MALVA: FOOD, MEDICINE AND CHEMISTRY

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Keywords: *Malva*, *M. sylvestris*, antioxidant activity, ethnomedicine, flavonoids, medicinal uses.

Plants of the genus *Malva* (Malvaceae) have been used by humans for millennia. In addition to being an important nutritional source, they are used for many medicinal purposes. Modern research not only supports the ethnomedicinal uses of these plants but has discovered many others. Many review articles were published about the traditional uses of *Malva*, and some reviews were published about modern research findings of the medicinal and other properties of *M. sylvestris*. However, none of the review articles discussed both traditional and modern scientific knowledge about all plants of this genus. In the present article an attempt has been made to discuss both the aspects comprehensively. Conclusions have been drawn and future research possibilities suggested.

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Introduction

The genus *Malva* includes around 30 species.[1,2] The plants originally grew in Eurasia and North Africa, but humans have taken them to all continents except the two poles. Archeological findings in Jordan indicate a continuous use of *M. parviflora* by humans since ancient times.[3] Excavations in Isreal found an earlier use of *M. parviflora* and *M. aegyptiaca* dating around 23000 years before present.[4] These findings were confirmed and expanded by recent two studies of the same site.[5,6] Ancient Balkan inhabitants used *Malva* (unspecified sp.) as food sources and the materials of the plants were found in the remains of their teeth that go back at least 8600 years ago.[7]

The published literature about the *Malva* species is enormous but it focuses mainly on four of them: *M. neglecta*, *M. parviflora*, *M. sylvestris* and *M. verticillata*. The reported traditional uses and modern research findings of these species will be introduced in separate sections of this article, but they will be discussed jointly with the other species in the discussion section. Other species were little studied and for some others, there are no scientific publications at all. The last group includes *M. aethiopica*, *M. assurgentiflora*, *M. brasiliensis*, *M. campestris*, *M. canariensis*, *M. dendromorpha*, *M. hispanica*, *M. microcarpa*, *M. microphylla*, *M. pacifica*, *M. preissiana*, *M. pseudolavatera*, *M. qaiseri*, *M. stipulacea*, *M. subovata*, *M. transcaucasica*, *M. tournefortiana*, and *M. trifida*.

Many review articles were published about the traditional uses of *Malva* species and we will cite them here, but to the best of our knowledge, there are no published review articles that summarize the scientific literature about all *Malva* species that were studied so far.

M. verticillata was mentioned in a review article for its antidiabetic activity,[8] and wound healing potential of *M. neglecta*, *M. parviflora* and *M. sylvestris* was presented due to their anti-inflammatory properties.[9] Antitussive activity of *M. sylvestris* was reviewed among other medicinal herbs that have the similar activity.[10] A comprehensive review article about flavonoids in plants of the Malvaceae family (that includes the genus *Malva*) has been published recently and it shows some of the important natural products of this compound family.[11] In Figure 1, the structures of selected flavonoids are presented.

M. sylvestris is the most studied species of the Malva genus so far. An excellent review of traditional uses (food, ethnomedicine) and scientific research findings of this plant was published by J. Gasparetto et al. in 2011.[12] But it has three disadvantages. First, in terms of active natural products present in *M. sylvestris*, this review focuses only on polyphenols that are presented with structural formulae, while other compound families are mentioned but not presented like polyphenols. Second, a notable number of the cited references are patents that readers will not easily access. Third, despite being a very important research center of traditional uses and modern research of medicinal plants, Iranian publications are not sufficiently cited in this review.

Another review article that presents the biological activities of *M. sylvestris* was published by D. Paul.[13] It presents some traditional uses of the plant and most of its modern research findings of medicinal and other activities very briefly. The phytochemical part is very short and presents mainly polyphenols. The author presents seven major biological activities of the plant while ignoring many others. Finally, a review article that includes both traditional uses and scientific data about the medicinal properties of the plant was published by Shokrollahi and Ali.[14] Despite being supposed to include very much data, it presents it just partially and much of the known literature is not cited at all.

Traditional uses of *Malva* species

Three species possess the vast majority of publications, in terms of traditional-ethnobotanical uses viz., *M. neglecta*, *M. parviflora* and *M. sylvestris*. The details are presented in a separate tables (Tables 1-3), while the same about rest of the species are presented collectively in Table 4.

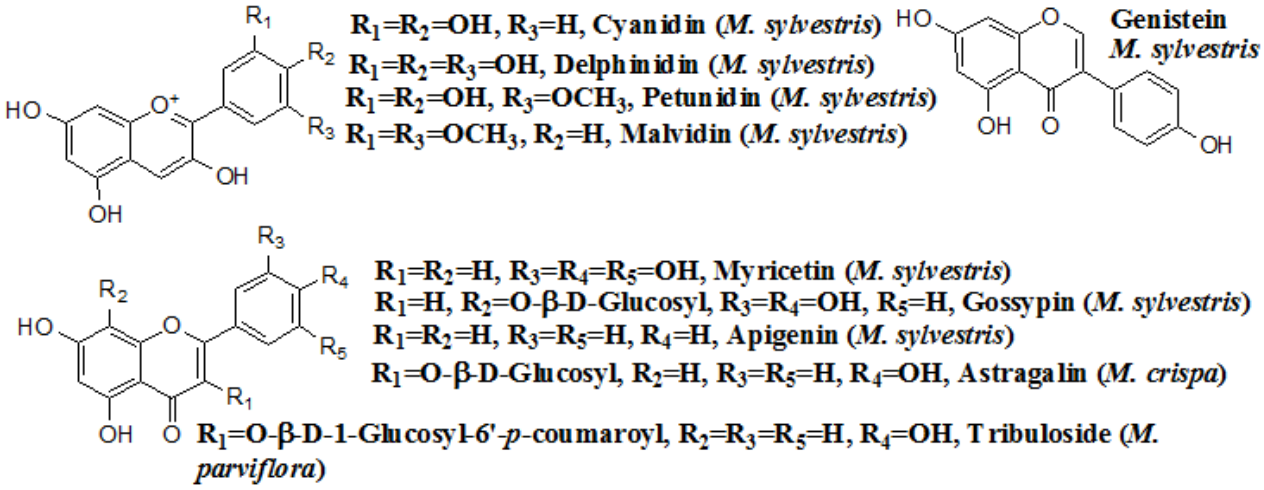


Figure 1. Selected flavonoids in three *Malva* species[11]

Table 1. Traditional uses of *M. neglecta*.

Country/Region	Used part/s	Use/s (reference)
Turkey/Germany	leaves	Compressed fresh leaves are used to treat abdominal pains[15]
Turkey	Stem, leaf, petiol	Eaten fresh or cooked[16]
Spain	Fruits	Immature, raw eaten as a snack[17]
Poland	Leaves, fruits, seeds	Leaves eaten in the past, immature, raw fruits still eaten, seeds grounded and added to bread[18]
Lebanon	Leaves	Infusion for treatment of gout and rheumatism[19]
Poland	Fruits	Immature, eaten raw [20]
Pakistan	Unspecified	Demulcent, aphrodisiac, laxative[21]
Pakistan	Shoots, roots	Shoots are used as potherb. The roots are used as purgative for young cattle[22]
Italy	Flowers, roots, leaves	To treat abdomenal pains. Leaves together with oil cure burns and zoster like inflammations. A hip-bath taken in the decoction soothes the uterus[23]
Turkey	Aerial parts	Decoction, to treat stomachache[24]
Pakistan	Roots	Purgative for young cattle[25]
India	Leaves	To heal broken bones and sooth baby's sore back.26 As anti diarrheal agent for calves and a food[28]
Turkey	Aerial parts	As food in various forms[27]
Iran	Aerial parts	Decoction to treat inflammation and sedative[29]
Pakistan	Roots, leaves, flowers	Roots used as purgative for young cattle. Leaves and flowers are used as demulcent, for bruise, inflammations, insect bites etc. Internally in the treatment of diseases of respiratory system digestive or urinary systems[30]
Pakistan	Whole plant	To treat piles and cough[31]
Iran	Flower, fruit	To treat sore throat and antitussive,[32,33] and as febrifuge[33]
Iran	Aerial parts	Decoction, poultice; laxative[34]
Spain	Aerial parts	Infusion to treat colds. Raw, immature fruits as food[35]
Pakistan	Stem	As food and to remove constipation and enhance digestion[36]
Pakistan	Leaves, roots	Leaves are used as food. Root extract is used to remove kidney stones[37]
Daghestan	Aerial parts	Food (cooked leaves, unripe fruits)[38]
Turkey	Aerial parts	Cooked or raw as salad[39]
Armenia	Aerial parts	Cooked or raw as salad[40]
Turkey	Whole plant	For large number of disorders[41]
Pakistan	Seeds	Crushed and used to cure cough and bladder ulcer[42]
Iran	Leaf, stem	Blood purification (unspecified method)[43]
Turkey	Leaves	To treat coughs and to treat abdominal pain[44]
Switzerland	Aerial parts	Ethnoveterinary: To treat skin afflications and orally to treat gastrointestinal disorders[45]

Table 2. Traditional uses of *M. parviflora*.

Country/Region	Used part/s	Use/s (reference)
Spain	Fruits, leaves	Immature, raw fruits as a snack, tender leaves and stems stewed[17]
Italy	Flowers, roots, whole plant	Flowers and roots are used against gastrointestinal pains as a laxative and as a diuretic. A decoction of the herb is used to treat gingivitis while cataplasms are used to treat furuncles and ulcerous wounds[23]
Turkey	Aerial parts	Food[27]
Pakistan	Leaves, roots, seeds	Seeds are used in cough and bladder ulcer. Leaf decoction is used for tap worm and profuse menstruation. Roots are used as sex tonic. Plant is also used as laxative[42]
Costa Rica	Whole plant	Ornamental plant[46]
Bolivia	Aerial parts	Anti-inflammatory, colds, fever, headache, vulnerary[47]
Canada	Aerial parts	Treat wounds of ruminants (unspecified method)[48]
South Africa	Unspecified	Poultice to treat sores and decoctions for neuralgia and sore throat[49]
South Africa	Leaves	To treat infected eye[50] and diarreea[51]
Pakistan	Seed, leaf	Seeds decoction is used as tea to treat common cold and cough. Leaves are cooked to treat constipation and used as vegetable[52]
Pakistan	Whole plant	Decoction used to cure cough flue and fever[53]
Iran	Leaves	Infusion, laxative, relieve cough and chest discomfort[54]
Argentina	Leaves	Decoction used in ethnoveterinary: intestinal colic, ocular diseases, wounds and injuries, mastitis and udders of goats and cows[55]
Bolivia	Leaves	Infusion, liver disorders, gastritis, stomach problems, renal inflammation, diuretic[56]
Iran	Seeds	Decoction to treat cold[57]
India	Whole plant	Decoction is used to treat cough, flu and fever[58]
Pakistan	Leaves	Food, decoction to treat constipation, cough and fever[59]
Egypt	Whole plant	Unspecified method, to treat pyorrhea, astringent[60]
Pakistan	Leaves, seeds	Infusion is used to lessen skin allergy, diaphoretic, headache[61]
Iran	Leaves, flowers	Food, treatment of kidney and bladder infections, emollient[62]
Pakistan	Leaves	Used by humans as vegetable, given to the hens as food[63]
Kashmir	Leaves	Eaten as vegetable, anthelmintic[64]
Chile	Unspecified	Antifungal[65]
Morocco	Leaves, stem	Decoction, respiratory disorders, cataplasm[66]
Kashmir	Shoot, leaf	Shoots are used for constipation, leaves are used to treat dry cough, bladder worm, diabetes and as vegetable and fodder[67]
Morocco	Leaves	Cataplasm: oral affection[68]
Pakistan	Seeds, leaves	Seeds used to relieve cough, bladder ulcer, leaves to treat tape worm, profuse menstruation[69]
Pakistan	Whole plant	Decoction, to treat cold, fever and cough[70]
Saudi Arabia	Leaf	Treatment of scorpion-sting[71]
Pakistan	Leaves, seeds	Leaves are emollient. Seeds are used to treat cough and ulcers in bladder[72]
Iraq	Leaves	Decoction: hair loss, abdominal pain, diarrhea[73]

Table 3. Traditional uses of *M. sylvestris*.

Country/Region	Used part/s	Use/s (reference)
Turkey/Germany	leaves	Compressed leaves are used to treat abdominal pains
Turkey	Stem, leaf,petiol	Eaten fresh (salad) or cooked[16]
Spain	Flowers, fruits, leaves	Flowers, as herbal tea and for making liqueur, immature fruits raw as a snack, tender leaves and stems stewed[17]
Poland	Leaves, fruits	Leaves used to be cooked in the past, immature, raw fruits eaten as a snack[18]
Lebanon	Leaves, flowers	Used to treat rheumatism and arthritis[19]
Poland	Fruits	Immature, eaten raw[20]
Pakistan	Unspecified	Medicinal, food for humans and animals[21]
Italy	Flowers, roots, leaves	To treat abdomenal pains, leaves are used to treat burns and zoster like inflammations, to soothe the uterus and as laxative and diuretic. It is used to treat furuncles and ulcerous wounds[23]
Turkey	Aerial parts	Used as food in many ways[27]
Iran	Flower, fruit	To treat febrifuge, respiratory ailments, depurative, mouth ulcers,[32] jaundicea and constipation[33]

Spain	Whole plant	Leaves and flowers are used for coughs, colds, sore throat, bronchitis, asthma and skin inflammations. Fflowers and leaves are used for fluid retention.[35]
Switzerland	Aerial parts	Used to treat skin afflications and gastrointestinal disorders in animals[45]
Costa Rica	Whole plant	Unspecified method: ornamental[46]
Argentina	Leaves	Used to treat intestinal colic, ocular diseases, wounds and injuries, and mastitis and udders of goats and cows[55]
Morocco	Leaves, roots	Decoction or cataplasm, respiratory or urinary disorders[66]
Arab countries	Leaves, roots, flowers	Many uses relates to *M. sylvestris* and *M. rotundifolia* together[74]
India	Leaves	Decoction mixed with lime juice to treat snake bite[75]
Italy	Different parts; Whole plant	Used to treat toothache, gingival inflammations, cough, cold, sore throat, mouth inflammations, diverse inflammations, furuncles, abscesses, wounds hemorrhoids, abdominal colic, warts, aphate, urinary infections and nail infections; also as perfume, analgesic, antitussive, anthelmintic, sedative and laxative.[76,79,80,82,85,88] To wash cows‘ udders;[83] in ethnoveterinary[88]
India	Unspecified	To treat tuberculosis[77]
Pakistan	Leaves	Unspecified Method: demulcent, aphrodisiac, laxative[78]
Cyprus	Leaves	Food, unspecified method, against cough and infection[84]
Spain	Aerial parts	Infusion: gastralgia, dysmenorrhoea, kidney malfunction, cold,[86] laxative, contusions, bruises, *Urtica diocia* stings and fever[87,91]
Portugal	Unspecified	Unspecified method: treatment of infections[89]
Syria	Leaves, flowers	Used as mouth wash, cough, respiratory infections, laxative[90]
Turkey	Aerial parts, whole plant	Wounds and furuncle,[92] hepatic and stomach disorders, cancer, sore throat, mumps, cough, cold, wounds, abscess, woman diseases, diabetes;[93] as food,[94] gynic problems, as green dye[102]
Slovakia	Aerial parts	Food[95]
Brazil	Unspecified	Infusion: cleanser, diuretic, boil, uterine inflammation, rheumatism, tonsillitis wound[96]
India	Aerial parts	Eaten twice a day to strengthen weak eye sight[97,112]
Algeria	Leaves	Unspecified method: laxative, hypoglymic[98]
Cyprus	Leaves	Cooked and consumed daily: antidiabetic[99]
Turkey	Leaves	Boiled and used to treat gastralgia, laxative[100]
Mexico	Flower, leaf	Capsules of extract (unspecified): weight loss, anti-inflammatory, laxative, antihyperglycemic[101]
Algeria	Aerial parts	Decoction: anti-inflammatory,weightloss[103]
India	Different parts of whole plant	Mucilaginous, cooling, anti-inflammatory, sore throat, jaundice, enlargement of spleen. cough, ulceration of urinary bladder, stimulates uterus, intestines[104]
Jordan	Leaves	Soaked (oral): emollient for intestinal mucosa[105]
Italy	Leaf, root, flower	Crushed leaves: teethache, whitlow. Leaves decoction or infusion: belly pain, cystitis, cough,cold, weightloss, bronchitis[106]
Iran	Flower	Infusion: jaundice, pharyngitis, furuncles, aphthous ulcers, antitussive[107]
Europe	Aerial parts	Abdominal colic, tympanism, rumination, diarrhea, constipation.[108]
Turkey	Roots	Infusion: abortive[109]
Algeria	Flower	Infusion: to treat abscesses, boils, swelling, insect bites, softening, antiseptic, astringent, abdominal pain, colic, otitis, asthma, constipation, colds, canker sores,[110] antiseptic for reproductive system[111]
Iran	Different parts	Immunomodulation, respiratory diseases of animals,[113] laxative, swellings, lubricant, clear the lung, expectorant, cough,[114] laxative, cough etc.[115]
Pakistan	Leaves	Unspecified method: bladder ulcer, diuretic, indigestion, anti-inflammatory, gastric mucus, relaxing activity[116]
Palestine	Leaves	Decoction: 10 g boiled in 100 mL of water, the affected is rubbed twice a day[117]

Table 4. Traditional uses of *Malva* species (excluding subspecies in Tables 1, 2 and 3).

Malva species	Country/Region	Use (reference)
M. cretica	Turkey	Food[27]
	Spain	Aerial parts, infusion: gastralgia[86]
M. moschata	Turkey	Food[27]
	Spain	Infusion to treat colds, raw, immature fruits as food[35]
M. nicaeensis	Turkey/Germany	Leaves: To treat abdominal pains[15]
	Spain	Immature, raw fruits eaten as a snack[17]
	Lebanon	Decoction of whole plant used to treat arthritis[19]

	Italy	Used against gastrointestinal pains, gingivitis, furuncles and wounds[23]
	Turkey	Food,[27] tosilitis, anpyretic, antitussive[41] Analgesic, ulcer, woman diseases, cough, digestive disorders, rheumatism, expectorant,[93] Urtica sp. Prickles,[94] abortive, cough, kidney disorders[109,119]
	Spain	Flowers, infusion: anticatarrhal[87]
	Israel	Whole plant: Cough, wounds and skin diseases[118]
M. pussila	Daghestan	Aerial parts, food (cooked leaves, unripe fruits)[38]
	Armenia	Cooked or raw as salad[40]
	Pakistan	Different parts are used to treat scurvy, piles, skin diseases, cough, bronchitis and inflammation of bladder[42]
	Slovakia	Food[95]
M. rotundifolia	Italy	Used for abdominal pains, burns, inflammations and soothing uterus[23]
	Arab countries	Many uses but this reference relates to *M. sylvestris* and *M. rotundifolia* together[74]
	India	Cough, inflammation, ulceration of urinary bladder, haemorrhoides, skin diseases, fever[104,120]
	Iran	Cancerous wounds,[121] oral sores[122]
M. verticillata	India	Cough, pectoral complaints, piles, ulcer, urine complaints, stmach ailments, swelling, kidney pain and food,[123,124,125]
	Ethiopia	External wounds, anthrax,[126] expulsion of placenta in cow,[127] fever,[128] vomiting, dysentery, neck tumor[129]
Unspecified	Spain	Leaves, infusion: anti-inflammatory, vulnerary (also after pig castration), antifurunculosa, stomachache, cholagogue, emollient, gingivitis, aphtae[130]
Unspecified	Canada/Trinidad	Aerial parts, unspecified method, respiratory (horses)[131]
Unspecified	Brazil	Leaves, infusion, soothing, headache, blood pressure[132]

Table 5. Modern research findings of some *Malva* species.

Malva species	Property	Major findings (reference)
M. aegyptiaca	Water soluble polysaccharides partial analysis	Water soluble were isolated and their monosaccharide units were identified: galactose, rhamnose, arabinose, mannose and glucuronic acid with the weight percentage of 56.86 %, 8.46 %, 9.04 %, 5.05 % and 20.57 %, respectively[133,134] (See note after ref. 133)
	Heavy metals accumulation	This plant accumulated Cd^{2+} more than other plants that were growing near phosphate treatment industry in Tinisia. Average concentration in the stems: 28.9 ppm[135]
	Chemical composition and antioxidant activity	Chemical composition was analyzed by GCMS for volatile compounds, and metal ions concentrations were determined. Total phenolic content was found and tested for antioxidant activity (strong, DPPH)[136]
	Chemical composition, antioxidant activity, bread additive	Chemical composition was determined focusing on flavonoids, triterpenoids and fatty acids. Antioxidant activity was determined by (DPPH, Fe^{3+} reduction). As bread additive, it was found to improve the quality and nutritional value[137]
M. crispa	High protein content	When cultivated protein content can reach up to 20 % (dried)[138]
	Flavonoids in flowers	Various glycosylated falvonoids were isolated from the flowers of the plant and characterized by chemical analysis and spectroscopic methods[139]
	Synthesis of gold nanoparticles	Leaves of the plants were used as reductant in the synthesis of AuNP's from HAuCl4. These AuNP's were tested against food borne bacterial pathogens[140]
	Synthesis of silver nanoparticles	Aqueous extract (reductant) of the leaves of the plant was used to prepare AgNP's. These were tested against various pathogen bacteria and found effective.[141] They were also highly toxic for zebra fish (Danio rerio)[142]
M. mohileviensis	Antiinflammatory and antioxidant	Ethanolic and aqueous extracts of seeds and aerial parts, as well as crude polysaccharides from cold and hot water extracts exhibited a significant anti-inflammatory and antioxidant (DPPH) activity[143]
M. moschata	Antibacterial	Hexane, dichloromethane and methonal extracts were prepared then the dry matter was suspended in DMSO. It was active against several types of bacteria[144]
	Plant pigments	This work focused on chlorophylls and carotenoids[145]
M. nicaeensis	Heavy metals accumlulator	Very good heavy metals accumulator from polluted soils, especially Zn and As. Promising bioremediation agent[146]
	Inhibition of pancreatic lipase	Dried aerial parts of the plant were extracted with methanol and the dry extract was suspended in DMSO and tested for PL inhibition. Strong activity[147]
	Inhibition of hormone sensitive lipase	Dried aerial parts of the plant were extracted with methanol and the dry extract was suspended in DMSO and tested for HSL inhibition. Strong activity[148]

M. pusilla	Polysaccharide isolation and activities	Water soluble polysaccharide was isolated and its monosaccharide units were determined (qualitatively). It was tested for anti-inflammatory activity (strong)[149]
M. rotundifolia	Composition	General composition was determined for macronutrients, fatty acids and some minerals. No alkaloids found[150]
	Antimicrobial	Ethanolic extract was dissolved in DMSO and tested for antimicrobial activity (very weak)[151]
M. sinensis	Cadmium accumulation	Contaminated soil from lead-zinc mines was treatred with this plant (also known as *M. cathayensis*) and found to be hyperaccumulator[152]

Modern Research Findings

The *Malva* species very extensively researched by modern techniques also. However, like in traditional uses of these plants, the vast majority of publications focus on four species of this genus: *M. neglecta*, *M. parviflora*, *M. sylvestris* and *M. verticillata*. Summary of research regarding each of these species are presented in a separate table. Like in traditional uses, *M. sylvestris* is most studied is this respect also.

Malva neglecta

Malva neglecta is a widespread edible plant that can be found in Eurasia and North Africa. It has many common names, sometimes in the same culture, and this might be misleading. Modern research findings approve its known traditional medicinal properties, and it is being studied more and more. A summary of these findings is shown in Table 6.

Malva parviflora

Malva parviflora is the second most widely studied *Malva* species after *M. sylvestris*. Despite the fact that its natural habitat overlaps with that of *M. sylvestris* and *M. nicaeensis*, it is relatively easy to distinguish *M. parviflora* from the other two: its leaves are more cycle shaped than of the other two species, and the plant itself is much lower than the two others. Modern research started studying *M. parviflora* only in the last four decades and the major findings are summarized in Table 7.

Malva sylvestris

Malva sylvestris is the most widely studied species of the *Malva* genus, and one of the most studied in the whole plant kingdom. In most parts of its natural habitat, it is very widespread, and most people mean it when they mention the words *Malva*, mallow or Khubbaiza in the Middle East. Modern reported literature about this plant is very large and published regularly. We have tried here to cite most important publications and summarized them in Table 8. We have cited together publications, published in the last twenty years (as of 2008), that report the same property. If notable differences are presented, the publications has been cited separately.

Malva verticillata

Among the four major *Malva* species listed in Tables 6-9, *M. verticillata* is the least investigated and modern research publications about it are fewer. In addition, traditional uses of this plant are also fewer than the other three. Despite this, a very comprehensive work has been carried out by studying the chemical composition and biological activities of seeds.

This exceptional work was done by a Japanese group lead by M. Tomoda and was published in nine articles between 1987 and 1992. This work has been presented collectively.

It is also notable that *M. verticillata* seeds are rich in polysaccharides that were thoroughly studied. It is interesting to pay special attention to the antidiabetic activity of *M. verticillata*, as this activity is one of the major properties of this plant.

Discussion

While studying the literature of traditional uses of Malva species, we found that some of them are in an ambiguous status as for their distinctiveness. For example, two of these species are M. alcea and M. excisa.[353] So, despite the fact that M. alcea was mentioned with other known Malva species (*Crispa*, *Pussila* and *sylvestris*) as having traditional antiviral infections activity of humans and animals,[354] we did not include this paper in Tables 3 and 4.

Al-Asmari et al. from Saudi Arabia reported that in ethnobotanical medicine of their country, leaves of *M. parviflora* are used to treat "scorpion sting envenomation."[71] They also cite another publication that is supposed to support their claim.[355] But reading this reference carefully reveals the fact that either the report or the citation or both are wrong: in reference 355 there is no mention of "Malva" and/or "parviflora", and authors indicate *Eryngium creticum* Lam. as a plant that is used in traditional Palestinian medicine to relieve pains of scorpion stings and snake bites.

Malva species are used for dye production.[102] The colored compounds of these plants, especially flavonoids/anthocyanins are the major source for these colors.

These compounds are naturally produced (see Figure 1), but this production can be enhanced by irradiation of the plants with UV,[285] or by the addition of other growth promoters. These results were confirmed by later publications.[287,288] J. Pinela and his colleagues from Portugal reported using Gamma radiation for the same purposes in M. neglecta.[356] Scientifically speaking, new results were obtained, and this report should be included in Table 6. We did not include it there for two reasons. One, this method is very expensive, and two, there are no follow up studies about the effect of this powerful radiation on other compounds in the plant, and maybe diverse results in terms of toxic materials production.

One of the very interesting medicinal activities of Malva plants is their potential use as antiobesity agents. In most publications, this activity is mentioned or studied along with the antidiabetic activity. *M. sylvestris* is traditionally used for this matter (weight loss) in Iran,[101,103] and this use is not "very unusual and rarely mentioned," as Menale and Muoio indicated.[106] Modern research found a possible explanation for this potential activity of *Malva* species. Y. Bustanji et al studied the antiobesity activity of *M. nicaeensis*, through the inhibition of pancreatic lipase (PL) and hormone sensitive lipase (HSL).[147,148] PL inhibition was also reported by *M. neglecta*.[171] These studies suggest the importance of followup studies on this subject.

Ameri et al indicated that the common name of *M. sylvestris* is "Jews mallow".[114] This is not correct because it refers to "Mulukhiyah" or *Corchorus olitorius*, a plant in the *Malvaceae* family but to the genus *Corchorus* not *Malva*.

Variations in chemical compositions of plants due to various factors such as locations, seasonality and weather conditions, are well known and widely reported. But such variations can also result not only from these external effects, but they can also result from internal factors of the plant e.g., the stage of growth or plant part. An interesting example of such variations has been reported by Zouari et al.[136]

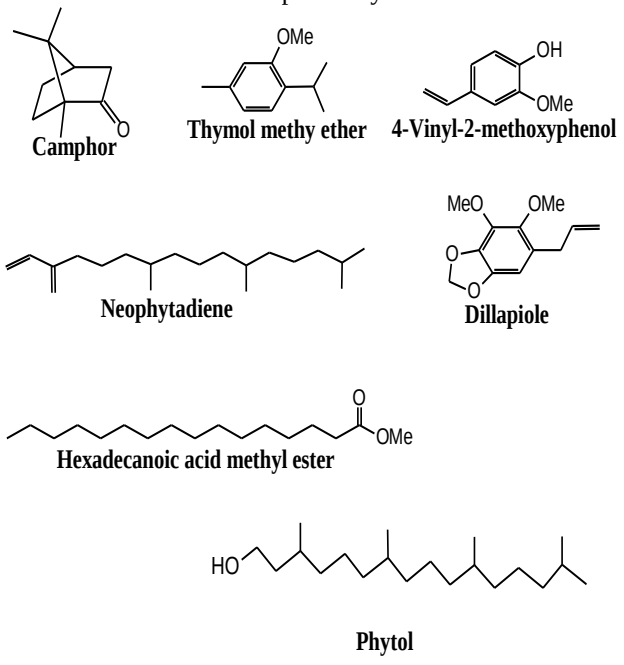


Figure 2. Compounds with notable concentration variations in *M. aegyptiaca* according to growth stage or plant part[136]

They have reported the different concentrations of volatile compounds according to three growth stages of *M. aegyptiaca* and also the concentration differences of macronutrients, metal ions and volatile compounds in leaves and fruits. Some of these compounds are presented in Figure 2, had notable variations according to growth stage.

Tunisian group lead by N. Zouari, published earlier this year another study[137] completing their previous report and evaluating the importance of *M. aegyptiaca* as bread additive. One of the interesting compounds they found was malvasterone (Figure 3), a steroidal triterpenoid that was first isolated from the roots of *M. parviflora*.[357] Steroidal units were also isolated later from *M. sylvest*ris (Figure 3).[286] These have an interesting lactone sub-unit, which grant them additional potential activities.

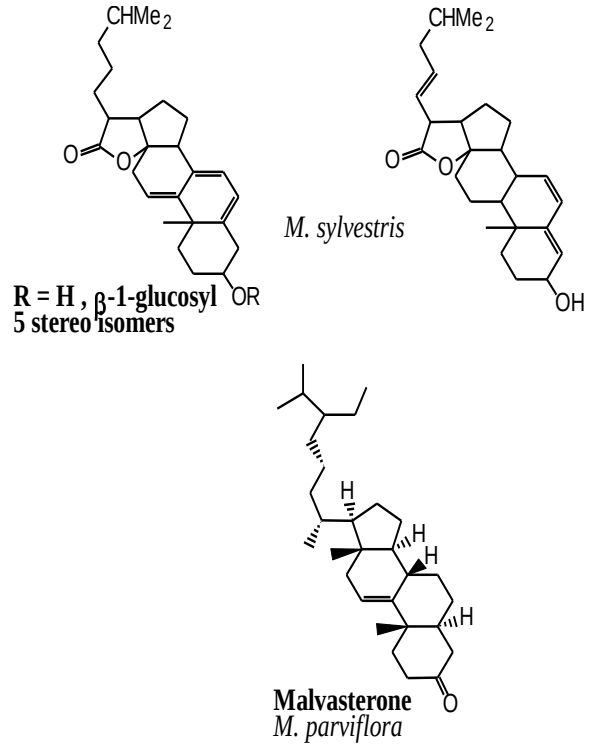


Figure 3. Structure of malvasterone.

Synthesis of nanoparticles of precious metals (or their oxides) using *Malva* species extracts has been reported by many groups.[140-142,172,188,216,303-304] In all these reports, aqueous extracts of leaves or flowers of the plants were used. The major quality that enables this kind of uses and reactions is the fact that these extracts are rich in flavonoids and anthocyanins. These compounds are good reductants, especially when hydroxyl (OH) groups are present in their structures.[358]

Beyrami-Miavagi and his colleagues,[164] have reported two properties of *M. neglecta*, antioxidant and contraceptive, as a safe alternative to prostodin (synthetic contraceptive), which causes oxidative stress and other damages in urinary system. There is no question about the antioxidants of Malva plants, but our intense search for research reports that support contraceptive activity of these plants was in vain, despite the fact that other plants with this activity are well known.[359,360,361]

The de-epoxidation of violaxanthin to zeaxanthin (Figure 4) is a biologically important process since it prevents photooxidative damages that might be caused to chloroplasts by excessive radiation.[362]

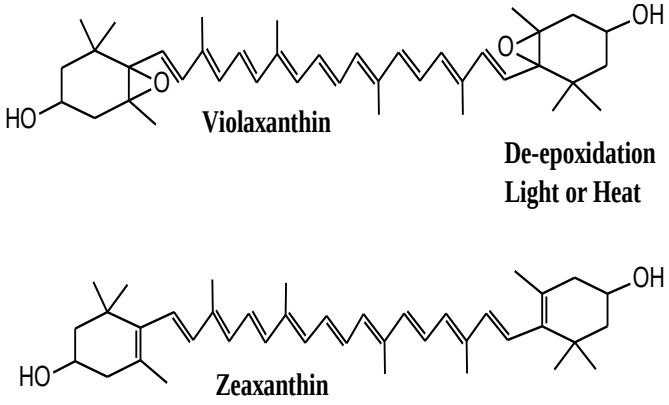


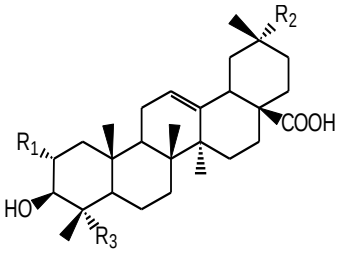
Figure 4. De-epoxidation of violaxanthin to zeaxanthin

This process occurring naturally has an additional importance when leaves of this plant are consumed as food since health benefits of zeaxanthin are more than those of violaxanthin. So it is favorable to expose leaves of the plant to light before cooking.

There seems to contradiction in two reports presented in Table 7 regarding the antidiabetic activity of *M. parviflora*. Phoboo[202] reported weak activity, however, strong activity has been reported by El-gizaewy.[204]

One can identify three sources of the difference. First the part of the plant used, leaves and seeds respectively; secondly, extraction solvent, water and n-hexane, and finally the testing model, in vitro enzyme inhibition (α-amylase and α-glucosidase) and in vivo treatment of streptozotocin (STZ) induced diabetic rats.

Isolation, characterization and three biological activities of a novel, natural derivative of the triterpenoid oleanolic acid has been reported.[210] Comparing the structures of oleanolic acid and the new compound (Figure 5), clearly shows that this derivative includes more polar functional groups.



Oleanolic acid: R_1=H, R_2=R_3=CH_3

Derivative (ref. 210): R_1=OH, R_2=R_3=CH_2OH

Figure 5. Oleanolic acid and its novel, natural derivative reported in reference 210

Oleanolic acid itself is physiologically very active compound,[363] and this new derivative should also be additionally studied and chemically modified to prepare new derivatives and test their activities.

Toxicity of Malva species to animals is very rare but was indicated in the research literature. *M. neglecta* was reported to cause hypocalcemia in cow,[205] but the mechanism of poisoning action was not reported. A controlled study with horses showed that consumption of large amounts of *M. parviflora* resulted in energy balance damages.[213] It is proposed that cyclopropene fatty acids contained in the plant are responsible for this, and elevation of acylcarnitine (Figure 6).

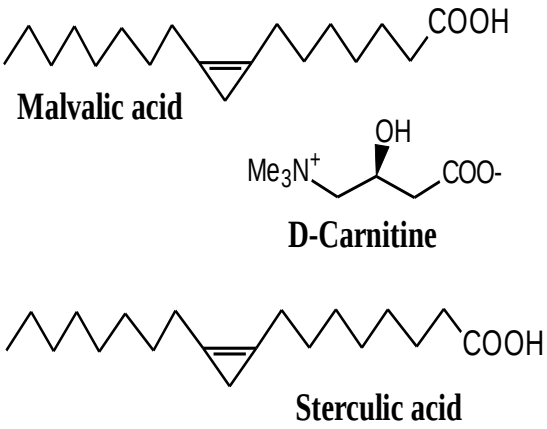


Figure 6. Structures of malvalic and sterculic acids and carnitine

Authors explain their findings by the rapid and easy oxidation of the unstable cyclopropene ring, which is consistent with earlier reports.[364]

In 2006, Ganai et al reported a detailed method of isolation and purification of the enzyme sulfite oxidase from leaves of *M. sylvestris*.[228] This work completes an earlier work by this author (and others), but we did not cite it in Table 8 due to its partial findings.[365] Sulfite oxidase catalysis the oxidation of sulfite to sulfate and it has very important role in sulfite detoxification in plants.[366]

Germination inhibition of plants by other plants is known as allelopathy. Many plants act as allelopathic for another plant and their growth can be inhibited by other plants. Cutillo and her colleagues found that two new terpenoids that they isolated from *M. sylvestris* and characterized have an allelopathic effect on *Lactuca sativa*.[229] The structures of these compounds are shown in Figure 7. Such findings are consistent with earlier and later reports of allelopathic effect of terpenoids on *L. sativa*.[367]

Wound healing and treatment of skin diseases by plant extracts and other pharmaceutics is a known phenomenon and has been extensively studied and published.[368] Plants of the *Malva* genus are among the most active as regard this activity. They were used for such purpose in many cultures.[35,42,45,61,76,81-83,104,118]

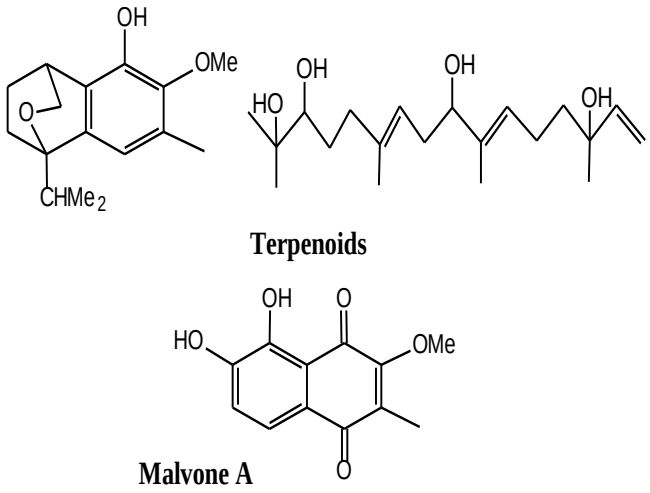


Figure 7. New terpenoids isolated from *M. sylvestris* (ref. 229) and Malvone A (ref. 230).

Modern research findings confirm the traditional knowledge.[161,183,248-258] But carefully reviewing this data reveals an interesting and not always consistent results. For example, it is reported that chloroform and n-hexane extracts of *M. parviflora* are irritant.[183] However, others found counter-irritant activity in chloroform and other extracts of the same plant.[369] Moreover, chloroform extract of M. sylvestris was also reported as having wound healing activity.[249,250] These contradictions must be resolved by future more extended studies.

Mineral content of *Malva* species has been published in several research articles. There is a common result in all of them. The genus Malva is rich with potassium and calcium (*M. neglecta*;[150] *M. parviflora*;[201] *M. sylvestris*[223,229,260,262,263]). Several methods were used to determine the metal content and one of the best, yet simplest was reported by S. Terfi and his colleagues.[264] Related to that, some studies were conducted to test the capacity of *Malva* species to accumulate heavy/toxic metals from contaminated soil or aqueous solutions. We present the results of these publications in Table 10.

Table 6. Modern research findings of *Malva neglecta.*

Property	Methods and major findings (reference)
Chemical composition	Alkaloids, flavonoids, saponins are present but tannins are absent.[153]
Antioxidant activity	Moderate activity was detected in methanolic and aqueous extracts DPPH and TBA methods.[154]
Poisoning	Hypocalcemia reported in a cow which ate a large amount of the plant.[155]
Antibacterial	Ethanolic extract of flowers was tested against 10 types of bacteria. Six of them were resistant[156]
Antibacterial	Aqueous, ethanolic, chloroform and acetone extracts show moderate activity against four types of bacteria.[157]
Antimicrobial	Aqueous, methanolic, n-hexane, chloroform, ethyl acetate and n-butanol extracts did not show any activity against four types of bacteria.[158]
Antioxidant	Stong antioxidant capacity of the phenolic content.[159]
Antioxidant	Hydroalcoholic (1:3) extract showed strong activity[160]
Antibacterial	Aqueous, ethanolic and chloroform extracts of M. neglecta and M. sylvestris were tested against seven types of bacteria that cause wound infections. All extracts were active, and ethanolic was most active for both plants. Extract of M. sylvestris was more efficient[161]
Mineral content	K^+ was highest with 230 mg kg^{-1} [162]
Antiinflammatory	Methanol extracts show moderate activity against some types of inflammation.[163]
Contraceptive	Female rats were treated with hydroacoholic (1:8) extract and prostodin, a synthetic contraceptive. The extract caused lesss oxidative stress and other damages in kidneys and urinary space[164]
Kidney stones preventive	Production of kidney stones (CaOx) and tubulointerstitial damage, induced in male rats by ethylene glycol and ammonium chloride, was reduced on treatment with aqueous extract of the plant.[165]
Antiinflammatory	Aqueous extract was tested against various inflammatory agents in patients with osteoarthritis and found as potent inhibitor[166]
Antibacterial	Ethanolic extract found active against antibiotic-resistant S. aureus[167]
Mucilage uses	Mucilage was separated from fresh leaves and precipitated by acetone, contains carohydrates and flavonoids. It was used to bind the synthetic analgesic of diclofenac sodium and produce granules[168]
Antioxidant	Hydrocolloid water extract of plant leaves was prepared in various temperatures (55-95 °C). The products of higher temperatures showed excellent antioxidant activity (DPPH)[169]
General composition, antioxidant, antibaterial	General composition of fresh leaves was determined by three classes of components: macronutients, metals and total phenols. The methanolic extract was tested for antioxidant and antibacterial activities: both were found moderate comparing with other plants in this study[170]
Health benefits, antioxidant and enzymes inhibition	This study connects the traditional known health benefits of the plant (very good food photos) and its medicinal properties. Aqueous extract showed antioxidant activity and pancreatic lipase and α-glucosidase inhibition[171]
Synthesis of silver nanoparticles	Aqueous extract was used as a reductant in the synthesis of AgNP's from silver nitrate[172]
Composition, anticholinesterase, antimicrobial, antioxidant, aflatoxin content	The aqueous extract was analyzed by LC-MS/MS for total phenolic content and determination of single phenolic compounds. It showed anticholinesterase, antimicrobial and antioxidant activities, and no aflatoxin content. The essential oil was analyzed by GC-MS for fatty acids content and volatile compounds[173]

Table 7. Modern research findings of *Malva parviflora.*

Property	Methods and major findings (reference)
Thiamine content and safety to ruminants	Thiamine content of the plant is relatively high compared with other plants in this study. This is in accordance with very low levels of thiamine destroying enzyme, thiaminase, that consumption of large amounts of it may lead to cerebrocortical necrosis in ruminants.[174]
De-epoxidation of in leaves	Temperature and light (λ=505 nm) on the de-epoxdation of violaxanthing to zeaxanthin. Leaves were sensitive to radiation and less to temperature, especially under 24 °C.[175]
Antifungal proteins	Two antifungal proteins were isolated and characterized from seeds of the plant. The proteins were found fungisatic instead of fungicidal.[176]
AChE inhibition	Ethanolic extracts of leaves are better inhibitor of acetylcholine esterase (AChE) than aqueous extracts and most efficient concentration was 0.025 mg ml^{-1}.[177]
Antibacterial, antiinflammatory	Extracts of plant parts showed antibacterial and anti-inflammatory activities. Authors suggested synergism of two unidentified anti-inflammatory compounds.[178]
Proximate composition, antioxidant	Protein, total phenolic content and metal content was determined. The plant is calcium rich. 80% Aqueous methanol extract showed moderate antioxidant activity (DPPH).[179]
Total phenolics, antioxidant	Total phenolic content was detemined and two of their sub-classes. Ruduction power (Ferric ion) and DPPH, ABTS quenching capacity were also determined[180]
Anti-inflammatory, anti-allergic	Aqueous extract of the flowers found active againts allergen-induced eosinophilia[181]
Anti-inflammatory, analgesic	Methanol extract of aerial parts has anti-inflammatory and analgesic activities.[182]
Antibacterial, antifungal, irritant	Hexane, chloroform, ethanol and aqueous extracts showed antibacterial and antifungal activities. Most extracts had irritant effect on inner surface of ear of male albino rabbits.[183]
Anti-inflammatory, antioxidant, metal chelating	Methanolic extract had stronger anti-inflammatory activity. Methanolic and aqueous extracts showed strong antioxidant (DPPH) and ferrous ion chelating activities.[184]
Phytochemical screening, antioxidant	Fresh leaves and stems were found to contain phenols, flavonoids, sponins, alkaloids, resins and tannins. Aqueous extract of both parts had antioxidant activity.[185]
Antioxidant	Ethanolic extract of leaves had strong antioxidant activity.[186]
Hypoglycemic	Extract of aerial parts showed promising antidiabetic activity.[187]
Silver nanoparticles preparation	Fresh leaves were extracted with 70% ethanol/water and the extract was used as reductant in synthesis of AgNP'S from $AgNO_3$.[188]
Phytochemical analysis	Seven phytosterol, two polyphenols and 14 fatty acids were identified from 85% ethanol extract. Alcoholic extract had significant anti-inflammatory and cytotoxic activities and aqueous extract antimicrobial activity.[189]
Phytochemical analysis	Very partial phytochemical analysis of aerial parts that were extracted with chloroform.[190]
Toxicity to Flour beetle	Ethanolic (see remarks in the discussion section) extract of leaves was prepared and found fatal for the larvae of *Tribolium confusum*[191]
Growth promoter	Aqueous extract (plant part/s not indicated) promoted the growth of cowpea (*Vigna Unguiculata*)[192]
Cytotoxicity	95% Ethanolic extract showed weak activity against breast cancer cell lines.[193]
Hepatoprotective	Whole plant was extracted by 70% ethanol/water. The extract was analyzed for major chemical constituents and tested against paracetamol induced hepatotoxicity: very active[194]
Neuroprotective	Leaves ethanolic extract is active against amyloid-β- (Aβ-) mediated alzheimer's disease.[195]
Pharmacognostic variables	Pharmacognostic variables were determined for all parts of the plant in order to standardize herbal medicines data.[196]
Heavy metals accumulation	Heavy metals concentrations was determined in aerial parts of the plant grown in normal soil. Results showed that heavy metals did not exceed healthy limits.[197,198]
Oil contamination removal	Soil was contaminated with oil (0.1 and 0.5%) and was treated by the plant for oil removal. After 30 days, 88.5% of the oil was removed.[199]
Adsorption of Cr(III)	Conatminated water with Cr(III) was treated by inserting the plan's roots in and the concentration change was measured under various pH and temprature values. Moderate activity[200]
Nutrients, antioxidant	Major nutrients, minerals, total phenolic content and anthocyanins were determined in aerial parts. High ntioxidant (DPPH) activity[201]
Antidiabetic, antioxidant, antihypertensive	Watet extract of aerial parts was prepared and its major chemical constituents were determined. It was tested for antidiabetic (weak), antioxidant (moderate) and antihypertensive (very weak) activities[202]
Drying process effect on content	Leaves were dried by four methods and total phenolic content and antioxidant activity of the products were determined[203]
Fatty acids content, antioxidant, antidiabetic	Dried seeds were extracted by *n*-Hexane to prepare fixed oil. The fatty acid content of this oil (9, saturated and unsaturated) and its antidiabetic (high) and antioxidant (high) activities were determined[204]
Antiprotozoal, antimicrobial	75% Ethnol/water extract of the leaves was tested for antiprotozoal and antimicrobial activities. It showed moderate antimalarial and high anti-leishmanial and weak antimicrobial activities[205,206]
Ulcerative colitis inhibition	Methanolic and aqueous extracts were prepared from leaves. Methanolic extract was more efficient in attenuating inflammation and tissue damage induced acetic acid[207]

Growth inhibition by eucalyptus leaf extract	Eucalyptus leaves aqueous extract was found relatively effective but only in high concentrations as herbicide against seeds (germination control) and adult plants of *M. parviflora*.[208]
Antioxidant	This study combines ethnobotanical uses (Brazil) and antioxidant (3 methods) test of the aqueous extract of leaves: high[209]
Hypolipidemic, hypoglycemic, anti-inflammatory,	A novel triterpenoidic acid, 2α,3β,23α,29α tetrahydroxyolean-12(13)-en-28-oic acid was isolated and was found to have hypolipidemic, hypoglycemic and anti-inflammatory activities.[210]
Memory retention	80% Ethanol/water extract showed memory retention in mice.[211]
β‑sitosterol, antibacterial	Chloroform and ethanolic extracts of roots showed high antibacterial activity against small number of bacteria. It is suggested that β-sitosterol in chloroform extract is the active compound[212]
Horse poisoning	Four horses, fed with large amounts of the plant, had myocardial disease and myopathy compared to control. Cyclopropene fatty acids in the plant may cause negative energy balance and abnormal acyl carnitine profiles.[213]
Zinc accumulation	High concentrations of Zn were found in roots but not aerial parts of the plant that grew around steel industries. [214]
Cd, Cu accumulation	Plants irrigated with sewage water, accumulated copper and cadmium up to six folds compared with control.[215]
Gold nanoparticles	70% Ethanol/water extract of the plant was used as reductant in the synthesis of AuNP's from $HAuCl_4$ [216]

Table 8. Modern research findings of *Malva sylvestris*.

Property	Methods and major findings (reference)
Antibacterial	Hexane, dichloromethane and methonal extracts were prepared then the dry matter was suspended in DMSO. Its antibacteria activity was very weak[144]
Plant pigments	Chlorophylls and carotenoids were isolated and identified[145]
Antibacterial	Aqueous, ethanolic and chloroform extracts of *M. neglecta* and *M. sylvestris* were tested against seven types of bacteria that cause wound infections. All extracts were active, and ethanolic was most active for both plants. Extract of *M. sylvestris* was more efficient[161]
Flavonoid glucoronides	Glucoronides (glucosyl derivatives) of various flavonoids from leaves of the plant, including a glucoronide sulphate[217,218]
Anti-complementary mucilage	Water extraction of fresh leaves afforded mucilage with average molecular weight of $6x10^6$. It consists L-rhamnose, D-galactose, D-galacturonic acid and D-glucurnic acid, with molar ratio of 6:3:2:2, respectively. This mucilage has anti-complementary activity[219]
Anti-complementary polysaccharide	Water extraction of fresh leaves yielded a polysaccharide with molecular weight of $1.1x10^4$. It consists L-rhamnose, D-galactose, D-galacturonic acid and D-glucurnic acid, with molar ratio of 22:6:22:11, respectively. This mucilage has anti-complementary activity[220]
Scopoletin isolation	Scopoletin (7-Hydroxy-6-methoxycoumarine) was first isolated from the plant by aqueous extraction (yield is higher than methanolic)[221]
Acidic polysaccharides	High molecular ($1.3\text{-}1.6x10^6$) acidic polysaccharides (mucilage) were isolated by water extraction. No activity reported[222]
Mineral content	Mineral content was determined from plant ash by means of atomic absorption. Among studied seven edible plants, *M. sylvestris* had the highest content of phosphorus and potassium[223]
Radical scavinging, Fe(II) chelating	50 % Methanol/water extract was tested for antioxidant activity (DPPH, H_2O_2) using low concentrations of the extract. For DPPH test it was inactive and for H_2O_2 it had moderate activity. Fe(II) chelating high[224]
Anthocyanin inhibibs lipid oxidation	"Homemade" anthocyanin samples from the plant were tested for radical scavinging in high fat albino rats. In concentration of 0.2 mg mL^{-1} it showed very strong activity of plasma lipid oxidation inhibition[225]
Anthocyanin antibacterial activity	"Homemade" anthocyanin samples from the plant were tested against several types of bacteria, and found active against some of them[226]
AChE inhibition, antioxidant	Ethanolic extract was prepared from aerial parts and tested for acetyl choline esterase inhibition: active only in high concentrations. Antioxidant activity was high[227]
Sulfite oxidase purification and kinetics	Sulfite oxidase was purified from leaves by acetone fractionation, heat treatment and several analytical methods. The kinetics, optimal pH, optimal tempretaure and the activation energy of the ezyme activity were detemined[228]
Novel terpenoids, growth inhibition of *Lactuca sativa*	Novel terpenoids (Figure 7) and other known were isolated from the aqueous extract. The new compounds were tested for germination inhibition of *L. sativa* and found moderately active[229]

Malvone A, antifungal	New phenolic 1,4-quinone (malvone A, Figure 7) was isolated from the stem bark by aqueous-acetone solution that contains ascorbid acid. The synthesis of malvone A in the plant was enhanced by plant pathogen *Verticillium dahliae* and it has antifungal activity against the same fungus[230]
Alkaloid content	Total alkaloids content was isolated from methanolic extract that was treated by acid then base: 35 mg in 100 g plant aerial parts[231]
Antiproliferative (inactive)	70 % Ethanolic/water extract of leaves was tester for antiproliferative activity against four types human tumor cell lines: inactive. *n*-hexane fractionation yielded campesterol, stigmasterol and γ-sitosterol[232]
Effect of aqueous sulfur dioxide	Treating the plant leaves with various concentrations of aqueous sulfur dioxide solution resulted in decrease of all biochemical activities especially antioxidant capacity[233]
Immunomodulatory	Carbohydrate rich water extract was tested for immunomodulatory activity in BALB/c mice and found active in some test types[234]
Anti-inflammatory, antioxidant	70 % Ethanolic extract was prepared and fractionated with 90 % CH_3OH and *n*-hexane. Tests showed antioxidant (DPPH) and anti-inflammatory (croton oil-induced ear oedema in mice) activities[235]
Anti-inflammatory	In the tests of cream prepared from water extract of aerial parts[236] and 70 % ethanol extract of flowers[237] against carragenin-induced edema in rats, and in tests of ethanolic extract of leaves against 12-O-tetradecanoylphorbol-acetate induced in mice active compounds were indicated. Quantification of prostaglandin by LC-MS/MS validated the tests of ethanolic extract of leaves was tested against activity of various inflammatory agents.[239] Different fraction of ethanolic extracts of leaves were tested against *A. actinomycetemcomitans.*[240]
Antinociceptive	Leaves water extract was not found active by hot-plate model against four pain agents, writhing test, neurogenic and inflammatory phases of formalin model, capsaicin-induced pain.[241]
Anti-inflammatory, anti-ulcerative	Aqueous extract of aerial parts showed anti-inflammatory and anti-ulcerative activities in rat model (drinking water)[242]
Antioxidant	Aqueous extract of leaves was tested for antioxidant activity (DPPH, superoxide radical), then analyzed to yield eleven active compounds, that each one of them was tested.[243] Total phenolic content and antioxidant activity (three methods: FRAP, DPPH, TAC-Mo^{VI}) of leaves (highest), stems and seeds.[244] Total phenolic content and antioxidant (DPPH) activity were determined for methanolic extract of whole plant.[245] Methanolic extract of leaves was teasted for antioxidant activity (DPPH).[246] Methanolic (with ammonium citrate) of aerial parts was teasted for antioxidant activity (DPPH)[247]
Skin disorders and wound healing	Burn wounds in rats were reated with diethyl ether extract of flowers, resulting notable healing.[248] Excision wounds were treated with chloroform extract of flowers, resulting wounds healing.[249,250] Fifty patients with hand eczema treated with ointment showed partial healing and no adverse effects.[251] Alloxan-induced diabetic rats with blade injury[252] and burn injury[253] showed complete and 80 % healing on treatment with dietheyl ether extract of flowers for 18 days. Blade-induced injury in palatal mucosa of rats showed on healing effect of 70% ethanol/water extract of stems and leaves.[254] 70% Ethanol/water extract of flower was prepared as cream with 5 and 10%. It was tested for treatment of burn (hot plate) injuries. Complete healing after 35 days.[255] Polyherbal cream (PHC) that contains aqueous extract of leaves was used to treat second-degree burn wounds in rats (110°C, 10 s). After 14 days, 87% of the wounds healed. Total phenolic content, antimicrobial and antioxidant activities PHC were determined.[256] A cream (1%) was prepared from aqueous extract of flowers used to treat surgical blade induced wounds in mice. After 10 days healing was almost complete.[257] 40% Ethanol/water leaves extract was used to treat inflammation (formalin induced) and tested for linear incised wound healing in rats and found effective[258]
Metal ion composition and heavy metal accumulation	Calcium and potassium were found in relatively high concentrations in leaves.[259] Unspecified plants showed high concentrations of calcium and potassium after burning.[260] Accumulation of major elements and heavy metals in plants (aerial parts) grew in industrial contaminated soil. The plant was classified as hyperaccumulator.[261] Concentrations of metals in leaves were measured in populated areas. Results are around standard except lead which was higher.[262] Metal composition of edible parts was determined by inductively coupled plasma optical emission spectroscopy. Results showed that washing the plants as done before cooking, reduces the content of metals notably.[263] This study reports three methods of extracting toxic metals from the plant leaves, finding that dry ashing method using 4:1 HNO_3:HCl was most efficient.[264] Dried flowers were sieved in different meshes and used as green biosorbent of Pb(II) from aqueous solution. Maximum biosorption capacity was 25.64 mg/g.[265] Dried leaves were powdered and dried again and the resulting mesh was used to Hg(II) from aqueous solutions comparing with charcoal and found more efficient.[266] Synergism of plant powder and charcoal yielded high removal of Hg(II) from aqueous solutions[267]
Antimicrobial, antibacterial, antifungal	Whole plant extract (96% EtOH/Water, traditionally used to treat gastrointestinal disorders) found active against *Helicobacter pylori*.[268] Methanolic extract of aerial parts and three fotmulations of it were tested against several bacteria. The extract was very active gainst *S. aureus*.[269] *n*-Hexane, dichloromethane and methanolic extracts of leaves and flowers were prepared (separately) and tested

	for antimicrobial and and antifungal activities. Only methanolic extract was active.[270] Tincture (no preparation method) was most active among other plants, against *Candida albicans* and *C. tropicalis*.[271] This study tested the components antimicrobial activity of commercial mouthwash Malvatricin: tyrothricin, hydroxyquinoline and the plant tincture. It revealed that activity is only a result of hydroxyquinoline presence.[272] Aerial parts were extracted with 50% methanol water and the extract was tested for urease inhibition: weak.[273] Methanolic extract of leaves was tested for urease inhibition (moderate) and against *Helicobacter pylori*: inactive.[274] Aqueous, ethanolic and *n*-hexane were prepared and tested against oral bacteria: inactive.[275] Roots were extracted with 48% EtOH/water and tested against oral *Streptococci* bacteria and found active against some of them.[276] Acetone/water (7:3) extract was tested for antifungal activity (moderate) and analyzed for major compound families and some single active compound.[277] Ethanol/water (7:3) extract of aerial parts was tested for antibacterial activity: active against *Pasteurella multosida*, inactive against *Salmonella enteritidis*.[278] Aerial parts aqueous extract was tested against *Candida albicans* infection in mice and found moderately active.[279] Vaginal protection medical products based on extracts of the plant (with extract of *Calendula officinalis*) are used, especially in pre-pubertal age.[280] Aerial parts 96% ethanol/water extract was tested against *Candida albicans* infection in mice and found moderately active.[281] Leaves were extracted with 3:1 methanol:water and the extract was tested against four types of bacteria: inactive.[282] Aqueous and ethanolic extracts of all parts were prepared and tested against *C. albicans* biofilm formation. All extracts were active but most active was the ethanolic extract of roots[283]
Chemical composition and some related properties	Methanolic extract of aerial parts was tested with four methods for antioxidant activity. Chemical composition was determined on three levels: macrontrients, major compound families and major compounds in each family.[284] Anthocyanin production was increased by UV irradiation of the flowering plant.[285] Three steroidal lactones and three glycosyl derivatives were isolated and characterized from methanoic extract of the friuts (see Figure 3).[286] Silver nitrate, abscisic acid and UV-B radiation used as growth-stressers and had different effects on growth of the palnt, but they all increased anthocyanin production.[287] Same findings of previous publication concerning silver nitrate.[288] Leaves and petioles methanol extract was analyzed (GCMS) for proximate composition: fatty acids, metal ions, total flavonoids and mucilage. The antioxidant capacityof the extract was tested by four methods.[289] Lipid content of seed oil (extracted with petroleum ether) was determined by GCMS for saponifiables (fatty acids by preparation of their methy esters) and unsaponifiables (mainly phytosterols). The antioxidant of the oil was determined by DPPH assay.[290] Ethanolic extract (plant parts not indicated) was tested fot antioxidant activity (DPPH) and partitioned with other solvents. Total content of the following compound families was determined: free monosaccharides (none), saponins, tannins (very low), terpenoids (very low), flavonoids and alkaloids.[291] Etherial, aqueous and ethanolic extracts of seeds and stems (separately) of the plant were prepared, and were for main compound groups (phenolics, flavonoids, alkaloids …etc.). Then they were analyzed by TLC and some known compounds were identified.[292] Essential oil of flowers was extracted by hydrodistillation and analyzed by three sucessive methods, identifying volatiles and odor activity values: β-damascenone was highest.[293] Total phenolic content in aqueous and ethanolic extracts (plant parts not indicated), as well as quantitative analysis of the extracts by HPLC. All known compounds.[294] Qualititaive analysis of fruits by extracting with several solvents and detection of the content of major compound families.[295] Crude fiber content of stems and leaves was determined, along with influences of locality an seasonality. The isolated crude fiber was fed to rat causing an icrease of faecal weight, indicating laxative activity.[296] Whole plant (before flowering) was extracted with acetone/*n*-hexane (1:1) and analyzed by GCMS for poly aromatic hydrocarbons (PAH's) and poly chlorinated benzenes (PCB's), in plants that grew in contaminated soils. PAH's were below detection limit but PCB were accumulated in the plant.[297] Flowers were extracted with methanol and total phenolic content, saponins and alkaloids were determined. The antioxidant of the extract was tested by several methods.[298] Ethanolic extract of flowers was analyzed for total phenolic content, total flovonoids, anthocyanins, carotenoids and fatty acids. Antioxidant activity of the extract was tested (4 methods, high) and hypoglycemic activity (α-amylase and α-glucosidase inhibition, very high)[299]
Polysaccharides and their properties	Leaves were extracted with 80% EtOH/water and extract fractionated to yield polysaccharides.No analysis for monosaccahrides is reported but detailed theoretical is presented for extraction and antioxidant activity of the polysaccharides.[300] Aerial parts was sequentially extracted with *n*-hexane, ethanol and water to yield 9.6% polysaccaride, which consists galactose, glucose, uronic acids, arabinose, and rhamnose (4:5:14:6:1, MW= $1.3x10^6$ KD). The polysaccharide has anti-ulcerative activity in rats.[301] Leaves enzyme (cellulase) assisted extraction of some polysaccharides. Theoretical is presented and antimicrobial, antitumor and antioxidant activities are reported[302]

Nanoparticles, synthesis, uses	Leaves aqueous extract and $CuCl_2$ were used to prepare CuONP's and their antibacterial activity was tested.[303] Leaves aqueous extract and $AgNO_3$ were used to prepare AgNP's and their mosquito larvicide activity was tested. These AgNP's have almost no effect on other aquatic organisms[304]
Antioxidant applications	Aqueous decoction of leaves and flowers was prepared and tested for antioxidant activity (DPPH, NBT) and gainst ammonium metavanadate (NH_4VO_3) kidney toxicity in rats.[305] 80% Methanol/water extract was prepared (plant part not indicated) and its antioxidant activity (DPPH, fenton reagent) was determined. Also, protection of fatty acids was measured *in* vitro[306]
Sedation, anti-anxiety, anesthetic, radiation side effects relief, anti-seizure	Methanol:chloroform (7:3) extract was prepared from stems and leaves. It was tested in rats for sedation, pre-anesthetic and anti-anxiety effect compared with with diazepam (valium, stronger)[307] Patients with radiation therapy of prostate cancer and experiencing severe dysuria, were treated with plant powder (parts not indicated), showing notable improvement of pain relief[308] Plant powder (parts not indicated) were extracted with 85% ethanol/water. The extract was found anti-seizure active in PTZ-induced seizure models on mice[309] Equal portion of the powder of the *M. sylvestris* and *Alcea digitata* (plants parts not reported) were used to treat patients with xerostomia (dry mouth) after radiotherapy of head or neck cancer.[310] Hydroalcoholic extract (no ratio, no plant parts) was used to treat mice with convulsion induced anxiety.[311] Whole plant aqueous extract was found protective against UV-B radiation in mice.[312]
Enzyme related activities	Methanol:water (4:1) extract was prepared (plant parts not indicated) and was tested for angiotensin converting enzyme (ACE) inhibition: moderate.[313] Catalase was partially purified and immobilized onto chitosan and its catalytic properties were studied[314]
Interaction with drugs and toxic compounds	Aerial parts aqueous extract was administered to Leghorn chickens along with Bromhexine HCl. The extract reduced the adverse side effects of the drug.[315] Whole plant was extracted with 95% aqueous methanol and the extract was tested against paracetamol-induced hepatotoxicity and found significantly active[316] Most (87%) patients at basic health units in Brazil reported using *M. sylvestris* products as an alternative and complementary therapy[317] Leaves aqueous extract ameliorated motor asymmetry in rats induced by 6-hydroxydopamine but had no protective effect neurons[318] 50% Methanolic (water) extract was prepared, analyzed for major compound families, minerals and tested for antioxidant activity (2 methods). Also, it was tested for reduction of lithium carbonate damages (oxidation, body weight gain, kidney) in rats: very positive[319] 50% Methanolic (water) extract was prepared, analyzed polysaccharides and tested for Fe(II) chelating and antioxidant activity. Also, it was tested for reduction of lithium carbonate damages (heart, testicles) in rats: very positive[320] Ethanol-water (4:1) extract was tested against sodium fluoride nephrotoxicity and found active[321]
Constipation relief	Flowers aqueous extract was administered to people with constipation and stool problems, Constipations decreased and stool form changed from hard to normal (self reported).[322] Constipation in rats was induced by loperamide and treared with leaves aqueous exreact and yohimbine as control laxative (see Figure 8)[323]
Mouth and throat diseases	A herbal mouthwash consisting of *Althaea officinalis*, *Salix alba* and *M. sylvestris* leaves (ratio, 5:1.25:1, respectively). Leaves extracted with ethanol and the dry extract was suspended with water (0.31%). This suspension was used to treat people with chronic periodontitis and using chlorhexidine as control, and positive results were obtained.[324] Flowers 95% ethanol/water extract was tested for sore throat treatment: inactive[325]
Corrosion prevention	Leaves methanolic with metal corrosion prevention activity was analyzed to determine major compounds responsible for this activity: furfural; levoglucosenone and Levoglucosan, two seven membered multi oxygenated heterocycles; 1,4:3,6-Dianhydroalpha-d-glucopyranose, six membered multi oxygenated heterocycle[326]
Functional foods for pets	Special food that contains human food ingredients suc as *M. sylvestris* was fed to pets to treat atopic dermatitis: positive results[327]
Multiple activity	Leaves ethanolic extract was prepared and fractionated with *n*-hexane, chloroform and ethyl acetate. The extract and fractions were tested for anti-inflammatory, anti-osteoclastogenic and antioxidant activities *in vitro* and *in vivo*[328]

Table 9. Modern research findings of *Malva verticillata*

Property	**Methods and major findings (reference)**
Isolation, analysis, characterization and activities of seed polysaccharides	A novel polysaccharide was isolated and characterized from seeds. It is composed of L-arabinose, D-galactose and D-glucose (3:6:7)[329] Another two novel polysaccharides were isolated and characterized: L-arabinose, D-galactose and D-mannose (14:28:1, MW= 57000); D-glucose, D-galactose and D-mannose (10:1:1, MW= 10400).[330] Peptidolycan was isolated from seeds and analyzed to reslt 43 % polysaccharide and 57 % protein, with total molecular weight of 22000 kD. The detailed amino acid composition is reported (page 2791) and the polysaccharide is composed of L-arabinose, D-xylose, D-galactose, L-rhamnose and D-galacturonic acid (6:5:3:8:24).[331] Branched

	acidic polysaccharide was isolated from seeds. It cosists mainly of arabinose, xylose, galactose and galacturonic acid, and has phagocytic activity.[332] Seven polysaccharides and peptidogylcans were isolated from seeds, and some of them showed anti-complementary and hypoglycemic activities.[333] Novel acidic polysaccharide was isolated from seeds, and it showed phagocytic and anti-complementary activities (L-arabinose, D-xylose, D-galactose, D-glucose, L-rhamnose and D-galacturonic acid (30:15:20:3:2:10, MW= 26000).[334] A neutral, branched polysaccharide was isolated and analyzed by chemical and enzymatic tools (glucose, galactose and arabinose), and it showed phagocytic activity[335] Branched acidic polysaccharide was isolated and analyzed showing anti-complementary activity.[336] Branched acidic polysaccharide was isolated from seeds, and it has phagocytic activity.[337]
Heavy metals accumulation	Compared with three other plants, *M. verticillata* was found to be moderate toxic metals accumulator, even though Cd accumulation was highest in some samples.[338] Out of four plants, *M. verticillata* was found to be good metal accumulator in average, and highets for both Cd and Pb.[339]
Antimicrobial, antidiabetic, antibacterial	Leaves methanolic and n-hexane extract were prepared. Methanolic extract which contained mainly steroids and flavonoids, showed moderate activity against *E. Bacillus*, *S. coli* and *S. aureus*, while hexane extract showed moderate activity against the first two bacteria.340 Seeds were extracted with ethanol followed by fractionation with n-hexane, chloroform, ethylacetate, n-butanol and water. The original extract had significant antidiabetic activity. Among the fractions, the hexanic had the highest activity.[341] Leaves methanolic extract was tested against alloxan-induced diabetes in rats:high. 70 % Methanol (water) leaves extract was tested against eleven bacteria species: inactive.[342] Leaves methanolic extract was tested for glucose-lowering activity in rats:high.[343]
Antioxidant, anti-inflammatory, anti-dermatitis	80 % Methanolic (water) extract (plant part not indicated) was tested for antioxidant activity by two methods (moderate) and total phenolic content (low).[344] Seeds were extracted with seeds or other parts of seven additional plats. The extract found to be anti-inflammatory, heme oxygenase-1 inhibitor and immunomodulatory.[345] Hydrodistillation of leaves yielded an oil that found active against LPS induces dermatitis.[346] Leaves aqueous extract found active against ulcerative inflammation induced by reserpine in mice.[347] Seed ethanolic extract was fractionated with methylene chloride, ethyl acetate and water. The extract and the fractions were tested in Wnt/β-catenin reporter activity assay. It modulated the β-catenin pathway of dermal papilla cells.[348]
Osteoclastogenesis and bone resorption supression	Seed aqueous extract inhibited osteoclastogenesis stimulated by receptor activator of nuclear factor-kB. The extract was analyzed by GCMS and 14 compounds were identified. Authors conclude that medicinal activity should be related to synergims of compounds.[349] (see note after this reference).
New compounds	Seeds were extracted with ethanol followed by fractionation with methylene chloride extract, ethyl acetate and water. Each fraction was analyzed by liquid chromatography and a new compound was isolated: verticilloside, 3-O-[β-D-(6'-linoleoyl)glucopyranosyl]-β-sitosterol (see Figure 9).[351] Leaves were extracted successively with petroleum ether and ethyl acetate. Two new compounds were isolated (Figure 9) and tested for antibacterial activity.[352]

Table 10. Reported heavy/toxic metals accumulation capacity of *Malva* species.

Malva species	Metal(s)	Method	Capacity (reference)
aegyptiaca	Cd(II)	plant from soil	high135
nicaeensis	Zn(II), As(III)	plant from soil	very high[146]
sinesis	Cd(II)	plant from soil	very high[152]
parviflora	general	plant from soil	low[197,198]
parviflora	Zn(II)	plant from soil	medium[214]
parviflora	Cd(II), Cu(II)	plant from soil	high[215]
sylvestris	general	plant from soil	very high[261]
sylvestris	general	plant from soil	medium for Pb(II)[262]
sylvestris	Pb(II), Ni(II)	plant from soil	medium[263]
sylvestris	Pb(II)	dry sieves from aqueous solution	very high[265]
sylvestris	Hg(II)	dry sieves from aqueous solution	very high[266]
sylvestris	Pb(II)	dry sieves with charcoal from aqueous solution	very high[267]
verticillata	general	plant from soil	medium (high for Cd)[338]
verticillata	general	plant from sewage	High for Cd and Pb[339]

If the inconsistency of references 261 and 263 can be ignored, *Malva* species as living plants or as fabricated sieves, can be used for removal of heavy metals from soil or water. It is also clear that *Malva* species are successful cadmium and lead accumulators.

Many of the studies that we cited here report antimicrobial, antibacterial and/or antifungal activities. Among those, it is interesting to notice the contradiction between the data reported in references 270 and 271: while the first reports the antifungal activity of *M. sylvestris* tincture, the second found no antimicrobial activity of the plant tincture, which is a component of commercial mouthwash. Despite this, the antibacterial, antimicrobial and antifungal activities of *Malva* species are proven beyond any doubt (see tables 6-9).

One of the interesting reports of the uses of *M. sylvestris* in herbal-traditional medicine, was published by S. G. Oliviera *et al*. in 2015.[317] They indicated that about 87 % of their study sample of people, reported the use of this plant and its products along with allopathic medicines or without them. Authors warn (page 5) that people are unaware of the plant possible toxicity, citing M. R. Ritter *et al*.[370] But reading carefully the publication of M. R. Ritter shows that there is no mentioning of *M. sylvestris* toxicity. Moreover, it was shown by Consolini & Ragone, that this plant is completely safe for all potential uses.[371]

In recent decades, there is growing interest in reducing damages of synthetic drugs by using natural plant extracts or other plant products. Among these synthetic drugs and chemicals, both organic, but mainly inorganic chemicals are widely used, and have some severe adverse effects.[372,373] A. A. Ben Saad and his colleagues, presented very promising results of using *M. sylvestris* aqueous extract to reduce the side effect of lithium carbonate.[319,320] Similar reports were published by other groups. For example, petroleum ether extract of *Solanum trilobatum* has a protective effect against lithium carbonate,[374] but unlike *M. sylvestris* that is soft to touch and completely safe,[375] *S. trilobatum* is a thorny plant and mildly toxic. The same Tunisian group of A. Ben Saad *et al*. is searching for other plants that can ameliorate damages of lithium carbonate, and recently they have published the positive results of their study of juice of *Opuntia ficus-indica* (cactus) thorny cladodes.[376]

Use of *Malva* species for constipation relief is known in most traditional medicines of Asia (*M. neglecta*[36,41,52,59], *M. parviflora*[67] and *M. sylvestris*[108,110,115]). This activity is recently investigated by several groups. One of the interesting reports was published by a M-A. Jabri and his colleagues.[323] They induced constipation in rats by loperamide (Figure 8), a synthetic alkaloid, usually marketed as the commercial Imodium for diarrhea relief.

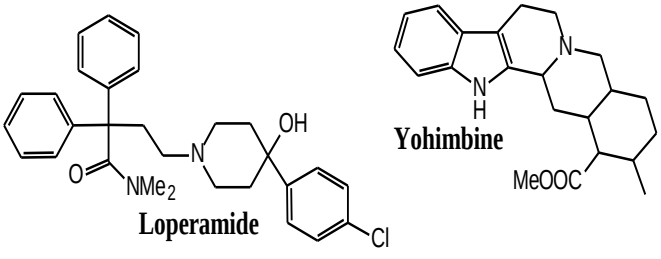


Figure 8. Structures of loperamide andf yohimbine[323]

Constipation was successfully treated with aqueous extract of *M. sylvestris* leaves. As control laxative, they used yohimbine (Figure 8), naturally occurring major alkaloid found in the bark of *Pausinystalia johimbe*.[377]

The anti-constipation activity of *M. sylvestris* leaves extract explained by the authors as a result of the antioxidant capacity, and they present possible mechanism of action (page 6). M. Elsagh *et al*. reported the successful use of flowers aqueous extract for the same goal.[322] Since both leaves and flowers of this plant are flavonoid-rich, these results of these two reports are consistent.

The presence of polysaccharides in *Malva* species drew the much attention from research groups. The isolated and characterized (fully or partially) polysaccharides were also tested for various activities viz., *M. aegyptiaca*,[133] *M. mohileviensis* (anti-inflammatory, antioxidant),[143] *M. pussila* (anti-inflammatory),[149] *M. sylvestris* (anti-complementary,[220] antioxidant,[222] anti-ulcerative, antimicrobial, antitumor and antioxidant[300-302]). All polysaccharides in these species are acidic, containing glycoronic acids, and relatively, water soluble. Polysaccharides isolated from seeds of *M. verticillata* are neutral,[329,330] and acidic with high acid content.[331] Later on, this Japanese group reported that some of these acidic polysaccharides (or peptidoglycans) have medicinal activities such as phagocytic,[332,337] anti-complementary and hypoglycemic,[333] phagocytic and anti-complementary,[334] and anti-complementary.[336] Phagocytic activity was also found in the neutral polysaccharide.[335] This extensive study that was done with *M. verticillata* should be done with other common *Malva* species.

Treating hair loss with *Malva* species products is known from traditional medicine of Iraq (*M. parviflora*),[73] and Iran (*M. sylvestris*).[115] Modern research confirmed these uses and E. Y. Lee *et al*. report that *M. verticillata* ethanolic extract and its fractions are modulating the Wnt/β-catenin pathway of dermal papilla cells, and thus, it's a good candidate for treating hair loss.[348] Their analysis revealed that the active compound is myristoleic acid (C14: 1 *cis* 9).

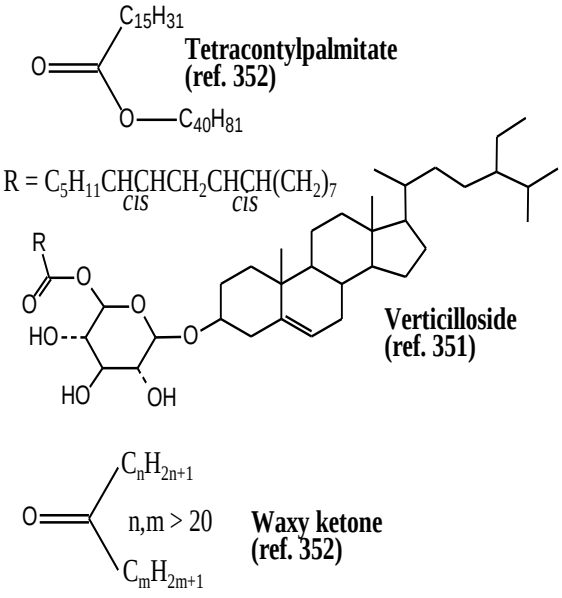


Figure 9. Structures of verticilloside[351] and two waxy compounds[352]

Another medicinal property that is known to traditional medicine and was confirmed lately by modern research is the ability of *Malva* extracts to repair bones. *M. neglecta* is used in traditional medicine of India (leaves),[26] and Turkey (whole plant),[41] to repair fractured bones. K-S. Shim *et al*. from Korea, report that water extract of *M. verticillata* suppresses osteoclastogenesis and bone resorption.[349]

M. verticillata is still providing modern research with new and very interesting compounds. One of these compounds was isolated and characterized by and her colleagues from ethanolic extract of the plant: verticilloside (Figure 9).[351]

Another two new compounds were isolated from leaves extract: tetracontanyl palmitate ($C_{56}H_{112}O_2$) and a waxy ketone (Figure 9), but the exact structure of the ketone was not completely elucidated.[352]

Conclusions

While studying the vast mass of publications about the genus *Malva*, we reached some important understandings that must be conveyed to interested readers. Some of these publications are inaccurate, to say the least (reference 71 and others). Moreover, some publications do not report any new findings of plants of *Malva* genus. M. Ishtiaq and his colleagues report an ethnomedicinal survey of the plants of Samahni valley in Pakistan.[378] In fact, there is no new information at all about *M. parviflora*, which is listed there, and for this reason, it was not included in table 2. Same consideration was taken for the report of Jeambey et al from Lebanon.[379] They cite previous reports and plants consumption as food (*M. sylvestris*), but again, no real information was provided concerning health or medicinal use of this plant.

During the writing itself, we discovered a strange fact: despite being one of the most useful species of *Malva*, *M. nicaeensis* was very poorly studied for medicinal-biological activities. It is widespread in the Middle East, especially in the Western part of it, and it is used as food in various ways (see table 4). It is also worth noticing that compared with other major Malva species, its traditional medicinal uses were very partially reported. Such reports were lately published.

M. Mosaddegh and his colleagues from Iran report that its roots and flowers decoction is traditionally used to treat stomach pains.380 Nasab & Khosravi (Iran) present the ethnomedicinal use of M. nicaeensis, along with M. parviflora and M. sylvestris.381 Its fruits decoction is used to treat cold and sore throat. S. Baydoun and her colleagues from Lebanon report that leaves decoction to have several uses to treat: catarrhs, renal infections, kidney stones, respiratory infections, constipation and skin diseases.[382] Strangely enough, only three reports were published about medicinal activities of this plant,[146-148] and its chemical composition, partial or complete, was never published. Moreover, for other major species, some same activities were reported by many groups or the same group more than once: antioxidant, antibacterial, anti-inflammatory. These activities were never published for *M. nicaeensis*.

Our group is currently working on these studies.

Therefore, we conclude and recommend:

(1) There is a need for extensive, systematic study of *M. nicaeensis*.
(2) Contradicting reports of medicinal activities of *Malva* species must be resolved by follow up studies.
(3) Proven and very useful medicinal activities of *Malva* species (antidiabetic, antiobesity) must draw more attention of researchers to convert this potential to practical drug treatments.
(4) It is very important to re-evaluate contradicting and inaccurate reports by further studies.
(5) It is important and useful to isolate the natural product/s responsible for medicinal activities of the plants, and study the mechanism of action. This can open a window of improving the activity.

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Received: 11.06.2017.
Accepted: 12.07.2017.