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Medical benefit of *Malva neglecta* – A review

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Abstract: *Malva neglecta* is a common traditionally used medicinal plant, contained alkaloids, tannins, saponins, hydroxycinnamic acids, flavonoids, flavonols, proanthocyanidins, anthocyanins, organic acids, protein, oils and sugars. It possessed antimicrobial, antioxidant, anti-inflammatory, anti-ulcerogenic, hepatoprotective, anti-urolithiasis, anticholinesterase and angiotensin converting enzyme, α-amylase, α-glucosidase and pancreatic lipase inhibitory inhibitory effects. This review will highlight the chemical constituents and pharmacological effects of *Malva neglecta*.

Keywords: constituents, pharmacology, *Malva neglecta*

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I. INTRODUCTION

As a result of accumulated experience from the past generations, today, all the world's cultures have an extensive knowledge of herbal medicine. Two thirds of the new chemicals identified yearly were extracted from higher plants. 75% of the world's population used plants for therapy and prevention. In the US, where chemical synthesis dominates the pharmaceutical industry, 25% of the pharmaceuticals are based on plant-derived chemicals[(1)]. Recent reviews revealed that the medicinal plants possessed central nervous, cardiovascular, antioxidant, reproductive, gastro-intestinal, respiratory, antidiabetic, galactagogu, antimicrobial, antiparasitic, dermatological, anticancer, anti-inflammatory, antipyretic and analgesic, immunological, hepato and reno-protective and many other pharmacological effects[(2-40)]. *Malva neglecta* is a common traditionally used medicinal plant, contained alkaloids, tannins, saponins, hydroxycinnamic acids, flavonoids, flavonols, proanthocyanidins, anthocyanins, organic acids, protein, oils and sugars. It possessed antimicrobial, antioxidant, anti-inflammatory, anti-ulcerogenic, hepatoprotective, anti-urolithiasis, anticholinesterase and angiotensin converting enzyme, α-amylase, α-glucosidase and pancreatic lipase inhibitory inhibitory effects. This current review highlighted the chemical constituents and pharmacological effects of *Malva neglecta*.

Plant profile:
Synonyms:
Malva neglecta is the only accepted name of this species[(41)].
Taxonomic classification:
Kingdom: Plantae, **Subkingdom**: Tracheobionta, **Superdivision**: Spermatophyta, **Division**: Magnoliophyta, **Class**: Magnoliopsida, **Subclass**: Dilleniidae, **Order**: Malvales , **Family**: Malvaceae, **Genus**: *Malva*, **Species**: *Malva neglecta*[(42)].
Common names:
Arabic: Khubbaizah; **English**: common mallow, dwarf mallow; **German**: Käsepappel, Weg-Malve; **Swedish**: skär kattost; **Turkey**: ebegumeci, develik, gomec, komec, ebegomeci, tolık[(43-44)].

Distribution:

It is native to **Africa** (Macaronesia, Algeria, Morocco); **Asia** (Saudi Arabia, Azerbaijan, Georgia, China, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan, Mongolia, Afghanistan, Iran, Iraq, Palestine, Jordan, Lebanon, Syria, Turkey, India, Pakistan); **Europe** (Belarus, Lithuania, Moldova, Ukraine, Austria, Belgium, Czech Republic, Germany, Hungary, Netherlands, Poland, Slovakia, Switzerland, Denmark, Ireland, Norway, Sweden, United Kingdom, Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Greece, Italy, Macedonia, Montenegro, Romania, Serbia, Slovenia, France, Portugal, Spain); and has become naturalised outside its native range, in temperate regions[(43)].

Distribution:

Herbs biennial, 50-100(-120) cm tall; stem sparsely stellate velutinous. Stipules ovate-lanceolate, 3-5 × 2-4 mm, stellate puberulent; petiole 2-8(-15) cm, puberulent in adaxial groove, glabrescent; leaf blade reniform or round, (3-)5-11 × (2-)5-11 cm, both surfaces very sparsely strigose or subglabrous, 5-7-lobed, lobes rounded or acute, margin crenate-serrate. Flowers 3- to many-fascicled, axillary. Pedicels 2-15(-40) mm. Epicalyx lobes

filiform- lanceolate, (3-)5-6 mm, ciliate. Calyx cup-shaped, 5-8 mm, lobes broadly triangular, sparsely stellate strigose. Corolla whitish to reddish, slightly longer than sepals; petals 6-8 mm, apex retuse; claw glabrous or sparsely hairy. Filament tube 3-4 mm, glabrous or with a few simple hairs. Style branches 10-11. Schizocarp flat-globose, 5-7 mm in diam.; mericarps 10-12, abaxially smooth, ca. 1 mm thick, angles rounded and rugose, sides reticulate. Seeds purple-brown, reniform, ca. 1.5 mm in diam., glabrous[45].

Traditional uses:

Due to its high mucilage content, it was used as soothing demulcent herbs, especially for cases of inflammation, either for the urinary, digestive or respiratory systems. Pregnant women or new mothers used mallow leaves as a source of iron, zinc and vitamins. *Malva neglecta* was substituted for spinach in many dishes, including soups, salads, gnocchi and quiche[46].

Leaves and flowers were used for the treatment of constipation, sore throat, women sterility, wound, hemorrhoids, miscarriage swellings, rheumatic pain, stomachache, abdominal pain, abscess, renal diseases, cough, throat infection, common cold, bronchitis, peptic ulcer and indigestion. Stems and roots were used as abortifacient[47-49].

Malva neglecta was used in the treatment of common cold and to relieve cough in different parts of Iran. It was also used as a valuable and useful medicine to relieve the bruise, inflammation and mosquito bite. It was consumed for the treatment of urinary tract or digestive system diseases as well[50]. The pulverized mallow seeds are used to treat bladder ulcers and coughs[51].

In Italy the plant was used as tea in inflammation and as a gargle in sore throat. It also was also used to treat acne, broken bones, help in abdominal pain and to treat swelling, dermatitis, burns and throat infection[52-53].

Malva neglecta fruit was an edible traditional medicinal plant used in Anatolia to cure multiple medical conditions such as asthma, stomachache and diarrhea. It also used to promote maturation of abscesses, in wound healing, abdominal pains and cancer[54-55]. The plant was also used in mild cathartic[56].

Parts used medicinally:

Fruits, roots, stems, leaves, flowers and seeds[47-49, 51].

Physecochemical characteristics:

The physecochemical characteristics of *Malva neglecta* leaves gum were: moisture 0.43%, nitrogen 1.37% crude protein 0.62%, total ash 0.30%, whole sugar 0.83%[57].

Chemical constituents:

The preliminary analysis showed that *Malva neglecta* contained alkaloids, tannins, saponins, hydroxycinnamic acids, flavonoids, flavonols, proanthocyanidins, anthocyanins, organic acids, protein and sugars[55, 57-59].

Forty one components were identified in the essential oils, constituting 95.0% of the essential oil composition of *Malva neglecta* (whole plants in flowering stage). The main constituents of the essential oil were cineole, hexatriacontane, tetratetracontane and α-selinene. However, the identified compounds (%) were: octane 1.7, isononane 1.3, α-pinene 1.6, camphene 1.1, β-pinene 2.9, β-Myrcene 0.8, limonene 1.0, cineole 18.8, 2-methyl decane 0.8, camphor 1.4, 1,3-di-tert butyl benzene 2.4, carvone oxide 0.8, anethole 2.2, valencene 1.7, α-selinene 4.2, β-Himachalene 1.2, α-muurolene 0.9, cadalene 1.1, 2-methyl heptadecane 1.6, octadecane 1.6, 2-methyl-1-hexadecanol 2.3, hexadecanoic acid 0.9, heneicosane 1.8, 1-nonadecanol 1.8, butyl phthalate 1.1, 2-eicosanol 1.8, Z-8-octadecen-1-ol acetate 1.4, docosane 1.3, 9-hexyl heptadecane 0.7, 2,5-Di-tert octyl-p-benzoquinone 4.0, arachidic acid 1.3, tetracosane 2.3, 3-ethyl-5-(2-ethylbutyl)octadecane 1.5, heptacosane 0.8, 1-hexacosanol 2.8, choleic acid 0.9, nonacosane 1.3, ethyl iso-allocholate 0.8, 17-pentatriacontene 1.5, hexatriacontane 7.8 and tetratetracontane 7.8[44].

Fatty acid compositions of *Malva neglecta* (whole plants in flowering stage) (%) were: 10-undecenoic acid 1.6, myristic acid 7.8, palmitic acid 36.8, phytol 2.9, linoleic acid 17.8, oleic acid 4.6, linolenic acid 13.2, stearic acid 6.8, arachidic acid 2.3, 6-hexadecenoic acid 2.3, behenic acid 1.8, saturated fatty acids 55.5 and unsaturated fatty acids 42.4[44].

The chemical analysis of the essential oils of the aerial parts of *Malva neglecta* from Torbat-e Heydarieh region-Iran, showed that they characterized by high percentage of spathulenol (27.0%), 1,7-diepi-α-cedrenal (10.6%), valencene (6.0%), tetrametyl neophytadiene (4.1%) and carotol (3.7%) represented the most abundant compounds. Oxygenated sesquiterpenes (49.8%) constitute about half of the total constituents followed by non-terpene hydrocarbons 26.2%, sesquiterpene hydrocarbons 6.0%,, dieterpene hydrocarbons 4.0% and oxygenated monoterpenes 2.0%[60].

The totol phenolics in the methanol extract of *Malva neglecta* (whole plants in flowering stage) was 68.29±0.14 μg pyrocatechol equivalents /mg extract and the total flavonoides was 15.58±0.19 μg quercetin

equivalents /mg extract. The phenolic compounds identified in the methanol extracts of *Malva neglecta* were: quinic acid 155.93±7.44, malic acid 13108.97±694.77, tr-Aconitic acid 284.98±13.91, protocatechuic acid 282.76±14.38, caffeic acid 70.38±3.65, p-coumaric acid 263.32±13.41, 4-OH benzoic acid 1694.92±88.09 and salicylic acid 1456.04±72.80µg /g extract[44].

The total phenolics (mg GAE/g DW), hydroxycinnamic acids (mg CAE/g DW), flavonoids (mg RE/g DW), flavonols (mg RE/g DW), proanthocyanidins (mg CE/g DW) and anthocyanins (mg C3-GE/g DW) contents in the root extract of *Malva neglecta* were 3.4 ± 0.3 0.48 ± 0.04, 0.97 ± 0.02, 0.52 ± 0.03, 0.004 ± 0.003 and 0.05 ± 0.01; in the stem extract were: 4.8 ± 0.1, 0.64 ± 0.01, 1.34 ± 0.10, 0.86 ± 0.03, 0.007 ± 0.001 and 0.05 ± 0.01; in the leaf extract were: 17.4 ± 0.3, 2.56 ± 0.06, 7.21 ± 0.28, 4.88 ± 0.21, 0.027 ± 0.003 and 0.65 ± 0.01; in the flower extract were: 11.6 ± 0.5, 1.85 ± 0.03, 5.43 ± 0.56, 3.00 ± 0.11, 0.015 ± 0.001 and 0.35 ± 0.04; in the fruit extract were: 5.0 ± 0.3, 0.88 ± 0.03, 2.63 ± 0.28, 1.43 ± 0.05, 0.027 ± 0.001 and 0.33 ± 0.01; and in the whole plant were: 6.6 ± 0.3, 0.95 ± 0.01, 2.95 ± 0.16, 1.46 ± 0.04, 0.011 ± 0.001 and 0.15 ± 0.02 respectively[55].

The lyophilized ethanol-based hydrophilic extract of *Malva neglecta* fruits was investigated for phenolic composition. Flavonoid glycosides were detected as the major phenolic compounds. Traces of rutin, chlorogenic acid, hydroxybenzoic acid and hydroxybenzoic acid-*O*-hexoside were detected in the extract[54].

Many organic acids were identified in the extracts of *Malva neglecta* included oxalic, quinic, malic, citric, succinic and fumaric acids[59].

Pharmacological effects:

Antimicrobial effect:

Malva neglecta acetone extract (whole plants in flowering stage) possessed antibacterial activity when used at concentration of 10, 20, and 30 mg/ml, the lowest concentration (10 mg/ml) showed inhibitory zones of 12±0.3, 12±0.1, 11±0.3, 10±0.1 and 16±0.2 mm against *Escherichia coli, Streptococcus pyogenes, Staphylococcus aureus, Pseudomonas aeruginosa* and *Candida albicans* respectively. Methanolic extract also showed antibacterial at the same concentrations, the lowest concentration (10 mg/ml) showed inhibitory zones of 10±0.2, 11±0.1, 10±0.2, 12±0.1 and 12±0.3 against the same pathogens respectively[44].

The antimicrobial activity of *Malva neglecta* was studied against 3 isolates of *Pseudomonas aeruginosa*, and one isolate of *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Staphylococcus aureus* and *Streptococcus pyogenes.* The aqueous extract of the leaves of *Malva neglecta* did not possess antibacterial effect against the tested bacterial isolates, the methanol extract clearly demonstrated an ability to inhibit the growth of the tested isolates. The methanol extract of the plant was also capable of inhibiting the formation of biofilms by many of the tested clinical isolates[61].

All extracts of *Malva neglecta* (crude, n-hexane, chloroform, ethyl acetate and aqueous) possessed antibacterial effect against *Klebsiella pneumoniae* (12.5-19 mm) and *Salmonella typhi* (11-14.5mm), all extracts except ethyl acetate extract showed antibacterial activity against *Bacillus subtilis* (12-18mm), only chloroform and aqueous extracts showed antibacterial activity against *Escherichia coli* (12 and 10 mm respectively) and all extracts showed no activity against methicillin resistant *Staphylococcus auerus*. All extracts possessed antifungal activity against *Aspergillus flavus*, All extracts except hexane extract showed activity against *Aspergillus niger* and *Fusarium solani*, while only crude and aqueous extracts possessed antifungal activity against *Aspergillus fumigates*[62].

The antibacterial activity of *Malva neglecta* ethanolic flower extract (0.05-4.0 mg/ml) was investigated against *Bacillus anthracis, Bacillus cereus, Staphylococcus aureus, Staphylococcus epidermidis, Listeria monocytogenes, Streptococcus pyogen, Escherichia coli, Salmonella typhi, Klebsiella pneumonia* and *Pseudomonas aeruginosa.* The extract possessed antibacterial activity against *Bacillus anthracis* (8-10 mm), *Staphylococcus aureus* (8-13 mm), *Staphylococcus epidermidis* (13-22 mm), *Pseudomonas aeruginosa* (7-10 mm), while other tested bacteria were resistant[663].

The ethanol, chloroform and aqueous extracts of *Malva neglecta* possessed wide range of antimicrobial activity. MICs of the ethanolic extract against *Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus pyogenes, Proteus vulgaris, Aspergillus niger, Aspergillus fumigates* and *Candida albicans* were 0.70, 0.60, 0.60, 0.75, 0.80, 1.00 and 0.95 mg/ml, MICs of chloroform extract were 0.95, 1.00, 0.95, 1.20, 0.80, 1.00 and 0.95 mg/ml and MICs of aqueous extract were 0.90, 0.90, 0.90, 0.90, 0.70, 0.95 and 0.90 mg/ml, respectively[64].

The methanol extract of *Malva neglecta* possessed antibacterial effects against *E. coli* (12mm), *Salmonella spp* (14mm), *Shigella spp* (31mm) and *Clostridium spp* (16mm), while it showed no activity against *Klebsiella spp*[65].

The ethanolic extract of *Malva neglec*ta possessed antibacterial activity against antibiotic-resistant *Staphylococcus aureus*. MIC and MBC of the extract were 6.5 and 13 mg/ml respectively[50].

Antioxidant effect:

Acetone, methanol, and petroleum ether extracts of *Malva neglecta* (whole plants in flowering stage) were tested for antioxidant activity using *β*-carotene-linoleic acid test system, DPPH free radical, ABTS cation radical scavenging activity and cupric reducing antioxidant capacity (CUPRAC) methods. The extracts showed good lipid peroxidation activity (IC_{50}: 45.92, 23.42 and 29.62 µg/ml, respectively). The methanolic extract showed moderate activity (IC_{50}: 60.51 µg/ml) in DPPH free radical scavenging activity. Methanolic and water extracts showed IC_{50}: 45.81 and 55.02 µg/ml in ABTS cation radical scavenging assay, respectively[44].

The lyophilized ethanol-based hydrophilic extract of *Malva neglecta* fruits was tested for *in vitro* antioxidant capacity (FCR, FRAP and ORAC assays) and enzyme inhibitory activities. The extract exhibited pronounced Folin–Ciocalteu reducing activity (12.8 ± 0.7 mg gallic acid Eq/g DW), ferric reducing antioxidant power (174.3 ± 9.8 µmol Fe^{2+}/g DW) and oxygen radical scavenging activity (1656.9 ± 69.7 µmol Trolox Eq/g DW)[54].

The antioxidant activity of hydroalcoholic solution extracts of *Malva neglecta*, *Urtica dioica* and their mixture was studied using *in vitro* models. Both extracts exhibited strong total antioxidant activity. At the concentration of 100 µg/ml, hydroalcoholic extracts of *Urtica dioica* seed, *Urtica dioica* root, *Urtica dioica* flower, *Urtica dioica* leaf, *Malva neglecta* flower, *Malva neglecta* leaf, and *Urtica dioica* + *Malva neglecta* showed 81.7%, 79.8%, 78.3%, 76.4%, 77.3%, 74.1%, and 80.7% inhibition on peroxidation of linoleic acid emulsion, respectively compared with 100 µg/ml of standard antioxidants BHA, BHT and *α*-tocopherol which exhibited 66.2%, 70.6%, and 50.1% inhibition by the same test, respectively. *Urtica dioica* + *Malva neglecta* showed strong superoxide anion radical scavenging activity compared with *Urtica dioica* root, *Urtica dioica* flower, *Urtica dioica* leaf, *Malva neglecta* flower, and *Malva neglecta* leaf extracts[66].

The antioxidant effect of the leaves, stems, flowers and roots extracts of *Malva neglecta* was studied using oxygen radical absorbance capacity (ORAC assay) and total reducing capacity (ferric reducing antioxidant power and FRAP assay). The total reducing capacity (FRAP assay) ranged from 190.3 ± 6.7 (leaf) to 39.2 ± 1.2 µmol Fe^{+2}/gDW (root), ORAC values ranged from 898.9 ± 14.9 (flower) to 425.3 ± 6.7 (root) µmol TE/gDW[55].

Antiinflammatory effect:

The effect of aqueous extract of *Malva neglecta* extract on the main inflammatory biomarkers in osteoarthritis was studied in synoviocytes and and THP -1 cells as a model of monocyte/ macrophage and human cartilage cells in osteoarthritis. Lipopolysaccharide (LPS) was used to induce production of inflammatory cytokines in both cells. *Malva neglecta* extract reduced TNF-α, IL-1β, iNOS, IL-18 and COX-2 expression in synoviocytes. Expression of all of these factors was also reduced by the extract in THP-1 cells. Furthermore, the production of PGE_2 and NO in the LPS-induced THP-1 cells was also reduced by *Malva neglecta* extract[67].

The effect of *Malva neglecta* on reducing the production of inflammatory mediators (inflammatory cytokines IL-1B, TNF-α, PGE2) was also investigated in lipopolysaccharide stimulating chondrocytes and monocytes like cells/ human macrophages. The aqueous extract of *Malva neglecta*, effectively suppressed the expression of pro-inflammatory cytokine genes. The expression of cytokine TNF-α gene decreased to 95.04%, the expression of cytokine IL-1B gene decreased to 73.81% and the expression of COX-2 gene decreased to 93.79% in the presence of the aqueous extracts of *Malva neglecta* and LPS [68].

Anti-ulcerogenic effect:

The anti-ulcerogenic potential of the extract of aerial parts of *Malva neglecta* was investigated in ethanol-induced ulcerogenesis in rats. *Malva neglecta* extract was nearly completely protected rat stomach from any visible damage. It induced 81.9% inhibition at a dose of 1243 mg/kg bw. Histologically, animal group treated with *Malva neglecta* extract, showed regenerative improvements of the lamina epithalis [69].

Hepatoprotective effect:

The hepato-protective effect of *Malva neglecta* hydroethanolic extract (300and 600 mg/ kg) was investigated in rats. The serum liver enzymes were increased in rats intoxicated with CCl_4 compare to the control group ($p<0.001$) and decreased significantly in rats treated with the extract ($p<0.01$). Histological finding revealed that CCl_4 caused hepatic tissue necrosis, while the extract reduced necrosis and enhanced hepatocytes regeneration[70].

Anti-urolithiasis effects effect:

The anti-urolithiasis effects of aqueous extracts of *Malva neglecta* (intraperitoneal injections of 200 and 800 mg/kg for 28 days) was investigated in ethylene glycol and ammonium chloride induced kidney stones in rats. The extract significantly decreased CaOx deposits and tubule-interstitial damage ($p<0.001$) in the

preventive groups. In curative groups, a low dosage of extract, reduced kidney oxalate deposits and tubule-interstitial damage ($p<0.05$). However, high dosed was more effective in both preventive and curative groups ($p \leq 0.001$)[71].

Anticholinesterase activity:

Extracts (methanol, petroleum ether and acetone) of *Malva neglecta* (whole plants in flowering stage) showed moderate activity against acetyl-and butyryl-cholinesterase enzymes. Methanol extract exerted the highest activity among all the tested extracts against acetyl-and butyryl-cholinesterase enzymes. At 200 µg/ml methanol extract possessed (53.68 and 63.95% inhibition), acetone extract (38.65±1.39 and 57.69±0.63% inhibition) and petroleum ether extract showed (30.13±1.32 and 43.68±1.12 % inhibition) against acetyl- and butyryl- cholinesterase enzymes respectively[44].

Angiotensin converting enzyme inhibitory effect:

In studying of the angiotensin converting enzyme suppressive effect of six traditional medicinal tea (*Verbascum cheiranthifolium, Anchonium elrichrysifolium, Plantago lanceolata, Phlomis armeniaca, Phlomis armeniaca, Malva neglecta* and *Salvia limbata*) infusions. The highest angiotensin converting enzyme inhibitory activity was displayed by *Malva neglecta* (34.0%) herbal infusions at the concentration of 0.6 mg/ml[55].

α-amylase, α-glucosidase and pancreatic lipase inhibitory effects:

The lyophilized ethanol-based hydrophilic extract of *Malva neglecta* fruits was weakly suppressed the activity of α-amylase (IC_{50}: 15.2 ± 0.8 mg/ml), α-glucosidase (IC_{50}: 14.19 ± 0.10 mg/ml) and pancreatic lipase (IC_{50}: 17.55 ± 0.20 mg/ml)[54].

Side effects and toxicity:

The side effects of *Malva neglecta* hydroalcoholic extract (200 and 500 mg/kg/day) were studied in comparison with prostodin on kidney tissue in rats. Creatinine and urea levels decreased significantly in the groups treated with *Malva neglecta* extract and increased significantly in the group receiving prostodin ($p<0.05$). Histopathologically, glomerular hypertrophy was observed in the rats treated with prostodin, while, in the groups treated with *Malva neglecta*, the glomeruli structure appeared normal, with tubular damage in some tubes[56].

II. CONCLUSION

Malva neglecta possessed wide range of pharmacological effects included antimicrobial, antioxidant, anti-inflammatory, anti-ulcerogenic, hepatoprotective, anti-urolithiasis, anticholinesterase and angiotensin converting enzyme, α-amylase, α-glucosidase and pancreatic lipase inhibitory inhibitory effects. The current review discussed the chemical constituents and pharmacological effects of *Malva neglecta* .

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