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REVIEW

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Malva species: Insights on its chemical composition towards pharmacological applications

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Malvaceae family is typical from the Mediterranean region, contains 240 genera and more than 4,200 species. They are most commonly used as ornamental plants, although they can also be conceived as a food resource and remedy for various diseases, such as digestive, respiratory, genitourinary, throat infections, and skeletal and skin disorders, as also injuries where they are profoundly applied for skin care and as antiseptic and demulcent. They also possess diuretic, lenitive, spasmolytic, and laxative effects, besides to be used as antidiarrheal. Thus, the present review provides in-depth data on *Malva* spp. potential applications and phytochemical composition for food and pharmaceutical industries. Habitat and cultivation conditions and the clinical reports related to its biological effects are also emphasized. *Malva* spp. possess a wide variety of chemical constituents (such as polysaccharides, coumarins, flavonoids, polyphenols, vitamins, terpenes, and tannins) found in different plant organs, especially in leaves and flowers, connected to their biological activity. In general, *Malva* spp. have rather moderate antimicrobial activity, high antiinflammatory and wound healing activities, strong antioxidant activity, and anticancer properties. Results from in vitro and in vivo experiments encourage more in-depth studies, namely clinical trials, towards to improve knowledge on the use of *Malva* spp. for the treatment of various health conditions in humans.

KEYWORDS

habitat, *Malva*, pharmacological properties, phytochemistry, traditional uses

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1 | INTRODUCTION

Malva genus comprises a widespread group of tropical and temperate plants belonging to the Malvaceae family (Zohary, 1987). This genus includes at least 25–30 different species, widespread throughout the temperate, subtropical, and tropical regions of Africa, Asia, and Europe as also in China, India, central of Asia, Mediterranean, South America, America, and Mexico (M. Ray, 1998). *Malva sylvestris* L. is the most important *Malva* species. These plants grow quickly and are used as garden flowers, whereas some of them grow as invasive weeds, especially in the United States, where are not native. The cultivation of this plant is done by seed and in early spring (Vogl et al., 2013). The young leaves of the plant that look like lettuce sound are processed as Greens in the west and used as rice stuffing (Veshkurova et al., 2006).

Malva species have been used in medicine since ancient times. In Catalonia (Spain), the leaves are used to treat urticaria or *Urtica dioica* L. (Vogl et al., 2013), whereas in Austrian, medicine has been used as tea to treat skin disorders and respiratory and gastrointestinal tract infections (Vogl et al., 2013). In traditional Iranian medicine, leaves are used to treat cut wound, eczema, dermal infected wounds, bronchitis, digestive problems, and inflammatory disorders in *Unani* medicinal literature (Henry & Piperno, 2008). Nowadays, the researches on *Malva* plants have shown critical therapeutic properties, such as antiulcerogenic, antioxidant, anticancer, skin tissue integrity, and antiinflammatory (Barros, Carvalho, & Ferreira, 2010; Quave, Plano, Pantuso, & Bennett, 2008). Many species of this genus have shown to be effective in cough, bladder ulcers, intestinal infections, colitis, tonsillitis, gastroenteritis, as cholesterol and lipid-lowering agent, as antihypertensive, antioxidant, analgesics, emollient, pectoral girdle, and on arteriosclerosis treatment (Abdel-Ghani, Hassan, & El-Shazly, 2013).

When looking at chemical composition, amino acids derivatives/proteins, phenolic compounds, mucilages, terpenoids (monoterpenoids, diterpenoids, and sesquiterpenoids), enzymes, coumarins, vitamins, and fatty acids/sterols have been pointed as the most effective and bioactive ingredients (Shehata & Galal, 2014).

Thus, given the promissory aspects highlighted above, the present review aims to provide in-depth data on the potential applications of *Malva* plants and as well as their phytochemical compositions for food and pharmaceutical industries. Moreover, it covers the habitat and cultivation conditions, clinical trials performed using *Malva* plants, and revises the main biological effects reported so far.

2 | MATERIALS AND METHODS

Data on *Malva* spp. were collected, analyzed, and assessed regarding their habitat, cultivation, medicinal use, phytochemistry, and pharmacology effects using Google scholar, science direct, Entrez PubMed, and among others.

3 | HABITAT AND CULTIVATION OF *MALVA* PLANTS

Among the 4,200 species belonging to the Malvaceae family, *Malva* spp. are in the group of the economically important ones (Kintzios, 2002). Besides in its natural habitats, *Malva* plants also grow as weeds of many agricultural plants or cultivated in gardens and fields. The name originates from the Greek word “malasso,” referring to their emollient properties, mostly attributed to the mucous canals, cavities, and epidermal cells located in both roots and aboveground plant parts. *Malva* species are annual, biennial, or perennial terrestrial herbs, widespread almost all over the world, however, predominately inhabiting Europe, Asia, North Africa, and America (Figure 1).

Those found in Australia (*M. rotundifolia* L., *M. parviflora* L., *M. verticillata* L., and *M. sylvestris*) are primarily considered naturalized

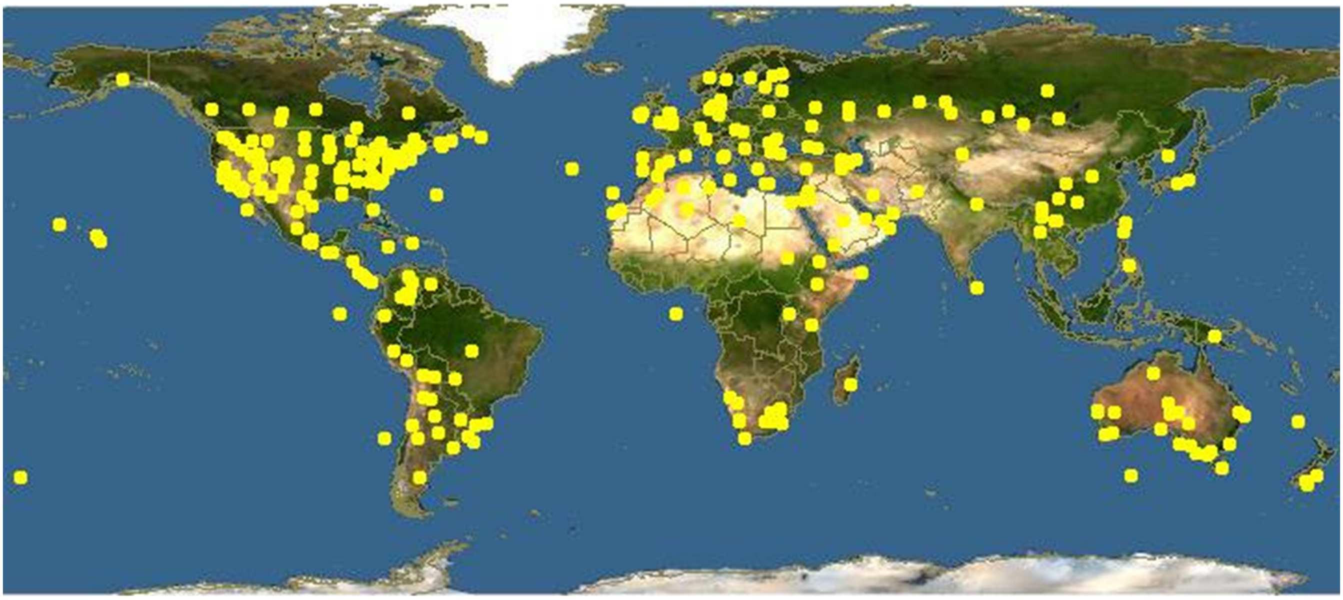

FIGURE 1 Distribution of Malva species (CalPhotos, 2012) [Colour figure can be viewed at wileyonlinelibrary.com]

weeds. The origin of *Malva* species is uncertain, and as the plausible centers of diversity are listed the regions of the Mediterranean and South-Western Asia. Vegetative parts are commonly cover with hairs; indumentum is variable. Leaves are simple, alternate, more or less palmatisect, with stipules. Flowers are actinomorphic, hermaphrodite, with five sepals and five petals. Bracteoles form an epicalyx and fruit are a schizocarp with numerous one-seeded mericarps. Depending on classification, there are up to 40 species within the genus (Barker, 1977; Hanf, 1983; Michael, 2006; M. F. Ray, 1995; Vadivel, Sriram, & Brindha, 2016; Valdés, 2011).

Most of *Malva* species are nitrophilous plants, requiring nitrogen-rich soils to grow correctly. Their habitats are generally warm and brightly lit, set mostly in temperate zones. The plants thrive on moderately dry soils that are with a common variation of the moisture content, a neutral to alkaline chemical reaction, and somewhat aerated. *Malva* species are commonly found in ruderal habitats and meadows (Landolt, 2010; Tutin et al., 1968-1980).

4 | CHEMICAL COMPOSITION OF *MALVA* PLANTS: ESSENTIAL OILS AND PLANT-DERIVED EXTRACTS

Essential oils are mainly depicted as the mixture of 20–80 complex volatile compounds, present in meager amount in different plants parts. Seasonal, climatic, harvest period, distillation techniques, and geographic conditions highly affect the chemical composition of essential oils. Many reports are available assessing the phytochemical composition of *M. sylvestris*. The presence of malvone A, a naphthoquinone, and differently known monoterpenes, aromatic compounds, and a tetrahydroxylated acyclic diterpenes were found (Conner & Beuchat, 1984). Preliminary photochemical analysis on *M. sylvestris* showed the presence of polysaccharides, coumarins, flavonoids, malvin, malvidin 3-(6″-malonylglucoside)-5-glucoside, malvone A, malvaline, scopoletin, polyphenols, niacin, folic acid, vitamins A, C, and E, and tannins (Cutillo, D'Abrosca, Dellagreca, Fiorentino, & Zarrelli, 2006). Other important flavonoids constituents found in *M. sylvestris* are gossypetin 3-sulphate-8-O-β-D-glucoside, hypolaetin 3′-sulphate, and three 8-hydroxyflavonoids (Flack, 1983; Table 1). Terpenoids, such as sesquiterpenes, diterpenes, and monoterpenes, were also present in *M. sylvestris* (Flack, 1983). Indeed, gas chromatography and mass spectroscopy analysis of *M. sylvestris* leaves methanolic extract showed the presence of 31 major peaks, with components including 2-(2-hydroxyethyl)piperidine, 1-butanamine, 2-methyl-N-(2 methylbutylidene), 4-(pyrrolidin-2-ylcarbonyl)morpholine, dithiocarbamate, l-gala-l-ido-octonic lactone, 2-methoxy-4-vinylphenol, pterin-6-carboxylic acid, cyclopropa nedodecanoic acid, pyrazole[4,5-b]imidazole, 1-formyl-3-ethyl-6-β-d-ribofuranosyl-, diethyl mercaptal, pentaacetate, tributyl acetylcitrate, dasycarpidan-1-methanol, acetate (ester)-, 9-desoxo-9-x-acetoxy-3,8,12-tri-O-acetylingol, and stigmasterol with documented antimicrobial and antiviral activities (Al-Rubaye et al., 2017).

The essential oils composition of *M. neglecta* gas chromatography/flame-ionization detection (GC/FID) and GC/mass spectrometry (MS) analyses revealed 41 components with cineole (18.8%), hexatriacontane (7.8%), tetratetracontane (7.8%), and α-selinene (4.2%) as the main constituents (Tables 1 and 2; Haşimi et al., 2017). Many reports reveal different concentrations of volatile compounds, macronutrients, and metal ions according to the three growth stages of *M. aegyptiaca* L. (Zouari et al., 2011). The GC and GC/Ms analyses of mature *M. aegyptiaca* revealed hexadecanoic acid (20.75%), ethyl linoleolate (18.76%), phytol (11.92%) and neophytadiene (5.15%), terpenyl acetate (3.76%), caryophyllene oxide (3.72%), tetradecanoic acid (3.35%), and 6,10,14-trimethyl-2-pentadecanone (3.24%) as major components (Table 1; Zouari et al., 2011). The hierarchical cluster analysis of *Malva* species based on relative percentage areas their essential oil constituents revealed likeness

TABLE 1 Chemical composition (%) of the essential oil from *Malva species* (Al-Rubaye, Kaizal, & Hameed, 2017; Haşimi et al., 2017; Zouari et al., 2011)

Compound	*Malva sylvestris*	*Malva neglecta*	*Malva aegyptiaca*
(cis)-Cadin-4-en-ol	1.31	–	–
(E)-Anethole	0.91	–	–
1,3-Di-tert butyl benzene	–	2.4	–
1,8-Cineol	18.14		–
11,14-Eicosadienoic acid methyl ester	–	–	–
17-Pentatriacontene	–	1.5	–
1-Hexacosanol	–	2.8	–
1-Nonadecanol	–	1.8	–
1-Undecyne	–	–	–
2,5-Di-tert octyl-p-benzoquinone	–	4	–
2-Eicosanol	–	1.8	–
2-methyl decane	–	0.8	–
2-Methyl heptadecane	–	1.6	–
2-Methyl-1-hexadecanol	–	2.3	–
2-Pentadecanone, 6,10,14-trimethyl	–		3.24
3-Ethyl-5-(2-ethylbutyl)octadecane	–	1.5	
4-Vinyl-2-methoxy phenolc	–	–	–
5, 8, 11,14-Eicosatetraenoic acid methyl ester	–	–	–
7,10,13-Eicosaterienoic acid methyl ester	–	–	–
9,12,15-Octadecatrienoic acid methyl ester	–	–	1.58
9,12-Octadecadienoic acid methyl ester	–	–	0.64
9,17-Octadecadienal	–	–	–
9-Hexadecenoic acid methyl ester	–	–	–
9-Hexyl heptadecane	–	0.7	–
9-Octadecenoic acid methyl ester	–	–	–
Anethole	–	2.2	–
Arachidic acid	–	1.3	–
a-Terpineol	–	–	0.17
a-Terpinolene	–	–	0.12
Benzene acetaldehyde	–	–	–
Berneol	–	–	0.89
b-Eudesmol	–	–	1.16
Bicyclogermacrene	–	–	–
b-Ionone	–	–	1.28
Bornyl acetate	–	–	0.94
b-Sesquiphellandrene	–	–	–
Butyl phthalate	–	1.1	–
Cadalene	–	1.1	–
Camphene	–	1.1	–
Camphor	–	1.4	0.28
Carvacrol	1.72	–	–
Carvone oxide	–	0.8	–
Caryophyllene oxide	0.98	–	3.72

(Continues)

TABLE 1 (Continued)

Compound	*Malva sylvestris*	*Malva neglecta*	*Malva aegyptiaca*
Choleic acid	–	0.9	–
Cineole	–	18.8	–
Dillapiolec	–	–	1.54
Docosane	–	1.3	–
Dodecanoic acid	–	–	1.36
epi-α-Muurolol	8.45	–	–
Ethyl iso-allocholate	–	0.8	–
Ethyl linoleolatec	–	–	18.76
Geranyl acetone	3.5	–	–
Germacrene-D	0.74	–	–
Heneicosane	–	1.8	–
Heptacosane	–	0.8	–
Heptadecanoic acid methyl ester	–		–
Hexadecanoic acid	–	0.9	–
Hexadecanoic acid methyl ester	–	–	0.45
Hexadecanoic acidc	–	–	20.75
Hexatriacontane	–	7.8	–
Isononane	–	1.3	–
Limonene	–	1	–
Linalool	1.94		–
Megastigmatrienone	–	–	0.32
Methyl eugenol	3.5	–	–
Methyl thymyl etherc	–	–	0.22
Neophytadienec	–	–	5.15
Nonacosane		1.3	–
Nonanal	–	–	–
Nonanoic acid	–	–	1
Octadecane	–	1.6	
Octadecanoic acid	–	–	1.13
Octadecanoic acid methyl ester	–	–	–
Octane	–	1.7	–
O-Cymene	0.69	–	–
p-Cymene	–	–	–
Pentacosane	–	–	0.66
Pentadecanal	–	–	0.55
Phytolc	–	–	11.92
Sabinene	2.32	–	–
Selinene	3.22	–	–
Spathulenol	2.54	–	0.52
Terpenyl acetate	–	–	3.76
Terpinen-4-ol	–	–	0.24
Tetracosane	–	2.3	–
Tetradecanoic acid	–	–	3.35
Tetratetracontane	–	7.8	–

(Continues)

TABLE 1 (Continued)

Compound	*Malva sylvestris*	*Malva neglecta*	*Malva aegyptiaca*
Thymol	1.19	–	–
trans-b-Damascenone	–	–	1.28
trans-Carveol	–	–	0.33
Tricosane	–	–	–
Valencene	–	1.7	–
Viridiflorol	–	–	0.89
Z-8-octadecen-1-ol acetate	–	1.4	–
α-Cadinol	11.5	–	–
α-Muurolene	–	0.9	–
α-Pinene	0.93	1.6	–
α-Selinene	–	4.2	–
α-Terpineol	1.33	–	–
α-Terpinyl acetate	14.87	–	–
β-Himachalene	–	1.2	–
β-Myrcene	–	0.8	–
β-Pinene	0.95	2.9	–
γ-Cadinene	8.71	–	–
γ-Terpinene	0.43	–	–
δ-Cadinene	1.14	–	–

TABLE 2 Aroma-active compounds from *Malva sylvestris* L

No.	Compounds [a]	μg/kg [b]	Odor description [c]	FD-factor [d,e]
2	Furfural	190	bumet	4
5	2-Pentyl furan	120	green	1
8	Limonene	440	orange, peel-like, fresh	5
9	Phenylacetaldehyde	740	floral	8
10	(E)-β-Ocimene	130	spicy	8
15	Nonanal	170	stale, green	3
17	Phenylethyl alcohol	380	sweet	2
20	Camphor	430	Camphoreous	1
21	Lilac aldehyde	50	fresh, flowery	6
25	Borneol	620	balsamic, sweet	7
26	Menthol	1030	fresh	3
27	Terpinen-4-ol	240	green, sweet	2
32	Decanal	90	floral, green	1
35	2,3-Dihydrobenzofuran	1440	fruity, fatty	1
48	α-Copaene	180	sweet, floral	3
50	β-Damascenone	410	sweet	9
62	(*E*)- β-Ionone	650	flowery	6
71	Dodecanoic acid	400	flowery	1
92	Phenanthrene	2090	carthy	1
117	1-(2-Methylene-3-butenyl)-1-methlenepropyl)-cyclopropane	430	floral	1

between *M. sylvestris* and *M. aegyptiaca* in terms of chemical composition (Figure 2).

Some of these compounds had important variations according to the growth stage. A Tunisian group led by Zouari published another study completing their previous report and evaluating the importance of *M. aegyptiaca* as bread additive (Fakhfakh, Abdelhedi, Jdir, Nasri, & Zouari, 2017). One of the exciting compounds they found was malvasterone, a steroidal triterpenoid that was first isolated from *M. parviflora* roots (Puckhaber, Stipanovic, & Bell, 1998). Steroidal triterpenoids have also been isolated later from *M. sylvestris*. The presence of a lactone sub-unit might be responsible for the malvasterone additional potential activities. On another note, many *Malva* species extracts-based nanoparticles of precious metals (or their oxides) have been made. The significant quality that enables this kind of uses and reactions is the fact that these extracts are rich in flavonoids and anthocyanins that are good reductants, especially when hydroxyl (OH) groups are present in their structures.

Toxicity of *Malva* species to animals is very rare but was indicated in the literature. *M. neglecta* Wallr. was reported to cause hypocalcemia in cow, but the mechanism of poisoning action was not stablished. A controlled study with horses showed that consumption of large amounts of *M. parviflora* resulted in energy balance damages. It is proposed that cyclopropene fatty acids contained in the plant are responsible for this and elevation of acylcarnitine (Wisetmuen, Pannangpetch, Kongyingyoes, Kukongviriyapan, & Itharat, 2008).

5 | FOLK MEDICINAL USES OF *MALVA* PLANTS

Malva plants, primarily *M. sylvestris*, also *M. moschata* L., *M. neglecta*, *M. alcea* L., and *M. rotundifolia*, are widely recognized for food and medicinal purposes (Celka, Buczkowska, Baczkiewicz, & Drapikowska, 2010; Gasparetto, Martins, Hayashi, Otuky, & Pontarolo, 2012). Commonly, these are ornamental plants, although they may be used as a food resource and remedy for various diseases (Al-Rubaye et al., 2017). There are several medicinal and edible uses reported to *Malva* species in different parts of the world (Table 3).

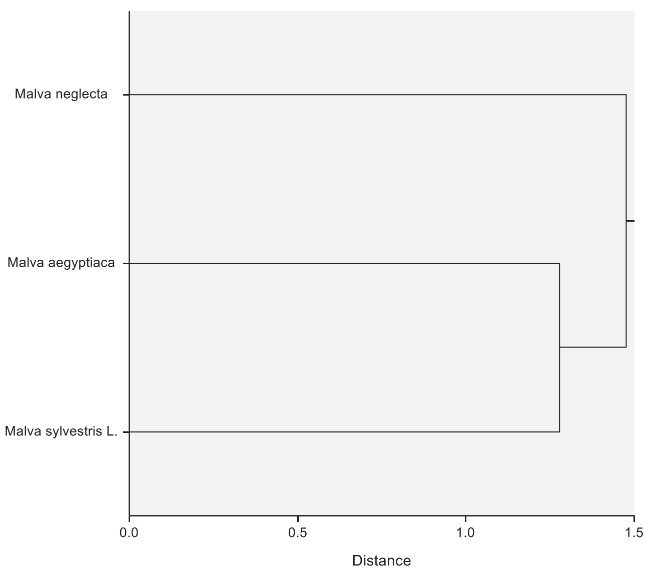

FIGURE 2 Hierarchical cluster analysis of *Malva* species based on normalized relative percentage areas of essential oil constituents (Distance measure: Euclidean; Software: NCSS 2019, v19.0.2)

Malva is widely used in Asia, Europe, Egypt, and the Himalayan region. The medicinal value of *Malva* includes the treatment of coughs and throat infections, as is the case of the traditional Persian medicine, in which *M. sylvestris* is used as mucolytic and antiseptic (Heydarirad, Rezaeizadeh, Choopani, Mosavat, & Ameri, 2017). In the Mediterranean region, *Malva* species have a long history of use for food and medicinal purposes. For example, *M. sylvestris* uses were reported since 2800 BC. Traditionally, *Malva* species are used for distinct clinical purposes, such as digestive, respiratory, genitourinary, skeletal, and skin disorders. *Malva* species have also diuretic, lenitive, spasmolytic, and laxative effects and are used as expectorant, antitussive, antidiarrheal, and profoundly applied for skin care as antiseptic and demulcent. As formerly reported, the most widely used *Malva* species part is the flower and leaf. In Nepal, powdered flowers of *M. verticillata* are also mixed with powdered flowers of *Anisodus luridus* Link and taken with milk to treat cold cough and tonsillitis. In Jordania, the infusion of *M. parviflora* leaf is used as emollient and laxative. A cataplasm leaf is used as antihemorrhoid for colorectal disorders. In traditional Lebanese, medicine leaves of *M. nicaensis* All. and *M. parviflora* are used for renal infections and kidney stones. In Iran traditional medicine, the juice from the flowers is used as emollient and laxative. The infusion of leaves and fruits is used to treat coughs, and the infusion of fruits to treat urinary organs irritation. Moreover, the infusion of flowers, leaves, and aerial parts of *M. sylvestris* is used as a mild laxative and to heal menstrual pains in both Albanians and Italians traditional medicine.

In addition to the traditional uses, the focuses of the recent studies are on the possible roles of these plants in sustainable agriculture and other practices related to environment preservation. The extracts of *M. sylvestris* are applicable as fungicide in bean anthracnose control (Andrade Pinto, Souza, & Oliveira, 2010) and for nanoparticles synthesis with potential use in medicine and industry (Feizi, Taghipour, Ghadam, & Mohammadi, 2018), whereas dry leaves act as a low-cost adsorbent to remove mercury and copper from seawater, wastewater, and water (Ramavandi & Asgari, 2018; Ramavandi, Rahbar, & Sahebi, 2016). Despite the apparent need for quantities of raw materials that are sufficient to satisfy the demands of pharmaceutical and other industries, most of *Malva* plants are collected from natural habitats. The practice is generally labor-demanding and time-consuming, leading to ecosystem degradation and even species endangerment, often resulting in a material of uneven or poor quality. Most of constraints could be overcome by introducing *Malva* plants in production systems. The additional reason to favor cultivated about collected material is the plant property to accumulate certain pollutants, for example, heavy metals cadmium and chromium. It has even been proposed for biomonitoring contaminants in the environment. Although of benefit when it comes to the stabilization of degraded areas, the high

TABLE 3 Traditional medicine uses of *Malva* plants

Botanical name	Place of consumed	Plants part uses	Traditional medicinal uses	Method of application	References
Malva sylvestris L.	Turkey	Flowers and leaves	Asthma, diarrhea, cutaneus abscesses, laxative	A poultice or drinking a decoction	(Dulger & Gonuz, 2004; Sezik, Zor, & Yesilada, 1992)
	Iran	Flowers	Cut wound, eczema, dermal infected wounds, bronchitis, digestive problems, inflammatory, laxative, coughs, protector of gastric and bladder mucous, burns, insect and scorpion stings	Infusions	(Ghasemi Pirbalouti, Yousefi, Nazari, Karimi, & Koohpayeh, 2009; Miraldi, Ferri, & Mostaghimi, 2001)
	European country (Portugal, Spain, Italy, France)	Roots	Toothache, genital tract, dermatitis	Chewed, decoction	(Barros et al., 2010)
		Young leaves	Skin, injuries, burns, stomach, diarrhea pectoral, rheumatism	Decoctions, infusions, cataplasm	
		Shoots	Toothache, constipation, genital tract, haemorrhoids	Decoctions, infusions, vapor baths	
		Flowers	Acne, skin condition, eyes, throat pain, cough	Decoctions, baths, gargles, lotions, vapor bath, syrups	
		Leafy-flowered, stems	Cold, cough, throat pain, tonsils, bladder rheumatism	Ointments, poultices, baths, decoctions, infusions, liniments	
		Seeds/ mericarps	Inflamed or injured skin	Maceration	
	Bulgaria	Flowers, leaves	Spasmolytic, antitussive, sedative, cystitis, cholagogue	Infusion	(Leporatti & Ivancheva, 2003)
	Italy	Flowers, leaves, aerial parts	Emollient, laxative, soothing, expectorant	Infusion	(Pieroni & Quave, 2005)
	Albanian	Flowering tops, aerial parts	Mild laxative, menstrual pains, al sore throat and bronchitis, as intestinal depurative		(Pieroni & Quave, 2005)
Malva neglecta Wallr.	Turkey	Leaf, aerial parts, stem, root, fruit	Abdominal pain, mouth pain, infertility, promote maturation of abscess, Menstrual disorders, Beneficial for intestines, Abortifacient, Tension, cancers, gynaecological disorders, hemorrhoids, muscle pain, kyphos, coughs, menstrual aches, diabetes, Kidney stone, afterbirth care, Diarrhea, weakness, asthenia, respiratory tract inflammation, Urinary inflammation	Infusion, cataplasm, eaten cooked with salt; root is washed and inserted in vagina; boiled in water, after filtering drunk as tea on an empty stomach	(Dalar, Türker, & Konczak, 2012; Gurbuz, Ozkan, Yesilada, & Kutsal, 2005; Tabata et al., 1994)
Malva verticillata L.	Nepal	Flowers	Cold, cough, tonsillitis, headache	Powdered flower of *M. verticillata* together with the powdered flower of *Anisodus luridus* is taken with milk	(Gewali, 2008)
Malva nicaensis All.	Eastern region of the Mediterranean	Whole plant	Coughing and wounds	Decoction	(Azaizeh, Saad, Khalil, & Said, 2006)
	Lebanon	Leaves	Catarrhs, Renal infections, Kidney Stones, Respiratory infections, Constipation, Skin diseases	Decoction	(Baydoun, Chalak, Dalleh, & Arnold, 2015)
	Turkey	Aerial parts	Expectorant and cough	Infusion is consumed as tea	(Uzun et al., 2004)
Malva parviflora L.	Jordanian	Leaves	Emollient, carminative, laxative, antihemorrhoid	Infusion and cataplasm of leaf	(Al-Khalil, 1995)
	Lebanon	Leaves	Catarrhs, Renal infections and kidney Stones, Respiratory infections, Constipation	Decoction	(Baydoun et al., 2015)

(Continues)

TABLE 3 (Continued)

Botanical name	Place of consumed	Plants part uses	Traditional medicinal uses	Method of application	References
	Zapotitlán de las Salinas, Puebla (México)	Root	Dysentery	Infusion	(Hernández et al., 2003)
	Ethiopian	Root	To treat asthma and wounds		(Tadeg, Mohammed, Asres, & Gebre-Mariam, 2005)

pollutant accumulation decreases the plant raw material quality and may pose a risk for human health (Ceccanti, Landi, Benvenuti, Pardossi, & Guidi, 2018; Terzi, Acemi, Ergül, & Özen, 2016; Unver, Ugulu, Durkan, Baslar, & Dogan, 2015). Therefore, to avoid possible raw material contamination, it would be recommended to produce *Malva* plants within organic or another sustainable agricultural system. Having in mind the weather, soil, and different specificities of the particular areas, plant-environment interactions, as well as the restrictions regarding mineral nutrition and pesticide application that are characteristic for organic production, comprehensive studies are required to balance the quality and yield inputs in cultivated plants (Brdar-Jokanović et al., 2018; S. Delfine et al., 2012; Jaradat, Abualhasan, & Ali, 2015; Nazemi Rafi, Kazemi, & Tehranifar, 2019; Nourafcan, Pouyanfar, & Mahmoudirad, 2015).

6 | PHARMACOLOGICAL PROPERTIES OF *MALVA* PLANTS

In the course of the various preclinical studies performed with *Malva* species, its antimicrobial, antioxidant, antidiabetic, anticancer, antiinflammatory, antihypertensive, and wound healing effects appear as the most prominent ones, as described below and briefly summarized in Figure 3.

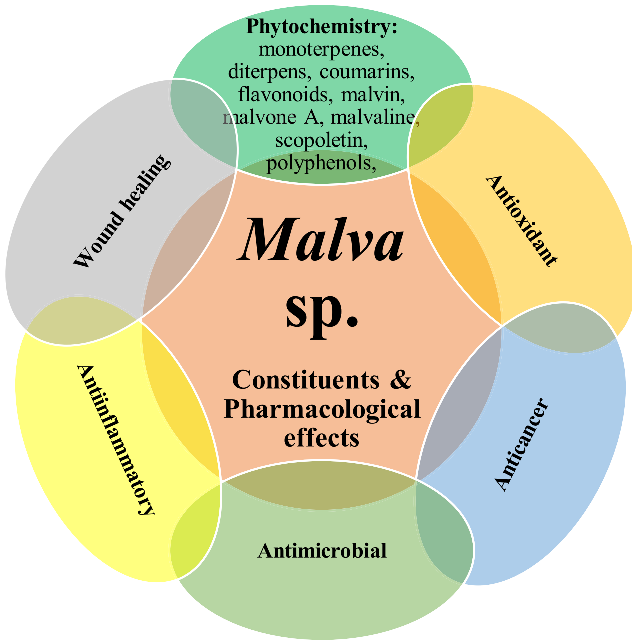

FIGURE 3 Major *Malva* species pharmacological effects [Colour figure can be viewed at wileyonlinelibrary.com]

6.1 | Antimicrobial activities of *Malva* plants

Plants from *Malva* genus have shown antimicrobial activity against a wide variety of bacteria and fungi (Table 4). Numerous studies investigated the *M. sylvestris* and *M. parviflora* extracts antimicrobial activity against standard bacteria (*Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa)* and fungi (*Candida albicans and Aspergillus niger*). Moreover, many other species were investigated in vitro by disc diffusion method (Table 4). Benso et al. showed activity of *M. sylvestris* leaves extract and its fractions for cells infected by *Aggregatibacter actinomycetemcomitans*—bacterium often associated with aggressive periodontitis (Benso et al., 2015). *M. sylvestris* hydroalcoholic extract showed antibacterial effect on *A. actinomycetemcomitans* (MIC = 156.2 μ g/ml). However, further studies in animal models will allow not only ascertain its efficacy but also safety prior any use in mouthwashes to prevent periodontal biofilm (Vahabi, Hakemi-Vala, & Gholami, 2019). *M. sylvestris* extract antibacterial activity was also reported for *Helicobacter pylori* strains (Cogo et al., 2010). Not only the whole *Malva* extracts but also their fractions and isolated compounds were tested as antimicrobials. The antimicrobial activity of an anthocyanin extracted from *M. sylvestris* was also reported, being found a great bacteriostatic activity on *S. aureus* (Cheng & Wang, 2016). Also, pheophytin a, a chlorophyll derivative of Malvaceae, exhibited strong antimicrobial effects against both Gram-positive and -negative bacteria, as well as *Candida* spp. (Gomes et al., 2015). Another compound, malvone A extracted from *M. sylvestris* stems, appears to be the most active ingredient and responsible for the antimicrobial potential of this plant (Veshkorova et al., 2010). Therefore, *M. sylvestris* extracts seem to be promisor for biopesticides formulation. In turn, three *M. parviflora* seeds-derived antimicrobial proteins revealed distinct homologies as well as a wide antimicrobial spectrum (Wang et al., 2001). *M. sylvestris* extracts and fractions showed strong anti-HIV activity in nanomolar or picomolar range in a model with epithelial and blood cell lines with reduction by 60% of infectivity, viral particles modulation of cytokines, and signaling inflammatory markers: interleukin (IL)1-alpha, IL-beta, IL-6, IL-8, and granulocyte-macrophage colony-stimulating factor (Benso et al., 2016)

Overall, studies found that *Malva* spp. have rather moderate activity against tested microorganisms in comparison with standard antibiotics. However, the results of numerous studies confirm that, due to

TABLE 4 *In vitro* antimicrobial activity of *Malva* species

Malva spp.	Plant part	Extract	Antimicrobial action	Reference
Malva neglecta	Whole plant	Methanol	*K. pneumoniae, B. subtilis, S. typhi, Aspergillus niger, A. flavus, A. fumigatus, Fusarium solani*	(Imtiaz et al., 2012)
		Methanol acetone	*E. coli, St. pyogenes, Staph. aureus, Ps. aeruginosa, C. albicans*	(Haşimi et al., 2017)
Malva parviflora	Whole plant	Hexane chloroform ethanol	*B. subtilis, S. aureus, E. coli, Proteus vulgaris, A. niger, A. oryzae*	(Islam, Ali, Saeed, Jamshaid, & Khan, 2007-2010)
	Root bark B-sitosterol	Petroleum ether chloroform ethanol	*Staph. aureus, E. coli*	(Ododo, Choudhury, & Dekebo, 2016)
	Seeds	Chloroform	*S. albus* (syn. *S. epidermidis*), *B. anthracis, B. pumilus, B. subtilis, Vibrio cholerae, Xanthomonas campestris, X. malvacearum*	(Parihar & Jadhav, 2017)
	Leaves, roots	Hexane methanol Water ultrasounds	*Micrococcus luteus, B. subtilis, S. aureus, S. epidermis, E. coli, P. aeruginosa, K. pneumoniae*	(Shale, Stirk, & van Stade, 2005)
	Roots	Methanol	*S. aureus, E. coli, P. aeruginosa, C. albicans, A. niger, Trichophyton mentagrophytes*	(Tadeg et al., 2005)
	Seeds proteins: Cw-3, cw-4, cw-5	-	*Fusarium graminearum, Phytophthora infestans,*	(Wang, Bunkers, Walters, & Thoma, 2001)
Malva preta	Pheophytin a	Hexane	*S. aureus, S. epidermidis, B. subtilis, P. aeruginosa, E. coli, Shigella flexneri, C. albicans, C. krusei, C. tropicalis, C. guilliermondii*	(Gomes et al., 2015)
Malva sylvestris	Whole plant	Methanol	*P. aeruginosa*	(Akgunlu et al., 2016)
		N-hexane	*Acinetobacter baumannii, Salmonella enteritidis, S. aureus, Enterococcus faecalis, Bacillus subtilis, C. albicans, C. krusei*	
	Leaves	Ethanol	*Aggregatibacter actinomycetemcomitans, Fusobacterium nucleatum, Prevotella intermedia, Porphyromonas gingivalis*	(Benso, Rosalen, Alencar, & Murata, 2015)
		Ethanol	*Helicobacter pylori*	(Cogo et al., 2010)
	Flowers, leaves	Water	*E. coli, S. aureus, Salmonella* spp., *Penicillium* spp., *Rhizopus* spp.	(Mihaylova, Popova, Denkova, Alexieva, & Krastanov, 2015)
	Flowers, leaves	N-hexane Dichloromethane methanol	*Erwinia carotovora, S. aureus, Streptococcus agalactiae, Enterococcus faecalis*	(Razavi, Zarrini, Molavi, & Ghasemi, 2011)
	Leaves	Water	*E. coli, S. saprophyticus, P. aeruginosa*	(Karm, 2017)
	Leaves, roots and flowers	Methanol	*E. coli, S. aureus, P. aeruginosa*	(Walter, Shinwari, Afzal, & Malik, 2011)
	Seed oil	-	*E. faecalis, Listeria monocytogenes, B. cereus, E. coli, C. albicans*	(Zohra, Meriem, & Samira, 2013)
	Anthocyanin	Water	*Staph. aureus*	(Cheng & Wang, 2016)

the increasing rate of antibiotics-acquired microbial resistance, there is a huge need to explore the potential of *Malva* species-derived bioactives. For example, *M. sylvestris* shows antibacterial activity against methicillin-resistant *S. aureus* (Razavi et al., 2011). Indeed, microorganisms with acquired antimicrobials resistance trigger serious problems in the world for hygienic and health programs. These problems need the search for new antimicrobial agents. Also, except possible applications in medicine and food industry, *Malva* species extracts may be used in modern agriculture as biocontrol agents. It is documented that, despite the effective results achieved with the use of synthetic pesticides in pests' control, these molecules exert harmful effects both on human health and environment. Thus, naturally occurring bioactives present in *Malva* spp. could be promisor alternatives for pest control also ensuring an environmentally friendly agriculture (Razavi et al., 2011).

6.2 | Antioxidant activities of *Malva* plants

Reactive oxygen and nitrogen species have been concerned in many diseases, including inflammation, autoimmune, cardiovascular, diabetes, neurodegenerative diseases, and even cancer (Mavi, Terzi, Özgen, Yildirim, & Coşkun, 2004). Due to the imperative role of antioxidants in the diseases' pathogenesis, the antioxidant ability of different medicinal plants has been assessed through several preclinical studies (Sharififar, Moshafi, Shafazand, & Koohpayeh, 2012)

Different *Malva* species have shown significant antioxidant effects, and there are numerous studies that describe the antioxidative effects of *Malva* plants from diverse regions. Moreover, distinct plant parts, including leaves, flower, petioles, stem, and seeds, have been investigated for antioxidant efficacy, and some results are shown in Table 5 . As it is observed, most studies were carried out in *M. sylvestris*, followed by *M. parviflora* and *M. verticillata*.

6.2.1 | Antioxidant properties of M. sylvestris

M. sylvestris is used traditionally to treat a wide range of diseases, including cough, cold, bronchitis, digestive problems, eczema, antimicrobial and antiinflammatory, rheumatism, and wound healing. *M. sylvestris* revealed to exert significant antioxidant effects due to its richness in antioxidant molecules (Dipak, 2016). Tabaraki et al. assessed the in vitro antioxidant potential of ethanolic extracts from *M. sylvestris* leaves and petioles. The antioxidant activity of leaves was higher than petioles that can be relevant to more presence of flavonoid compounds in the leaves as they are typical phenolic compounds with powerful antioxidant activity. 2-Methoxy-4-vinylphenol was the main phenolic compound present, according to the GC–MS analysis of the extract (Tabaraki, Yosefi, & Asadi, 2012). Antioxidant capacities of *M. Sylvestris* flower methanolic extract assessed by DPPH, ferric reducing/antioxidant power (FRAP), ferrous ion chelating capacity, peroxidase (POX), and catalase (CAT) activity revealed a reducing power inhibition of 0.355 at 0.5 mg/ml, whereas synthetic antioxidant butylated hydroxyl toluene (BHT) and ascorbic acid showed much higher FRAP of 0.715 and 1.854 at the same concentration, respectively. Although its EC_{50} value was higher (21.52 μg/ml) than that of the positive controls, BHT and α-tocopherol (3.23 and 2.25 μg/ml, respectively), *M. sylvestris* flower extract exhibited notable antioxidant activity through scavenging different reactive oxygen and metal chelation, POX activities and hydrogen-donating, which is possibly conferred by phenolic constituents (Mohajer, Taha, Ramli, & Mohajer, 2016). *M. sylvestris* leaves extract and fractions from Brazil revealed the aqueous fraction as the bioactive fraction using ABTS and DPPH assays. Its phytochemical analysis identified rutin as the major compound (Benso et al., 2016). Baghdad et al. assessed both phenolics and flavonoids content of *M. sylvestris* leaves, stems, flowers, and seeds, in addition to their in vitro antioxidant potential. Their findings demonstrated that all extracts displayed dose-dependent antioxidant effects. As the same as other studies, leaf and seed extracts presented the highest and lowest levels of total phenolic compounds, respectively (Beghdad et al., 2014).

M. sylvestris leaves ethanolic extract collected in Portugal showed 43.1% inhibition of DPPH radical at 0.1 mg/ml. Results of this study indicated that the antioxidant ability is not exclusively related to the phenolic composition, because it was not found a linear correlation between rosmarinic acid amounts and the whole activity (Jabri, Wannes, Marzouki, & Sebai, 2017). By other studies, strong antioxidant activities for *M. sylvestris* leaves were also noted and related to the presence of phenols, flavonoids, carotenoids, and tocopherols (Barros et al., 2010), being their abundance higher than ones reported in Italian species (Conforti et al., 2008).

The essential oils were also investigated for free radical scavenging potential in the study by Delfine et al., and results revealed that essential oils do not have any radical scavenging activity in DPPH test, whereas in FRAP test, the antioxidant effect appeared higher for all the samples, though less than BHT. They concluded that essential oils samples have not free radicals scavenging activity but are notable ferric reduction/antioxidant agents. The essential oils sample indicated the main ferric ion reducing ability at 0.57 mmol TE/L, where based on chemical analysis, the phenolic composition is higher. It contained high amounts of 4-vinylguaiacol and eugenol. The obtained results confirmed the formerly published reports, concluding that polar solvents extracts act more efficiently than essential oils or other extracts as antioxidant agents (S Delfine et al., 2017). The lowest level of phenols, flavonoids, and carotenoids were found in fruits, as well as lowest antioxidant activity in all assays (Barros et al., 2010). The Tunisian *M. sylvestris* leaves extract exhibited EC_{50} value of 333.5 mg/ml in DPPH assay, which was considerably lower than that of ascorbic acid (97.01 μg/ml). In this study, the reducing potential (Fe^{3+} to Fe^{2+}) revealed to be dose-dependent. The researcher attributed the antioxidant activity to the presence of gallic, catechic, epicatechic and vanillic acids, and coumarin along with rutin, quercetin, kaempferol, and luteolin (Ben Saad et al., 2016). The antioxidant activity of *M. sylvestris* seed oil from Serbia was also estimated, and the seed oil from *M. sylvestris var. mauritiana* (EC_{50} = 28.97 mg/ml was two times stronger than *M. sylvestris* seed oil. Because both had fairly the same composition of fatty acids and sterols, the antioxidant activity may have been associated with some phenolic compounds and tocopherols (Tešević et al., 2012). Other studies were also performed

TABLE 5 Antioxidant activity of *Malva* species

Malva species	Extract/fraction	Experimental method	Results IC_{50} (μg/ml)/ % Inhibition	Reference
M. aegyptiaca	Crude water-soluble polysaccharides from leaves	Fe^{2+} chelating activity FRAP β-Carotene bleaching DPPH	IC_{50} = 1.15 μg/ml IC_{50} = 1.22 μg/ml IC_{50} = 1.56 μg/ml IC_{50} = 1.94 μg/ml	(Fakhfakh et al., 2017)
M. neglecta Wallr.	Leaves hydrophilic extract	FRAP (μFe^{+2}/g) ORAC (μmol TE/g)	190.3 μFe^{+2}/g 898.9 μmol TE/g	(Dalar et al., 2012)
	Stems		51.5 μFe^{+2}/g 506.2 μmol TE/g	
	Flowers		109.8 μFe^{+2}/g 795.2 μmol TE/g	
	Roots		39.2 μFe^{+2}/g 425.3 μmol TE/g	
	Fruits		56.4 μFe^{+2}/g 448.1 μmol TE/g	
	Whole plant		67.5 μFe^{+2}/g 582.3 μmol TE/g	
	Flower hydroalcoholic extract	FTC FRAP Superoxide anion radical scavenging Hydrogen peroxide scavenging	77.3% 27% 84.2% 85.3% 59.0 46.4%	(Güder & Korkmaz, 2012)
	Leaf hydroalcoholic extract	DPPH Metal chelating activity	74.1%, 32% 75.4% 78.1% 62.1% 37.3%	
M. parviflora	Whole plant methanol extract	DPPH ABTS	9.3% 94.3%	(Afolayan et al., 2008)
	Polyphenols extract	DPPH	33.31%	(Abd El-Salam & Morsy, 2019)
	Leaves ethanol extract	DPPH	IC_{50} = 2.61 mg/ml	(Messaoudi et al., 2015)
	Leaves aqueous extract	ABTS FRAP DPPH	82.58% 65.41 μM Fe^{2+}/100g IC_{50} = 76.67 μg/ml	(H. Bouriche et al., 2011; Teixeira et al., 2016)
	Leaves methanol extract	DPPH	IC_{50} = 89.03 μg/ml	(H. Bouriche et al., 2011)
M. sylvestris	Ethanol extract Leaves	DPPH ABTS (μmol Trolox/g)	IC_{50} = 2.62 mg/ml 0.34 μmol Trolox/g	(Benso et al., 2016)
	Aqueous fraction		IC_{50} = 1.01 mg/ml 1.30 μmol Trolox/g	
	Ethyl acetate fraction		IC_{50} = 0.94 mg/ml 1.10 μmol Trolox/g	
	Leaves ethanol extracts	TBA DPPH FRAP TAC	>1 mg/ml 16.691–606 μg/ml 0.144 μmol Fe^{2+}/mg 0.138 mg EAA/g	(Beghdad et al., 2014; Conforti et al., 2008)
	Flowers	DPPH FRAP TAC	IC_{50} = 13.92 mg/ml 0.040 μmol Fe^{2+}/mg 0.114	(Beghdad et al., 2014)
	Stems		IC_{50} = 76.483 mg/ml 0.152 μmol Fe^{2+}/mg 0.087 mg EAA/g	

(Continues)

TABLE 5 (Continued)

Malva species	Extract/fraction	Experimental method	Results IC_{50} (µg/ml)/ % Inhibition	Reference
	Seeds		IC_{50} = 59.39 mg/ml 0.091 µmol Fe^{2+}/mg 0.155 mg EAA/g	
	Aerial parts essential oil	DPPH FRAP	−0.57 mmol TE/L	(S Delfine et al., 2017)
	Leaves and flowers aqueous extract	DPPH NBT	IC_{50} = 0.68 g/l IC_{50} = 1.0 g/l	(Marouane et al., 2011)
	Leaves methanol extract	DPPH	40.2% 37.1%	(Jaradat et al., 2015)
M. sylvestris	Leaves aqueous extract	DPPH	43.1%	(Jabri et al., 2017)
	Aqueous extract	DPPH MO reducing power	24% 38%	(DellaGreca et al., 2009)
	Leaves water-soluble polysaccharides	DPPH $OH^{\bullet}$ scavenging Reducing power (absorb.)	67.1% 65% 0.75	(Rostami & Gharibzahedi, 2017)
	Leaves hydroalcoholic extract	DPPH FRAP	IC_{50} = 0.071–0.077 mg/ml 0.129–0.149 mmol Fe^{2+}/g	(Tabaraki et al., 2012)
	Petioles hydroalcoholic extract		IC_{50} = 0.071–0.075 mg/ml 0.046–0.051 mmol Fe^{2+}/g	
M. sylvestris	Leaves crude polysaccharides	DPPH $OH^{\bullet}$ scavenging	89% 87%	(Samavati & Manoochehrizade, 2013)
	Leaves methanol extract	Metal chelating β-carotene bleaching test	0.42 0.72	(Saad et al., 2017)
	Flower methanol extract	DPPH Fe^{2+} chelating FRAP POX activity CAT	21.52 176.72 0.355 146.25 65.016	(Mohajer et al., 2016)
	Leaves methanol extract	DPPH FRAP	333.5 670 mmol Fe^{2+}/g	(Ben Saad et al., 2016)
M. verticillata	Leaf ethanolic extract	DDPH (mg AAE/g) FRAP (mmolTrolox/100 g) ABTS (mg Trolox/g)	22.14 421.48 363.83	(Bao, Bao, Li, Wang, & Ao, 2018)
	Stem		5.15 169.13 46.72	
	Seed		12.62 313.59 76.47	

Abbreviations: CAT, catalase; FRAP, ferric reducing/antioxidant power; FTC, ferric thiocyanate; NBT, *nitroblue tetrazolium;* OH, hydroxyl; ORAC, oxygen radical absorbance capacity; POX, peroxidase; TAC, total antioxidant capacity; TBA, thiobarbituric acid; TEAC, Trolox equivalent antioxidant capacity.

to assess the antioxidant activity of *M. sylvestris* polysaccharides (MSP) besides to consider phenolic compounds. Water-soluble MSP extracted via enzyme-assisted extraction by Rostami et al. and three purified homogeneous fractions, comprised of galactose, glucuronic acid, arabinose, rhamnose, and mannose, revealed a dose-dependent increase in antioxidant activity. Overall, the findings gained in this study demonstrate that MSP fractions have high reactive oxygen scavenging and reducing activities. This was justified by the fact that as MSP molecule possesses many hydroxyl groups in their structure, they can act as electron donors and deliver the perfect antioxidant action (Rostami & Gharibzahedi, 2017). This result agrees with the dose-dependent scavenging activity observed in vitro for DPPH and OH radicals, which was previously published for crude polysaccharides from *M. sylvestris* leaves. That study revealed high scavenging activities of crude polysaccharides derivatives from the plant leaves, with DPPH and hydroxyl radicals scavenging activity of 89 and 87%, respectively. The wild *M. sylvestris* leaves were found to possess higher antioxidant activity when compared with the cultivated species (Samavati & Manoochehrizade, 2013), further confirmed by Jaradat et al. (Jaradat et al., 2015).

There is consistent literature regarding *M. sylvestris* antioxidant effects. In the study by Ben saad et al., the effects of *M. sylvestris* extract against lithium carbonate-induced oxidative damages in the kidney of male rats have been reported. Oxidative stress influenced by lithium carbonate caused a significant increase in lipids peroxidation level along with a decrease in CAT, superoxide dismutase, and glutathione peroxidase activities. Pretreatment with *M. sylvestris* restituted all mentioned factors and prohibited toxicity. They have hypothesized that occurrence of a high level of Na^+ and K^+ monitored in mallow extract could recompense the loss of electrolytes induced by lithium-supplemented rats as well as the phenolic and flavonoid components in the plant afford protection against oxidative injury (Ben Saad et al., 2016). In addition, the hydroalcoholic *M. sylvestris* extract administration in gentamicin-induced nephrotoxicity in rat led to an improvement in kidney and liver (aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase) function, a decrease in proinflammatory factors (TNF-alpha and ICAM-1 mRNA) expression levels, reduction of oxidative stress (malondialdehyde and FRAP), and to a decrease in tissue injuries (Z. Mohamadi Yarijani et al., 2019).

The results were in conformance with outcomes of their other similar study carried out to assess the positive effects of *M. sylvestris* on the testes and heart of male rats. A considerable protective effect of plant extract was found against lithium-induced toxicity in both organs associated with the existence of complex polysaccharides (Saad et al., 2017). According to the report by Marouane et al., the administration of *M. sylvestris* extract also could decrease lipids peroxidation levels and superoxide dismutase, CAT and glutathione peroxidase activities in the abnormal features observed in kidney slices from vanadium-poisoned rats in rat kidney, which had already enhanced by vanadium treatment (Marouane, Soussi, Murat, Bezzine, & El Feki, 2011). Jabri et al. have studied the protective effect of *M. sylvestris* aqueous extract against oxidative stress induced by loperamide in rat jejunum. They found that treatment with mallow extract blocked antioxidant enzymes activity depletion, lipids peroxidation, reduced glutathione level, and inhibited jejunal overload of hydrogen peroxide and free iron induced by loperamide. These effects were related to antioxidant molecules present in this plant, like malvidin, delphinidin, quercetin, apigenin, malvin, and kaempferol (Jabri et al., 2017). The effects of *M. sylvestris* hydroalcoholic extract on the toxicity effects of cisplatin in kidneys and liver were also investigated, and results showed protective of mallow supplementation in these organs, along with reduction of oxidative stress and inflammation (Mohamadi Yarijani, Godini, Madani, & Najafi, 2018).

6.2.2 | Antioxidant properties of M. parviflora

M. parviflora is another *Malva* species that have appeared as an extremely talented antioxidant species. Widely distributed in Africa, it is used in folk medicine to treat some inflammatory illnesses. The methanolic extract of *M. parviflora* whole plant inhibited 94.3% of $ABTS^{\bullet+}$ radical cation and 9.3% of DPPH, meaning more capacity to quench $ABTS^{\bullet+}$, comparable with that of BHT (97.57%) and rutin (79.45%), as standards. Flavonoid content was higher than phenolics and proanthocyanidins, and a linear correspondence was observed between polyphenols and antioxidant activities, thus concluding that frail DPPH inhibition is probably relevant to very low phenolic content, with $ABTS^{\bullet+}$ radical scavenging capacity being attributed to the different antioxidant reactions mechanisms (Afolayan, Aboyade, & Sofidiya, 2008).

M. parviflora leaves methanol and aqueous extracts showed noticeable quenching effects with IC_{50} values of 89.03 and 76.67 μg/ml, respectively, comparable with the standard BHT. Alhough the EDTA standard displayed a higher chelating activity, both extracts could chelate ferrous ions in a concentration-dependent manner, whereas methanol extract exhibited lower activity than the aqueous one (Bouriche, Meziti, Senator, & Arnhold, 2011).

Study on the effect of drying process on total phenolic compounds content and antioxidant ability of *M. parviflora* leaves revealed that microwave drying at 350 W was the best operative method even if the difference was not too much. IC_{50} in DPPH test differed from 2.57 to 3.10 mg/ml for all examined working conditions. Authors explained the increase of antioxidants in dried leaves owing to their release improvement by heat treatment and expedition in their extraction (Messaoudi et al., 2015). *M. parviflora* antioxidant activity in the study by Teixeira et al. proved a noteworthy positive association between ABTS and FRAP tests, phenol content and ABTS and FRAP tests. Thus, phenolic compounds seem to be responsible for the antioxidant activity as primary components (Teixeira, Cruz, Franco, Vieira, & Stefenon, 2016). More recently, polyphenols extract from *M. parviflora* L. leaves, consisting mainly of naringenin, rho-coumaric acid, apigenin-7-glucoside, luteolin, and cinnamic acid, showed DPPH radical scavenging activity with 33.31% inhibition (Abd El-Salam & Morsy, 2019).

6.2.3 | Antioxidant properties of *M. neglecta*

M. neglecta leaves and flowers have been effectively used for cough, digestive, and respiratory system problems and for its antiulcerogenic effects (Güder & Korkmaz, 2012). *M. neglecta* leaves are used in Turkish traditional medicine as main plant materials (Dalar et al., 2012). Hydroalcoholic extracts from *M. neglecta* flower and leaves (FE, LE) at 100 μg/ml showed antioxidant properties (Table 1) with 77.3% (FE) and 74.1% (LE) total antioxidant activity (ferric thiocyanate), 84.2% (FE) and 75.4%(LE) superoxide radical scavenging potency, and 85.3%(FE) and 78.1% (LE) H_2O_2 scavenging ability. DPPH and FRAP flower extract revealed to be stronger than the leaf extract. Total phenols and flavonoid as catechin equivalent in 1 mg of lyophilized extracts were identified at MNF 136.1, 46.7 (μg/mg) in flower and 106.1, 22.9 (μg/mg) in leaf. No correlation was stated between total phenols and antioxidant activity (Güder & Korkmaz, 2012). As well, *M. neglecta* hydrophilic leaf extract showed higher antioxidant potential than flower, stem, fruit, and root extracts, respectively, and portrayed a higher phenolic composition (17.4 mg GAE/g) as main components of leaves, involved mostly flavonoids (7.21 mg RE/g) and 4-hydroxycinnamic acids (2.56 mg CAE/g). The average level of total phenolics in *M. neglecta* whole plant was 6.6 mg GAE/g. In this study, also flavonols and anthocyanins were assessed, as they have been incriminated in the antioxidant capabilities and health profits. Consequently, flavonols were recognized as the main flavonoid compounds (67.70% in leaf; Dalar et al., 2012). *M. neglecta* was also reported as a safe alternative to prostodin, a synthetic contraceptive, but the published literature so far supports that the contraceptive effects of these plants were in vain, even though other plants with this activity are well-known (Sandeep et al., 2010).

6.2.4 | Antioxidant properties of *Malva aegyptiaca*

M. aegyptiaca is a wild spontaneous and mucilaginous plant belonging to *Malva* genus, more prevalent in North Africa and used in the treatment of fevers, wounds, and pain. A study in Tunisia assessed the antioxidant effects of crude water-soluble polysaccharides extracts. The extract prepared by precipitation with cetylpyridinium chloride presented significant chelating, β-carotene peroxidation inhibition, and scavenging activities. Extract revealed a remarkable dose-dependent chelating ability and β-carotene bleaching. Authors postulated that polysaccharides could transform free radicals to stable components as electron donors and that the presence of more sulfated groups and total sugars triggers upper antioxidant activity. Although the crude water-soluble polysaccharides extract activity, it was lower than standards (Fakhfakh et al., 2017). In sum up, in can be supposed that different *Malva* species possess strong antioxidant activity, associated with their richness in phenolic compounds, as well as other constituents, like polysaccharides. Among the different organs, in general, leaves appear to be the main contributors to the antioxidant potential, followed by flowers. It is noticeable that the whole antioxidant potential is also related to the region and diversity of geographical environments, including soil, sunlight, temperature, humidity, altitude, precipitation, and so on. Thus, the antioxidant effects differ with variations in plants chemical composition. Anyway, as oxidative injury is connected to degenerative and inflammatory diseases, such as arthritis, cardiovascular diseases, cancer, rheumatism, immune system problems, brain dysfunction, and others (Bouriche, Meziti, & Senator, 2010), the therapeutic potential of *Malva* species due to its remarkable antioxidant constituents can be considered for further medicinal investigations.

6.3 | Antidiabetic activities of *Malva* plants

There seems to be a contradiction in two reports regarding *M. parviflora* antidiabetic activity (Smith-Palmer, Stewart, & Fyfe, 1998). Some authors have reported weak antidiabetic activity (Phoboo, Kalidas, & Tahra, 2015), whereas others reported strong effects (El-gizawy & Hussein, 2015). Basically, these differences are due to plant parts, extraction solvents, and even the test models used (Veshkurova et al., 2006). However, the n-BuOH fraction from *M. verticillata* induced significant recovery of alloxan-damaged pancreatic islets in zebrafish. Two isolated major components, alone or in combination, were able to recover alloxan-damaged pancreatic islets and for their KATP channel-blocking mechanism using diazoxide in zebrafish (Ko et al., 2018). One of the targets of the antidiabetic drug is alpha-amylase, whose inhibition limits glucose absorption by suppressing carbohydrate digestion. The lipophilic and hydrophilic fractions of *M. sylvestris* leaves were able to inhibit porcine pancreatic alpha-amylase activity and, thus, may be used as supplements (Hawash et al., 2019).

6.4 | Anticancer activities of *Malva* plants

Cancer is one of the main leading causes of death and disability worldwide, with more than 18.1 million of new cases and 9.6 million deaths per year (Bray et al., 2018). The use of biological medicines for cancer treatment is highly controversial, because patients are more likely to refuse the conventional therapeutic strategies, thus presenting a higher risk of death (Johnson, Park, Gross, & Yu, 2018). For many people from third world countries, it is the only treatment available (Hill, Mills, Li, & Smith, 2019), whereas in developed countries, these are used as a complementary therapy to ameliorate some undesirable side effects of conventional treatments (Fitzsimmons et al., 2019; Keene, Heslop, Sabesan, & Glass, 2019). However, it is necessary to study the impact of a combination between conventional drugs and active herbal ingredients (Fu et al., 2018). The chemopreventive effect of *M. verticillata* has been recently attributed to glycosyl glycerides, isolated from the aerial parts, and identified as (2S)-1-*O*-*β*-*D*-galactopyranosyl-3-*O*-isostearoyl (malvaglycolipid A Compounds 1 and 2). Most of glycosyl glycerides showed cytotoxicity on HepG2, AGS, HCT-15, and A549 human cancer cells suggesting that *M. verticillata* may prevent cancer through inducing cellular cytotoxicity and apoptosis (Ko et al., 2018).

Medicinal plants, such as *Malva* species, have shown promising effects for chemo-radiotherapy-induced mucositis (Bahramsoltani, 2017). Its traditional use as mucolytic and expectorant has encouraged the research on the alleviation of mouth dryness in patients with xerostomia and oral mucositis derived from chemo and radiotherapy treatments, mostly for head and neck cancer (HNC). In addition, *M. sylvestris* may reduce xerostomia through increasing the salivary secretion or maintaining the mucosal water content in oral cavity. The reduction of cisplatin-induced renal and hepatic side effects has also been demonstrated in rats ($n = 56$; male rats of 9- to 11-weeks old) by using *M. sylvestris* hydroalcoholic extract. Pretreatment with mallow extract protected kidney and liver from cisplatin-induced side effects and reduced both oxidative stress and inflammation (Mohamadi Yarijani et al., 2018).

6.5 | Insights into the antiinflammatory and wound healing properties of *Malva* plants

Among *Malva* species, only two species, viz. *M. sylvestris* and *M. parviflora* extracts, were studied in vivo for their antiinflammatory and wound healing properties (Table 6). The study of the antiinflammatory

TABLE 6 Antiinflammatory and wound healing activity of *Malva* species

Malva spp.	Plant part	Extract	Action	Reference
M. sylvestris	Leaves, flowers	Diethyl Ether	Wound healing	(Pirbalouti, Azizi, Koohpayeh, & Hamedi, 2010; Pirbalouti & Koohpyeh, 2011; A.G. Pirbalouti, Yousefi, Nazari, Karimi, & Koohpayeh, 2009)
	Leaves	Ethanol	Wound healing	(Kovalik et al., 2014)
	Areal part	Water	Antiinflammatory	(Sleiman & Daher, 2009)
	Aerial parts	Water	Antiinflammatory	(Prudente et al., 2013)
	Leaves	Water	Antiinflammatory, antiosteoclastogenic	(Benso et al., 2016)
	Leaves	Water/Ethanol	Antiinflammatory	(Conforti et al., 2008)
M. parviflora	Leaves and roots	Hexane Methanol Water Ultrasounds	Antiinflammatory	(Shale et al., 2005)
	Leaves	Water Methanol	Antiinflammatory	(H Bouriche et al., 2010)
	Roots	Methanol	Treatment of skin disorders	(Tadeg et al., 2005)

activity of *M. parviflora* leaf hydroalcoholic extract on Alzheimer's disease pathology in lean and obese transgenic 5XFAD mice showed neuroinflammation suppression through inhibiting microglia proinflammatory M1 phenotype and promoting microglia phagocytosis. This suggests that *M. parviflora* can be effectively used to prevent or delay Alzheimer's disease progression (Medrano-Jimenez et al., 2019). Indeed, *M. sylvestris* significantly reduced neuronal injury by mechanisms involving raise in superoxide dismutase and CAT activities, suppression of nuclear factor kappa B, IL-1 and IL-6, and glial fibrillary acidic protein expression confirming its neuroprotective effects on central nervous system (Keshavarzi et al., 2019). The role of the aqueous extract from *M. sylvestris* aerial parts was assessed in rat models with induced inflammation (Sleiman & Daher, 2009). Later, it was confirmed that malvidin 3-glucoside appears to be the main responsible bioactive compound for the antiinflammatory effect (Prudente et al., 2013). Also, Martins et al. suggested that *M. sylvestris* extracts antiinflammatory effects seem to be related to special antiinflammatory mediators induction—prostaglandins PGE_2 and PGD_2 (Martins et al., 2014). Besides, several studies documented wound healing effects to *M. sylvestris*. For example, Pirbalouti et al. and Kovalik et al. evaluated the wound healing activity of *M. sylvestris* extracts in rats and found a significant reduction in wound size in *M. sylvestris* extract-treated mice (Kovalik et al., 2014; Pirbalouti et al., 2009; Pirbalouti et al., 2010; Pirbalouti & Koohpyeh, 2011). The mechanism through which *M. sylvestris* exert its wound healing potential is not clearly established. However, it was suggested that *M. sylvestris* act on fibrosis-free granulation tissue formation in skin (Medellin-Luna, Castaneda-Delgado, Martinez-Balderas, & Cervantes-Villagrana, 2019).

6.6 | Antihypertensive effect of *Malva* species

Hypertension is a disease with high prevalence and morbidity, where vascular inflammation and associated oxidative stress (endothelial dysfunction) are the underlying causes of this pathology. Lagunas-Herrera et al. reported the antihypertensive activity of *M. parviflora* extracts and fractions in mice with chronic and acute hypertension, with values of pharmacological constants of ED_{50} = 0.038 mg/kg and Emax = 135 mmHg for systolic pressure and ED_{50} = 0.046 mg/kg and Emax = 98 mmHg for diastolic pressure by modulating parameters, such as IL-1beta, IL-6, IL-10, TNF-alpha, and malondialdehyde. *M. parviflora* also prevented inflammatory and oxidative damage in kidney by thwarting the effect of chronic and acute administration of angiotensin II on hypertension. As well, isolated compounds viz. oleanolic acid, tiliroside, and scopoletin showed ED_{50} = 0.01 and 0.12 mg/kg and Emax = 33.22 and 37.74 mmHg for scopoletin and tiliroside, respectively, for systolic pressure, whereas that for diastolic pressure data were ED_{50} = 0.01 and 0.02 mg/kg, with an Emax = 7.00 and 6.24 mmHg, suggesting that they are responsible for the antihypertensive activity (Lagunas-Herrera et al., 2019).

7 | CLINICAL EFFECTIVENESS OF *MALVA* PLANTS IN HUMANS

7.1 | Dry mouth/xerostomia

More information on clinical benefits of using *Malva* species are available in case of the dry mouth, also known as xerostomia, that is one of the most common complications of radiotherapy in patients with HNC. Several clinical trials have been performed to evaluate the efficacy of *M. sylvestris* compounds in the treatment of this symptom in HNC patients. Data obtained support the efficacy of this preparation in the treatment of dry mouth in these patients (Ameri et al., 2016). Also, at the same time, a pronounced improvement in quality of life in HNC patients with radiation-induced xerostomia was observed (Heydarirad et al., 2017). Moreover, in a randomized, open-labeled, active-controlled trial, Heydarirad et al., 2017 studied the efficacy of *Alcea digitata* Alef and *M. sylvestris* in the quality of life of HNC patients (*n* = 60) with radiation-induced xerostomia. Results showed a significant improvement in terms of pain, swallowing, speech, and eating in the intervention group compared with the control group (Heydarirad et al., 2017). A similar study was done by Rezaeipour et al. on prevention of radiation-induced acute mucositis in patients (*n* = 23) with HNC, where the herbal mixture of *A. digitata* and *M. sylvestris* was administered for 7 weeks. Patients from the control group showed more severe mucositis from second week, compared with the administered drug group; hence, the severity of mucositis and the mouth pain score mean in the control group was significantly more severe in comparison with the drug group (Rezaeipour et al., 2017). Both studies showed the efficacy of the herbal mixture containing *A. digitata* and *M. sylvestris* on prevention of radiation-induced acute mucositis and xerostomia. Several similar studies have been performed with this herbal mixture in the treatment of cough, but it was not possible to determine the specific contribution of *Malva* species.

7.2 | Prostate cancer

A clinical trial performed in patients undergoing external beam radiation therapy for prostate cancer was conducted to assess the effectiveness of *Malva* species in preventing radiation-induced dysuria, being found strong protective effects (Mofid et al., 2015). The combination of *A. digitata* and *M. sylvestris* was also tested on prevention of acute radiation proctitis in patients with prostate cancer (*n* = 65) in double-blind, randomized controlled studies (Moeini et al., 2018). Proctitis is the most common adverse effect of radiotherapy on pelvic organs cancer, causing diarrhea or loose stools, anal pain, tenesmus, mucus discharge, urgency and frequency, and bleeding. The infusion of a combination of the two powdered flowers prevented the gastrointestinal side effects of prostate radiotherapy, such as anal discomfort, and delayed the need for analgesics and antidiarrheals, although mobility did not decrease significantly (Moeini et al., 2018).

7.3 | Functional constipation

In a placebo-controlled trial, it was confirmed that *M. sylvestris* flowers aqueous extract syrup (1 g extract per day) is effective and safe for treating functional constipation in adult patients (Elsagh et al., 2015). In the same study, some moderate side effects were observed, including diarrhea, acid regurgitation, nausea, worse constipation, epigastric pain, heartburn, and urticaria. Also, in the literature, two cases of acute liver and kidney damage after oral *M. sylvestris* and *M. sylvestris var. grandiflora* consumption were described (Aktas et al., 2014). In both cases, the patients ate mallow as a meal, and the nature of organ damage was acute. However, there is no scientific support for its toxicity when used in safe doses and under therapeutic indications. Although toxicological data are limited, the long-term history of human use as a food resource highlights the absence of safety concerns when looking at the use of oral preparations.

7.4 | Asthma

Short-term administration of an herbal mixture (ASMATUS^{TM}) consisting in *Matricaria chamomilla*, *Althaea officinalis*, *M. sylvestris*, *Hyssopus officinalis*, *Adiantum capillus-veneris*, *Glycyrrhiza glabra*, and *Ziziphus jujube* for 5 days during a double-blind randomized clinical trial in 46 children (7–12 years old) with intermittent asthma significantly decreased the severity of cough and nighttime awakenings compared with placebo. However, further studies are needed to determine the right herbal combination, dose, and herbal treatment regimen (Javid et al., 2019).

8 | CONCLUSIONS AND FUTURE PERSPECTIVES

Despite the traditional use of *Malva* plants in various cultures, very limited data are available from clinical trials. The folk use of *Malva* flowers and leaves has been documented in several medicinal handbooks, and available data obtained from preclinical studies legitimate its benefits. But to date, data are lacking that confirm the folk usage of *Malva* plants throughout clinical trials. Limited data from clinical trials consist mainly of studies on xerostomia, prostate cancer, and functional constipation. Meanwhile, results from preclinical experiments in animals encourage further clinical trials with *Malva* species towards to discover effective treatments of various conditions in humans.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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