quorum sensing regulated virulence functions and biofilm of uropathogenic bacteria: *In vitro* and *in silico* insights. **J King Saud Univ Sci** 33: 101588. **https://doi.org/10.1016/j.jksus.2021.101588**

Amsalu N, Bezie Y, Fentahun M, Alemayehu A, Amsalu G. 2018. Use and conservation of medicinal plants by

indigenous people of Gozamin Wereda, East Gojjam Zone of Amhara Region, Ethiopia: An ethnobotanical approach. **Evid Based Complement Alternat Med** 2018: 1 - 23. **https://doi.org/10.1155/2018/2973513**

Aparna MS, Yadav S. 2008. Biofilms: microbes and disease. **Braz J Infect Dis** 12: 526 - 530. **https://doi.org/10.1590/S1413-86702008000600016**

Askari SF, Jahromi BN, Dehghanian A, Zarei A, Tansaz M, Badr P, Azadi A, Mohagheghzadeh A. 2020. Effect of a novel herbal vaginal suppository containing myrtle and oak gall in the treatment of vaginitis: a randomized clinical trial. **Daru J Fac Pharm Tehran Univ Med Sci** 28: 603 - 614. **https://doi.org/10.1007/s40199-020-00365-6**

Badalamenti N, Ilardi V, Rosselli S, Bruno M, Maggi F, Leporini M, Falco T, Loizzo MR, Tundis R. 2020. *Ferulago nodosa* Subsp. *geniculata* (Guss.) Troia & Raimondo from Sicily (Italy): Isolation of essential oil and evaluation of its bioactivity. **Molecules** 25: 3249. **https://doi.org/10.3390/molecules25143249**

Barac A, Donadu M, Usai D, Spiric VT, Mazzarello V, Zanetti S, Aleksic E, Stevanovic G, Nikolic N, Rubino S. 2018. Antifungal activity of *Myrtus communis* against *Malassezia* sp. isolated from the skin of patients with pityriasis versicolor. **Infection** 46: 253 - 257. **https://doi.org/10.1007/s15010-017-1102-4**

Bekhechi C, Malti CEW, Boussaïd M, Achouri I, Belilet K, Gibernau M, Casanova J, Tomi F. 2019. Composition and chemical variability of *Myrtus communis* leaf oil from northwestern Algeria. **Nat Prod Commun** 14: 1934578X1985003. **https://doi.org/10.1177/1934578X19850030**

Bellu E, Diaz N, Kralovič M, Divin R, Sarais G, Fadda A, Satta R, Montesu MA, Medici S, Brunetti A, Pinheiro Barcessat AR, Jarošíková T, Rulc J, Amler E, Margarita V, Rappelli P, Maioli M. 2022. Myrtle-functionalized nanofibers modulate vaginal cell population behavior while counteracting microbial proliferation. **Plants** 11: 1577. **https://doi.org/10.3390/plants11121577**

Ben Hsouna A, Dhibi S, Dhifi W, Mnif W, Nasr HB, Hfaiedh N. 2019. Chemical composition and hepatoprotective effect of essential oil from *Myrtus communis* L. flowers against CCL_4-induced acute hepatotoxicity in rats. **RSC Adv** 9: 3777 - 3787. **https://doi.org/10.1039/C8RA08204A**

Berendika M, Drozdek SD, Odeh D, Oršolić N, Dragičević P, Sokolović M, Garofulić IE, Đikić D, Jurčević IL. 2022. Beneficial effects of laurel (*Laurus nobilis* L.) and myrtle (*Myrtus communis* L.) extract on rat health. **Molecules** 27: 581. **https://doi.org/10.3390/molecules27020581**

Birhanie MW, Walle B, Rebba K. 2016. Hypnotic effect of the essential oil from the leaves of *Myrtus communis* on mice. **Nat Sci Sleep** 8: 267 - 275. **https://doi.org/10.2147/NSS.S101493**

Boelens MH, Jimenez R. 1992. The chemical composition of Spanish Myrtle oils. Part II. **J Essent Oil Res** 4: 349 - 353. **https://doi.org/10.1080/10412905.1992.9698084**

Bouaoudia-Madi N, Boulekbache-Makhlouf L, Madani K, Silva AMS, Dairi S, Oukhmanou–Bensidhoum S, Cardoso SM. 2019. Optimization of ultrasound-assisted extraction of polyphenols from *Myrtus communis* L. pericarp. **Antioxidants** 8: 205. **https://doi.org/10.3390/antiox8070205**

Bouzabata A, Cabral C, Gonçalves MJ, Cruz MT, Bighelli A, Cavaleiro C, Casanova J, Tomi F, Salgueiro L. 2015. *Myrtus communis* L. as source of a bioactive and safe essential oil. **Food Chem Toxicol** 75: 166 - 172. **https://doi.org/10.1016/j.fct.2014.11.009**

Brahmi F, Mokhtari O, Yahyaoui MI, Zraibi L, Bentouhami NE, Abdeslam A, Legssyer B. 2023. Phytochemical composition, antioxidant, and antifungal activity of essential oil from *Myrtus Communis* L. **Mater Today Proc** 72: 3826 - 3830. **https://doi.org/10.1016/j.matpr.2022.09.510**

Bruna S, Portis E, Cervelli C, De Benedetti L, Schiva T, Mercuri A. 2007. AFLP-based genetic relationships in the Mediterranean myrtle (*Myrtus communis* L.). **Sci Hortic** 113: 370 - 375. **https://doi.org/10.1016/j.scienta.2007.04.007**

Cannas S, Molicotti P, Ruggeri M, Cubeddu M, Sanguinetti M, Marongiu B, Zanetti S. 2013. Antimycotic activity of *Myrtus communis* L. towards *Candida* spp from isolates. **J Infect Dev Ctries** 7: 295 - 298. **https://doi.org/10.3855/jidc.2799**

Capetti F, Cagliero C, Marengo A, Bicchi C, Rubiolo P, Sgorbini B. 2020. Bio-guided fractionation driven by *in vitro* α-amylase inhibition assays of essential oils bearing specialized metabolites with potential hypoglycemic activity. **Plants** 9: 1242. **https://doi.org/10.3390/plants9091242**

Caputo L, Capozzolo F, Amato G, De Feo V, Fratianni F, Vivenzio G, Nazzaro F. 2022. Chemical composition, antibiofilm, cytotoxic, and anti-acetylcholinesterase activities of *Myrtus communis* L. leaves essential oil. **BMC Complement Med Ther** 22: 142. **https://doi.org/10.1186/s12906-022-03583-4**

Chalchat JC, Garry RP, Michet A. 1998. Essential oils of myrtle (*Myrtus communis* L.) of the mediterranean littoral. **J Essent Oil Res** 10: 613 - 617. **https://doi.org/10.1080/10412905.1998.9700988**

Cordeiro L, Figueiredo P, Souza H, Sousa A, Andrade-Júnior F, Barbosa-Filho J, Lima E. 2020. Antibacterial and antibiofilm activity of myrtenol against *Staphylococcus aureus*. **Pharmaceuticals** 13: 133. **https://doi.org/10.3390/ph13060133**

Cruciani S, Santaniello S, Garroni G, Fadda A, Balzano F, Bellu E, Sarais G, Fais G, Mulas M, Maioli M. 2019. Myrtus polyphenols from antioxidants to anti-inflammatory molecules: Exploring a network involving cytochromes P450 and vitamin D. **Molecules** 24: 1515. **https://doi.org/10.3390/molecules24081515**

Dhifi W, Jazi S, El Beyrouthy M, Sadaka C, Mnif W. 2020. Assessing the potential and safety of *Myrtus communis* flower essential oils as efficient natural preservatives against *Listeria monocytogenes* growth in minced beef under refrigeration. **Food Sci Nut** 8: 2076 - 2087. **https://doi.org/10.1002/fsn3.1497**

Eslami S, Ebrahimzadeh MA, Biparva P. 2018. Green synthesis of safe zero valent iron nanoparticles by *Myrtus communis* leaf extract as an effective agent for reducing excessive iron in iron-overloaded mice, a thalassemia model. **RSC Adv** 8: 26144 - 26155. **https://doi.org/10.1039/C8RA04451A**

Flamini G, Cioni PL, Morelli I, Maccioni S, Baldini R. 2004. Phytochemical typologies in some populations of *Myrtus communis* L. on Caprione Promontory (East Liguria, Italy). **Food Chem** 85: 599 - 604. **https://doi.org/10.1016/j.foodchem.2003.08.005**

Franco AM, Tocci N, Guella G, Dell'Agli M, Sangiovanni E, Perenzoni D, Vrhovsek U, Mattivi F, Manca G. 2019. Myrtle seeds (*Myrtus communis* L.) as a rich source of the bioactive ellagitannins oenothein B and eugeniflorin D2. **ACS Omega** 4: 15966 - 15974. **https://doi.org/10.1021/acsomega.9b02010**

Ghodrati M, Farahpour MR, Hamishehkar H. 2019. Encapsulation of Peppermint essential oil in nanostructured lipid carriers: *In-vitro* antibacterial activity and accelerative effect on infected wound healing. **Colloids Surf Physicochem Eng Asp** 564: 161 - 169. **https://doi.org/10.1016/j.colsurfa.2018.12.043**

Giuliani C, Bottoni M, Milani F, Todero S, Berera P, Maggi F, Santagostini L, Fico G. 2022. Botanic garden as a factory of molecules: *Myrtus communis* L. subsp. *communis* as a case study. **Plants** 11: 754. **https://doi.org/10.3390/plants11060754**

González de Peredo A, Vázquez-Espinosa M, Espada-Bellido E, Jiménez-Cantizano A, Ferreiro-González M, Amores-Arrocha A, Palma M, Barroso CG8, Barbero GF. 2018. Development of new analytical microwave-assisted extraction methods for bioactive compounds from myrtle (*Myrtus communis* L.). **Molecules** 23: 2992. **https://doi.org/10.3390/molecules23112992**

González-Varo JP, Arroyo J, Aparicio A. 2009. Effects of fragmentation on pollinator assemblage, pollen limitation and seed production of Mediterranean myrtle (*Myrtus communis*). **Biol Conserv** 142: 1058 - 1065. **https://doi.org/10.1016/j.biocon.2009.01.017**

González-Varo JP, Albaladejo RG, Aparicio A, Arroyo J. 2010. Linking genetic diversity, mating patterns and progeny performance in fragmented populations of a Mediterranean shrub: Fragmentation effects on plant progeny performance. **J Appl Ecol** 47: 1242 - 1252. **https://doi.org/10.1111/j.1365-2664.2010.01879.x**

Gortzi O, Lalas S, Chinou I, Tsaknis J. 2008. Reevaluation of bioactivity and antioxidant activity of *Myrtus communis* extract before and after encapsulation in liposomes. **Eur Food Res Technol** 226: 583 - 590. **https://doi.org/10.1007/s00217-007-0592-1**

Gülbol Duran G, Terzi MY. 2021. Investigation of anti-inflammatory effects of *Myrtus communis* L. essential oil on IL-1β Induced human bronchial epithelial cell line. **Turk Klin J Med Sci** 41: 470 - 477. **https://doi.org/10.5336/medsci.2021-81607**

Hager R, Pitsch J, Kerbl-Knapp J, Neuhauser C, Ollinger N, Iken M, Ranner J, Mittermeier-Kleßinger V, Dawid C, Lanzerstorfer P, Weghuber J. 2021. A high-content screen for the identification of plant extracts with insulin secretion-modulating activity. **Pharmaceuticals** 14: 809. **https://doi.org/10.3390/ph14080809**

Hayder N, Bouhlel I, Skandrani I, Kadri M, Steiman R, Guiraud P, Mariotte AM, Ghedira K, Dijoux-Franca MG, Chekir-Ghedira L. 2008. *In vitro* antioxidant and antigenotoxic potentials of myricetin-3-o-galactoside and

myricetin-3-o-rhamnoside from *Myrtus communis*: Modulation of expression of genes involved in cell defense system using cDNA microarray. **Toxicol in Vitro** 22: 567 - 581. **https://doi.org/10.1016/j.tiv.2007.11.015**

Hosseinzadeh H, Khoshdel M, Ghorbani M. 2011. Antinociceptive, anti-inflammatory effects and acute toxicity of aqueous and ethanolic extracts of *Myrtus communis* L. aerial parts in mice. **J Acupunct Meridian Stud** 4: 242 - 247. **https://doi.org/10.1016/j.jams.2011.09.015**

Jabri MA, Rtibi K, Ben-Said A, Aouadhi C, Hosni K, Sakly M, Sebai H. 2016. Antidiarrhoeal, antimicrobial and antioxidant effects of myrtle berries (*Myrtus communis* L.) seeds extract. **J Pharm Pharmacol** 68: 264 - 274. **https://doi.org/10.1111/jphp.12505**

Khaleghi M, Khorrami S. 2021. Down-regulation of biofilm-associated genes in mecA-positive methicillin-resistant *S. aureus* treated with *M. communis* extract and its antibacterial activity. **AMB Express** 11: 85. **https://doi.org/10.1186/s13568-021-01247-z**

Khan N, Rasool S, Ali Khan S, Khan SB. 2020. A new antibacterial dibenzofuran-type phloroglucinol from *Myrtus communis* Linn. **Nat Prod Res** 34: 3199 - 3204. **https://doi.org/10.1080/14786419.2018.1556657**

Khezri K, Farahpour MR, Mounesi Rad S. 2020. Efficacy of *Mentha pulegium* essential oil encapsulated into nanostructured lipid carriers as an *in vitro* antibacterial and infected wound healing agent. **Colloids Surf Physicochem Eng Asp** 589: 124414. **https://doi.org/10.1016/j.colsurfa.2020.124414**

Koo H, Allan RN, Howlin RP, Stoodley P, Hall-Stoodley L. 2017. Targeting microbial biofilms: current and prospective therapeutic strategies. **Nat Rev Microbiol** 15: 740 - 755. **https://doi.org/10.1038/nrmicro.2017.99**

Kordali S, Usanmaz A, Cakir A, Komaki A, Ercisli S. 2016. Antifungal and herbicidal effects of fruit essential oils of four *Myrtus communis* genotypes. **Chem Biodivers** 13: 77 - 84. **https://doi.org/10.1002/cbdv.201500018**

Kreutz T, Carneiro SB, Soares KD, Limberger RP, Apel MA, Veiga-Junior VF, Koester LM. 2021. *Aniba canelilla* (Kunth) Mez essential oil-loaded nanoemulsion: Improved stability of the main constituents and *in vitro* antichemotactic activity. **Ind Crops Prod** 171: 113949. **https://doi.org/10.1016/j.indcrop.2021.113949**

Kwasny SM, Opperman TJ. 2010. Static biofilm cultures of Gram-positive pathogens grown in a microtiter format used for anti-biofilm drug discovery. **Curr Protoc Pharmacol** 13 **https://doi.org/10.1002/0471141755.ph13a08s50**

Mahmoudvand H, Fallahi S, Mahmoudvand H, Shakibaie M, Harandi MF, Dezaki ES. 2016. Efficacy of *Myrtus communis* L. to inactivate the hydatid cyst protoscoleces. **J Investig Surg Off J Acad Surg Res** 29, 137–143. **https://doi.org/10.3109/08941939.2015.1088601**

Mansour RB, Beji RS, Wasli H, Zekri S, Ksouri R, Megdiche-Ksouri W, Cardodo SM. 2022. Gastroprotective effect of microencapsulated *Myrtus communis* essential oil against ethanol/HCl-induced acute gastric lesions. **Molecules** 27: 1566. **https://doi.org/10.3390/molecules27051566**

Marsh PD. 2004. Dental plaque as a microbial biofilm. **Caries Res** 38: 204 - 211. **https://doi.org/10.1159/000077756**

Maxia A, Frau MA, Falconieri D, Karchuli MS, Kasture S. 2011. Essential oil of *Myrtus communis* inhibits inflammation in rats by reducing serum IL-6 and TNF-alpha. **Nat Prod Commun** 6: 1545 - 1548.

Mechchate H, Alves CEC, Es-Safi I, Amaghnouje A, Jawhari FZ, Oliveira RC, Gomes AF, Conte R, Pontes GS, Bousta D, Grafov A. 2022. Antileukemic, antioxidant, anti-inflammatory and healing activities induced by a polyphenol-enriched fraction extracted from leaves of *Myrtus communis* L. **Nutrients** 14: 5055. **https://doi.org/10.3390/nu14235055**

Mehrbod P, Safari H, Mollai Z, Fotouhi F, Mirfakhraei Y, Entezari H, Goodarzi S, Tofighi Z. 2021. Potential antiviral effects of some native Iranian medicinal plants extracts and fractions against influenza A virus. **BMC Complement Med Ther** 21: 246. **https://doi.org/10.1186/s12906-021-03423-x**

Migliore J, Baumel A, Juin M, Médail F. 2012. From Mediterranean shores to central Saharan mountains: key phylogeographical insights from the genus *Myrtus*: Phylogeography of the genus *Myrtus*. **J Biogeogr** 39: 942 - 956. **https://doi.org/10.1111/j.1365-2699.2011.02646.x**

Mimica-Dukić N, Bugarin D, Grbović S, Mitić-Ćulafić D, Vuković-Gačić B, Orčić D, Emilija Jovin MC. 2010.

Essential oil of *Myrtus communis* L. as a potential antioxidant and antimutagenic agents. **Molecules** 15: 2759 - 2770. **https://doi.org/10.3390/molecules15042759**

Mir MA, Bashir N, Alfaify A, Oteef MDY. 2020. GC-MS analysis of *Myrtus communis* extract and its antibacterial activity against Gram-positive bacteria. **BMC Complement Med Ther** 20: 86. **https://doi.org/10.1186/s12906-020-2863-3**

Moazeni M, Davari A, Shabanzadeh S, Akhtari J, Saeedi M, Mortyeza-Semnani K, Abastabar M, Nabili M, Moghadam FH, Roohi B, Kelidari H, Nokhodchi A. 2021. *In vitro* antifungal activity of *Thymus vulgaris* essential oil nanoemulsion. **J Herb Med** 28: 100452. **https://doi.org/10.1016/j.hermed.2021.100452**

Mulas M, Melis RAM. 2011. Essential oil composition of myrtle (*Myrtus communis*) leaves. **J Herbs Spices Med Plants** 17: 21 - 34. **https://doi.org/10.1080/10496475.2011.556986**

Nabati F, Mojab F, Habibi-Rezaei M, Bagherzadeh K, Amanlou M, Yousefi B. 2012. Large scale screening of commonly used Iranian traditional medicinal plants against urease activity. **DARU J Pharm Sci** 20: 72. **https://doi.org/10.1186/2008-2231-20-72**

Nicoletti R, Salvatore M, Ferranti P, Andolfi A. 2018. Structures and bioactive properties of Myrtucommulones and related acylphloroglucinols from Myrtaceae. **Molecules** 23: 3370. **https://doi.org/10.3390/molecules23123370**

Nishikawara F, Nomura Y, Imai S, Senda A, Hanada N. 2007. Evaluation of cariogenic bacteria. **Eur J Dent** 1: 31 - 39.

Nomura R, Matayoshi S, Otsugu M, Kitamura T, Teramoto N, Nakano K. 2020. Contribution of severe dental caries induced by *Streptococcus mutans* to the pathogenicity of infective endocarditis. **Infect Immun** 88: e00897-19. **https://doi.org/10.1128/IAI.00897-19**

Odeh D, Oršolić N, Berendika M, Đikić D, Domjanić Drozdek S, Balbino S, Greche H. 2022. Antioxidant and anti-atherogenic activities of essential oils from *Myrtus communis* L. and *Laurus nobilis* L. in rat. **Nutrients** 14: 1465. **https://doi.org/10.3390/nu14071465**

Onal S, Timur S, Okutucu B, Zihnioğlu F. 2005. Inhibition of alpha-glucosidase by aqueous extracts of some potent antidiabetic medicinal herbs. **Prep Biochem Biotechnol** 35: 29 - 36. **https://doi.org/10.1081/PB-200041438**

Ouedrhiri W, Mechchate H, Moja S, Mothana RA, Noman OM, Grafov A, Greche H. 2021. Boosted antioxidant effect using a combinatory approach with essential oils from *Origanum compactum*, *Origanum majorana*, *Thymus serpyllum*, *Mentha spicata*, *Myrtus communis*, and *Artemisia herba-alba*: Mixture design optimization. **Plants** 10: 2817. **https://doi.org/10.3390/plants10122817**

Ozbeyli D, Sen A, Cilingir Kaya OT, Ertas B, Aydemir S, Ozkan N, Yuksel M, Sener G. 2020. *Myrtus communis* leaf extract protects against cerulein-induced acute pancreatitis in rats. **J Food Biochem** 44. **https://doi.org/10.1111/jfbc.13130**

Ozcan O, Ipekci H, Alev B, Ustundag UV, Ak E, Sen A, Emekli Alturfan E, Sener G, Yarat A, Cetinel S, Akbay TT. 2019. Protective effect of Myrtle (*Myrtus communis*) on burn induced skin injury. **Burns** 45: 1856 - 1863. **https://doi.org/10.1016/j.burns.2019.07.015**

Ozcan O, Ipekci H, Alev B, Ustundag UV, Sen A, Emekli-Alturfan E, Sener G, Yarat A, Tunali-Akbay T. 2020. The effect of *Myrtus communis* L. ethanol extract on the small intestine and lungs in experimental thermal burn injury. **J Therm Biol** 93: 102685. **https://doi.org/10.1016/j.jtherbio.2020.102685**

Patel M. 2022. Oral cavity and *Candida albicans*: Colonisation to the development of infection. **Pathogens** 11: 335. **https://doi.org/10.3390/pathogens11030335**

Poli JP, Guinoiseau E, de Rocca Serra D, Sutour S, Paoli M, Tomi F, Quilichini Y, Berti L, Lorenzi V. 2018. Anti-Quorum sensing activity of 12 essential oils on chromobacterium violaceum and specific action of cis-cis-p-Menthenolide from Corsican *Mentha suaveolens* ssp. *Insularis*. **Molecules** 23: 2125. **https://doi.org/10.3390/molecules23092125**

Rahimvand L, Niakan M, Naderi NJ. 2018. The antibacterial effect of aquatic and methanolic extract of *Myrtus communis* on *Actinobacillus actinomycetemcomitans*, *Porphyromonas gingivalis* and *Prevotella intermedia*. **Iran J Microbiol** 10: 254 - 257.

Sadeghi-Nejad B, Moghimipour E, Yusef Naanaie S, Nezarat S. 2018. Antifungal and antibacterial activities of

polyherbal toothpaste against oral pathogens, *in vitro*. **Curr Med Mycol** 4: 21 - 26. **https://doi.org/10.18502/cmm.4.2.65**

Samareh Fekri M, Mandegary A, Sharififar F, Poursalehi HR, Nematollahi MH, Izadi A, Mehdipour M, Asadi A, Fekri MS. 2018. Protective effect of standardized extract of *Myrtus communis* L. (myrtle) on experimentally bleomycin-induced pulmonary fibrosis: biochemical and histopathological study. **Drug Chem Toxicol** 41: 408 - 414. **https://doi.org/10.1080/01480545.2018.1459670**

Saraiva C, Silva AC, García-Díez J, Cenci-Goga B, Grispoldi L, Silva AF, Almeida JM. 2021. Antimicrobial activity of *Myrtus communis* L. and *Rosmarinus officinalis* L. essential oils against *Listeria monocytogenes* in Cheese. **Foods** 10: 1106. **https://doi.org/10.3390/foods10051106**

Sateriale D, Imperatore R, Colicchio R, Pagliuca C, Varricchio E, Volpe MG, Salvatore P, Paolucci M, Pagliarulo C. 2020. Phytocompounds vs. dental plaque bacteria: *In vitro* effects of myrtle and pomegranate polyphenolic extracts against single-species and multispecies oral biofilms. **Front Microbiol** 11: 592265. **https://doi.org/10.3389/fmicb.2020.592265**

Selvaraj A, Jayasree T, Valliammai A, Pandian SK. 2019. Myrtenol attenuates MRSA biofilm and virulence by suppressing sarA expression dynamism. **Front Microbiol** 10: 2027. **https://doi.org/10.3389/fmicb.2019.02027**

Selvaraj A, Valliammai A, Sivasankar C, Suba M, Sakthivel G, Pandian SK. 2020. Antibiofilm and antivirulence efficacy of myrtenol enhances the antibiotic susceptibility of *Acinetobacter baumannii*. **Sci Rep** 10: 21975. **https://doi.org/10.1038/s41598-020-79128-x**

Sen A, Yuksel M, Bulut G, Bitis L, Ercan F, Ozyilmaz-Yay N, Akbulut O, Cobanoğlu H, Ozkan S, Senerl G. 2017. Therapeutic potential of *Myrtus communis* Subsp. *communis* extract against acetic acid-induced colonic inflammation in rats: Therapeutic potential of *Myrtus communis* subsp. *communis* extract. **J Food Biochem** 41: e12297. **https://doi.org/10.1111/jfbc.12297**

Serce S, Ercisli S, Sengul M, Gunduz K, Orhan E. 2010. Antioxidant activities and fatty acid composition of wild grown myrtle (*Myrtus communis* L.) fruits. **Pharmacogn Mag** 6: 9. **https://doi.org/10.4103/0973-1296.59960**

Seyoum G, Zerihun G. 2014. An ethnobotanical study of medicinal plants in Debre Libanos Wereda, Central Ethiopia. **Afr J Plant Sci** 8: 366 - 379. **https://doi.org/10.5897/AJPS2013.1041**

Shaapan RM, Al-Abodi HR, Alanazi AD, Abdel-Shafy S, Rashidipour M, Shater AF, Mahmoudvand H. 2021. *Myrtus communis* essential oil: Anti-parasitic effects and induction of the innate immune system in mice with *Toxoplasma gondii* infection. **Molecules** 26: 819. **https://doi.org/10.3390/molecules26040819**

Sharifzadeh A, Shokri H. 2016. Antifungal activity of essential oils from Iranian plants against fluconazole-resistant and fluconazole-susceptible *Candida albicans*. **Avicenna J Phytomed** 6: 215 - 222.

Sisay M, Engidawork E, Shibeshi W. 2017. Evaluation of the antidiarrheal activity of the leaf extracts of *Myrtus communis* Linn (Myrtaceae) in mice model. **BMC Complement Altern Med** 17: 103. **https://doi.org/10.1186/s12906-017-1625-3**

Sisay M, Bussa N, Gashaw T, Mengistu G. 2019. Investigating in vitro antibacterial activities of medicinal plants having folkloric repute in Ethiopian traditional medicine. **J Evid-Based Integr Med** 24: 2515690X1988627. **https://doi.org/10.1177/2515690X19886276**

Skandrani I, Bouhlel I, Bhouri W, Ben Sghaier M, Hayder N, Marie-Geneviève DF, Ghedira K, Chekir-Ghedira L. 2012. *In vitro* antioxidant and antigenotoxic potentials of 3,5-O-di-galloylquinic acid extracted from *Myrtus communis* leaves and modulation of cell gene expression by H_2O_2: Antioxidant and antigenotoxic potentials of DGQA. **J Appl Toxicol** 32: 333 - 341. **https://doi.org/10.1002/jat.1655**

Snoussi A, Essaidi I, Ben Haj Koubaier H, Zrelli H, Alsafari I, Živoslav T, Mihailovic J, Khan M, El Omri A, Veličković TC, Bouzouita N. 2021. Drying methodology effect on the phenolic content, antioxidant activity of *Myrtus communis* L. leaves ethanol extracts and soybean oil oxidative stability. **BMC Chem** 15: 31. **https://doi.org/10.1186/s13065-021-00753-2**

Soomro S, Mesaik MA, Shaheen F, Khan N, Halim SA, Ul-Haq Z, Ali Siddiqui R, Choudhary MI. 2019. Inhibitory effects of myrtucommuacetalone 1 (MCA-1) from *Myrtus Communis* on inflammatory response in mouse macrophages. **Molecules** 25: 13. **https://doi.org/10.3390/molecules25010013**

Torabi I, Sharififar F, Izadi A, Ayatollahi Mousavi SA. 2022. Inhibitory effects of different fractions separated from standardized extract of *Myrtus communis* L. against nystatin-susceptible and nystatin-resistant *Candida albicans* isolated from HIV positive patients. **Heliyon** 8: e09073. **https://doi.org/10.1016/j.heliyon.2022.e09073**

Touaibia M. 2017. Composition and anti-inflammatory effect of the common myrtle (*Myrtus communis* L.) essential oil growing wild in Algeria. **Phytothérapie https://doi.org/10.1007/s10298-017-1100-9**

Tuberoso CIG, Barra A, Angioni A, Sarritzu E, Pirisi FM. 2006. Chemical composition of volatiles in Sardinian myrtle (*Myrtus communis* L.) alcoholic extracts and essential oils. **J Agric Food Chem** 54: 1420 - 1426. **https://doi.org/10.1021/jf052425g**

Usai M, Marchetti M, Culeddu N, Mulas M. 2020. Chemotaxonomic evaluation by volatolomics analysis of fifty-two genotypes of *Myrtus communis* L. **Plants** 9: 1288. **https://doi.org/10.3390/plants9101288**

Waters CM, Bassler BL. 2005. Quorum sensing: cell-to-cell communication in bacteria. **Annu Rev Cell Dev Biol** 21: 319 - 346. **https://doi.org/10.1146/annurev.cellbio.21.012704.131001**

Wenzel RP. 2007. Health care–associated infections: Major issues in the early years of the 21st century. **Clin Infect Dis** 45: S85 - S88. **https://doi.org/10.1086/518136**

Yangui I, Younsi F, Ghali W, Boussaid M, Messaoud C. 2021. Phytochemicals, antioxidant and anti-proliferative activities of *Myrtus communis* L. genotypes from Tunisia. **South African J Bot** 137: 35 - 45. **https://doi.org/10.1016/j.sajb.2020.09.040**

Zougagh S, Belghiti A, Rochd T, Zerdani I, Mouslim J. 2019. Medicinal and aromatic plants used in traditional treatment of the oral pathology: The ethnobotanical survey in the economic capital Casablanca, Morocco (North Africa). **Nat Prod Bioprospecting** 9: 35 - 48. **https://doi.org/10.1007/s13659-018-0194-6**