Constituents And Pharmacological Effects Of*leontice Leontopetalum*- A Review

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Abstract:

Phytochemical analysis showed that *Leontice leontopetalum* contained many quinolizidine alkaloids, tannins, phenolic, flavonoids, and many other bioactive contents. The pharmacological studies revealed that *Leontice leontopetalum* possessed antioxidant, antidiabetic, convulsant and anti convulsant, cytotoxic, anticholinesterase cardiovascular and smooth muscle contractile effects. The current mini-review discussed the chemical constituents and pharmacological effects of *Leontice leontopetalum*.

Keywords: *Leontice Leontopetalum***,** Pharmacology, Constituents

Introduction:

In the last few decades, there has been an exponential growth in the field of herbal medicine. It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects. Plants generally produce many secondary metabolites which are bio-synthetically derived from primary metabolites and constitute an important source of chemicals which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides, and food additives. Many recent reviews showed that medicinal plants possessed antiurolithiatic[1], reproductive[2], gastrointestinal[3-5], analgesic and antipyretic[6], anti-inflammatory[7], nephro- and hepato-protective[8-9], dermatological[10], antidiiabetic [11], and central nervous effects[12]. Phytochemical analysis showed that *Leontice leontopetalum* contained many quinolizidine alkaloids, tannins, phenolic, flavonoids, and many other bioactive contents. The pharmacological studies revealed that *Leontice leontopetalum* possessed antioxidant, antidiabetic, convulsant and anti convulsant, cytotoxic, anticholinesterase cardiovascular and smooth muscle contractile effects. The current mini-review was designed to highlight the chemical constituents and pharmacological effects of *Leontice leontopetalum*.

Plant profile:

Synonyms: *Leontice brevibracteata, Leontice leontopetalum subsp. ewersmannii, Leontice eontopetalum subsp. leontopetalum*[13-14].

Taxonomic classification:

Kingdom: Plantae, **Phylum**: Spermatophyta, **Subphylum**: Angiospermae, **Class**: Dicotyledonae, **Order**: Ranunculales, **Family**: Berberidaceae, **Genus**: *Leontice*, **Species**: *Leontice leontopetalum*[15].

Common names:

Arabic: Taqiq**,** Kaf Al-Asad, Aslaj Al-Asad, Rakf, Khmerat Al-Dar, Kibkab, Artanitha; **English**: Lion foot, lion leaf, lion turnip; **Russian**: Leontitsa Evermana; **Swedish**: lejonblomma; **Uzbek**: Yersovun[14, 16].

Distribution:

It was distributed in **Africa** (Algeria, Egypt), **Asia** (Iran, Iraq, Jordan, Palestine, Lebanon, Syria, Turkey, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan, Pakistan), and **Europe** (Italy, Bulgaria and Greece)[14, 17].

Description:

Tuber large and deep. The stem and leaves are waxy, hairless, emerging from different spots from the ground. Leaves pinnate. Inflorescence much-branched, with many yellow flowers. Flower with 6 sepals, 6 petals (6 nectaries are hidden under 6 scales at the petals bases) and 6 anthers. The fruit is an inflated, egg-like reticulate capsule after drying, the plant is detached from the ground, tumbles and disperses its seeds[18].

Traditional uses:

The tuber was used in the treatment of epilepsy and leprosy. It was also used as snakebite opium poisoning antidotes. A soap was obtained from the plant, it was used in removing stains from cloth[17, 19]. The plant roots were used in the treatment of rheumatism, joint pain and inflammation in Iran[20].

It was recommended to prevent benign prostatic enlargement, preventing breast, lymphoblastic, uterine and prostate cancers and for irregular menstrual periods, prevent menstrual cycle and postmenstrual syndrome, migraine, and development of myoma[21].

Tuber of *Leontice leontopetalum* subsp. *leontopetalum* was used for haemorrhoids in Turkey, the tubers were pulled out of the ground and sliced, then swallowed as a pill twice a day[22].

Parts used: Roots, tubers, and whole plant[20, 23].

Chemical constituents:

Leontice leontopetalum contained many alkaloids, 19 quinolizidine alkaloids were detected in the plant, the alkaloid pattern of *Leontice leontopetalum* was characterized by quinolizidine alkaloids of the lupanine-type with lupanine as the main compound. In *Leontice leontopetalum* L. subsp. *ewersmannii* 15 quinolizidine alkaloids were detected, in contrast to *Leontice leontopetalum, L. ewersmannii* accumulated quinolizidine alkaloids of the matrine-type, and the α-pyridone-type was the major compounds[24].

The plant contained tannins up to 1.5%, alkaloids 7.4 ±0.32 mg/g to27.12 ±1.18 mg/g dry weight (leontidine, leontine, leontamine, lupanine, 13α-hydroxy lupanine, α- isolupanin, 3α-hydroxylupanin, leontiformidine, d-leontiformine, pachycarpine, oblongine, petaline, (+) O-methyldihydro secoquettamine and (+) dihydrosecoquettamine) and up to 30% starch. The plant also contained flavones and saponins with a hemolytic index of 1:240 in the aboveground portion of the plant[16, 24-31].

The total phenolic and flavonoid contents of the crude methanol and water extracts of the tubers of *Leontice leontopetalum* L. subsp. *ewersmannii* were 77.13 ± 3.05 and 12.23 ± 0.04 µg PEs/mg extract, and 94.41 ± 1.76 and 13.02 ± 0.17 µg QEs/mg extract, respectively[18]. Isorhamnetin-3-rutinoside (narcissin) and quercetin-3-glucoside were isolated from the leaves and stems of *Leontice leontopetalum*[32].

Pharmacological effects:

Cardiovascular effects and smooth muscles effects:

The effects of (−) oblongine chloride, on blood pressure, heart rate, and blood flow were studied in anaesthetized guinea-pig. Oblongine chloride caused a doses ranging (0.5 to 30 mg/kg, iv) reduction of systolic and diastolic blood pressure. These effects were associated with an increase in heart rate. Propranolol (5 mg/kg) failed to block the effects of oblongine chloride on systolic and diastolic blood pressure but significantly reduced the increase in heart rate observed with low doses (0.5–6 mg/kg) of oblongine chloride. Oblongine chloride also caused doses ranging (0.05 to 0.5 mg/kg) increase in blood flow. Larger doses (1.5, 4.5, 15 and 30 mg/kg) caused an initial decrease followed by an increase of blood flow. The net effect of cumulative doses was an increase in

blood flow over the control value. Accordingly, oblongine chloride possessed potential haemodynamic effects, which were not mediated by β-adrenergic receptor stimulation[33].

Low concentrations of petaline chloride (1-300 micrograms/ml), a quaternary alkaloid from *Leontice leontopetalum,* caused relaxation of the epinephrine-contracted aorta, contraction of the ileum, and no effect on the trachea. It also increased, in a concentration-dependent manner, the contractions of the spontaneously-beating atrium and the isolated perfused heart. These effects were not affected by propranolol but were significantly reduced in the presence of quinacrine, suggesting the participation of arachidonic acid metabolism to this effect. Larger concentrations (up to 3 mg/ml) caused nonsustained large contractions of the aorta and the trachea and increased the amplitude of the phasic contractions of the ileum. The contractile effects were not inhibited by atropine. In anesthetized rats, petaline chloride (0.3-3 mg/100 g body weight; ip) increased both the systolic and diastolic blood pressure and increased the heart rate[29].

Oblongine chloride (3 x 10^{5}-10^{-3} M), a quaternary alkaloid from *Leontice leontopetalum*, caused concentration-dependent relaxation of guinea-pig isolated ileal longitudinal segments, the effect was not blocked by propranolol (10^{-6} M) alone or in combination with prazosin (3 x 10^{-8} M), or by indomethacin (10^{-6} M), but was reduced by desensitization of the preparation by prior exposure to a combination of propranolol and yohimbine (3 x 10^{-6} M). Oblongine chloride (10^{-5-3} x 10^{-3}) M) also caused concentration-dependent relaxation of epinephrine-precontracted guinea-pig isolated main pulmonary artery rings. The effect was not affected by propranolol or by indomethacin but was significantly attenuated by pretreatment with 3 x 10^{-5} M ATP and potentiated by pretreatment with quinacrine (10^{-5} M). Oblongine chloride (10^{-5} M-3 x 10^{-3} M) caused concentration-dependent increase in the contractility of guinea-pig atrium but did not affect the rate of the atrium. It also caused concentration-dependent increase in the contractility of the isolated perfused heart except that large concentrations of oblongine (10^{-3}, 3 x 10^{-3} M) which inhibited both contractility and rate of the heart. The inotropic effects of oblongine on the atrium were not blocked by propranolol or indomethacin but were significantly blocked by quinacrine[28].

Antioxidant effects:

Lupanine, a quinolizidine alkaloid isolated from the tubers of *Leontice leontopetalum* subsp. *ewersmannii* caused high inhibition of lipid peroxidation at 100 µg/ml, it produced the same ABTS cation radical scavenging activity of BHT, α-tocopherol and (+)-catechin at the same concentration[30].

The phenolic contents and antioxidant and scavenging of superoxide radical activities were studied using *in vitro* models. The highest and lowest reducing power was found in leaves and tubers of *Leontice leontopetalum* (1.146±0.055 and 0.889±0.037) respectively. Free radical superoxide scavenging activity was greater than 27% in all cases. The correlation of antioxidant activities, FRAP and reduction power, with, phenolic contents indicated significant correlations except for radical superoxide scavenging activity. Alkaloid content was only significantly associated with reducing power. Accordingly, *Leontice leontopetalum* can be a source of natural antioxidant[26].

Antidiabetic effects:

The effect of the extract of *Leontice leontopetalum* was studied in human pancreatic beta cell-treated with streptozotocin (STZ). *Leontice leontopetalum* extracts (1, 10, 100, and 1000 ug/ml) were supplemented in media for twenty-four hours and after STZ treatment (10 and 20 mM). Cells survivals (MTT), cells proliferation were recorded. Insulin content and releasing were measured at 1.1, 8.4 and 16.7 mM glucose concentrations. The result showed that cell survival was decreased, and cell proliferations in STZ groups were attenuated in a dose-dependent manner. Co-treatments with *Leontice leontopetalum* with STZ enhanced insulin-releasing decreased by STZ[34].

Convulsant and anti convulsant effects:

The alkaloid petaline chloride, obtained from extracts of *Leontice leontopetalum* was more potent convulsant poison than leptazol. However, it reduced the convulsant activity of leptazol and gave some protection from electrically induced seizures at lower dose. It depressed both the patellar tendon reflex and the crossed extension reflex, it also possessed muscle relaxant activity and increases the rate, force and amplitude of the beat of the isolated auricle depressed in a low calcium medium[35].

Cytotoxic effect:

The cytotoxicity of the crude methanol extract of the roots of *Leontice leontopetalum* was studied against MCF-7, HepG2, WEHI, and MDBK cell lines. The results showed that IC_{50} values of the crude methanol extract of the roots of *Leontice leontopetalum* were >100 against all the tested cell lines[36].

Anticholinesterase effects:

Lupanine, a quinolizidine alkaloid isolated from the tubers of *Leontice leontopetalum* subsp. *ewersmannii*, showed almost the same butyrylcholinesterase inhibitory activity with galantamine at 200 µg/ml[30].

Conclusion:

The chemical analysis of *Leontice leontopetalum* showed that it contained many biologically active metabolites included quinolizidine alkaloids, tannins, phenolic, and flavonoids. The pharmacological studies revealed that *Leontice leontopetalum* possessed antioxidant, antidiabetic, anticonvulsant, cytotoxic, anticholinesterase cardiovascular and smooth muscle contractile effects. The current review discussed the chemical constituent, pharmacological and therapeutic effects of *Leontice leontopetalum* as promising herbal drug in the treatment of diabetes, epilepsy, cancer, heart failure, and smooth muscles atony.

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