

The Pharmaceutical Importance of *Althaea officinalis* and *Althaea rosea* : A Review

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Abstract: Two species of the genus *Althaea* (Malvaceae) were grown in Iraq, *Althaea officinalis* and *Althaea rosea*. *Althaea officinalis* contained pectins 11% , starch 25-35% , mono-, and di-saccharide, saccharose 10% , mucilage 5%, flavonoids (Hypolaetin-8-glucoside, isoquercitrin, kaempferol, caffeic, pcoumaric acid), coumarins, scopoletin, phytosterols, tannins, asparagine and many amino acids. The previous studies showed that *Althaea officinalis* possessed antimicrobial, antiinflammatory, immunomodulatory, demulcent, soothing, antitussive and many other pharmacological effects. *Althaea rosea* contained high molecular weight acidic polysaccharides (1.3 to 1.6 million Dalton) known as mucilages which found in flowers and leaves. These mucilages were composed of glucuronic acid, galacturonic acid, rhamnase and galactose. It also contained proteins, alkaloids flavonoids and minerals. It possessed many pharmacological effects including antimicrobial, cardiovascular, prevention of urolithiasis, antiestrogenic, cytotoxic and immunomodulating effects. The aim of this review is to highlight the chemical constituents and the pharmacological and therapeutic effects of *Althaea* species grown in Iraq.

Key words: *Althaea officinalis* , *Althaea rosea* , constituents, pharmacology.

Introduction :

Using plants from the Malvaceae family for herbal therapy is very common in the Middle East, of these plants are *Althaea officinalis* and *Althaea rosea*. *Althaea officinalis* is native to Asia, Europe and United States of America. It is widely used traditionally for the treatment of the irritation of oral, pharyngeal mucosa and associated dry cough, mild gastritis, skin burns and for insect bites. It is also used in catarrh of the mouth and throat, gastrointestinal tract and urinary tract complains, as well as for inflammation, ulcers, abscesses, burns, constipation and diarrhea⁽¹⁾ .

Althaea rosea (L.) is a popular garden plant. It is native to China, southern Europe, the Middle, Near east, Mediterranean and Central Asian regions. It was used traditionally as expectorant, cooling, diuretic, expectorant, and emmenagogue. Decoction of flowers is used as anti-inflammatory, febrifuge, demulcent and astringent agent. The roots are used in the treatment of ulcers. Flowers as well as roots are used in the treatment of inflammation of the kidneys and the uterus. Seeds are thought to be diuretic and febrifuge⁽¹⁻³⁾.

Many compounds were extracted from different parts of *Althaea officinalis*, these included pectins 11%, starch 25-35%, mono-, and di-saccharide saccharose 10%, uucilage 5%, flavonoids (Hypolaetin-8-glucoside,

isoquercitrin, kaempferol, caffeic, p-coumaric acid), coumarins, scopoletin, phytosterols, tannins, asparagine and many amino acids⁽⁴⁻¹⁰⁾.

Althaea rosea contained high molecular weight acidic polysaccharides (1.3 to 1.6 million Dalton) known as mucilages which found in flowers and leaves. These mucilages were composed of glucuronic acid, galacturonic acid, rhamnose and galactose. It also contained proteins, alkaloids flavonoids and minerals⁽¹¹⁻¹⁴⁾.

The previous studies showed that *Althaea officinalis* possessed antimicrobial, anti-inflammatory, immunomodulatory, demulcent and soothing, antitussive and many other pharmacological effects. *Althaea rosea* also possessed many pharmacological effects including antimicrobial, cardiovascular, prevention of urolithiasis, antiestrogenic, cytotoxic and immunomodulating effects. The objective of the present review is to highlight the chemical constituents and the pharmacological and therapeutic effects of *Althaea* species grown in Iraq.

I-Althaea officinalis

Synonym : Malva officinalis

Common names: English name : Althaea, Marshmallow, Arabic name: khatma , Khatmi

Distribution: Native to Asia, Europe and United States of America.

Traditional use: *A. officinalis* is widely used in the irritation of oral, pharyngeal mucosa and associated dry cough, mild gastritis, skin burns and for insect bites. It is also used in catarrh of the mouth, throat, gastrointestinal tract and urinary tract, as well as for inflammation, ulcers, abscesses, burns, constipation and diarrhea⁽¹⁾.

Part used: Leaf, root, flowers

Physicochemical properties⁽²⁻³⁾ :

Total ash: not more than 6% in the peeled root and not more than 8% in the unpeeled root, acid-insoluble ash : not more than 3% in the peeled root, water-soluble extractive : not less than 22%, loss on drying : not more than 12%, and swelling index : not less than 10.

Chemical constituents :

Many compounds were extracted from different parts of the plants, these included pectins 11%, starch 25-35%, mono-, di-saccharide saccharose 10%, mucilage 5%, flavonoids : hypolaetin-8-glucoside, isoquercitrin, kaempferol, caffeic, p-coumaric acid, ferulic acid, p-hydroxybenzoic acid, salicylic acid, p-hydroxyphenylacetic acid, vanillic acid, coumarins, scopoletin, phytosterols, tannins, asparagine and amino acids⁽⁴⁻¹⁰⁾.

Mucilage polysaccharides contents reached 5-11.6% (depending on vegetative period). They were consisted of the mixture of colloiddally soluble polysaccharides, particularly of acid arabinogalactans, galacturonic rhamnans, arabans and glucans acidic heteropolysaccharide (with a MW ca 30 000) containing D-galactose, L-rhamnose, D-glucuronic acid and D-galacturonic acid in the molar ratios 1.2:1.0:1.0:1.0, L-arabinans and D-glucans. Dominant neutral mucilage component is (1-6)-D-glucan. By partial acid hydrolysis *Althaea* mucilage O, the following oligosaccharides were obtained: O- (D-galactopyranosyluronic acid)-(1-2)-L-rhamnopyranose, O- (D-glucopyranosyluronic acid)-(1-3)-O- (D-galactopyranosyluronic acid)-(1-2)-L-rhamnopyranose and hexasaccharide, nonasaccharide, dodecasaccharide composed of a repeating unit having the structure of the trisaccharide through position 4 of the D-galacturonic acid residue^(8,15-21).

Valiei *et al* extracted many compounds from extracts of flower and root of *Althaea officinalis*, these included : undecyene, nonanoic acid methyl ester (nonanoic acid), phenol, 2,6-bis(1,1-dimethylethyl)-4-methyl, tetradecanoic acid methyl ester (tetradecanoic acid), pentadecanoic acid methyl ester (pentadecanoic acid), 9-hexadecenoic acid methyl ester (9-hexadecenoic acid), hexadecanoic acid methyl ester (hexadecanoic acid), cyclopropaneoctanoic acid 2-hexyl methyl ester (cyclopropaneoctanoic acid, 2-hexyl), heptadecanoic acid methyl ester (heptadecanoic acid), octadecyene-5, 7,10-octadecadienoic acid methyl ester (7,10-octadecadienoic acid), 9,12-octadecadienoic acid(-6) methyl ester (9,12-octadecadienoic acid), 8,11-octadecadienoic acid,

methyl ester(8,11-octadecadienoic acid), 9,12,15-octadecatrienoic acid (-3) methyl ester (9,12,15-octadecatrienoic acid), octadecanoic acid methyl ester (octadecanoic acid), naphthalene, decahydro-2,6-dimethyl , 10-nonadecenoic acid methyl ester (10-nonadecenoic acid), cyclopropaneoctanoic acid, 2-octyl, methyl ester (cyclopropaneoctanoic acid,2-octyl), dihydroionone, 3-heptadecen-5-yne, heneicosane, methyl 2-octylcyclopropene-1-heptanoate, eicosanoic acid, methyl ester (eicosanoic acid) , tetracosan, heneicosanoic acid methyl ester (heneicosanoic acid), pentacosane, docosanoic acid methyl ester (docosanoic acid), tricosane, tricosanoic acid methyl ester (tricosanoic acid), heptacosane, tetracosanoic acid methyl ester (tetracosanoic acid), octacosane, squalene, nonacosane , -sitosterol⁽²²⁾ .

Pharmacological effects :

Antimicrobial activity :

A methanolic extract prepared by exhaustive extraction from marshmallow root has been shown to possess an inhibiting activity able to diminish significantly the periodontal pathogens resident in the oral cavity (*Porphyromonas gingivalis*, *Prevotella spp.*, *Actinomyces odontolyticus*, *Veilonella parvula*, *Eikenella corrodens*, *Fusobacterium nucleatum*, *Peptostreptococcus spp.*). Antimicrobial activity against *Pseudomonas aeruginosa*, *Proteus vulgaris* and *Staphylococcus aureus* has been documented for chloroform and methanolic extracts of marshmallow roots⁽¹⁸⁾. The hexane extracts of flower and root of *Althaea officinalis* exerted antimicrobial activity against Gram-positive and Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Bacillus subtilis*, *Enterococcus faecalis*, *Staphylococcus aureus* and *Staphylococcus epidermidis*), as well as three fungi (*Aspergillus niger*, *Candida albicans* and *Saccharomyces cerevisiae*)⁽²²⁾.

Rashidi *et al* also found that 80 % ethanolic *Althaea officinalis* extract was active against *Aspergillus niger*, *Aspergillus fumigatus*, and *Aspergillus flavus* species. MIC of *Althaea officinalis* 80 % ethanolic extract 50-100 mg/ml⁽²³⁾. However , ethanol, water and hexane extracts of the dried seed at a concentration of 10.0 mg/ml, were inactive on *Candida albicans* and *Candida tropicalis*⁽²⁴⁾. Ethanolic extract of dried whole plant, in cell culture at variable concentrations is inactive on adenovirus, coxsackie B2 virus, Herpes virus type 1, measles virus, poliovirus 1 and Semlicki-Forest virus vs plaque inhibition (Berghe, 1978). Water extract of the dried leaf, in cell culture at a concentration of 10.0%, was inactive on Herpes virus type 2, influenza virus A2, poliovirus 11 and vaccinia virus A⁽²⁵⁾.

Antiinflammatory:

Aqueous extracts of the roots stimulated phagocytosis, and the release of oxygen radicals and leukotrienes from human neutrophils *in vitro*. The aqueous extract also induced the release of cytokines, interleukin-6 and tumour necrosis factor from human monocytes *in vitro*, thereby exhibiting anti-inflammatory and immune stimulant activity⁽²⁶⁾.

A polysaccharide fraction (500mg/ml) isolated from a root extract had anticomplement activity in human serum *in vitro*⁽²⁷⁾. Marshmallow mucilage polysaccharides administered intraperitoneally to mice at a dose of 10 mg/kg produced a 2.2-fold increase in phagocytic activity of macrophages in the carbon-clearance test⁽²⁴⁾. However, with a dry 80% ethanolic extract administered orally (100 mg/kg b.w.), no inhibition of carrageenan induced rat paw oedema has been proved⁽²⁹⁾.

Hypolaetin 8-glucoside has been tested for its anti-inflammatory, analgesic and anti-ulcer activity in rats. This flavonoid (30, 60 and 90 mg/kg i.p.) was more potent than phenylbutazone (30, 60 and 90 mg/kg i.p.) in suppressing the acute phase of adjuvant carrageenan-induced inflammation but had less effect in the prolonged inflammatory phase. In contrast to phenylbutazone, it did not cause gastric erosions. Analgesic activity of hypolaetin 8-glucosid has been found to be lower than the one of phenylbutazone . Hypolaetin 8-glucoside was also more potent than troxerutin (both at the doses of 100, 200, 300 and 400 mg/kg s.c.) in inhibiting histamine-induced capillary permeability in rats⁽¹⁸⁾ .

An ointment containing an aqueous marshmallow root extract (20%) applied topically to the external ear of rabbits reduced irritation induced by UV irradiation or by tetrahydrofurfuryl alcohol. The ointment has been compared to pure dexamethasone 0.05% ointment and a combined marshmallow and dexamethasone product.

The anti-inflammatory effect of marshmallow ointment was lower than that of a dexamethasone ointment. The combined product had higher anti-inflammatory effect than the ointments with the individual ingredients⁽¹⁸⁾. Scopoletin exert anti-inflammatory activity in croton oil induced mouse ear edema⁽³⁰⁾.

Immunomodulatory effects :

Althaea-mucilage O, an acidic polysaccharide isolated from marshmallow root, has been demonstrated to have an anti-complement activity on normal human serum in concentrations of 100 – 1000 ug/ml⁽²⁷⁾.

An extract (extraction medium 45 % 1,3-butylene glycol solution) of marshmallow root was found to inhibit intracellular calcium mobilisation in normal human melanocytes activated by endothelin-1, and to strongly inhibit endothelin-1-induced proliferation of melanocytes. The extract can diminish the physiological effect of endothelin-1 on normal human melanocytes following UVB irradiation⁽¹⁸⁾.

Scopoletin produced dual action on tumoral lymphocytes exhibiting both a cytostatic and a cytotoxic effect on the cell, and also exert apoptosis. Proliferation of normal T lymphocytes was found due to the interaction with kinase C (PKC) protein. It indicates that scopoletin may be a potential anti-tumoral compound⁽³⁰⁾.

Demulcent and soothing :

The demulcent effects of Radix Althaeae are due to its high content of polysaccharide hydrocolloids, which form a protective coating on the oral and pharyngeal mucosa, soothing local irritation and inflammation⁽¹⁾. However, weak inhibition (17%) of mucociliary transport in isolated, ciliated epithelium of the frog oesophagus was demonstrated after treatment of the isolated tissues with 200 ml of an aqueous root macerate (6.4 g/140 ml)⁽³¹⁾. Polysaccharides from marshmallow root showed moderate adhesion to epithelial tissue of porcine buccal membranes⁽¹⁸⁾.

Antitussive effects :

Marshmallow root extract and isolated mucilage polysaccharide were tested for antitussive activity in unanaesthetised cats of both sexes at oral doses of 50 to 100 mg/kg body weight, in a cough induced by mechanical stimulation, in a comparison with the cough-suppressing effects of Althaea syrup (1000 mg/kg), prenoxdiazine (30 mg/kg), dropropizine (100 mg/kg) and codeine (10 mg/kg). Both the extract and isolated polysaccharide significantly reduced the intensity and the number of cough efforts from laryngopharyngeal and tracheobronchial areas. The root extract was less effective than the isolated polysaccharide. The antitussive activity was found to be lower than that of codeine, but higher than those of prenoxdiazine and dropropizine^(18,32).

Polysaccharides of Marshmallow exhibited statistically significant cough-suppressing activity, which was noticeably higher than that of the non-narcotic drug used in clinical practice to treat coughing. By testing many plants, the most expressive antitussive activity was observed with the polysaccharide from marshmallow, containing the highest proportion of the uronic acid constituent⁽³³⁾.

In a double blind clinical study, Rouhi and Ganji used *Althaea officinalis* in patients with hypertension who had been developed cough during taking of angiotensin converting enzyme inhibitors. The patients received 40mg of *Althaea officinalis* three times daily as 20 drops for four weeks. The Mean scores of the severity of the cough in the group which have been treated by *Althaea officinalis* had a significant change from the score of 2/66+0.958 (to) 1/23+1.006. Eight patient in the *Althaea officinalis* group showed almost complete cough abolition⁽³⁴⁾.

Other pharmacological effects :

Polysaccharide from the root of *A. officinalis* (Althaeamucilage-O) administered intraperitoneally to nondiabetic mice significantly reduced blood glucose⁽³⁵⁾.

Scopoletin (7-hydroxy-6-methoxy coumarin) is therapeutically evaluated in rats for hyperthyroidism, lipid peroxidation and hyperglycemia. Scopoletin (1.00 mg/kg, p.o.) administered daily for 7 days decreased the

levels of serum thyroid hormones and glucose as well as hepatic glucose-6-phosphatase activity. Scopoletin also mimic hepatic lipid peroxidation and promote antioxidants activity, superoxide dismutase and catalase. It indicated that scopoletin produce anti-thyroid activity and hyperglycemia without hepatotoxicity⁽³⁶⁾.

Ethanol/water f(1:1) extract of the dried entire plant, at a concentration of 5.0 mcg/ml, produced weak activity vs superoxide anion when estimated by the neotetrazolium method⁽³⁷⁾. The extract of *A. officinalis* exhibited strong antioxidant activity in different antioxidant tests⁽³⁸⁾. Their antioxidant activity is accounted for approximately 69% of the activity of the reference compound alpha-tocopherol⁽⁴⁰⁾. Sadighara et al examined three colors of petals of *Althaea officinalis* flowers, i.e., pink, reddish pink, and white were examined for total antioxidant activity. The results showed that the reddish pink flowers of *A. officinalis* have more antioxidant activity and the power of antioxidant activity was reddish pink > pink > white⁽⁴⁰⁾.

II-Althaea rosea

Common names : English name : garden Hollyhock , Arabic name : Khatma wardi , Khatmi wardi.

Distribution : It is native to China , southern Europe , the Middle and Near east , Mediterranean and central Asian regions. The plant grows best in medium-fertile, moist, but well-drained soil. The plant can not grown in the shades. It can be found in woodlands, cultivated beds and sunny edges.

Traditional use: It is used as expectorant, cooling and diuretic, cough mixtures, and emmenagogue. Decoction of flowers is used as anti-inflammatory, febrifuge, demulcent and astringent agent. As a demulcent and astringent, the roots are useful in the treatment of ulcers. Flowers as well as roots are used in the treatment of inflammation of the kidneys and the uterus. Seeds are thought to be diuretic and febrifuge⁽⁴¹⁻⁴³⁾.

Physicochemical properties⁽¹¹⁾

Total ash 7.3 ± 0.32 % , acid insoluble ash 1.48 ± 0.16 % , water soluble ash 3.33 ± 0.24 % , and loss on drying in crude drug (%) 8.2 ± 0.38 % .

Successive extraction (% Extractable matter) : petroleum ether extract 8.18 ± 0.85 % , chloroform extract 2.76 ± 0.12 % , methanol extract 3.63 ± 0.32 % , and aqueous extract 11.24 ± 0.14 % .

Chemical constituents:

Althaea rosea contained high molecular weight acidic polysaccharides (1.3 to 1.6 million Dalton) known as mucilages which found in flowers and leaves. These mucilages were composed of glucuronic acid, galacturonic acid, rhamnose and galactose⁽¹²⁾.

Fahamiya found that aqueous extract of the seeds of *Althaea rosea* Linn contain alkaloids, carbohydrates ,phenolic compounds and flavonoids, while methanolic extracts contained all the above compounds as well as glycosides . However, chloroform extract contained only carbohydrate⁽¹¹⁾.

Dudek *et al* investigated the distribution of phenolic acids in the flowers of *Althaea rosea var. nigra* . They studied the methanolic and methanolic-aqueous extracts of whole flowers, petals and calyxes of *Althaea rosea* (L.) Cav. var. *nigra*. They found that the plant contained, cinnamic (ferulic, *p*-coumaric, caffeic), benzoic (*p*-hydroxybenzoic, vanillic, syringic) acids and *p*-hydroxyphenylacetic acid. *p*-Coumaric, syringic and *p*-hydroxybenzoic acids were detected almost in all fractions. In the petals almost all of detected phenolic acids were found (except caffeic acid in methanolic extract, syringic and *p*-ydroxyphenylacetic acids in methanolic-aqueous extract). In the calyxes the vanilic and *p*-hydroxyphenylacetic acids were not found. The total content of phenolic acids in whole flowers was 60 mg%, in petals , 120 mg% and 30 mg% in calyxes⁽¹³⁾.

Raknimov and Mezthlumyan found that the amount of pectins in the stems was greater than in the roots. Sugars isolated from the plant stems and roots included arabinose, rhamnose , galactose, xylose and galacturonic acid. The percentage of hemicelluloses was 26.6 % in the stems and 14.1% in the roots. The amount of proteins in the stems was 11.3% and in the roots 12.1%. 17 amino acids were found in *Althaea rosa* stems and roots. The amino acid composition included valine, threonine, methionine, isoleucine, leucine, lysine, phenylalanine, histidine and arginine. The predominant amino acid were asparagine, glutamine and leucine. The amount of hemicellulose was 26.6% in the stems and 14.1 % in the roots. trace elements in *Althaea rosa* were determined.

The amount of microelements : Pb , Cd , Cu, Zn, Sn, Cr, and Fe in the stems were 30.1 , 0.67 , 30.0, 93.6, 23.1, 196.0 mg/kg and 106.0, while, their amounts in the roots were 26.1, 0.83, 24.2, 37.5 , 18.5 , 200.5 , and 790 mg/kg respectively⁽¹⁴⁾.

Pharmacological activities :

Antimicrobial effects :

The antimicrobial activities of n-hexane, methanol, ethanol, ethyl acetate and water extracts of *Althaea rosea* L. flowers were reported against *Escherichia coli* ATCC 29998, *Escherichia coli* ATCC 25922, *Escherichia coli* ATCC 11230, *Staphylococcus aureus* ATCC 6538, *Staphylococcus aureus* ATCC 29213, *Staphylococcus epidermidis* ATCC 12228, *Salmonella thyphimurium* CCM 5445, *Enterobacter cloacae* ATCC 13047, *Enterococcus faecalis* ATCC 29212, *Pseudomonas aeruginosa* ATCC 27853 as bacteria and *Candida albicans* ATCC 10239 by disc diffusion method⁽⁴⁴⁾.

Cardiovascular effects

Alcoholic extract of the flower of *Althaea rosea* (L.) increased the outflow of coronary artery of isolated guinea pig's heart and markedly dilated the blood vessels in the hind-limbs of rats. The extract showed a transient hypotensive effect on anesthetic cats. It inhibited platelet aggregation induced by ADP and showed an inhibitory effect on experimental thrombosis formation⁽⁴⁵⁾.

Prevention of urolithiasis

In both preventive and curative protocols, treatment of rats with hydroalcoholic extract of *Althaea rosea* roots significantly reduced the kidney calcium oxalate deposits compared to ethylene glycol group. Administration of *Althaea rosea* extract also reduced the elevated urinary oxalate due to ethylene glycol⁽⁴⁶⁾.

Anti-estrogenic effects :

In traditional folk medicine the *Althaea rosea* flowers were regarded as an emmenagogue. Literature data have proved that the infusion and methanolic extract of *Althaea rosea* influence hormonal activity and affected the morphology of the sexual organs of the rats. It exerted estrogenic activity, but exact component of this plant responsible for this activity was not determined. The *in vivo* test proved that *p*-hydroxybenzoic acid was estrogenic. Dudek *et al* proved that this compound present in different parts of *Althaea rosea* and could be responsible for its estrogenic activity⁽¹³⁾.

Effect on Immune system :

Water extract of *Althaea rosea* produce the following effects on immune system⁽⁴⁷⁾ :

- 1- Induced a transient non-specific polyclonal response indicated by the production of IL-4 in treated, non-immunized mice.
- 2- Initially boosted the production of anti-EA antibodies and IL-4, a T- helper 2 cytokine.
- 3- Suppress production of gamma-interferon, a T- helper 1 cytokine.

Cytotoxic effects:

The cytotoxic activity of n-hexane, methanol, ethanol, ethyl acetate and water extracts of *Althaea rosea* L. was investigated by brine shrimp assay. Ethyl acetate extract showed cytotoxic activity against brine shrimp⁽⁴⁴⁾.

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