

Review Article

Phytochemical compounds and biomedical properties of *Althaea officinalis*.

Baiken Baimakhanova , Amankeldi Sadanov , Irina Ratnikova , Saltanat Orasymbet , Erik Shorabaev , Gul Baimakhanova , Alma Amangeldi , Zaru Kapassova , Nurgali Rakhymbayev , Zhalgaskali Arystanov , Zere Zhalimova , Akzharkyn Saginbazarova , Aknur Turgumbayeva 

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Abstract

The purpose of this review is to provide a comprehensive overview of the research conducted on the chemical constituents and biological characteristics of *Althaea officinalis*. **Methods:** A comprehensive search of scientific databases, including Medline, Scopus, Web of Science, EMBASE, CINAHL, Google Scholar, Researchgate, was conducted. The search included keywords such as “*Althaea officinalis*”, “*Althaea officinalis* compounds”, “*Althaea officinalis* phytochemicals”, “*Althaea officinalis* pharmacological”, and “*Althaea officinalis* traditional uses”. **Results:** *Althaea officinalis*, commonly known as marshmallow root, is a perennial herbaceous plant native to Europe and western Asia. It belongs to the *Althaea* genus of the Malvaceae family. Throughout history, people have recognized the plant ability to relieve symptoms such as a sore throat, dry cough, stomach ulcers, and wounds. Modern pharmacological studies have shown that the extract from this plant has various positive effects, including antitussive, anti-inflammatory, antioxidant, antibacterial, and wound-healing properties. Recent analyses of its chemical composition have revealed that *Althaea officinalis* contains numerous bioactive compounds, including mucopolysaccharides, flavonoids, phenolic acids, tannins, coumarins, steroids, caffeic acid, ferulic acid, triterpenoids etc. The roots and leaves of *Althaea officinalis* are used in teas, salads, emollients, and sedatives due to their edible and medicinal qualities. Furthermore, this particular plant is frequently grown for its beautiful flowers, making it a popular choice for ornamental purposes. Currently, *Althaea officinalis* can be found worldwide due to its widespread cultivation in the agricultural industry. It offers various benefits in the fields of food, healthcare, and dietary supplements. **Conclusion:** *Althaea officinalis*, a well-known traditional herbal plant, is readily available and widely used. Recent research efforts have successfully identified numerous chemical components of *Althaea officinalis*, including flavonoids, polysaccharides, phenolic acids, coumarins, and steroids. These diverse chemical compounds contribute to the plant's various pharmacological properties, such as its ability to alleviate coughs, reduce inflammation, provide antioxidant effects, fight against bacterial infections, and promote wound healing.

Keywords: *Althaea officinalis*; antibacterial; anti-inflammatory; wound healing, antioxidant

Baiken Baimakhanova. Candidate of Biological Sciences, Research and Production Center for Microbiology and Virology, Almaty, Kazakhstan. bbbayken@mail.ru

Amankeldi Sadanov. Doctor of Biological Sciences, Professor, Research and Production Center for Microbiology and Virology, Almaty, Kazakhstan. a.sadanov1951@gmail.com

Irina Ratnikova. Doctor of Biological Sciences, ass. Professor, Department of microbial preparations, Research and Production Center for Microbiology and Virology, Almaty, Kazakhstan. iratnikova@list.ru

Saltanat Orasymbet. Candidate of Biological Sciences, Department of microbial preparations, Research and Production Center for Microbiology and Virology, Almaty, Kazakhstan. s_orazymbet@inbox.ru

Erik Shorabaev. Candidate of Biological Sciences, Department of microbial preparations, Research and Production Center for Microbiology and Virology, Almaty, Kazakhstan. eshorabaev@mail.ru

Gul Baimakhanova. PhD, Department of Ecological and Agricultural Microbiology, Research and Production Center for Microbiology and Virology, Almaty, Kazakhstan. bgulb@mail.ru

Alma Amangeldi. PhD, Department of food microbiology, Research and Production Center for Microbiology and Virology, Almaty, Kazakhstan. almashka91@mail.ru

Zaru Kapassova. Senior lecturer, Department of Pharmaceutical Disciplines, Astana Medical University, Astana Medical University, Astana, Kazakhstan. zaru60@mail.ru

Nurgali Rakhymbayev. PhD, Senior lecturer, Department of Organization, Management and Economics of Pharmacy and Clinical Pharmacy, Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan. nr_farma@mail.ru

Zhalgaskali Arystanov. Doctor of Pharmaceutical Sciences, Professor of the Department of Pharmaceutical Disciplines, Astana Medical University, Astana, Kazakhstan. arystanov.zh@amu.kz

Zere Zhalimova. Master of medical science, Lecturer of Pharmaceutical Disciplines, West Kazakhstan Medical University named after Marat Ospanov, Aktobe, Kazakhstan. zere_zhalimova@mail.ru

Akzharkyn Saginbazarova. Associate professor, Head of Department of Pharmaceutical Disciplines, West Kazakhstan Medical University named after Marat Ospanov, Aktobe, Kazakhstan. akzharkyn.sab@mail.ru

Aknur Turgumbayeva*. PhD, ass. Professor, Department of Fundamental Medicine, al-Farabi Kazakh National University, Almaty, Kazakhstan. turgumbayeva.agnur@med-kaznu.com



INTRODUCTION

Due to their numerous health benefits and therapeutic properties, herbs and plant metabolites/extracts are becoming increasingly popular¹. This trend is particularly noticeable in the modern era, where there is a growing resistance to drugs and concerns about the negative effects of chemicals. Unlike traditional chemical remedies, herbal treatments have fewer adverse reactions². A notable example is *Althaea officinalis*, a plant that has been highly esteemed for centuries. *Althaea officinalis*, commonly known as marshmallow, is a perennial herb from the Malvaceae family. It is typically found in moist areas with damp soil and is indigenous to Western Asia and Europe. The stems can reach a height of 1.5 meters and have a diameter of 5 centimeters. *Althaea officinalis* is now cultivated globally for its beneficial applications in food, healthcare, and dietary supplements. Additionally, it is often grown as an attractive plant due to its vibrant flowers^{3,4}.

The roots and leaves of the *Althaea officinalis* plant, which are edible and medicinal, are utilized in teas, salads, as well as for their emollient and sedative properties⁵. Pharmaceutical raw materials are derived from the roots or leaves of a plant, and biological compounds can also be found in its flowers and seeds. The roots are typically collected in autumn or spring, either in the first or second year of cultivation. The leaves, on the other hand, are obtained during the flowering phase. Many countries worldwide make use of the roots, leaves, and flowers of this plant for both culinary and medicinal purposes. Traditionally, *Althaea officinalis* root has been utilized to treat various conditions such as irritation of the mouth and throat mucosa, dry cough, mild gastritis, skin burns, insect bites, catarrh, ulcers, abscesses, constipation, and diarrhea^{6,7}.

Modern pharmacological studies have shown that *Althaea officinalis* possesses properties such as antitussive, antioxidant, anti-inflammatory, antibacterial, and wound-healing effects⁸. The key components of *Althaea officinalis* include mucopolysaccharides (5–11.6%), flavonoids, phenolic acids, tannins, coumarins, steroids, caffeic acid, ferulic acid, and triterpenoids⁹. The chemical makeup of *Althaea officinalis* can differ due to various factors, including the particular cultivar, the colour of its flowers and leaves, its scent, the climate it grows in, how it is dried, and how it is stored¹⁰. The aim of this review was to provide the scientific community with information about the bioactive compounds and medicinal properties of *Althaea officinalis*, primarily based on recent research discoveries.

MATERIALS AND METHODS

A comprehensive search of scientific databases, including Medline, Scopus, Web of Science, EMBASE, CINAHL, Google Scholar, Researchgate, was conducted. The search included keywords such as “*Althaea officinalis*”, “*Althaea officinalis* compounds”, “*Althaea officinalis* phytochemicals”, “*Althaea officinalis* pharmacological”, and “*Althaea officinalis* traditional uses”.

RESULTS & DISCUSSION

Traditional Use

The leaves, flowers, and roots of *Althaea officinalis* have long been utilized in various traditional herbal remedies. The name *Althaea* is derived from the Greek term “*althein*,” which translates to “to heal.” Pliny suggested that a decoction of marsh mallow mixed with milk should be consumed after dinner for five consecutive days to alleviate coughs². In Iranian traditional medicine, the flowers of *Althaea officinalis* are employed to address inflammatory conditions of the respiratory system and warm catarrh, characterized by redness in the eyes and face, sharp yellow discharges, and a burning sensation in the nose and throat. The renowned physician Ibn Sina, who lived around 980–1037, asserted that the leaves and flowers of *Althaea officinalis* provide relief for coughs stemming from a hot and dry chest, while its seeds help to smooth the windpipe. Theophrastus, a philosopher from around 370 to 285 BCE, also recognized the benefits of *Althaea officinalis*, noting its effectiveness in wine as a remedy for ruptures and coughs⁴. In the realm of Unani medicine, *Althaea officinalis* is regarded as possessing a temperament that can be classified as either cold-wet or hot-wet, which is thought to negatively impact the stomach and lungs.

To mitigate these effects, practitioners often recommend combining *Althaea officinalis* with corrective substances such as honey, *Foeniculum vulgare*, or *Berberis vulgaris*. Additionally, alternatives to *Althaea officinalis* include the roots of *Centaurea behen* Linn., the fruits of *Malva sylvestris* Linn., the flowers of *Nymphaea lotus*, *Acacia arabica* gum, and the manna from *Bambusa arundinaceae*. In treating conditions like bronchitis, catarrh, coryza, cough, and asthma, the seeds of *Althaea officinalis* are typically prepared as a decoction. Furthermore, its seeds are prepared as paste and massaged on the chest in conditions like pleurisy and pneumonia⁵.

In Bolivia, the infusion of *Althaea officinalis* is commonly utilized as an expectorant. Meanwhile, in India, people consume an infusion made from the dried flowers of *Althaea officinalis* for its expectorant properties, while the boiled roots combined with black pepper are used to alleviate asthma symptoms. Italians have historically employed decoctions of dried flowers and leaves as a remedy for asthma, and they also prepare root infusions to treat bronchial catarrh. In the United States, a hot water extract of dried *Althaea officinalis* roots is taken orally to serve as an expectorant, and the dried roots are also used to relieve coughs and sore throats⁷.

Additionally, in Germany, the leaves, flowers, and roots of *Althaea officinalis* are incorporated into traditional medicine to address mucosal irritations in the mouth and throat, respiratory tract catarrh, and dry coughs¹. The residents of Gallies, located in Abbottabad, Northern Pakistan, utilize various parts of *Althaea officinalis* — such as its leaves, roots, seeds, and flowers—to treat conditions like asthma, bronchitis, and pneumonia⁶. In Turkey, the freshly ground aerial parts of *Althaea officinalis* are applied to wounds³. This highlights the significance of *Althaea officinalis* as a well-regarded herbal remedy across various



traditional medicine practices for addressing coughs and other respiratory issues.

Chemical compounds

The scientists have successfully isolated and identified 46 substances from different parts of *Althaea officinalis*, which include flavonoids, phenolic acids, coumarins, steroids, terpenoids, and amino acids. Flavonoids make up the primary components of *Althaea officinalis*. Currently, researchers have isolated 17 flavonoids from the plant. Along with this, research has indicated that *Althaea officinalis* harbours steroids and triterpenoids. To date, one steroid and one triterpenoid have been isolated from the roots and seeds. At the same time, the roots of *Althaea officinalis* yielded three coumarins. Moreover, the researchers found polysaccharides in *Althaea officinalis*. The mucus contained 5-11.6% polysaccharides, depending on the growing season. These polysaccharides consisted of a combination of colloid-soluble polysaccharides, including acid arabinogalactans, galacturonic rhamnans, arabans, and glucans. Other compounds have also been discovered from *Althaea officinalis* and identified respectively as phenolic acids, phenolic compounds and fatty acids.

To extract bioactive compounds from *Althaea officinalis*, various traditional methods like polar and non-polar maceration have been employed. These methods involve the use of different solvents such as methanol, ethanol, dichloromethane, ethyl acetate, 10% H₂O₂, oily solvents, and aqueous solvents. Additionally, other extraction techniques have also been utilized to separate chemical compounds from the plant using solvents like butanol, hexane, ethyl acetate, water, and others. The chemical composition of *Althaea officinalis* can vary qualitatively and quantitatively depending on factors like growth stage, drying methods, and storage conditions¹.

Antioxidant activity

A research conducted by Benbassat et al. investigated the antioxidative properties of root extracts by employing various solvents for the extraction process. They employed ABTS•⁺, hypochlorous acid removal, and lipid peroxidation tests to evaluate the activity. The findings indicated that the extract prepared with water as the solvent did not exhibit any antioxidative activity. However, the extracts prepared with ethanol:water as the extracting agent displayed robust antioxidative activity. Interestingly, lower concentrations of ethanol in the mixed solvent (50:50 and 70:30, v/v) demonstrated higher scavenging activity for ABTS•⁺ radicals and hypochlorite ions in comparison to the extract with a higher concentration of ethanol (90:10, v/v). These results correlated with the phenolic and flavonoid content of the extracts. The findings indicated that the extract obtained with the least amount concentration of ethanol had the highest phenolic content. Additionally, the phytochemical analysis of the extracts in the study demonstrated a greater total flavonoid content for the extracts obtained through extraction with lower ethanol concentrations in the mixed solvent and correlated with their antioxidant capacity²⁷.

In a similar study, the total antioxidative capacity of ethanol

extracts from *Althaea officinalis* was measured using FRAP and single electron transfer with a Naxifer™ kit. The findings revealed a total antioxidative capacity of 1.2 mmol Fe²⁺/L. As researchers report the total antioxidant capacity of plant is related to compounds such as phenols, phenolic compounds, and flavonoids²⁸. The presence of hydroxyl groups in the flavonoids and phenolic compounds of *Althaea officinalis* is responsible for its antioxidant activity. These hydroxyl groups have the capability to absorb DPPH. The redox and radical scavenging properties of phenolic compounds are attributed to the hydroxyls they contain. Flavonoids function as antioxidants by scavenging reactive nitrogen species and reactive oxygen species. Additionally, in certain cases, they can chelate transition metal ions in a structure-dependent manner. The antioxidant properties of flavonoids are determined by the number and arrangement of phenolic hydroxyl groups attached to their ring structures.

The antioxidant activity of *Althaea officinalis* polysaccharides assessed using the DPPH test showed good results. The findings showed a significant increase in free radical scavenging ability as the concentration of polysaccharides rose from 0.25 to 4 mg/mL ($P < 0.05$). However, when compared to vitamin C, the absorption activity of *Althaea officinalis* solutions was consistently lower at all concentrations. The IC₅₀ value, which represents the concentration needed to eliminate 50% of DPPH free radicals, was determined to be 1.53 mg/mL for *Althaea officinalis*. This value was higher than that observed in the vitamin C assay²⁹. Similar study discovered that polysaccharides from *Althaea officinalis* have the ability to eliminate DPPH radicals also within the concentration range of 1.0–5.0 mg/mL. These polysaccharides exhibited a dose-dependent capacity to create stable DPPH compounds, ranging from 28% to 57%. However, when compared to BHT at a concentration of 100 µg/mL, the cleansing effect of the polysaccharides (at a concentration of 5.0 mg/mL) was lower. The IC₅₀ value for the polysaccharide was determined to be 4.77 mg/mL^{34,35}.

Another study also uncovered the DPPH radical scavenging properties of polysaccharides obtained from the roots of *Althaea officinalis*. The research findings determined that the optimal values for four crucial factors, in order to achieve the highest antioxidant activity of polysaccharides isolated from *Althaea officinalis* roots (84.94%), are an extraction temperature of 55.51 °C, an extraction time of 12.11 hours, a W/S ratio of 39.75, and a particle size of 12.18 mm. The antioxidant activity displayed an upward trend as the W/S ratio increased within the tested ranges. The increase in antioxidant activity of *Althaea officinalis* root polysaccharides at higher W/S values during the extraction process is a result of diluting the raw material with liquid, consequently reducing the presence of oxygen molecules. However, longer extraction times resulted in reduced rates of free radical scavenging. The decline in antioxidant activity at higher extraction temperatures attributed to the degradation of antioxidant polysaccharides at elevated temperatures^{30,31}.

The antioxidant activity of the polysaccharides influenced by factors such as monosaccharide composition, glycosidic bonds,



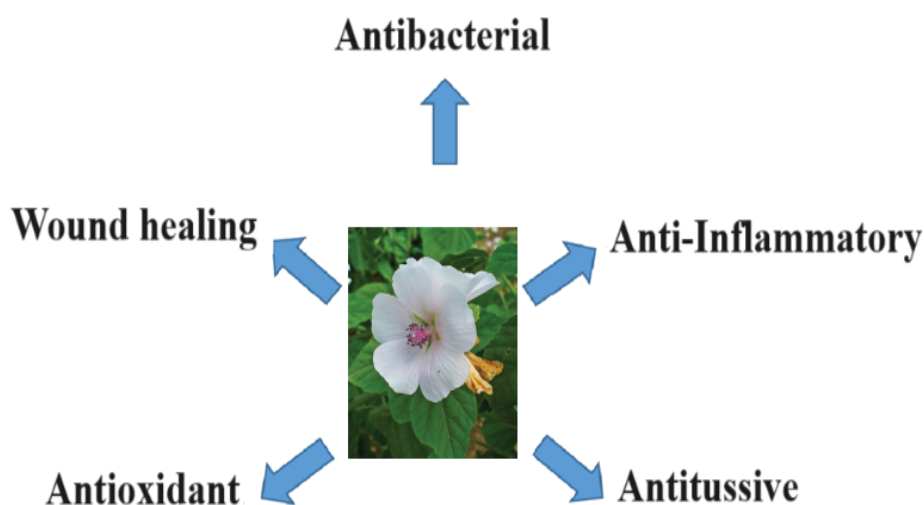


Figure 1. Pharmacological properties of *Althaea officinalis*

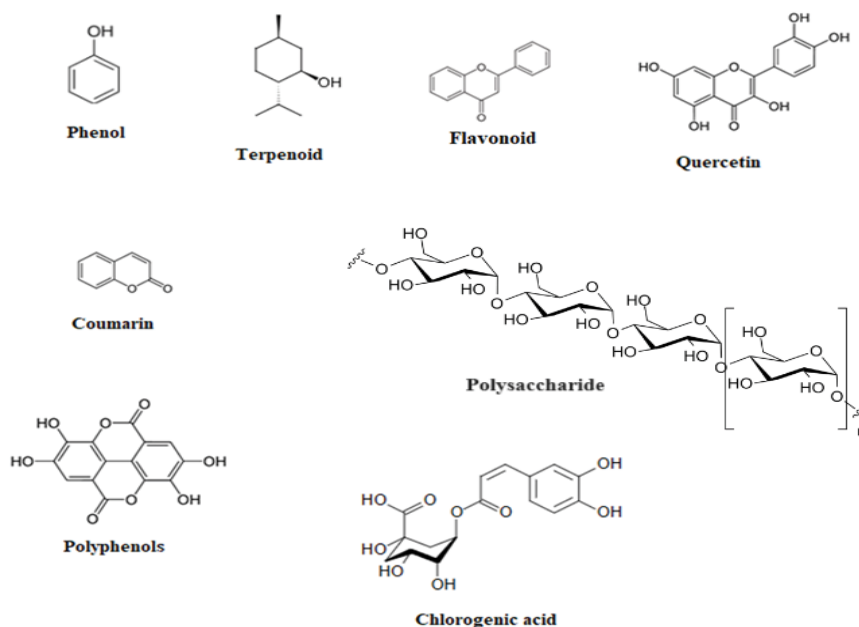


Figure 2. Chemical structure of the main biologically active substances of the *Althaea officinalis*.

the presence of functional groups, and molecular weight. The antioxidant activity of polysaccharides due to the presence of hydroxyl and carboxyl groups in their structure, which reduced free radicals by giving hydrogen. In addition, it due to the formation of cross-bridge between divalent ions and -COOH groups in uronic acid.

A study conducted by Bohdanovych et al. examined the flavonoid content, antioxidant activity, and iron ion reduction ability of alcoholic extracts from hairy roots of *Althaea officinalis* and roots of in vitro cultured control plants (source). The researchers focused on two groups of hairy root lines. The first group consisted of hairy roots obtained through transformation with the wild strain *Agrobacterium rhizogenes* A4, while the second group was initiated by transformation with a strain of A.

rhizogenes carrying the human interferon- $\alpha 2b$ gene controlled by the sugar beet root-specific MII promoter. The study found no significant differences between the two groups of hairy root lines, suggesting that additional genes did not play a role in the antioxidant status of the hairy roots. Both groups exhibited lines with varying levels of antioxidant activity, ranging from low to medium to high values. The reducing power of the extracts also varied, with the highest activity recorded at $\text{EC}_{0.5} = 7.10 \text{ mg}$ and the lowest activity at $\text{EC}_{0.5} = 29.24 \text{ mg}$. This variation was found to be correlated with the total flavonoid content in the extracts. Considering the association discovered between the overall flavonoid content and the reducing activity of extracts derived from the hairy roots of *Althaea officinalis*, researchers inferred that the presence of flavonoids in plants belonging

to this species contributes to this activity. The findings of this investigation support that flavonoids actively participate in antiradical reactions within the cells of *Althaea officinalis*' hairy roots^{36,37}.

In a separate study, the petroleum ether portion of *Althaea officinalis* displayed a significant ability to scavenge hydroxyl radicals, with an IC₅₀ value of 9.7 mg. The highest impact in blocking hydroxyl radicals was observed in the *Althaea officinalis* and ascorbic acid at a concentration of 20 mg/mL, with percentages of 94.8% and 81.6%, respectively. At a concentration of 20 mg/mL, the *Althaea officinalis* root exhibited a higher capacity for scavenging radicals (93.4%) compared to other portions. It has been established that the absorbing effect of *Althaea officinalis* portions on DPPH radicals increases linearly with concentration. The cleansing effect is linked to the presence of uronic acid (12.25%) in the *Althaea officinalis* root, which has the potential to eliminate hydroxyl ions. DPPH free radicals accept an electron or hydrogen radical and become a stable neutral molecule^{32,33}.

Antibacterial activity

The investigation into the antibacterial properties of *Althaea officinalis* methanol extract against standard strains of *Klebsiella aerogenes* (*K. aerogenes*), *Streptococcus pneumoniae* (*S. pneumoniae*), *Staphylococcus aureus* (*S. aureus*), and *Pseudomonas aeruginosa* (*P. aeruginosa*) yielded promising results in both in vitro and in vivo studies. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of the extract were determined to be 100 mg/mL and 200 mg/mL, respectively, for *S. aureus*, and 50 mg/mL and 100 mg/L for the other pathogens. In agar diffusion analysis, the extract at a concentration of 100 mg/mL exhibited inhibitory activity against all bacteria. At a concentration of 50 mg/mL, it inhibited the growth of *S. aureus*, *P. aeruginosa*, and *S. pneumoniae*, while at 25 mg/mL, it inhibited *S. aureus* and *S. pneumoniae*. MIC and MBC values of *Althaea officinalis* were lower for *P. aeruginosa*, *K. aerogenes*, and *S. pneumoniae* than for *S. aureus*. These results correlated with high flavonoid content in the methanol extract of *Althaea officinalis*, which exhibited significant inhibitory effects against both gram-positive and gram-negative bacteria^{38,39}.

The antibacterial properties of the alcoholic extract obtained from *Althaea officinalis* against antibiotic-resistant strains of *Staphylococcus aureus* showed good results. The study involved the use of *S. aureus* strains that were obtained from patients. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of the extract were determined using broth microdilution and agar dilution methods. The findings revealed that the MIC/MBC of the ethanolic extract of *Althaea officinalis* L. against *S. aureus* was 3.2/6.5 mg/mL^{40,41}.

In a similar study conducted by Arab et al., the antibacterial impact of alcoholic extracts was examined on two species of bacteria. The flower, leaf, stem, and root of *Althaea officinalis* were assessed against two types of pneumonia bacteria (*Bacillus cereus* and *Klebsiella pneumoniae*) in vitro. To evaluate

the antimicrobial activity of alcoholic extracts and *Althaea officinalis* essence at various concentrations were exposed to these bacteria using the disk diffusion method. Positive controls such as penicillin, ampicillin, gentamicin, and vancomycin were utilized, while negative controls included ethanol, ethyl acetate, and DMSO solvents. The extraction of essence was carried out following the Clevenger system. The outcomes demonstrated that the stem alcoholic extracts and essences of *Althaea officinalis* (at a concentration of 100 mg/mL) exhibited the highest antimicrobial properties against *K. pneumoniae*. The alcoholic extract demonstrated activity against two species of pneumonia bacteria in all tested concentrations, and the essence of *Althaea officinalis*, at a concentration of 12.5 µL/mL, showed efficacy against both bacteria. From 56 combinations of *Althaea officinalis* essence, more than 93% of the main combinations consisting of thymol, p-cymene, γ-terpinene, β-pinene, terpineol, carvacrol were extracted. It was observed that the antibacterial properties and inhibitory halo diameter increased with higher concentrations of extracts and essences^{42,43}.

Another study demonstrated the antibacterial effects of a water-ethanol extract obtained from *Althaea officinalis* against standard strains of *Listeria*, *Staphylococcus aureus*, *Pseudomonas*, and *Escherichia coli*. The results demonstrated that the extract exhibited a bacteriostatic effect with a MIC value of 330 ± 0.1 µg/mL against *Staphylococcus aureus*. Additionally, at a concentration of MIC = 660 ± 0.2 µg/mL, extract displayed a bactericidal effect against *Staphylococcus aureus*, but did not exhibit any impact on the other bacteria tested. The MIC for *Listeria* was observed at a concentration of 250 ± 0.15 µg/mL, MBC not detected. Hydroethanolic extract of *Althaea officinalis* did not demonstrate any effect on gram-negative bacteria^{44,45}. In a comparable investigation, Haghighi et al., conducted assess and compare the impact of different concentrations of ethanol extract from *Althaea officinalis* root, 0.2% chlorhexidine (CHX), and penicillin on *Streptococcus mutans* and *Lactobacillus acidophilus* in vitro. The findings revealed that *Althaea officinalis* extract exhibited a bacteriostatic effect with a minimum inhibitory concentration (MIC) of 102 mg/mL, while at a concentration of 212.5 mg/mL, it demonstrated a bactericidal effect against *S. mutans*. The MIC for *L. acidophilus* was observed at 212.5 mg/mL, with the minimum bactericidal concentration (MBC) also being 212.5 mg/mL. The MIC and MBC values for the plant extract were higher than those of penicillin and 0.2% CHX for both bacterial species. As the concentration of the extract increased, there was an increase in the inhibitory effect on both types of bacteria. Notable differences were found in the average zones of growth inhibition at the same concentrations of 6%, 25%, 50%, and 100% for both *S. mutans* and *L. acidophilus*. The extract exhibited a greater effectiveness against *S. mutans* compared to *L. acidophilus*^{46,47}.

The antibacterial effect of *Althaea officinalis* extracts is primarily due to their biological active components. The antibacterial activity correlated with high flavonoid content in the extracts of *Althaea officinalis*, which exhibited significant inhibitory effects against both gram-positive and gram-negative bacteria. Flavonoids exhibit antibacterial activity

Table 1. Main biological active compounds of *Althaea officinalis*

Extracts	Plant Part	Method	Biological active compounds	Pharmacology activity	Country	Ref.
			Flavonoid			
Ethanolic	Leaves	HPLC, ¹ H- NMR	Tilioside, kaempferol-3-glucoside , quercetin-3-glucoside	Antioxidant, Antimicrobial, Anti-Inflammatory	Poland	[12]
Ethanolic	Leaves	HPLC, ¹ H- NMR	Hypolaetin-8 -glucoside, hypoletin-8-β-gentiobioside	Antioxidant and Anti-Inflammatory,	Poland	[13]
Ethanolic, Methanolic	Stem, leaves	HPLC, GC-MS	Astragalin, kaempferol 7-O-glucoside	Antimicrobial and Antioxidant	France	[14]
Ethanolic	Root, leaves	HPLC, ¹ H- NMR	Hypolaethin-8-O - β-D-(2''-O-sulfo)-glucopyranoside, 4'-O-methylhypolaethin-8-O-β-D-(2''-O-sulfo)-glucopyranoside, 4'-O-methylhypolaethin-8-O-β-D-(3''-O sulfo)-glucuronopyranoside, 4'-O-methylisoscuteallarein 8-O-β-D-(3''-O-sulfo)-glucuronopyranoside, hypolaethin-8-O-β-D-(3''-O-sulfo)-glucuronopyranoside (theograndin II), hypolaethin-8 -O-β-D-glucopyranosyl-(1'''→4'')-β-D-glucuronopyranoside	Antioxidant, Anti-Inflammatory	Germany	[15]
Ethanolic, n-hexane	Leaves	LC, GC-MS	Quercetin, kaempferol	Wound healing, Antiviral, Antimicrobial	Bulgaria	[16]
Ethanolic, Methanolic	Root	UV, ¹ H-NMR, ¹³ C-NMR	Hypolaethin 8-O - β-D-glucoside, isoscuteallarein 4'-methyl ester 8-O-β-D-glucoside-2''-SO ₃ K	Antimicrobial and Antioxidant	Poland	[17]
			Steroid			
Ethanolic	Root	¹ H-NMR	β-sitosterol	Antimicrobial and Antioxidant	India	[18,19]
			Triterpenoid			
Methanolic	Seed	¹ H-NMR	Lanosterol	Antimicrobial and antioxidant	India	[18]
			Coumarins			
Ethanolic, Methanolic	Root, leaves	HPLC, ¹ H- NMR	5,6-dihydroxycoumarin-5-dodecanoate, 6β-D-glucopyranoside, scopolin-6'-O-α-L-rhamnopyranosid, and scopoletin	Antioxidant, Antimicrobial, Anti-Inflammatory	Germany, Poland, India	[15,17,18]
			Polysaccharides			
Ethanolic	Root	GLC-MS	Arabinanogalactans, galacturonic rhamnans, arabans and glucans.	Antioxidant, Anti-Inflammatory	Germany, Slovakia, Japan	[20-22]
Aqueous	Root	LC-MS	D-galactose, L-rhamnose, D-glucuronic acid and D-galacturonic acid	Antimicrobial and Antioxidant	Poland	[23,24]
Aqueous	Root	LC-MS	L-arabinans, D-glucans and (1-6)-α-D-glucan	Antimicrobial and Antioxidant	Germany, Poland	[25,26]
			Phenolic acid			
Ethanolic, Methanolic	Stem, leaves, root	HPLC, ¹ H-NMR, ¹³ C-NMR	Caffeic acid, p-hydroxyphenylacetic acid, chlorogenic acids, ferulic acid	Antioxidant and Anti-Inflammatory	France, Poland	[14,17]
			Phenolic compounds			
Ethanolic, Methanolic	Stem, leaves, root	HPLC, ¹ H-NMR, ¹³ C-NMR	4-hydroxycinnamic acid, vanillic acid, salicylic acid, 2β-hydroxycalamene, 3,4-dihydroxybenzyloctadecane	Antioxidant and Anti-Inflammatory	France, Poland, India	[14],[17-19]
			Phenolic amides			
Ethanolic, Methanolic	Stem, leaves, root	HPLC, ¹ H- NMR	N-(E)-caffeoyl-L-dopa, N-(E)-caffeoyl-L-tyrosine, N-(E)-coumaroyl-L-dopa, N-(E)-coumaroyl-L-tyrosine	Antioxidant and Anti-Inflammatory	France, Germany	[14,15]
			Fatty acid			
Ethanolic, Methanolic	Root, seed	¹ H-NMR, ¹³ C-NMR	Lauric acid, n-triacontanoic acid	Antimicrobial and Anti-Inflammatory	Poland, India	[17,18]



Table 2. Investigation methods and pharmacological activities of *Althaea officinalis*

Pharmacological activity	Plant part	Extract	Concentration / Used Dose	Method	Constituent	Ref.
Antioxidant	Leaves	Ethanol	-	ABTS, lipid peroxidation assay	Phenol, flavanoid	[27]
	Leaves	Ethanol	-	FRAP	Flavanoid, phenolic compound	[28]
	Leave	Ethanol	0.25 - 4 mg/mL	DPPH	Polysaccharides	[29]
	Root	Methanol	50 mg/mL	DPPH	Polysaccharides	[30,31]
	WP	Petroleum ether fraction	20 mg/mL	DPPH	Uronic acid	[32,33]
	Leaves, seed	Hydroalcoholic	1.0 – 5 mg/mL	DPPH	Polysaccharides	[34,35]
	Root	Alcoholic	25 - 50 mg/mL	DPPH	Flavanoid	[36,37]
Antibacterial	Leaves	Methanol	25 – 200 mg/mL	Agar diffusion	Flavonoid	[38,39]
	Leaves	Alcoholic	100 mg/mL	Microdilution and agar dilution	-	[40,41]
	Leaves	Water-ethanol	250 - 500 mg/mL	Agar diffusion	Phenolic compounds	[42,43]
	Leaves, stem	Ethanol, ethyl acetate	100 mg/mL	Disk diffusion	Thymol, p-cymene, γ-terpinene, β-pinene, terpineol, carvacrol	[44,45]
	Leaves	Ethanol	100 – 250 mg/mL	Disk diffusion	-	[46,47]
	AP	Methanol, water	100 -400 mg/mL	Agar well-diffusion	Triterpenoid, fatty acid	[48,49]
Anti-Inflammatory	Root	Water	100 mg/mL	Immunosorbent assay, scratch assay, PrestoBlue® viability assay, crystal violet cell quantification assay	Flavanoid, phenolic compounds	[50,51]
	Root	Ethanol	100	Extract treatment, immunosorbent assay, scratch assay	Flavanoid, coumarins	[52,53]
	Leaves	Combined mixture (N-diethylnitrosamine + silymarin + water extract of <i>Althaea officinalis</i>)	250, 500, 750 mg/ mL	Intraperitoneal administration	Flavanoid	[54,55]
Wound healing	Leaves	Polyherbal ointment (<i>Althaea officinalis</i> water extract + R. x damascena essential oil + L. angustifolia essential oil in a eucerin base; 20:20:10:50)	25 – 50 mg/mL	Wound excision test	Quercetin, kaempferol	[56,57]
	Leaves	Water-ethanol	5% and 10 %	Stereological techniques	Quercetin	[58,59]
	AP	Water-alcoholic	50, 100 mg/mL	Wound excision test	Kaempferol, ferulic acid	[60,61]
	Leaves	Water-ethanol	25 – 100 mg/mL	Wound excision test	-	[62,63]
Antitussive	Flower	Mucilage	5%, 10% and 15%	Topical application	Polysaccharides	[64,65]
	Leaves	Water	-	Administered in the form of lozenges and syrup	-	[68]
	Leaves	Water	40 mg	Administered in the form of syrup, measure spirometry data	-	[69]
	Leaves	Water	2.5 – 10 ml	Administered in the form of syrup, measured cough intensity, cough frequency, cough intensity during the day	-	[70]
	Leaves	Water	1-5 ml		-	[71]
	Leaves	Water	5- 10 ml		-	[72]
	Leaves	Water	1-10 ml		-	[73]
	Leaves	Water	20 ml		-	[74]
	Leaves	Water	20-40 ml		-	[75]

through various mechanisms including the inhibition of nucleic acid synthesis, disruption of cytoplasmic membrane function, interference with energy metabolism, prevention of bacterial adhesion, and inhibition of biofilm formation. On the other hand, flavonoids can inhibit the function of cell membrane porins, alter membrane permeability, and attenuate bacterial virulence. At the same time, based on the research findings, it has been discovered that *Althaea officinalis* extract possesses the capability to hinder the growth of bacteria as a result of its abundant concentration of phenolic compounds. These compounds exert various effects on microorganisms by modifying the permeability of microbial cell membranes through the buildup of hydrophobic groups in the phospholipid bilayer. Additionally, they can bind to enzymes and impede their functions, including those associated with protein, DNA, and RNA synthesis. Moreover, polyphenols exert their anticariogenic effects by inhibiting bacterial growth and interfering with bacteria adhesion and affecting the enzymatic activity of cariogenic bacteria. One of the antibacterial effects of the extract of *Althaea officinalis* on Gram-positive bacteria is due to its adhesion to N-acetyl glucosamine found in the bacterial cell wall. In addition, antibacterial activity attributed to the antioxidative effects of the plant extract components. The antibacterial effect of the extract also explained by the fact that the plant polyphenols, plays a major role, exert their inhibitory effects on bacterial growth by producing hydrogen peroxide. Another factor that influenced the plant extract's antibacterial efficacy was identified as the extraction method and the choice of solvents. Various methods and solvents were employed to obtain extracts from plants, resulting in varying antibacterial outcomes against specific bacteria.

A research conducted by Khamees et al. demonstrated that *Althaea officinalis* exhibits significant antimicrobial properties against specific gastrointestinal pathogens when compared to commonly used antibiotics. The methanol extract of *Althaea officinalis* at concentrations of 100 and 200 mg ml⁻¹ displayed a greater zone of inhibition against all tested microorganisms when compared to the aqueous extract. However, both extracts exhibited a similar zone of inhibition against *Salmonella typhimurium*, with a value of $p < 0.001$. Furthermore, the methanol extract at the indicated concentrations demonstrated higher efficacy against *Klebsiella pneumonia* than the standard antibiotic gentamicin, with inhibition zones measuring 15.3 and 17.9, respectively. The tested plant extracts also exhibited antimicrobial activity against the tested microorganisms at doses of 300 and 400 mg/ml. The methanol extract exhibited significant activity against *S. aureus*, *P. vulgaris*, and *Shigella Dysenteriae* at a dose of 400 mg/ml. All bacteria showed equal sensitivity to gentamicin. In comparison, the methanol extract had a higher activity than gentamicin against *Klebsiella pneumonia* at all concentrations, resulting in a zone of inhibition ranging from 15.3 mm to 21.2 ± 0.3 mm. *E. coli*, *K. pneumonia*, and *Shigella dysenteriae* also demonstrated zones of inhibition measuring 23.5 ± 0.2 mm, 21.2 ± 0.3 mm, and 18.7 ± 0.5 mm, respectively. These results were comparable to those obtained with ciprofloxacin (p value < 0.001). According to the authors, unlike other studies, the active components responsible for

the antibacterial activity in this study are triterpenoid and fatty acids. The *Althaea officinalis* extract contains triterpenoid compounds like lanosterol, which act on and destroy the cell membranes of microorganisms. Additionally, the presence of fatty acids is associated with the antibacterial activity. The *Althaea officinalis* extract is abundant in saturated and unsaturated fatty acids with carbon chains of 16 or more. Fatty acids with carbon chains of six or fewer inhibit Gram-negative bacteria, while fatty acids with carbon chains greater than twelve inhibit Gram-positive bacteria. Yeasts, on the other hand, are inhibited by fatty acids with carbon chains of ten to twelve^{48,49}.

Anti-inflammatory activity

Bonaterre et al. conducted a study to evaluate the anti-inflammatory or antioxidant properties of the ethanol extract of *Althaea officinalis* root in activating pro-inflammatory macrophages (MΦ) or inducing oxidative stress. The findings revealed that treatment of human THP-1 MΦ, which were differentiated using PMA, with *Althaea officinalis* root extract enhanced their viability without impacting the cell count. Root extracts of *Althaea officinalis* (REA) demonstrated the ability to safeguard human MΦ against H₂O₂-induced cytotoxicity and H₂O₂-induced ROS production. Both REA and diclofenac, utilized as a reference substance for anti-inflammatory purposes, equally inhibited the release of tumor necrosis factor-α (TNF-α) and IL6 in MΦ induced by LPS. Treatment with *Althaea officinalis* root extract did not compromise the mitochondrial membrane potential (MMP). Furthermore, REA stimulated the migratory capability of MΦ. Using medicinal extracts derived from the roots of *Althaea officinalis* elicited an immediate effect by forming a protective film on the inflamed mucous membrane. According to the results of the study, REA has anti-inflammatory effects through several mechanisms. Polysaccharides from *Althaea officinalis* have immune-boosting effects. Moreover, REA possesses antioxidant properties, which provoke the immune system's defence mechanisms in human BV-173 leukemic cells, and shields against the rise of intracellular ROS in human macrophages. On the other hand, the high molecular weight hyaluronic acid in REA triggers numerous effects on tissue, prompting the movement of leukocytes, stimulating of growth factors by epithelial cells, proliferation, differentiation which is advantageous for tissue regeneration^{50,51}.

Another investigation was carried out to evaluate the properties of *Althaea officinalis* root extract on human umbilical vein endothelial cells (HUVECs), including its anti-inflammatory, antioxidant, and migration-enhancing effects. HUVEC cells were exposed to *Althaea officinalis* root extract for 24 hours, followed by a 3-hour administration of lipopolysaccharide (LPS) or a 1-hour exposure to H₂O₂. The levels of intracellular reactive oxygen species (ROS) were measured using dichlorofluorescein (DCFDA), and the release of interleukin (IL-) 6 was quantified using an enzyme-linked immunosorbent assay (ELISA). The migratory capacity of HUVECs was assessed using a scratch assay. The results demonstrated that *Althaea officinalis* root extract at a concentration of 100 μg/mL reduced IL-6



release by 17% compared to the stimulation caused by 0.1 µg/mL LPS. Additionally, the extract at a concentration of 500 µg/mL inhibited IL-6 release by 24% in comparison to the response induced by LPS. In addition, following a 24-hour period of treatment, the root extract of *Althaea officinalis* at concentrations of 500 µg/mL and 1000 µg/mL demonstrated a decrease in ROS production by 18% and 16% respectively. When treated for 6 hours, the extract at a concentration of 500 µg/mL facilitated wound closure by 10%, while the concentration of 1000 µg/mL enhanced it by 13.5% in comparison to the control group^{52,53}.

Wang et al. conducted studies to evaluate the protective properties of *Althaea officinalis* flower extract against liver cell damage caused by N-diethylnitrosamine (DEN)-induced hepatocellular carcinoma. To investigate a group of 70 Wistar rats was divided into seven different groups (n=10/group): sham, DEN, silymarin treatment (SIL; DEN+SIL), *Althaea officinalis* treatment (DEN+250 and 500 *Althaea officinalis*), and combined SIL and *Althaea officinalis* treatment (DEN+SIL+250 and 500 *Althaea officinalis*). The impact of the *Althaea officinalis* extract on inflammation assessed by measuring the levels of pro-inflammatory substances like IL-1β and TNF-α, as well as the anti-inflammatory cytokine IL-10, using commercially available Novus Biologicals sandwich ELISA kits specifically designed for rodents. Analyzing the cytokine levels in the rats' serum, showed that DEN significantly (p<0.05) elevated the levels of all three pro-inflammatory cytokines (IL-6, IL-1β, and TNF-α) compared to the sham group. Furthermore, the secretion of the anti-inflammatory cytokine IL-10 was markedly suppressed (p<0.05) by DEN in comparison to the sham group. SIL alone demonstrated a significant decrease (p<0.05) in serum levels of IL-6 and TNF-α, along with a notable increase (p<0.05) in IL-10 levels when compared to the DEN group. Although there were in the group treated with *Althaea officinalis* extract, improvements in cytokine levels these changes did not reach statistical significance (p>0.05). However, in the co-treatment groups of *Althaea officinalis* + SIL, particularly the DEN + 500 *Althaea officinalis* + SIL group, all three pro-inflammatory cytokines exhibited a significant reduction (p<0.05) compared to the DEN group and the SIL group. Furthermore, significantly increased the level of the anti-inflammatory cytokine IL-10 (p<0.05) compared to both groups. The combination of *Althaea officinalis* with SIL effectively regulated liver biochemical parameters, improved antioxidant parameters in blood serum, and significantly diminished the levels of pro-inflammatory cytokines (p<0.05). *Althaea officinalis* extract, when given at doses of 250 and 500 mg/kg alongside SIL, resulted in a noteworthy reduction in the number of p53-positive cells (p < 0.05) and a noticeable increase in the number of Bcl-2-positive cells (p < 0.05). This indicates that *Althaea officinalis* has the ability to provide protection to normal cells by regulating the Bax/Bcl-2/p53 and PI3K/Akt/mTOR signaling pathways^{54,55}.

Wound healing activity

A study conducted by Momtaz et al. examined the effectiveness of a polyherbal ointment containing a combination of *L.*

angustifolia, *R. x damascena*, and *Althaea officinalis* for healing grade III skin cuts. In order to assess the wound healing properties of this polyherbal preparation, an ointment was formulated using an extract of *A. officinalis*, *R. x damascena* essential oil (2% essence), and *L. angustifolia* essential oil (2% essence) in a eucerin base (20:20:10:50). The wound excision test was performed for a period of 14 days, and the percentage of healing effect was calculated for each group. The anti-inflammatory activity of the same composition was evaluated using the formalin-induced edema method on the hind paw of rats. The results indicated that the group treated with the polyherbal formulation demonstrated a significantly higher rate of recovery compared to the other groups. These findings were further supported by histological studies, which showed notable advancements in re-epithelialization, angiogenesis, collagen deposition, and reduction in inflammation in the group treated with herbal formulations. The percentages of wound healing were documented as 99.07 ± 0.34, 99.22 ± 0.35, 98.45 ± 0.733, 98.75 ± 0.88, and 63.72 ± 5.64 for the polyherbal composition, *L. angustifolia* extracts, *R. damascena*, *Althaea officinalis*, and placebo groups, respectively. The polyherbal composition demonstrated the highest level of inhibitory activity, which was almost equivalent to that of dexamethasone. However, dexamethasone showed a more potent effect in reducing inflammation caused by formaldehyde compared to the herbal extracts. *L. angustifolia* and *Althaea officinalis* displayed a slower rate of wound healing during the initial 7-day treatment period, but they exhibited notable potential for the healing process by the end of the treatment duration. On the other hand, both *R. x damascena* and the polyherbal formulation effectively enhanced wound healing until day 14. The polyherbal formulation significantly reduced inflammation after 90, 135, and 180 minutes of inducing formalin edema (P < 0.001) when compared to the control and formalin groups. Other herbal extracts have demonstrated similar anti-inflammatory properties, although to a lesser extent than the polyherbal formulation. Furthermore, the wound healing capabilities of the polyherbal mixture have been confirmed through histopathological analysis. This analysis has shown the complete re-growth of epithelial cells, the formation of healthy granulation tissue, and a significant reduction in scarring. Reportedly, such effect could be chiefly ascribed to the antioxidant, anti-inflammatory, and antimicrobial traits of phenolic compounds. These properties contributed to a noteworthy enhancement in re-epithelialization and neovascularization, the neutralization of harmful free radicals, and a reduction in inflammation. Concurrently, a polyherbal concoction amplified the expression of transforming growth factor-β (TGF-β), collagen production, and skin fibroblast differentiation. In addition, the bioadhesive and mucilaginous polysaccharides in *Althaea officinalis* spurred the cellular physiology of epithelial cells and the physical creation of mucin-like atop irritated tissues, leading to the remedy of irritated mucous membranes as part of tissue regeneration. This leads to a speedier re-epithelialization, autolytic debridement, angiogenesis, enhanced migration of keratinocytes, and the generation of endogenous wound healing stimulants, thus providing an optimum condition for wound healing^{56,57}.



A separate study was conducted to assess the impact of *Althaea officinalis* (AO) water-ethanol gel on wound healing in rat models using stereological techniques. In this experiment, 48 male Wistar rats were randomly divided into four groups ($n = 12$): an untreated control group, a group treated with a gel base, and two groups treated with 5% and 10% *Althaea officinalis* gel respectively. The procedures were carried out every 24 hours. Various factors were evaluated, including the rate at which the wounds closed, the volumetric density of collagen bundles, hair follicles, and blood vessels, as well as the length density and average diameter of the vessels, and the population of fibroblasts. The initial size of the wounds in all four groups averaged $104.22 \pm 7.26 \text{ mm}^2$, with no significant differences observed between the groups. The rate of wound closure in the 5%-AO (6.03%/day) and 10%-AO (5.94%/day) groups was significantly higher compared to the control group (3.14%/day) and the group treated with a gel base (3.44%/day) ($p < 0.05$). The numerical density of fibroblasts in the groups that received 5% and 10% *Althaea officinalis* was 112.8% ($p = 0.021$) and 45.3% ($p = 0.049$) higher than that of the control group, respectively. Similarly, it was also 117.8% ($p = 0.018$) and 49.18% ($p = 0.027$) higher than that of the gel base group, respectively. The volumetric density of collagen bundles was significantly higher at 66.2% ($p < 0.001$) and 57.1% ($p < 0.001$) in the 10% *Althaea officinalis* group compared to both the control and baseline groups, respectively. However, there was no significant increase in the volume density of collagen bundles in the 5% *Althaea officinalis* treated group compared to the control and study groups. The volume density of hair follicles in the 5% and 10% *Althaea officinalis* treated groups was significantly higher compared to both the study group ($p = 0.038$ and $p = 0.008$, respectively) and control group ($p = 0.037$ and $p = 0.009$, respectively). On the other hand, there were no significant differences in vessel length and volume density between the 5% and 10% *Althaea officinalis* treated groups compared to the gel base and control groups. However, there were notable distinctions in the average vessel diameter when comparing the groups treated with *Althaea officinalis* to both the control group and the group treated with gel base. Results demonstrated that *Althaea officinalis* extract increases the volume density of collagen fibers and the population of fibroblasts, besides it improves the process of vascularization. It's related with various effects of the anti-inflammatory, antioxidant, and anti-microbial properties, as well as fibroblast proliferation-inducing effect. In addition, extract of *Althaea officinalis* has N-phenylpropenoyl-L-amino acids (NPA) which can stimulate keratinocytes and increases cellular activity of fibroblasts. Moreover, extract of *Althaea officinalis* has antioxidant activity that improves vascular endothelial function and stimulate tissue regeneration of epithelial cells^{58,59}.

Rezaei et al. conducted a study to assess the wound-healing properties of a water-ethanol extract derived from *Althaea officinalis*, comparing it to ciprofloxacin and gentamicin. Using a wound excision model, the researchers measured the percentage of wound healing over several days in three different groups. The results indicated that wounds treated with the hydroalcoholic extract of *Althaea officinalis* healed at a faster

rate compared to the control group. Significant improvement was observed within 6 days of treatment ($p < 0.05$). However, there were no statistically significant differences between the group receiving the hydroalcoholic extract of *Althaea officinalis* L. and the group receiving zinc oxide. The findings also revealed that the group receiving the hydroalcoholic extract of *Althaea officinalis* experienced variations in the connective tissue matrix and notable inflammatory reactions, unlike the other groups. By the 21st day of the experiment, the group that received the hydroalcoholic extract of *Althaea officinalis* displayed a decrease in the density of fibrous tissue cells, a shorter duration of inflammation, and a more advanced stage of granulation compared to the group that used zinc oxide ointment. There were no differences observed in the reorganization of skin tissue components between the two groups. After completing the treatment, both groups demonstrated intact formation of the outermost layer of skin and a reduction in scar size. Pathologically, the tissue samples treated with *Althaea officinalis* extract exhibited good healing characteristics, including a well-structured arrangement, minimal inflammation intensity, and faster recovery time. Wound healing potency of hydroethanolic extract attributed to free radical-scavenging action and the antimicrobial property of the phytoconstituents present in the extract. Hydroethanolic extract contains flavonoides which possess anti-haemorrhage properties which promotes and accelerate the healing processes of epithelial wounds by means of inhibition or activation of the enzymes. Plant-derived antioxidants such as phenolic acids, flavones, and flavonols, could delay or prevent the onset of degenerative diseases because of their redox properties. Moreover, results showed that hydroethanolic extract of *Althaea officinalis* had anti-inflammatory effects and reduced the severity of the inflammation which contribute to the wound healing as^{wel60,61}. A study with a similar focus investigated the efficacy of hydroalcoholic extracts derived from *Althaea officinalis* on the recovery of both large and non-infected wounds in rats. In this study, each extract was given to 50 injured rats for either 7 or 14 consecutive days. The findings from visual observations showed that the hydroalcoholic extracts had the ability to stimulate wound healing, as demonstrated by a significant increase in wound contraction. Additionally, further confirmation of the wound healing potential associated with the *Althaea officinalis* extract was obtained through histopathological examinations^{62,63}.

Valizadeh et al. conducted a study to investigate the effects of *Althaea officinalis* flower mucilage on the healing of wounds. The experiment involved dividing the animals into six groups, each containing five cases. These groups consisted of a control group that received no treatment, a positive control group treated with eucerin, a standard group treated with topical phenytoin at a concentration of 1%, and treatment groups treated with homemade ointment containing different concentrations (5%, 10%, 15%) of *Althaea officinalis* flower mucilage (AFM). The findings indicated that the 15% AFM ointment showed the most favourable results among the treatment groups. When applied topically, it significantly reduced the time required for wound healing. Both the 15%



AFM ointment and the 1% phenytoin group achieved complete closure of the wounds on days 14 and 15, respectively, with no significant difference in healing time between them. Additionally, the 15% AFM ointment was found to effectively reduce wound healing time without any noticeable difference compared to the 1% phenytoin ointment. The optimal recovery based on a macroscopic examination conducted 14 days after the treatment was seen in the 15% AFM ointment group, which had the shortest duration compared to the other groups. After completing the treatment, the macroscopic evaluation showed complete healing and variations in the thickness of the outer layer of skin across different groups. Additionally, the process of angiogenesis, the formation of new blood vessels, was evident. An increase in the number of fibroblasts, cells involved in collagen maturation and precipitation, was observed. Microscopic analysis revealed similar patterns of fibroblasts in all treatment groups, including those treated with 1% phenytoin and 5%, 10%, and 15% AFM ointment. The healing properties of *Althaea officinalis* are due to mucilage components, such as pectin, tannin, and polysaccharides. Tannic acid has the ability to promote the healing of excisional wounds by stimulating the formation of new blood vessels (angiogenesis) and exhibiting antibacterial activity. It also increases the levels of VEGF (vascular endothelial growth factor), which is a powerful and long-lasting stimulator of angiogenesis at wound sites. Tannin and arabinose aid in the healing process by coagulating surface proteins. Pectin plays a crucial role in providing moisture and oxygen at the wound site, which is essential for angiogenesis and epithelialization, while also exerting antibacterial effects. Polysaccharides stimulate the growth of new epithelial cells on the damaged tissue surface^{64,65}.

Antitussive activity

The effectiveness of *Althaea officinalis* in treating dry cough accompanied by irritation of the throat has been the main focus of clinical trials. The age of the patients plays a crucial role in these studies, as *Althaea officinalis* has been used to treat children and infants. One clinical trial observed 822 patients who were experiencing dry cough along with irritation of the throat. The objective was to assess the efficacy, tolerability, and satisfaction of an aqueous extract derived from the root of *Althaea officinalis*. The extract was administered in the form of lozenges and syrup. The patients were instructed to use the medication for a duration of 7 days. The results revealed that both the lozenge and syrup forms of the aqueous extract effectively relieved dry cough symptoms within just 10 minutes. Additionally, the treatment was well-tolerated, with only three minor adverse events reported in the group receiving the syrup⁶⁸.

In a separate investigation, a study was conducted to evaluate the efficacy of *Althaea officinalis* as a cough suppressant in 63 individuals who developed a dry cough due to the use of angiotensin-converting enzyme inhibitor medications. These individuals were divided into two groups and given either 20 drops of *Althaea officinalis* (40 mg) or a placebo every 8 hours for a period of 4 weeks. The severity of the cough was measured using a scale ranging from 0 to 4, and spirometric tests were

performed. The group that received *Althaea officinalis* showed a significant decrease in cough severity, with the average score dropping from 2.66 ± 0.958 to 1.23 ± 1.01 . After the treatment, eight out of the thirty patients in this group reported no cough at all. On the other hand, the placebo group had relatively high scores, with cough severity decreasing from 2.7 ± 0.79 to 2.33 ± 0.84 . No notable changes were observed in spirometry data (such as Forced Vital Capacity, Forced Expiratory Volume in 1 second, FEV1/FVC ratio, and Peak Expiratory Flow between 25% and 75% of vital capacity) for both the *Althaea officinalis* group and the placebo group⁶⁹.

In a post-marketing investigation of 313 children (0–3 years [$n = 100$], 3–6 years [$n = 115$], 6–12 years [$n = 98$]), who were suffering from irritation in the mouth and throat along with a dry cough, researchers examined the efficacy and tolerability of *Althaea officinalis* syrup. The syrup contained 35.61 grams or 76.45 milliliters of an aqueous extract derived from the root of *Althaea officinalis* (at a ratio of 1:19.5–23.5) per 100 grams of syrup. Over an average span of 3 days, the children were administered a dosage of 2.5–10 milliliters of syrup, taken 4–6 times daily. The study evaluated various symptoms including the severity and frequency of coughs, cough intensity during the day, as well as other cough-related symptoms such as difficulty in falling asleep, quality of sleep, neck pain, chest pain, and accompanying symptoms like catarrh and fever. The findings revealed that the treatment was highly effective and well-tolerated in 84.3% and 97% of cases, respectively. However, there were two instances of reported side effects, such as obstructive bronchitis and bronchopneumonia in the age group of 0–3 years⁷⁰.

In a retrospective observational study, the effectiveness of the *Althaea officinalis* syrup was assessed in 599 children (divided into various age groups: 0–3 months [$n = 61$]; 3 months to 3 years [$n = 128$]; 3–6 years [$n = 128$]; 3–6 years [$n = 61$]; $n = 188$]; 6–12 years [$n = 222$]) who experienced irritation in their mouth and throat mucous membranes, accompanied by a dry cough. The syrup was administered to the children at doses of 1–5 ml, 1–6 times daily, for a period of 3–14 days. The treatment demonstrated high effectiveness or effectiveness in 90% of cases. No adverse effects were reported during the study⁷¹.

In another clinical trial involving 60 patients who were experiencing cough associated with acute bronchitis, a double-blind method was utilized. The patients were randomly divided into two groups ($n = 30$) - one group receiving a placebo and the other group receiving herbal oral drops. The herbal oral drops contained 15 drops with 40 mg of *Zingiber officinalis* and 300 mg of hydroalcoholic extract of *Althaea officinalis*, while the placebo group received oral drops without any active ingredients. The patients were instructed to take the drops every 6 hours for a duration of 10 days. To assess the efficacy of the treatment, the patients were evaluated using a questionnaire that included measurements of cough severity, frequency of nighttime coughing attacks, frequency of waking up due to cough, and chest pain. After the treatment was finished, it was noted that a mere 2.7% of the patients who were administered the herbal oral drops reported experiencing

chest discomfort, compared to 50% of the patients in the placebo group who reported chest pain. Moreover, the herbal oral drops led to an 80% decrease in the severity of cough, whereas the placebo group experienced a 60% reduction in cough severity. Nevertheless, there was no noteworthy disparity between the two groups when it came to bone pain and muscle pain⁷².

In a separate investigation, a study was conducted to evaluate the effectiveness of a solution that contained extracts from *Zataria multiflora* and *Althaea officinalis*. The study included 200 patients who were suffering from a common cold and cough. The main objective was to compare the efficacy of this herbal solution with that of dextromethorphan syrup, which was administered three times a day for four consecutive days. The results showed that the herbal syrups led to a 65.5% improvement in cough symptoms, while dextromethorphan achieved a 39.4% improvement ($p = 0.001$)⁷³.

In a clinical trial of similar nature, the efficacy of a 5 mL dosage of herbal syrup containing an extract of *Zataria multiflora* combined with *Althaea officinalis* was examined in comparison to dextromethorphan syrup for patients (aged 10-85 years) suffering from persecutory and idiopathic cough. The trial assessed the visual analogue score (VAS) value and the improvement in cough before and after 24, 48, and 72 hours of treatment. At the beginning of the treatment, there were no significant variations between the two groups in terms of demographic characteristics, cough duration of less than 3 days, and VAS scores. However, a notable decrease in cough severity was observed at all stages following the treatment. After 96 hours, both patients receiving the herbal syrup and those receiving the dextromethorphan syrup experienced a similar improvement in cough. The corresponding VAS scores were 2.67 and 2.4, respectively⁷⁴.

In other clinical trial of 62 patients (16–89 years) with irritant cough associated with colds ($n = 29$), bronchitis ($n = 20$), and mucus-forming respiratory diseases ($n = 15$) assessed efficacy and safety. herbal syrup containing dry alcoholic extract, ivy leaf extract, infusions of thyme, anise and aqueous macerate of *Althaea ra dix mucus*. The recommended dosage was 1–2×5 ml per day for adults and 1–3×2.5 ml per day for children 6–12 years old. Changes in cough and expectoration parameters were used to assess effectiveness. Methods of exposure were based on safety. Patients used the syrup for 3–23 days, with an average duration of 12 days. At the end of treatment, improvement in symptom scores was observed. Efficacy and safety were rated as very good 86 and 97% of practicing physicians. One case of an undesirable effect (vomiting while eating) was reported⁷⁵.

CONCLUSION

Althaea officinalis, a well-known traditional herbal plant, is readily available and widely used. Recent research efforts have successfully identified numerous chemical components of *Althaea officinalis*, including flavonoids, polysaccharides, phenolic acids, coumarins, and steroids. These diverse chemical

compounds contribute to the plant's various pharmacological properties, such as its ability to alleviate coughs, reduce inflammation, provide antioxidant effects, fight against bacterial infections, and promote wound healing. Previous studies have also provided scientific evidence supporting the use of *Althaea officinalis* in both traditional and modern medicine for treating various ailments. However, more such trials are required to establish and validate the ethnopharmacological profile of *Althaea officinalis*. Subsequent investigations, therefore, need to be carried out on clinical disease models to test and confirm the herb's effectiveness in dealing with various diseases. It's crucial to mention that the curative actions of plants or their extracts come without adverse effects, unlike certain other medicinal agents used for identical health conditions. One significant drawback of using raw extracts for treatment is the insufficiency of active components in the extract required to trigger a sufficient therapeutic response. This issue can be addressed by identifying the active element responsible for its therapeutic impact and synthesising it on a larger scale, paving the way for further therapeutic and toxicity studies. Even though these active ingredients are sourced from nature, potential harmful side effects may emerge if they are consumed at high levels to achieve therapeutic outcomes. Future studies should focus on identifying the active elements within *Althaea officinalis*, and subsequently, their large-scale production, analysis of chemical characteristics, therapeutic assessments, and toxicity tests. This will facilitate the molecular modification of these active ingredients for the development of an appropriate treatment method suitable for mass production. Additionally, incorporating *Althaea officinalis* as a supplement to chemotherapy drugs could be considered, resulting in a reduction in the required quantities of synthetic drugs and consequently, lessening their harmful effects. Moreover, it is crucial to perform detailed mechanistic studies to uncover the underlying ways this esteemed medicinal plant works, thus confirming traditional knowledge surrounding this highly regarded medical plant. Enhancements in current extraction techniques, drug standardisation protocols and future clinical investigations on the health-promoting qualities of this herb would further broaden its practical applications. This review may serve as a valuable resource for researchers and scientists conducting further research on the potential of *Althaea officinalis* essential oil.

AUTHORS' CONTRIBUTIONS

Conceptualization, Baikun Baimakhanova, Amankeldi Sadanov, Irina Ratnikova; formal analysis and visualization, Saltanat Orasymbet, Erik Shorabaev, Gul Baimakhanova, Alma Amangeldi, Zhanat Toxanbayeva; writing—original draft preparation, Klara Zhumalina, Aigul Ibragimova, Rabiga Anarbayeva, Nesipkul Asylova; writing—review and editing, Kapassova Zaru and Aknur Turgumbayeva;

CONFLICTS OF INTEREST

The authors declare no conflict of interest.



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