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A mini-review on phytochemistry and pharmacological activities of *Scrophularia striata*

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ABSTRACT

Introduction: *Scrophularia striata* (Scrophulariaceae) is an important medicinal plant in Iran and in Iranian folk medicine it has been used for variety of disorders. The present article aims to provide a review at the studies done on phytochemistry and pharmacological effects of S. striata.
Methods: This mini review is based on a literature study of scientific journals from electronic sources, such as Science Direct, PubMed, Google Scholar, Scopus and Web of Science.
Results: The main chemical constituents which have been isolated and identified from Scrophularia striata are cinnamic acid, some flavonoids such as quercetin, isorhamnetin-3-O-rutinoside and nepitrin and one glycoside (acteoside1). This plant possesses anti-inflammatory, antibacterial, antioxidant, anticancer, analgesic and neuroprotective effects. In addition it accelerates wound healing process
Conclusion: *Scrophularia striata* has a potential for the treatment of several diseases and disorders, but there are only a few studies done to investigate the plant phytochemistry, thus further studies should be focused on isolation and identification of active compounds with pharmacological activities. Besides, the majority of pharmacological studies have been performed using aerial parts of plant, thus further studies are needed to investigate bioactivity of other parts of the plant.

Implication for health policy/practice/research/medical education:
The results of this review revealed that *S. striata* provides a wide range of research possibilities. This plant has potential to be used as a therapeutic agent in several clinical conditions such as inflammatory disorders, wounds, burns, anxiety and cancer and its bioactive compounds are potential candidates for drug development.
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Introduction

Scrophularia striata (Scrophulariaceae) is a perennial herbaceous plant found in western parts of Iran. This plant has different common names in different regions including Teshneh dari, Benjek mashineh and Benj ghan. It is well known among people who live in western parts of Iran. They claim that the plant is able to cure various conditions such as conjunctivitis, otitis, gastritis, common cold, hemorrhoids, infectious wounds and burns (1-3). All parts of plant have been used in tradition medicine. The aqueous extract of aerial parts of the plant is particularly used to treat second and third grade burns. Topical application of *S. striata* significantly accelerate the healing of burn injury with minimal scar formation. Several studies have been performed to reveal pharmacological potentials of *S. striata* during last decade. The aim of this review is to summarize the available information so that smooth the way for future researches.

Chemical composition

Only a few studies have been performed to investigating the chemical composition of *S. striata*. In one study the phytochemistry of this plant was investigated using gas chromatography-mass spectrophotometer analysis and the results of this study indicated that the ethanolic and aqueous extracts are rich in Bis (2-ethylhexyl) phthalate (25.17%, 25.855% respectively) and hydroalcoholic extract rich in oleyl alcohol (24.81%) (**4**). In a study

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performed by Mahboubi et al, the total phenolic content and total flavonoids of crude extracts of aerial parts of *S. striata* were determined by using the Folin-Ciocalteu spectrophotometric and the modified aluminum chloride colorimetric methods respectively (5). According to the results of this study the total phenolic contents in the ethanolic (79.7 mg gallic acid equivalent (GAE) /g) and ethyl acetate (65.5 mg GAC/g) extracts were higher than those of methanolic (49.1 mg GAC/g) and aqueous extracts (36.6 g GAC/g). In the ethyl acetate extract the total flavonoid content (27.5 mg quercetin/g) was greater than those of ethanolic (9.8 mg quercetin/g), methanolic (8.2 mg quercetin/g) and aqueous extracts (5.1 mg quercetin/g). Monsef-Esfahani et al isolated five compounds including cinnamic acid, quercetin, isorhamnetin-3-O-rutinoside and nepitrin and acteoside1 from aerial parts of *S. striata* Boiss. by using chromatographic methods. In this study the structures of isolated compounds were determined using spectroscopic techniques (Figure 1) (6). The phytochemical screening of *S. striata* was carried out by Azadmehr et al using thin layer chromatography which revealed the presence of phenyl propanoids, phenolic compounds and flavonoids in the ethanolic extract of this plant (2).

Pharmacological activities

Antimicrobial effects

Ethanolic, aqueous, methanolic and ethyl acetate extracts of *S. striata* whose antimicrobial activities were analyzed by the micro broth dilution assay, displayed activity against *Staphylococcus aureus, S. saprophyticus, S. epidermidis,* oral *Streptococcus sp (S. mutans, S. sobrinus, S. sanguis), Candida sp (C. albicans, C. glabrata)* and *A. parasiticus.* The ethanolic extract showed more antimicrobial activity than other extracts (7).

Sharafati-Chaloshtori et al focused on antibacterial activity of ethanolic extract obtained from aerial parts of *S. striata* against *Escherichia coli*. The ethanolic extract (100, 200 and 400 mg/mL) exhibited significant activity against *E. coli* (inhibition zones were 12±0.8, 14±0.8 and 16±0.8 mm, respectively). The aqueous extract had no activity against *E. coli* (7).

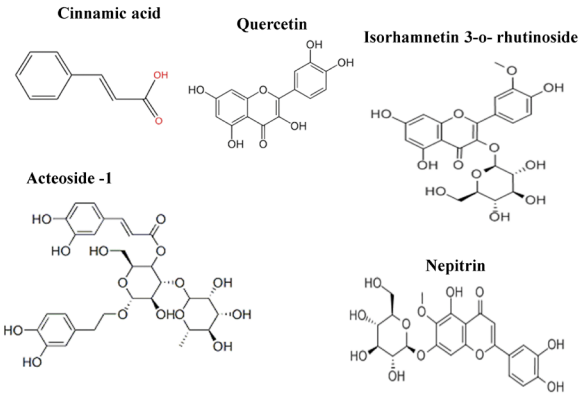

Figure 1. The chemical structure of some compounds isolated from *Scrophularia striata*.

The activities of crude extract obtained from aerial parts of *S. striata* against 50 resistant *Pseudomonas aeruginosa* were evaluated by Ayobi et al. The results of this study indicated that the antibacterial activity of water and methanol fractions was higher than that of crude extract. Water extract was also more potent as compared to methanol fraction (8).

Antibacterial activity of *S. striata* against *S. aureus* was reported by Zamanian-Azodi et al (9).

The results of a study performed by Ardeshiry Lajimi et al revealed that aqueous extract of *S. striata* (1-20 µg/mL) inhibited the growth of *E. coli* and *S. aureus* (10).

Zahiri et al reported the therapeutic effects of ethanolic extract of *S. striata* against localized cutaneous leishmaniasis due to *Leishmania* major (11).

Antiproliferative activity

Ardeshiry Lajimi et al investigated the effects of *S. striata* on the growth of astrocyte cancer cell line (1321). Their findings demonstrated that filtered leaf extract of *S. striata* had antiproliferative activity against 1321N1 cell line (12).

Azadmehr et al reported the *in vitro* anticancer activity of *S. striata* extract in human leukemia cell line (2).

Frahmandzad et al evaluated the effects of *S. striata* extract on expression of *Bax* (BCL2 Associated X, Apoptosis Regulator) gene in homo sapiens brain glioblastoma cells. Their findings indicated that the *S. striata* (0.1 mg/mL) could alter the *Bax* gene expression thereby inducing apoptosis in brain glioblastoma cells (1).

Healing effects

The wound healing activity of *S. striata* extract was reported by Hemmati et al. They investigated the effect of topical application of *S. striata* (2, 5 and 10% W/W) on open skin wound in rabbit. Their finding demonstrated that the rate of wound closure in animals who treated with plant extract was significantly higher than that of control groups. They suggested that the *S. striata* extract might stimulate collagen synthesis, angiogenesis, vessel dilatation and decrease of inflammation, bleeding and edema (13).

Ghasghaii et al evaluated the healing effects of methanolic extract of *S. striata* on full-thickness wound model in rat. Their results indicated that the plant extract promoted wound healing by attenuate the inflammation, increase fibroblast proliferation and tissue re-epithelialization (14).

The effect of *S. striata* on episiotomy wound healing was investigated by Sharifi et al. This clinical trial was conducted on 80 primiparous women who were referred to Ganjavian hospital in Dezful (Iran) in 2014-2015 and the researchers found that the rate and quality of wound healing in plant extract treated group were significantly

higher than those of control group (15).

Tanideh et al investigated the effect of *S. striata* ethanolic extract on burn wound healing compared with Silver Sulfadiazine. The results of this study showed that *S. striata* possessed antibacterial and wound healing activities (16).

Anti-inflammatory effects

Azadmehr et al evaluated the protective effects of *S. striata* on ovalbumin (OVA) induced airway inflammation in a mouse model of asthma. They treated sensitized mice with plant extract via intraperitoneal injection and they assessed the protective effects of plant extract base on the number of eosinophils and other inflammatory cells. In addition, the total immunoglobulin E (IgE) and OVA-specific IgE levels in serum, interleukin-4 (IL-4) and interleukin-5 (IL-5) cytokines in bronchoalveolar lavage fluid (BALF) were determined. According to the results of this study the number of inflammatory cells and T-helper 2 (Th2) cytokines including IL-4 and IL-5 in BALF were significantly reduced after treatment with *S. striata* extract. Also, *S. striata* caused a significant decrease in the serum IgE and OVA-specific IgE levels. These result suggest that *S. striata* may have therapeutic potential for treating allergic asthma via modulating Th2-mediated cytokines (17).

The effects of acetate extract of *S. striata* on macrophages pro-inflammatory cytokine secretion in cell culture was investigate by Azadmehr et al and their finding indicated that ethyl acetate fraction of *S. striata* has inhibitory effects on proinflammatory mediators (IL-1β, TNF-α and PGE2) production by lipopolysaccharide stimulated peritoneal macrophages (18).

The suppressive effects of ethanolic extract of *S. striata* on Nitric oxide production in mouse peritoneal macrophages was investigated by Azadmehr et al and the results of the study showed that different concentrations of plant extract (10, 50 and 100 g/mL) significantly decreased the Nitric oxide production *in vitro*. They also administered plant extract (50 and 100 g/mL) to Balb/c mice and found that lipopolysaccharide and IFN-ɣ induced production of Nitric oxide was inhibited by plant extract in the isolated mouse peritoneal macrophages *ex vivo* (19).

Antioxidant effects

The antioxidant activity of *S. striata* was evaluated and confirmed in several studies (2,5,20,21). Azadmehr et al evaluated the antioxidant and neuroprotective effects of *S. striata* extract *in vitro*. They treated PC12 cell line with different concentrations of plant extract and then exposed the cells to H2O2 for induction of oxidative stress and neurotoxicity. They measured cell viability, reactive oxygen species generation and apoptosis by MTT assay, fluorescent probe 20, 70-dichlorofluorescein diacetate, and annexin V/propidium iodide, respectively. Moreover they used DPPH method for evaluating antioxidant capacity of the plant extract. Their finding showed that the cell viability in extract (200 μg/mL) treated group was significantly higher than that of control group. The extract also decreased the intracellular reactive oxygen species production in a dose-dependent manner. In addition the plant extract showed antioxidant activity and decreased apoptotic cells (20). Mahboubi et al investigated the antioxidant activity of different extracts of *S. striata* using DPPH and BCBT assay. Their finding showed more antioxidant activity of aqueous, methanolic and ethanolic extracts compared to ethyl acetate extract (5).

Neuroprotective effects

The neuroprotective effect of extract obtained from aerial parts of *S. striata* against glutamate-induced neurotoxicity was reported by Salavati et al. The results of this study indicated that high polarity methanolic fraction of aerial parts of *S. striata* had a significant neuroprotective activity against glutamate induced neurotoxicity in cultured rat pups cerebellar granule neurons (22). In another study the neuroprotective effect of *S. striata* was reported by Azadmehr et al (20).

Matrix metalloproteinases inhibition

The results of a study showed that the high polarity methanol solution extract of *S. striata* had a significant inhibitory effect on matrix metalloproteinases (MMPs) activity *in vitro* (23). Monsef-Esfahani et al investigated the *S. striata* extract for the presence and characterization of matrix metalloproteinases inhibitor compounds. They identified two active compounds (acteoside and nepitrin) and suggested that nepitrin could inhibit MMPs activity at low concentrations, whereas acteoside showed inhibitory effect on MMPs activity at high\concentrations (24).

Effects on depression and anxiety

The antidepressant and anxiolytic effects of *S. striata* were studied in animal model using the elevated plus-maze and forced swimming test. The results of this study showed that *S. striata* ethanolic extract possessed antidepressant and anxiolytic effects. The beneficial effects of *S. striata* could be mediated through GABAergic mechanism (25).

Analgesic effects

Sofiabadi et al reported that the ethanolic extract of *S. striata* relieved the acute (doses of 100 and 200 mg/kg) and chronic pain (dose of 200 mg/kg) in rat (26). Another study performed by Alimohammadi et al using hot plate method demonstrated the analgesic effect of *S. striata* hydroalcoholic extract in acute pain in mice (27).

Preservative effects

Jebelli et al evaluated the *S. striata* water extract on the quality and shelf life of the rainbow trout (*Oncorhynchus*

mykiss) fillet during super chilled storage. Their finding indicated that incorporation of *S. striata* water extract (3%) in rainbow fillets caused delayed lipid peroxidation and hydrolytic spoilage and lower bacterial count. They suggested application of *S. striata* coating effectively maintained quality attributes and extended shelf life of the rainbow trout stored under superchilled condition (28).

Conclusion

Scrophularia striata is a powerful medicinal plant and provides a wide range of research possibilities. Since last decade several studies have been carried out focusing on its pharmacological activities. These studies make it possible to justify the traditional uses of the plant and to find new pharmacological activities. However the chemical composition of the plant has not been extensively studied and deserve more attention in near future because the phytochemistry analysis of the plants is a key component of medicinal plant research. Finally, we suggest more pharmacological studies to be carried out using different parts and active compounds isolated from the plant.

Conflict of interests

The author declares that there is no conflict of interests.

Ethical considerations

Ethical issues have been completely observed by the author.

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