JPP JOURNAL OF Pharmacy and Pharmacology
ROYAL PHARMACEUTICAL SOCIETY
JPP Journal of Pharmacy And Pharmacology
Review

Ethnobotanical and scientific aspects of *Malva sylvestris* L.: a millennial herbal medicine

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Keywords
ethnoveterinary medicine; food; *Malva sylvestris*; review; traditional medicine

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Received April 18, 2011
Accepted September 22, 2011

doi: 10.1111/j.2042-7158.2011.01383.x

Abstract

Objectives *Malva sylvestris* L., known as common mallow, is native to Europe, North Africa and Asia. In the Mediterranean region, this species has a long history of use as food, and due to its therapeutic relevance, some parts of this plant have been employed in traditional and ethnoveterinary medicines. The leaves in particular have been reported to have potent anti-inflammatory, antioxidant, anti-complementary, anticancer and skin tissue integrity activity. Additionally, an anti-ulcerogenic effect was recently proven, demonstrating that the aqueous extract was more effective than cimetidine, a potent medicine used to treat gastric ulcers. Due to its wide use and medicinal importance, many studies have been conducted; however, the information in the literature is very extensive and disseminated, making it difficult to use.

Key findings A complete review involving the ethnobotanical and scientific aspects of *M. sylvestris* has been made. The research has provided evidence that *M. sylvestris* has potential use as a medicinal plant and has highlighted a need for more studies involving clinical and toxicological aspects of its use.

Summary This review can contribute to the field with its historical context, and by describing the progress made, new ideas for researchers can arise.

Introduction

The use of plants and their products in curing diseases is known as herbal medicine, which is considered part of folk or traditional medicine.[1] For many centuries, treatment with medicinal plants was the only resource available for numerous ethnic groups, and nowadays, plants are still used in traditional medicine to treat, alleviate or prevent many diseases.[2]

Among the numerous species used in folk medicine, *Malva sylvestris* L. (Malvaceae) stands out due to its variety of uses, with its consumption reported to have originated in 3000 BC. In the region of Syria, archaeological studies have shown the existence of *M. sylvestris* seeds in dental calculus human fossils. The researchers concluded that the consumption of this species is long standing, due both to it being an edible plant and to its possible medicinal properties.[3]

Nowadays, the consumption of *Malva* is widespread, because new research has revealed important therapeutic properties, such as anti-ulcerogenic, antioxidant, anticancer, skin tissue integrity and anti-inflammatory.[4–10]

The entire plant has exhibited therapeutic properties, but in general the pharmacological effects of *Malva* are assigned to the leaves and flowers, especially due to the presence of some flavonoids and mucilages in these parts.[11–22]

Several recent studies involving different aspects of *M. sylvestris* have been conducted, but in the literature, this information is quite extensive and scattered, which makes it difficult to use in new research.

This work provides a short overview of the pharmacological, phytochemical, ethnopharmacological, agronomic and veterinary uses of *M. sylvestris*. Beyond validation of this plant's uses, this review can be used as an important tool for the development of new research.

Botanical Description

Native to Europe, Asia and North Africa, *M. sylvestris* L. (Figure 1) is a member of class Equisetopsida, subclass Magnoliidae, superorder Rosanae, order Malvales, family Malvaceae and genus Malva.[10,23,24] Details of its botanical descriptions can be found in official references such as the Brazilian, Helvetic, British and European Pharmacopoeias. For that reason, some information was translated and summarised in a single text for better understanding.

The flowers of *M. sylvestris* are almost odourless and have a mucilaginous taste when chewed. They are 3–5 cm wide and have an epicalyx; the rest of the stalk does not exceed 20 mm in length.[25] The flower consists of an epicalyx with three oblong or elliptical-lanceolate parts that are shorter than those of the calyx and are situated immediately below it; the calyx has five pubescent triangular lobes, and gamosepalous at the bases. A corolla three to four times longer than the calyx with five wedge-shaped, notched petals is fused to the stamen tube at their base. Numerous stamens, the filaments of which fuse into a stamina tube covered by small star-shaped trichomes and occasional simple trichomes are visible under magnification, and numerous wrinkled carpels, glabrous or sometimes pubescent, enclosed in the stamen tube are arranged into a circle around a central style that ends with numerous filiform stigmas. In cultivated varieties, the epicalyx is three to seven partite, the calyx is five to eight partite, and the corolla is five to 10 partite.[26,27]

The leaves are simple, membranous, pubescent and velvey on both sides. They are green even when dry, have long petioles and are orbicular to reniform, palminervous and lobed, with three, five, seven or nine shallow lobes. They have rounded or acute apexes, with a truncated subcordiform, dentate-crenate and measure 7–15 cm in diameter. Venation is actinodromous. First-order veins are prominent and straight; second-order veins show acute divergence angles; and third-order veins are cross-linked. The last, marginal, venation is incomplete, with simple venules and curves. The nipples show outright development and are large and polygonal in shape.[25,28] Details of the morpho-anatomical characters of the leaf are shown on Figures 2 and 3.

Traditional Medicine Use

Numerous studies involving the use of medicinal plants have demonstrated the worldwide importance of *M. sylvestris* in traditional medicine. As a medicinal food, *M. sylvestris* has been consumed as a mild laxative, a liver cleansing tonic, and against heartburn.[29,30] It can be prepared as soup but is most commonly prepared in salads.[30] In pharmaceutical preparations, it can be used to treat conditions such as gastrointestinal disorders, abdominal pain, diarrhoea and respiratory diseases.[19,31–35]

The leaves, flowers and aerial parts of *M. sylvestris* are known worldwide due to their anti-inflammatory prop-

Figure 1 *Malva sylvestris* L. (a) Leafy flowered stems; (b) young leaves; (c) immature fruits.[10]

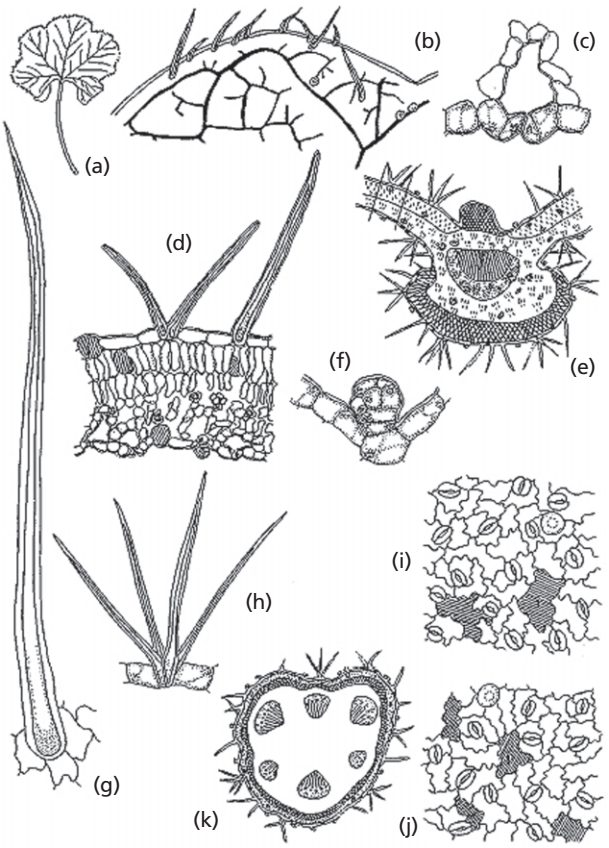

Figure 2 Morpho-anatomical characters of a leaf from *Malva sylvestris* L., Malvaceae. (a) Overall aspects; (b) leaf architecture showing perfect areole and polygonal; (c) detail of the stomata; (d) detail of the mesophyll with non-glandular trichomes; (e) overall appearance of the midrib; (f) glandular trichome; (g) non-glandular trichome; (h) stellar trichome; (i, j) epidermal cells of the adaxial and abaxial surfaces, respectively; (k) overall aspect of the petiole.[28]

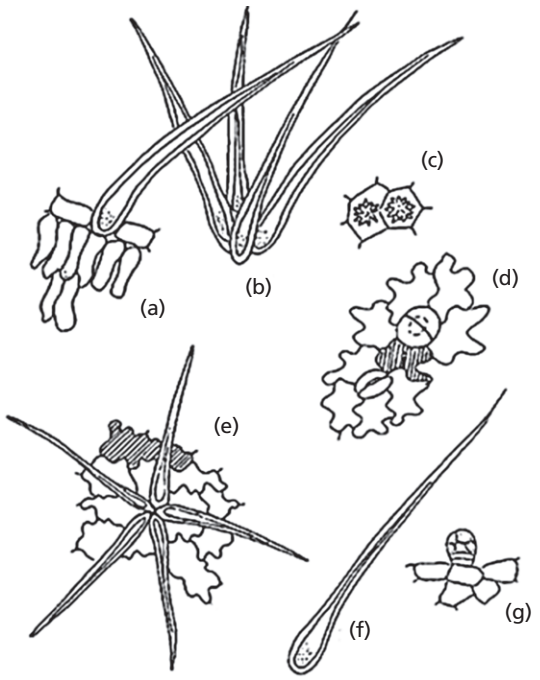

Figure 3 Morpho-anatomical characters of powdered leaf from *Malva sylvestris* L., Malvaceae. (a) Part of the palisade cells with non-glandular trichome; (b) stellar trichome; (c) druses of calcium oxalate; (d) adaxial surface showing the stomata and mucilaginous cell; (e) abaxial surface with the stellar trichome and mucilaginous cell; (f) non-glandular trichome; (g) detail of the epidermis with glandular trichome.[28]

erties, mainly against gingivitis, abscesses and tooth pain.[6,15,19,36,37] Additionally, the leaves and flowers have ample potential for use in the treatment of urological problems, insect bites, burns, furuncles and ulcerous wounds.[19,35,38,39] It is important to mention that the use of *M. sylvestris* in association with other medicinal species is a common practice that enhances their expected effects. Other details of the traditional use of *M. sylvestris* are shown in Table 1.[40–68]

Agronomic, Economical and Ecological Aspects

Many authors refer to *Malva* as a weed.[69–73] It can be found as an invasive plant in food crops, except in cereal crops, in which no development has been observed.[74]

M. sylvestris grows in different soil types, including rocky soils, and soil and media with different pH levels and with different amounts of phosphorus, nitrogen and organic carbon.[75,76] *Malva* can accumulate more nutrients (P, K, N and Mg) in their roots than tomatoes and beans when the species are grown together.[77] Pollination by different insects is extremely important for the maintenance and proliferation of *M. sylvestris*, but the scarification of seeds has been found to be the most effective way to guarantee their germination.[76,78,79]

Malva has host characteristics and is widely known due to its beneficial relationships with other organisms.[80,81] This plant is considered a better host than cotton and okra for *Aphis gossypii* and has been described as a host for several microorganisms, such as cucumber mosaic virus, *Cercospola malvícola*, *Malvapion malvae*, *Haritalodes derogatus*, *Meloidogyne* spp. and tospovirus.[80–86] The flowers play an important role in the maintenance of visiting insects because they are a vital source of nectar for bees, butterflies and hoverflies.[78–80]

Malva can be eliminated easily through the use of herbicides, but their presence can be of ecological and economical importance.[69–73,87,88] The methanolic extracts, for

Table 1 Traditional uses of *Malva sylvestris*

General use	Parts used	Preparation	Specific use
Gastrointestinal disturbance	Leaves	Decoction	Laxative, depurative, gastritis, intestinal disorders[6,15,17,31,34,35,38,40–42]
		Infusion	Laxative, constipation, stomach ache[11,43,44]
		Cooked	Constipation[17]
	Flowers	Infusion	Laxative, protector of gastric mucous, gastralgia, colic, stomach ache and dysentery[14,15,45–48]
		Decoction	Mild laxative (for children), soothing abdominal pains[11,31]
	Aerial parts	Decoction	Abdominal pains, intestinal disorders, depurative and mild laxative[18,23,49,50]
		Infusion	Diarrhoea, dyspepsia, gastritis, intestinal disorders, laxative, stomach ache, constipation[32,51,52]
		Cooked	Constipation, laxative[53]
	Roots	Infusion	Stomach ache[44]
		Decoction	Mild laxative, gastrointestinal afflictions[15,16,41]
	Whole plant	Decoction	Depurative or laxative effects, against abdominal pains[19]
	Green parts or roots	External compress	Stomach pain[19]
Dermatological ailments	Leaves and whole plant	Infusion, cataplasm and decoction	Burns, furuncles, ulcerous wounds, skin disease, chilblain[11,14,40,41,54,55]
	Leaves	Cataplasm	Nettle rash, skin eruptions, irritations and furunculosis[40,41]
		Infusion/decoction	Burns, urticaria, insect and scorpion stings[43,45,56]
		Cooked	Abscesses[17]
		Compress with *Linum* seeds	Drain abscesses[6,19]
		Fresh	Nettle stings[51]
	Leaves and flowers	Decoction, infusion	Acne, astringent[48,57]
		Bath/wash after boiling, cataplasm	Swellings, wounds, furuncles[33,58,59]
	Aerial parts	Compress (boiling the plant)	To heal furuncles and abscesses, cicatrising, to heal nail infections[2,33]
		Cream (mixed with pork fat or butter)	Antiwrinkle[19]
	Roots	Decoction	Emollient[17]
Menstrual pains	Aerial parts	Decoction	Relieve menstrual pains[18,23,50]
	Flowers	Infusion	Dysmenorrhoea[47]
	Roots	Decoction	Menstrual pain[41,60]
Haemorrhoidal	Leaves	Infusion, vapour	Antihaemorrhoidal[11,43]
Inflammation	Whole plant	Infusion and decoction	Genito-urinary, gastrointestinal system[45]
		Decoction	Internal anti-inflammatory[11,41,42,59]
	Leaves	Infusion	External anti-inflammatory[6,37,43]
		Cataplasm	Inflammation around wounds[37]
	Flowers, leaves and whole plant	Crushed plant (with olive oil)	Local application against arthritis, rheumatism[36]
		Boiled (compresses)	Treat rheumatisms[19]
		Infusion and decoction as mouthwash or gargles	Inflammation of the throat, mouth, eyes and diverse skin inflammation[31,33,34,59,61]
Urological disorders	Whole plant	Infusion	Bladder pains, chronic bladder ulcer[14,30,55,62]
		Decoction	Prostate ailments, diuretic[17]
		Food, soup or salad	Diuretic[29,30]
	Aerial parts	Decoction	Diuretic[6,15,17,31,34,35,38,40,41]
		Decoction/ infusion	Disinfectant of urinary and kidney diseases[19,32,60]
	Leaves/flowers	Infusion	Cystitis, kidney pain and malfunction[38,46,47]
	Fruit	Infusion	Protector of bladder mucous, irritation of urinary organs[45]
	Leaves	Bath/washing after boiling	Antiseptic of urinary system[43,59]

(*Continued*)

Table 1 (*Continued*)

General use	Parts used	Preparation	Specific use
Respiratory complaints	Leaves/flowers	Infusion/decoction	Pectoral emollient, cough, expectorant, spasmolytic and asthma[19,31,38,45,48,52,63,64]
		Decoction	Cough, sore throat and respiratory infections[15,19,57,60,65]
		Infusion	Cough[34,46,64]
.	Aerial parts	Decoction	Sore throat, bronchitis, cough, respiratory diseases[2,17,18,23,49,50,54,66]
		Infusion	Asthma, laryngitis and pharyngitis[32,60]
	Leaves	Boiling with milk and with *Citrus limon*	Tonsillitis, mumps and sedative[16,60]
	Flowers	Infusion	Sore throat, cough suppressant, bronchitis[11]
	Fruit	Infusion	Cough[30]
	Roots	Decoction, and decoction with *Laurus nobilis* and barley	Pectoral, sore throat[15]
Urological disorders	Leaves/flowers	Decoction/infusion	Treatment of urinary and kidney diseases[19,32]
		Infusion	Cystitis, kidney pain and malfunction[38,46,47]
	Fruit	Infusion	Protector of bladder mucous, irritation of urinary organs[45]
	Leaves	Bath/washing after boiling	Antiseptic for urinary system[43,59]
Pain	Root and leaves	Vapour of decoction (*M. sylvestris* association)	Lumbar ache[16]
	Green parts or roots	Compress (crushed fresh plants)	Labour pains[19]
	Leaves	Ointment	Contusions and bruises[51]
Oral diseases	Leaves/flowers	Chewed	Toothache[33]
		Decoction – mouthwash or gargle and cataplasm	Mouth/gums, toothache, gingival abscesses[34,57]
		Decoction, in gargles or washes	Gingival and mouth inflammation[33]
	Aerial parts	Gargle and to wash	Buccopharyngic anti-inflammatory and anti-odontalgic[43]
		Compress	Gingival inflammations and toothache[33]
		Cooked in milk or warm ashes	Dental abscesses and swollen gums[53]
	Leaves	Cataplasm	Dental abscesses[41,61]
	Root / leaves	Decoction	Toothache and stomatitis[41]
	Flowers	Infusion – mouthwashes	Aphthous ulcers[34]
	Whole plant	Decoction	Zoster-like inflammation, gingivitis[14]
	Roots	Decoction	Toothache[15]
Vaginal disorders	Leaves	Infusion	Anti-infectious[43]
	Leaves and flowers	Decoction	Vaginal itching[15]
Other relevant uses	Leaves	Soup	To enhance uterine contractions during parturition[67]
		Decoction (also with sugar and pork fat)	Anxiolytic, dislocation[34,41]
		Infusion/decoction	Slimming[15,34]
	Aerial parts	Decoction, or in a soup as food	Partum enhancer, post-partum[49]
		Decoction with a pinch of salt	Refreshing, personal cleanliness[19,53]
		Juice	Epilepsy[68]
	Flowery plant	Infusion	Gastralgia; dysmenorrhoea and kidney malfunction[47]
	Leaves/flowers	Infusion	Sedative, soothing[46,48]
	Roots	Decoction	Menstrual pain, hypertension, weakness, abortion and fever[41,51,60]

example, can be used as a fungicide against *Colletotrichum lindemuthianum*, which causes bean anthracnose.[89] *Malva* also has an important role in the recovery of degraded land (landfills) and soils rich in copper, because its roots can stabilise the soil by reducing the effects of copper toxicity through the exclusion of this metal.[90,91] Its mucilage has also been used in wastewater treatment, reducing turbidity by 96.3–97.4% in synthetic wastewater (12 mg/l mucilage) and by 61–66% (62.5 mg/l mucilage) for biological wastewater.[92]

Another relevant aspect of *M. sylvestris* is its hypersensitive response to ozone. In the leaves of *M. sylvestris*, ozone accesses the apoplastic fluid surrounding the cells where it is rapidly converted into reactive oxygen ($O_2^{-}\bullet$). The reactive oxygen accumulates around the veins, generating visible injuries that are heterogeneously distributed throughout the surface of the leaves. This property makes *M. sylvestris* a potential bio-indicator of different levels of ozone contamination. On the other hand, the sensitivity of *M. sylvestris* to ozone can be harmful because depending on the ozone levels, the occurrence of crop damage is possible. In addition to injuries, ozone may cause premature leaf senescence as well as significant reductions in leaf growth, shoot biomass, seed mass, inflorescence weight and germination rate and thus has a direct influence on plant development.[93–97] Nevertheless, the structural diversity of the dominant community of bacteria in the rhizosphere is not affected by the ozone exposure.[96]

Veterinary Uses

Several studies report the use of *M. sylvestris* for veterinary purposes. Decoctions of whole plants, sometimes boiled in oil, can be administered to livestock to treat colic and to unblock rumens.[19] The leaves when applied in enemas or compresses have shown high effectiveness in the treatment of mastitis in bovines and against swine constipation.[98]

Infusions and decoctions of blooming aerial parts have been used as laxatives in horses, but these preparations have also demonstrated activity against inflammation, wound infection, diarrhoea in young calves, respiratory problems in horse, and intestinal inflammation in cows and sows.[99,100] Applied in bath form, it can be used as a galactagogue in sows, and the enema preparation can be used against aphthous fever and as an antiseptic.[99]

By direct ingestion, the leaves have been used as a laxative, as an antimastitic and to decrease ruminal methane production.[51,61,98] The crushed plant has been applied externally to drain abscesses in cattle; use as a curative for skin, reproductive and nervous disorders has also been reported.[19,101]

Phytochemical Constituents

Amino acids/protein derivatives

High contents of arabinogalactan protein (AGP) have been found in cultures of callus cells (12.8% dry weight).[22] The most abundant components of AGP were galactose (57.6 mol%), arabinose (31.0 mol%), mannose (3.5 mol%), glucuronic acid (3.2 mol%), glucose (2.5 mol%), xylose (1.8 mol%) and rhamnose (0.4 mol%).

Using high performance thin-layer chromatography (HPTLC), the presence of the amino acids alanine, threonine, hydroxyproline, serine, glutamine, asparagine and arginine have been detected. Of these, only hydroxyproline was determined quantitatively, representing 0.8% of the total amino acid composition.[22] Additionally, the presence of trigonelline (1.9%, 1.0% and 0.05%, dry weight) and glycine betaine (0.07%, 0.002% and 0.002%, dry weight) has been described, in the leaves, flowers and roots, respectively.[102]

Flavonoids

Information involving the occurrence of flavonoids in the Malvaceae family is limited. However, flavonols and flavones with additional OH groups at the C-8 A ring and/or the C-5′ B ring positions are characteristic of this family, demonstrating chemotaxonomic significance.[103] *M. sylvestris* has significant quantities of these substances. In a study involving the nutraceutical potential of its extracts, the total flavonoids were 210.8, 46.6, 25.4 and 143.4 mg/g in the leaves, flowers, immature fruits and flowered stems, respectively.[10] In the leaves, gossypetin 3-sulphate-8-O-β-D-glucoside (gossypin) and hypolaetin 3′-sulphate were identified as the major constituents, followed by 3-O-β-D-glucopyranosyl-8-O-β-D-glucuronopyranoside, hypolaetin 4′-methyl ether 8-O-β-D-glucuronopyranoside, hypolaetin 8-O-β-D-glucuronopyranoside and isoscutellarein 8-O-β-D-glucuronopyranoside. [20,104,105]

Flavonoids have been found mostly in the flowers, especially anthocyanins such as malvidin 3,5-diglucoside (malvin), which occurs exclusively in the flavylium cationic form.[21,106–112] Malvidin 3-O-glucoside (oenin); malvidin; delphinidin 3-O-glucoside; malvidin 3-O-(6″-O-malonylglucoside)-5-O-glucoside; delphinidin; malvidin chloride; genistein; myricetin; and derivatives of apigenin, quercetin and kaempferol have also been found in the flowers, with total anthocyanin content ranging from 0.42 to 7.3% of dry matter.[21,103,108,113,114] Likewise, leucoanthocyanins, cyanidin and petunidin have been found, but in very low concentrations.[21] Figure 4 shows the chemical structures of some flavonoids found in *M. sylvestris*.

Mucilages

Among dicotyledonous plants, the order Malvales possesses the most abundant deposits of mucilages. This is particularly true of the Malvaceae family, especially the species *M. sylvestris*, in which the presence of polysaccharides has been reported for over 50 years.[115]

Mucilages are one of the major components responsible for the therapeutic effects of *Malva*, mainly due to their anti-complementary and cough suppression activities.[9,63]These substances are located in mucilage idioblasts, mucilage ducts, cavities and specialised epidermal cells.[116] The contents can vary according to the plant part, but in general, high percentages of crude mucilages can be found in the leaves (6.0–7.2%), flowers (3.8–7.3%) and roots (7.5%).[117–119] The mucilages consist mainly of glucuronic acid, galacturonic

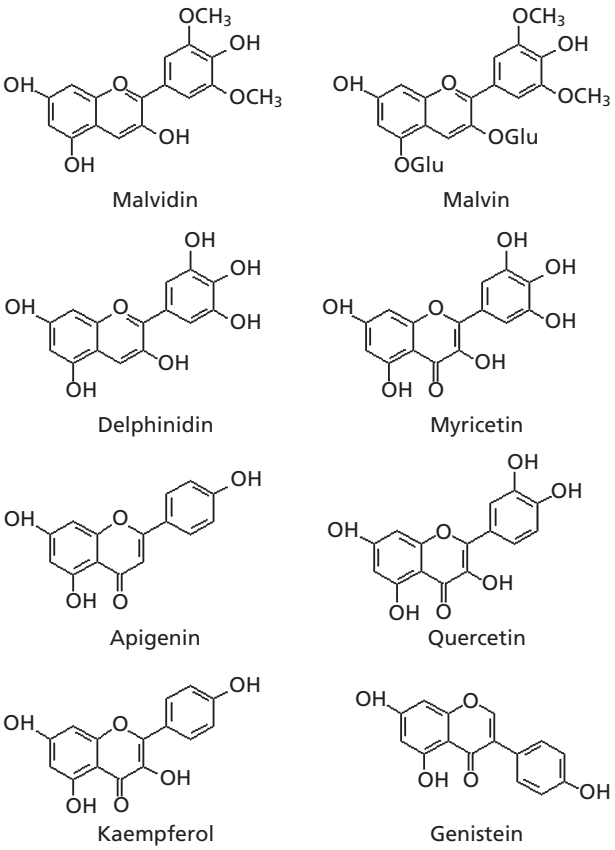

Figure 4 Some flavonoids found in *Malva sylvestris*.

acid, rhamnose, galactose, fructose, glucose, sucrose and trehalose, but uronic acid, arabinose, mannose, xylose, fucose, raffinose and 2″–*O*–α–(4–*O*–methyl–α-D-glucuronosyl)-xylotriose have also been found.[10,117,118,120]

Terpenoids

Several classes of terpenoids, including monoterpenes, diterpenes, sesquiterpenes and nor-terpenes, have been found in *M. sylvestris*. Aqueous extracts from fresh leaves have revealed the presence of linalool, linalool-1-oic acid, (6R,7E, 9S)-9-hydroxy-4,7-megastigmadien-3-one, (3S,5R,6S,7E, 9R)-5,6-epoxy-3,9-dihydroxy-7-megastigmene, blumenol A, (3R,7E)-3-hydroxy-5,7-megastigmadien-9-one, (+)-dehydrovomifoliol, (3S,5R,6R,7E,9R)-3,5,6,9-tetrahydroxy-7-megastigmene and (6E,8S,10E,14R)-3,7,11,15-tetramethylhexadeca-1,6,10-trien-3,8,14,15-tetraol.[121] In seed oil, the main terpene present is terpineol, and in the leaves, flowers and immature fruits, carotenoids, which are tetraterpenoids, are present.[10,122]

Among these substances, malvone A (2-methyl-3-methoxy-5,6-dihydroxy-1,4-naphthoquinone) stands out due to its resistance against the pathogen *Verticillium dahliae*; it is therefore considered an important antimicrobial agent.[123] The structure of malvone A is shown in Figure 5.

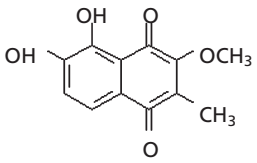

Figure 5 Chemical structure of malvone A, a phytoalexin found in *Malva sylvestris*.

Phenol derivatives

Many derivatives of phenolics have been found in extracts from different parts of *M. sylvestris*. The total phenolic compounds were found to be 386.5 mg/g in the leaves, 317.0 mg/g in flowered stems, 258.7 mg/g in flowers and 56.8 mg/g in immature fruits.[10] Despite the high concentration of these substances, only one study involving their isolation and identification has been reported.[121] It mentioned the presence of 4-hydroxybenzoic acid, 4-methoxybenzoic acid, 4-hydroxy-3-methoxybenzoic acid, 2-hydroxybenzoic acid, 4-hydroxy-2-methoxybenzoic acid, 4-hydroxybenzyl alcohol, 4-hydroxydihydrocinnamic acid, 4-hydroxy-3-methoxydihydrocinnamic acid, 4-hydroxycinnamic acid, ferulic acid and tyrosol.

Enzymes

Sulphite oxidase is the enzyme responsible for the final reaction in oxidative degradation of sulphur-containing amino acids. This enzyme is physiologically important because its absence may lead to death. Sulphite oxidase has been found in a variety of animals and bacteria, and it has also been found in the leaves of *M. sylvestris*.[124,125]

Coumarins

The presence of two coumarins, 7-hydroxy-6-methoxycoumarin (scopoletin) and 5,7-dimethoxycoumarin, has been reported in the leaves of *M. sylvestris*. The latter has been reported to be a phototoxic coumarin with probable anticancer activity.[114,126]

Vitamins

One of the biological activities of *M. sylvestris* is the antioxidant effect attributed to the presence of tocopherols (vitamin

E) and ascorbic acid (vitamin C). The presence of four forms of tocopherols (α, β, γ and δ) has been described, but α-tocopherol is the major form present in green plant tissues. It is the most potent antioxidant of the tocopherols, possibly due to its preferential absorption and distribution in the human body.[10] Quantitative analyses have demonstrated high concentrations of these substances in the leaves (106.5 mg%), as well as large quantities in flowered stems (34.9 mg%), flowers (17.4 mg%) and immature fruits (2.6 mg%).[10] In the same plant parts, ascorbic acid was also detected, at levels of 1.11 mg/g in flowers, 0.27 mg/g in immature fruits, 0.20 mg/g in flowered stems and 0.17 mg/g in leaves.[10] These results emphasise the importance of *M. sylvestris* as an antioxidant agent against reactive oxygen species.

Fatty acids/sterols

In the leaves of *M. sylvestris*, the presence of the steroids campesterol, stigmasterol and γ-sitosterol has been reported.[127] With regard to fatty acids, the seed oil has been found to consist mainly of palmitic acid (26.6%), oleic acid (23%), malvalic acid (11%), lauric acid (15.6%), myristic acid (6.6%), sterculic acid (5.6%), palmitoleic acid (5.6%), linoleic acid (4%), vernolic acid (1.6%) and traces of stearic acid.[122,128] The quantitative and qualitative composition of these substances depends directly on the plant growth conditions.[122]

Apart from seeds, lipids are found in the leaves, flowers, immature fruits and flowered stems.[10] These include caproic acid, caprylic acid, capric acid, lauric acid, myristic acid, myristoleic acid, pentadecanoic acid, palmitic acid, palmitoleic acid, heptadecanoic acid, stearic acid, oleic acid, linoleic acid, α-linolenic acid, arachidic acid, eicosenoic acid, *cis*-11,14-eicosadienoic acid, behenic acid, tricosanoic acid, lignoceric acid and *cis*-11,14,17-eicosatrienoic acid and heneicosanoic acid (C20:3n3 + C21:0). Leaf crude extract prepared by treatment with acetyl chloride and methanol has been found to contain 0.47% lipids, the most abundant being α-linolenic acid (42.2%).[129] For this reason, *M. sylvestris* has an important role as a nutraceutical food, especially due to the presence of essential fatty acids as such omega-3 and omega-6. The importance of consumption of omega-3 fatty acids has been confirmed, as these compounds can contribute to the prevention of several diseases, including cancer, diabetes and coronary artery disease.[10]

Radioecological compounds

Ruthenium-106 has radioecological importance and its absorption depends on soil-to-plant transfer factors. The uptake of ruthenium-106 has been related to the phylogeny of plants of the same order. *M. sylvestris* has 6570 Bq/g $^{103/106}$Ru activity.[130] Other elements found in *M. sylvestris* were strontium (Sr) and technetium-99 (^{99}Tc).[131,132]

Pigments

Qualitative analysis of *M. sylvestris* acetone extracts has been performed using paper-chromatography. These tests showed the presence of chlorophyll A, chlorophyll B and xanthophylls.[133]

Chemical elements

Leaves of *M. sylvestris* have been evaluated for the determination of non-metals, halogens and essential and non-essential metallic elements. Analysis performed using inductively coupled plasma optical emission spectrometry (ICP-OES) revealed the presence of Al, B, Ba, Bi, Ca, Co, Cr, Cu, Fe, K, La, Mg, Mn, Na, Ni, Pb, Si, Sn, Sr, Tl, U, Zn, Zr.[119] Quantitative analysis performed using polarised X-ray fluorescence spectrometry showed the presence (mg/kg) of K (27153.0), Mg (3340.0), Ca (19477.4), Fe (2198.5), Al (1953.9), Mn (99.6), Sr (52.1), Zn (40.8), Cu (16.7), Rb (12.0), Cr (10.4), Ni (8.4), Co (4.1), Pb (1.5), Sn (1.1), Cd (0.6), Hg (<0.1), S (5140.9), Cl (4971.4), P (3468.3), Br (51.7), I (6.1) and As (< 1.0).[134] It is significant that *Malva* has a high capacity to accumulate heavy metals (Cd, Cu, Ni, Pb and Zn) from soils rich in these substances. Therefore, there is a need to raise awareness about the health hazards of intake of these substances in populations that live in risk areas.[135]

Pharmacological Activity

Several studies have been conducted to evaluate the pharmacological activity of *M. sylvestris*. This species has demonstrated relevant properties, and therefore, several patents have been issued.

M. sylvestris has classically been indicated for the treatment of oral diseases and thus its antimicrobial and anti-inflammatory properties have been assessed using different extracts and preparations.

In a maximum inhibitory dilution (MID) assay, mouthwashes based on cetylpyridinium chloride (CPC) combined with *M. sylvestris* extract exhibited stronger antimicrobial properties than those containing only CPC. The combination of *Malva* and CPC demonstrated antimicrobial activity against 28 strains of *Staphylococcus aureus*, while mouthwashes containing only CPC were effective against only three strains. This study demonstrated a synergistic antimicrobial effect between *Malva* and CPC.[136]

The antimicrobial effects of ethanolic extracts obtained from *M. sylvestris* stems was assessed against methicillin-resistant *S. aureus* using planktonic growth and biofilm formation/adherence tests. The biofilm formation assay indicated that ethanolic stem extracts had moderate activity

against *S. aureus* (half maximal inhibitory concentration (IC50) values ≤ 32 μg/ml) with limited bacteriostatic effects in planktonic growth tests.[4]

A moderate to low antimicrobial response was also achieved against different strains of *Helicobacter pylori* using ethanolic extracts obtained from the leaves and inflorescences. Based on disk-diffusion, the hydroalcoholic extract (5 mg/disk) promoted inhibition zone ranged from 8 to 10 mm for *H. pylori* 26695 and *H. pylori* J99 strains, respectively. Concerning the minimum inhibitory concentration (MIC) assay, the lowest extract concentrations that inhibited the visible growth of the microorganisms ranged from 0.625 to >5.0 mg/ml and were not considered strong responses.[137]

Based on the diameter inhibition zones and agar-diffusion tests, lyophilised and crude methanolic extracts did not substantially inhibit strains of *Escherichia coli, Pseudomonas aeruginosa, Pseudomonas fluorescens*, *Klebsiella pneumoniae*, *Serratia marcescens*, *S. aureus, Staphylococcus epidermidis*, *Micrococcus luteus*, *Bacillus subtilis, Bacillus cereus*, *Bacillus pumilu, Bordetella bronchiseptica, Candida albicans* and *Saccharomyces cerevisiae*.[138,139] An aqueous extract of leaves was the only preparation of *M. sylvestris* that had significant antimicrobial properties against fungi. The aqueous extract at a concentration of 0.60 g/ml completely inhibited the growth of colonies of *Aspergillus candidus*, *Aspergillus niger*, *Penicillium* spp., and *Fusarium culmorum*; however, this extract was ineffective against *C. albicans*.[5,140]

The potential of *Malva* as an anti-inflammatory agent was also tested in mice taking a 100 mg/kg oral dose of the aqueous extract. Oedema induced by carrageenan and formalin was reduced by 60% in both the acute and chronic inflammation models, leading the investigators to conclude that this kind of extract could significantly reduce inflammation.[5]

The anti-inflammatory effects of creams containing different concentrations of *M. sylvestris* extract were assessed in carrageenan-induced oedema in rats. Carrageenan-induced oedema was significantly inhibited by a 5% malva cream compared with the placebo treatment. This effect was higher than that obtained with a cream containing 2% indometacin, which is a potent nonselective inhibitor of cyclooxygenase-2 (COX-2) that was used as a positive control.[7]

The hydroalcoholic extract obtained from *M. sylvestris* leaves was shown to have anti-inflammatory effects on croton oil-induced inflammation in the ears of mice (surface of 1 cm^2; application of 80 μg of croton oil suspended in 42% aqueous ethanol). At 300 $\mu g/cm^2$, the application of the extract reduced oedema by 21%. These data have demonstrated the topical anti-inflammatory effect of *M. sylvestris* in local inflammation.[6]

M. sylvestris has been shown to have analgesic properties. Studies conducted in mice have shown that lyophilised aqueous extract from *M. sylvestris* leaves had significant analgesic effects. In an abdominal constriction test, intraperitoneally administered extract (10 mg/kg) reduced acetic acid-induced abdominal constrictions by 76.4%. In a formalin-induced pain test, the treatment reduced intensive licking activity by 61.8% in the neurogenic phase and 46.6% in the inflammatory phase of the formalin model. In a capsaicin-induced pain model, the amount of time that the animal spent licking the injected paw was reduced by 62.9%. The hot-plate model was the only pain model in which the aqueous extract was not effective. These results suggested that the antinociceptive effects of the aqueous extract were related to the inhibition of the prostaglandin synthesis pathway cyclooxygenase and unrelated to the stimulation of the opioid receptors.[141]

The plant's antioxidant capacity has also been established in different assays. The aqueous extract at concentrations of 20 and 100 μg/ml reduced scavenging activity in a 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay by 24% and 30%, respectively. When measured with the β-carotene-linoleic acid assay, the 0.1 mg/ml aqueous extract had 87% antioxidant activity. A considerable effect (77% antioxidant activity) was also observed when *M. sylvestris* essential oil was used at the same concentration.[142,143] Overall, the ethanolic extracts obtained from the leaves and aerial parts as well as the *n*-hexane, dichloromethane and methanolic extracts obtained from the seeds had only moderate to low antioxidant activity.[6,144,145]

The antioxidant capacity of the methanolic extracts obtained from the leaves, flowers, immature fruits and flowered stems was evaluated using several different assays and models, including DPPH radical absorption, neutralisation of linoleate free radicals, malondialdehydethiobarbituric acid (MDA-TBARS) complex, and β-carotene models. All parts of the plant were shown to have antioxidant capacity (half maximal effective concentration (EC50) ≤ 0.6 mg/ml), except immature fruits, which had an EC50 value of 4.47 mg/ml by the DPPH assay.[10] In particular, methanolic extracts obtained from the leaves had very strong antioxidant properties including radical scavenging activity (EC50 = 0.43 mg/ml), reducing power (EC50 = 0.07 mg/ml), and lipid peroxidation inhibition in liposomes (EC50 = 0.04 mg/ml) and brain cell homogenates (EC50 = 0.09 mg/ml). The powerful antioxidant effects of the leaf methanolic extracts have been attributed to the presence of antioxidant substances, such as phenols, flavonoids, carotenoids and tocopherols, in this part of the plant.[10]

In a comparative study involving plants from different regions of Europe and Asia, the greatest antioxidant activity was found in the methanolic extracts obtained from plants collected in northeastern Portugal. These data demonstrated that the strength of the antioxidant capacity could be tied to the region where the plant has been collected.[10]

Table 2 Pharmacological activity of *Malva sylvestris*

Activity	Extract/pharmaceutical preparations	Models	Results
Acetylcholinesterase (AChE)	Ethanolic extract, decoction and essential oil fraction (aerial parts)	Enzymatic activity measured at visible wavelengths	28% of AChE inhibition using 0.1 mg/ml of essential oil; 25% of inhibition using 5 mg/ml of plant decoction and no inhibition observed through use of ethanolic extract[143]
Anticancer	Ethanolic extract (leaves)	Sulphorhodamide B assay	No anti-proliferative activity was observed using four human cancer cell lines (breast cancer MCF-7, prostate cancer LNCaP, amelanotic melanoma C32 and renal adenocarcinoma)[127]
	Hydroalcoholic extract (leaves)	MTT assay	Significant proliferative reduction of B16 and A375 cancer cell lines[8]
Anti-complementary	Mucilage (leaves)	IgM-haemolysin-sensitised sheep erythrocytes method	Potent anti-complementary activity compared with the positive control (arabinogalactan fraction from roots of *Angelica acutiloba*)[9]
Anti-inflammatory	Hydroalcoholic extract (leaves)	Topical anti-inflammatory activity evaluated by inhibition of the croton oil-induced ear oedema in mice	21% of oedema reduction[6]
	Malva extract cream (the plant part used was not specified)	Topical anti-inflammatory activity on carrageenan-induced oedema in rats	Significant inhibition of oedema obtained with 5% *M. sylvestris* cream[7]
	Aqueous extract (aerial parts)	Acute and chronic inflammation models induced in rats by carrageenan and formalin	Significant anti-inflammatory activity – optimum inhibition at 100 mg/kg body weight (60% inhibition)[5]
Antimicrobial	Commercial mouthwashes based on cetylpyridinium chloride (CPC) and mallow combination	Maximum inhibitory dilution test against 28 *Staphylococcus aureus* field strains	CPC+ mallow association inhibited the growth of all 28 *S. aureus* strains using 1/320 dilution against 1/160 dilution of CPC control[136]
	Ethanolic extract (stems)	Minimal inhibitory concentration test and modified microtitre dish system (biofilm formation and adherence test)	Limited bacteriostatic activity on planktonic growth of methicillin-resistant *S. aureus*; IC50 $\leq$ 32 μg/ml for biofilm inhibition[4]
	Ethanolic extract (leaves and inflorescences)	Agar-diffusion and minimal inhibitory concentration using thirteen *Helicobacter pylori* strains	Moderate activity by agar-diffusion test and low activity using minimal inhibitory concentration assay (> 5 mg/ml)[137]
	Lyophilised methanolic extract (flower)	Diameter inhibition zones test	No activity against *Escherichia coli, Pseudomonas aeruginosa, Pseudomonas fluorescens, Klebsiella pneumoniae, Serratia marcescens, Staphylococcus aureus Staphylococcus epidermidis, Micrococcus luteus, Bacillus cereus* and *Bacillus pumilu*; moderate activity against *Bordetella bronchiseptica*[138]
	Methanolic extract (aerial parts)	Agar-diffusion	Low antimicrobial activity against *Saccharomyces cerevisiae* and no activity observed for *Staphylococcus areus, Staphylococcus epidermidis, Escherichia coli, Bacillus subtilis, Micrococcus luteus* and *Candida albicans*[139]
	Aqueous extract (leaves)	Inoculation of 0.5 cm discs of individual fungus in culture medium composed of potato dextrose agar containing different extract concentrations	Growth colonies inhibition of *Aspergillus candidus, Aspergillus niger, Penicillium* spp., and *Fusarium culmorum* by use of 0.60 g/ml of the extract[140]
	Aqueous extract (aerial parts)	Disk diffusion technique	No potential against *Candida albicans* or against 11 hospital bacterial isolates[5]

(*Continued*)

Table 2 (*Continued*)

Activity	Extract/pharmaceutical preparations	Models	Results
Antioxidant	Aqueous extract (aerial parts)	1,1-Diphenyl-2-picrylhydrazyl (DPPH) assay	24% of DPPH scavenging activity at 20 μg/ml of the extract; antioxidant capacity observed using compounds isolated from the extracts[142]
		DPPH assay and β-carotene-linoleic acid assay	30% of antioxidant activity by DPPH assay and 87% of activity by β-carotene-linoleic assay, both at 0.1 mg of dry plant/ml water[143]
	Essential oil	β-carotene-linoleic acid assay	77% of antioxidant activity at 0.1 mg/ml[143]
	Hydroalcoholic extract (leaves and aerial parts)	DPPH assay, bovine brain peroxidation assay, β-carotene bleaching test	Low radical scavenging activity for DPPH assay; low antioxidant activity using bovine brain peroxidation assay; moderate activity by β-carotene bleaching test[6]
		DPPH radical assay, scavenging effect of H_2O_2 and chelating effect of samples on Fe^{2+}	No antioxidant effects on DPPH assay; concentration-dependent effects by hydrogen peroxide test; and > 86% of chelating effects after 60 min incubation in ferrous ion trials[144]
	Methanolic extracts (leaves, flowers, immature fruits and leafy flowered stems)	DPPH radical absorption, neutralization of linoleate free radical, MDA-TBARS complex, and β-carotene models	All samples proved to have antioxidant activity, particularly leaves (EC50 values < 0.4 mg/ml for all used models)[10]
	n-Hexane, dichloromethane and methanolic extracts (seeds)	Thin layer chromatograph (TLC) plate sprayed with DPPH solution; serial dilution of plant extracts mixed with 1 ml of DPPH reagent	Antioxidant properties by TLC qualitative plates test; by DPPH assay no activity was observed for dichloromethane extract and low activity for *n*-hexane and methanolic extracts[145]
Anti-ageing	Seed extract	DNA macro-array and quantitative reverse transcriptase-polymerase chain reaction	Increase of antioxidant gene expression (anti-ageing properties) [154]
Antinociceptive	Lyophilised aqueous extract (leaves)	Abdominal constriction test in mice. Abdominal constrictions induced by intraperitoneal injection of acetic acid (0.6%); formalin and capsaicin-induced pain, injecting 2.5% formalin solution or 1.6 μg/paw of capsaicin intraplantarly into the paw; hot-plate test observing the licking of paws, shaking paws or jumping off the surface at 56 ± 1°C	Significant antinociceptive effect against induced acetic acid abdominal constrictions (76.4%) and capsaicin-induced pain model (62.9%); inhibition of neurogenic (61.8%) and inflammatory (46.6%) phases of pain by formalin-induced pain test; no significant activity observed in central analgesic effect by hot-plate test[141]
Anti-ulcerogenic	Aqueous extract (aerial parts)	Ethanol-induced gastric ulcer in rats	Maximum protection (37%) at 500 mg/kg body weight (value higher than that observed with cimetidine (30%), a reference drug) [5]
Immunomodulatory properties	Aqueous extract (leaves)	Intraperitoneal injection of egg albumin (EA) and combinations of EA and extract.	*Malva sylvestris* extract did not have an adjuvant effect on anti-EA antibody production[1]
Bioadhesive mucous membranes	Aqueous extracts (flowers)	Ex-vivo system (mucous membranes prepared from tissue of the buccal region from freshly killed pigs)	Low bioadhesion to epithelial tissue. Not possible to correlate anti-irritative, anti-inflammatory or rehydration effects in this study[155]
Biochemical profile	Aqueous extract (aerial parts)	Extract intake via drinking water in rats	400 and 800 mg/kg body weight doses resulted in significant increases in serum triglycerides while other lipid, glycaemic and liver enzyme parameters (alkaline phosphatase, lactate dehydrogenase, alanine and aspartate transaminases) were unaffected[5]

Table 3 Pharmacological activities of *Malva sylvestris* claimed in patents

Activity	Extract/formulations	Observations
Alopecia and other capillary disorders	Hydroalcoholic extract (seeds or flowers) and associations	Loss of hair is stopped in 2–5 weeks. Hair regrowth takes 4–6 months[151]
	Malva association lotion also used as homeopathic composition	Causes regrowth of hair within 4–6 months and prevents hair loss within 2–5 weeks in most cases. Highly effective, even in patients who have lost hair for a long time[152]
	Solution of hair nutrients containing *M. sylvestris* association	Prevent hair loss – regeneration of the hair was observed[153]
	Lotion containing associations of *M. sylvestris* and other plant extracts	5α-reductase inhibitory and androgen receptor binding inhibitory activities – prevention and treatment of accelerated secretion of sebum (seborrhoea, pimple, male pattern alopecia) caused by excessive male hormones, hirsutism (polytrichosis), acne, prostatic hypertrophy and tumour[150]
Anti-inflammatory	Flowers hydroalcoholic extract and associations	Anti-inflammatory and anti-ulcer by topical application (reduce oedema within 24 h in a carrageenan test)[156]
Antioxidant	Associations containing *M. sylvestris*	Antioxidant activity better than α-tocopherol; same effects as synthetic butylated hydroxytoluene[157]
	Cosmetic containing *M. sylvestris* extract and other plants associations	High free-radical scavenging efficiency; alleviate skin irritation[141]
Biochemical profile	Ingestible composition of aqueous *M. sylvestris* extract and associations	Reduce the levels of triglycerides or uric acid in a mammal[142,143]
Insulin-like growth factor-1 (IGF1) factor	Extracts of *M. sylvestris* and associations	Improve glossiness of skin, restore softness of skin, increase bone density and muscle cell proliferation protein assimilation, improve carbohydrate metabolism, suppress inflammation, improve cognitive function, restore hair, enhance immunity and prevent or treat conditions such as senility accompanying physiological ageing[144]
Insecticide	96% alcohol natural insecticide containing *M. sylvestris* associations	Insecticide activity that does not cause the destruction of ecosystems, damage to mammals, wild animals and insects from the family Apidae[158]
Activity	Extract/formulations	Results
Integrity of skin and other tissues	Ingestible composition of *M. sylvestris* extract and association	Enhance the elasticity or structural integrity of skin, urogenital tissue, blood vessel walls, mucosal tissue of a human[159]
	Ingestible composition of aqueous *M. sylvestris* extract and association (administration in form of tablet, pill, capsule, powder or granule)	Effective to treat sagging and to strengthen tissues such as skin, mucosal and urogenital tissues and blood vessels[143]
	Topical composition comprised of a safe and effective amount of aqueous *M. sylvestris* extracts	Enhance the mucous production in mucosal tissue and increase elastin promoter activity in the presence of increasing doses of the extracts[159]
Skin ageing (topical)	Emulsion containing *M. sylvestris* and other plants associations	The extracts provide improve skin condition by elastase inhibition[160]
	Cosmetic containing *M. sylvestris*, ceramide liposome and other phytocomplex association	Prevent skin ageing, improve acne problems, increase skin elasticity and reduce the moisture loss of keratin[161]
	M. sylvestris association (aqueous or hydroalcoholic extract) useful as a serum, lotion, emulsion, cream, hydrogel, mask, stick or patch	Skin hydration and/or prevention or reducing signs of dry skin[162]
	Aqueous extract	Highly effective for enhancing the elasticity or structural integrity of skin or mucosal tissues by elastase inhibition and trypsin inhibition[142]
Skin whitening	*M. sylvestris* and *Mentha piperita* extracts associations	Strong skin-lightening effect[163]
	Cosmetic containing kojic acid and *M. sylvestris* association	Human skin freckles and spots removed[164]
	Cosmetic containing leaves and flowers of *M. sylvestris* and other plant extracts associations	Inhibition of tyrosinase activity and melanogenesis – improve skin colour and reduce pigmentation[165]
	Cosmetic comprised of *M. sylvestris, Primula veris*, co-enzyme Q10, β-carotene and tocopherol	Improve or prevent abnormal symptoms of skin pigmentation and excessive skin pigmentation by inhibiting melanogenesis of the skin; inhibiting and improving skin pigmentation such as melasma, freckles, and dullness[166]
	Topical composition containing *M. sylvestris* and other plant extracts	Excellent skin whitening and high pigmentation inhibition effect[167]

The antiproliferative activity of ethanolic and hydroalcoholic leaf extracts has been assessed in some human tumour cell lines. Significant reductions in the proliferation of B16 murine melanoma (97% relative to the control) and A375 human melanoma cells (58%) were observed using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) assay.[8] In contrast, antiproliferative activity was not observed in the MCF-7 cancer cell line, the LNCaP prostate cancer cell line, C32 amelanotic melanoma or renal adenocarcinoma in the sulphorhodamine B assay.[127]

M. sylvestris is most often linked to the maintenance of dermatological and mucous membrane integrity. As a consequence, several products such as cosmetics, topical compounds and moisturisers for the prevention of skin ageing have been developed and patented. These products have shown high efficiencies in relieving skin irritation, enhancing mucous production and scavenging free radicals.[146,147] Aqueous extracts and ingestible compounds have also been shown to enhance the structural integrity of skin and other human tissues.[58,148,149] Solutions and lotions were effective in preventing alopecia and other capillary disorders.[150–153]

Recently, the anti-ulcerogenic effect of *M. sylvestris* was demonstrated using aqueous extracts in rats with induced gastric ulcers. After a month of treatment at a dosage of 500 mg/kg body weight, a maximum protection of 37% was achieved. This level of anti-ulcerogenic activity was similar to that of cimetidine, a reference drug that showed 30% maximum protection.[5]

The biochemical profiles of rats ingesting aqueous extracts from plant shoots have also been evaluated.[5] When doses of 400 and 800 mg/kg body weight were administered, only serum triglycerides increased significantly, while the glycaemic, liver enzymatic and lipid profiles were not affected. This result disagreed with those from other studies that demonstrated reductions of triglyceride and uric acid levels after the intake of compounds containing the aqueous extract alone or in association with *Cotinus coggygria* extract.[58,148] It is important to mention that, despite the widespread use of *M. sylvestris* as a food or herbal medicine, only one toxicity test has been performed.[146] In this case, the Microtox Acute Toxicity assay showed that the hydroalcoholic extract had toxicity very close to the established maximum (20% of bioluminescence inhibition). Thus, further studies should be performed to assess the toxicity of *M. sylvestris* extracts.

The pharmacological aspects of *M. sylvestris* have been summarised in Table 2. Claimed patents have been listed in Table 3.

Conclusions

This review highlights the importance of *M. sylvestris* as a medicinal herb and functional food. Studies have proven its potential for treating inflammation, gastric ulcers and skin problems. Consequently, interest in this plant has increased worldwide, and in recent years, the number of patents has increased considerably. On the other hand, few studies involving clinical and toxicological research have been performed, making necessary further studies to elucidate the relationships between phytochemicals and mechanisms of disease treatment. It will then be possible to guarantee the benefits of safe *Malva* product use in the population.

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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