Pharmacological and Therapeutic Effects of Lallemantia royleana- A Review

Ali Esmail Al-Snafi

Department of Pharmacology, College of Medicine, Thi qar University, Iraq.

Corresponding Author: Ali Esmail Al-Snafi

Abstract: The chemical analysis of Lallemantia royleana seed showed that the seeds contained: protein 25.60%, fat 18.27%, fiber 1.29%, alkaloids, anthraquinones, flavonoids, glycosides, phlobatannin tannins, volatile oils, mixed fatty acids and terpenoids. It exerted many pharmacological effects included antimicrobial, antioxidant, antidepressant, anxiolytic, sedative, antiemetic, hypolipidemic, protective and many other pharmacological effects. The current review discussed the Lallemantia royleana as a beneficial medicinal plant.

Keywords: Lallemantia royleana, constituents, pharmacology

I. INTRODUCTION

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. Recent reviews revealed that the medicinal plants possessed central nervous, cardiovascular, antioxidant, reproductive, gastro-intestinal, respiratory, anti-diabetic, antimicrobial, antiparasitic, dermatological, anticancer, anti-inflammatory, antipyretic and analgesic, immunological, hepato and reno-protective, and many other pharmacological effects. The chemical analysis of Lallemantia royleana seed showed that the seeds contained: protein 25.60%, fat 18.27%, fiber 1.29%, alkaloids, anthraquinones, flavonoids, glycosides, phlobatannin tannins, volatile oils, mixed fatty acids and terpenoids. It exerted many pharmacological effects included antimicrobial, antioxidant, antidepressant, anxiolytic, sedative, antiemetic, hypolipidemic, protective and many other pharmacological effects. The current review will discuss the chemical constituents and pharmacological effects of Lallemantia royleana as a beneficial medicinal plant.

Plant profile:
Synonyms:
Dracocephaluminderiense, Dracocephalum royleanum and Nepeta erodiiifolia

Taxonomic classification:

Common names:
Arabic: Rehnanberry, balango; English: Lady’s mantle, balangu; Hindi: Tukhm-e-balanga; Pakistan: tukhme balangu, tukhmalanga; Unani: Baalango, Tukhm-e-Baalango; Urdu: Balangusherazi

Distribution:
It is distributed in Asia: Armenia, Azerbaijan, China, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan, Afghanistan, India, Pakistan, Syria, Iraq, Iran, Russian Federation-Western Siberia, and in Europe: Russian Federation-European part.

II. Description

It was an annual, unbranched, or branched from the base. Stems erect, quadrangular, 5-30 cm, with a dense indumentum of short eglandular retrorse hairs, leafy. Leaves simple, 15-20 x 7-15 mm, oblong-obovate, crenate, cuneate, below with short eglandular hairs and scattered sessile oil globules; petiole up to 15 (-20) mm. Inflorescence starting from near base of stem; verticillasters in axils of leaves, numerous, 6-8 flowered, distant or contiguous; bracts several, linear-oblong as long as or longer than calyx, sessile or shortly petiolate, cuneate, with marginal awns 2-4 mm long. Calyx tubular, 6-7 mm, veined or ribbed, with short glandular spreading hairs and a few sessile oil globules; upper lip with 3 ovate obtuse lobes; lower lip with 2 narrower lobes; all shortly
acminate; teeth clearly convergent in fruit and closing the mouth. Corolla pale lilac, blue to whitish pink, 7-8 mm, slightly longer than calyx; upper lip 1.5 mm long, nearly shorter than lower lip(31).

**Traditional uses:**

Seeds were used as cooling, diuretic, sedative; as a soothing agent during urinary troubles, fever, common cold, intestinal troubles. It was also used as cephalic astringent, cardiac tonic, carminative and for cough. A poultice of seeds was applied to abscesses, boils and inflammations. In Ivory Coast, Burkina Faso, Gabon and Tanganyika, different parts of the plant were used for the treatment of intercostals pain, rheumatic pain and fever. The leaf and root decoctions were used to treat pneumonia.(28, 32-33)

Muslim used its seeds in drinks as flavoring, cooling, soothing and sedative. Seeds also applied as one composition of herbal mixtures for anxiety and depression disorders. Seeds mucilage also applied as a liniment for skin complications. The seeds were used in Iranian traditional medicine as diuretic, tonic, aphrodisiac, and antitussive and for the treatment of various nervous, hepatic, and renal disorders. (27, 34-36).

**Chemical constituents:**

The chemical analysis of *Lallemantia royleana* seed showed that the seeds contained: dry matter 92.75%, ash 3.63%, crude protein 25.60%, crude fat 18.27%, crude fiber 1.29%, NDF (insoluble fiber in neutral detergent) 30.67% and ADF (insoluble fiber in acid detergent) 47.80%(37).

However, Farahnaky et al., showed that the whole seeds contained moisture 6.05 ± 0.06, protein 2.93 ± 0.20, fat 0.30 ± 0.06, ash 2.98 ± 0.23, fiber 24.24 ± 0.11 and total carbohydrate 87.74 ± 0.55%.(38)

The highest values of volatile oil percentage, volatile oil yield per hectar, specific gravity, density and refractive index of the seed oil of *Lallemantia royleana* reached 2.75%, 14.24/ha, 0.980 mg/microliter, 0.941 mg/microliter and 1.520 degree respectively(39).

The preliminary phytochemical investigation of the methanolic extract of seeds of *Lallemantia royleana* showed that the seeds extract contained alkaloids, anthraquinones, flavonoids, glycosides, phlobactin tannins, volatile oils, mixed fatty acids and terpenoids(40,41).

Seed oil contained 19.26%, fatty acid, 90.71% of them were unsaturated fatty acids (USFA) and 9.29% saturated fatty acids, linolenic acid and palmitic acid were the predominant acids in PUSFA, MUSFA and SFA seed oil, respectively. Seed oil also contained 427.8 ppm tocopherols and 210 ml/l polyphenols(42).

The oils of the aerial parts of *Lallemantia royleana*, grown in Isfahan Province, Iran were analyzed by GC and GC-MS. Forty-six compounds, constituting 94.5% of the total components were identified. The components of *Lallemantia royleana* aerial parts oil (%) were: tricyclic 1.0, α-pinene 0.3, 1-octen-3-ol 0.1, 6-methyl-5-hepten-2-one 0.9, 3-octanone 0.5, 2-octanone 0.1, β-myrcene 2.8,3-octanone trace, α-phellandrene 0.3, δ-3-carene 3.1, α-terpinene 2.0, β-cymene 1.9, limonene 5.7, benzyl alcohol 1.6, 1,8-cineole 1.8, β-cis-oicime 0.8, β-trans-oicime 7.4, γ-terpinene 1.1, isobutanol 0.9, terpinolene 2.7, butanol 0.2, dehydro-sabina ketone 0.5, iso-3-thujanol 0.7, sabina ketone 0.6, 3-thujene-2-one 7.8, myrtenal 1.7, myrtenol 0.2, verbenone 16.4, trans-carveol 9.8, cis-sabinene-hydrate acetate 0.2, cis-carveol 4.8, trans-sabinene-hydrate acetate 0.5, trans-sabinyl acetate 5.5, carvacrol 1.5, iso-dihydrocarvyl acetate trace, α-cubebeene 0.8, α-longipinne 0.1, β-bourbonene 2.7, β-cubebeene 8.9, α-cis-bergamotene trace, β-caryophyllene 0.6, α-trans-bergamotene 0.1, β-cis-farnesene trace, β-trans-farnesene trace, spathulenol 0.3 and α-muurolo 0.6%(43).

Sharifi-Rad et al., investigated the volatile constituents of the volatile parts of *Lallemantia royleana* using gas chromatography and gas chromatography–mass spectrometry. Thirty-seven compounds were identified and the main constituents were trans-pinocarvyl acetate (26.0%), pinocarvone (20.0%), β-pinene (1.5%), (E)-β-oicime (4.1%), terpinolene (1.1%), linalool (3.4%), trans-pinocarvyl acetate (1.6%), 3-thujen-2-one (5.1%), myrtunal (1.5%), verbenone (7.1%), trans-carveol (5.3%), cis-carveol (3.5%), pulegone (4.4%), carvacrol (1.6%), dihydrocarvyl acetate (2.5%) and β-cubebeene (2.1%) (43).

The *Lallemantia royleana* seed mucilage contained 75.87-76.74% carbohydrate, 2.71-3.86% protein, 8.24-9.92% ash, 8.51-9.48% moisture and 20.33% uralic acids. It was with high molecular weight (1.19×10^5 Da) polysaccharide, composed of galactose (33.54-36.28%), arabinose (35.96-37.88%), rhamnose (15.18-18.44%), xylose (6.02-7.38%) and glucose (4.11-5.20%) (44-45).

A water-soluble polysaccharide was isolated from the seeds of *Lallemantia royleana*. It contained 8.2% moisture, 13.1% ash, 1.6% protein and 77.1% carbohydrate. Analysis showed that it contained arabinose, rhamnose, mannnose, fructose, galactose, α-and β-d-glucose, glucuronic acid, galacturonic acid, and glucosamine. H1, 13C and COSY NMR spectroscopy demonstrated the presence of (1 → 4)-linked-α-D-GalpA, (1 → 3)-linked-β-D-Galp, (1 → 6)-linked-β-D-Galp, (1 → 2)-linked-α-L-Arap, (1 → 3)-linked-α-L-Rhap and (1 → 3)-linked-β-L-Arap in the polysaccharide sequence (46).

The water-extractable hemcellules from seeds of *Lallemantia royleana* was investigated. It appeared as branched hemcellules, monosaccharide and elemental analysis of the hemcellules obtained from
*Lallemantia royleana* showed the presence of arabinose 29.44 ± 0.31, galactose 1.41 ± 0.02, rhamnose 69.74 ± 0.51, galacturonic acid 1.82 ± 0.24 % of the total monosaccharides on anhydrous basis. The mass spectrometric study showed presence of β-1,2-linked rhamnose and β-1,3-linked arabinose units in the main chain with arabinose attached to the main chain through β-1,3-linkage[47].

The total phenolic content of *Lallemantia royleana* seeds was estimated using Folin-Ciocalteu method. Total phenolic content was 25.3 mg as gallic acid equivalent/g extract[44]. However, the *Lallemantia royleana* seed mucilage total phenolic content and antioxidant activity (IC₅₀) were equal to 82.56±1.6μgGAE/mg and 528.54±0.35μg/ml, respectively[44].

**Pharmacological effect:**

**Antimicrobial effects:**

The antibacterial activity of *Lallemantia royleana* seeds extracts was evaluated by using diffusion method at three different concentrations (100, 50 and 10 mg/ml) against *Staphylococcus aureus, Enterobacter cloacae* (IARS 7), *Pseudomonas aeruginosa* (IARS 9) and *Escherichia coli* (IARS 3). Except aqueous extracts, all organic extracts of *Lallemantia royleana* seeds (methanol, ethanol and chloroform) displayed significant anti-bacterial activity against all the tested bacteria. The chloroform extract exhibited highest anti-bacterial activity (diameter of zone of inhibition= 10.67 ± 1.44, 11.83 ± 3.79, 14.00 ± 1.5 and 14.67 ± 0.58 mm against *P. aeruginosa, E. coli, E. cloacae* and *S. aureus*, respectively) at a concentration of 100 μg/ml[27].

Antibacterial screening of *Lallemantia royleana* essential oil showed that it significantly inhibited the growth of *Staphylococcus aureus, Bacillus subtilis, Klebsiella pneumonia* and *Pseudomonas aeruginosa* (p < 0.05). MICs for *Staphylococcus aureus, Bacillus subtilis* and *Klebsiella pneumonia* were 5.6, 4.8 and 3.5 μg/ml, respectively. The antifungal screening of the essential oil of *Lallemantia royleana* showed that the oil significantly inhibited the growth of *Candida albicans* and *Aspergillus niger* (MIC = 3.1 and 2.5 μg/ml, respectively)[43].

The effect *Lallemantia royleana* seed mucilage edible coating on population of microbial pathogens (total viable count, psychrotrophic bacteria, *Escherichia coli, Staphylococcus aureus* and fungi), chemical changes (thiobarbituric acid, peroxide value and pH) and sensory attributes (color, odor and total acceptability of the beef slices at 4 °C for 18 days) were determined. *Lallemantia royleana* seed mucilage edible coating extended the microbial shelf life, oxidative stability and sensorial acceptability of beef[49].

The antibacterial activities of essential oils from different Iranian medicinal plants were evaluated against TEM gene positive ESBL-producing *Escherichia coli* strains isolated from urine samples of patients with urinary tract infections. The essential oils of the aerial parts of *Lallemantia royleana* displayed high inhibitory effects against ESBL-producing *Escherichia coli* strains with MIC of 1 mg/ml[48].

The methanolic seed extract of *Lallemantia royleana* (100, 200, 300 and 500 μg) was tested against *Aspergillus flavus* (NCIM 524), *A. niger* (NCIM 773), *A. parasitic* (NCIM 898), *Candida albicans* (NCIM 3471) and *Saccharomyces cerevisiae* (NCIM 3090). Almost all the fungal strains growth was inhibited by the crude plant extract. The methanolic seed extract of *Lallemantia royleana* showed inhibition in the growth of *Aspergillus flavus* and *Aspergillus parasiticus* at 200 μg concentration and more. *Saccharomyces cerevisiae* growth was inhibited at 100 μg concentration, while the growth of *Aspergillus niger* was inhibited at 500 μg concentration. The *Candida albicans* strain showed significant growth inhibition in the presence of methanolic extract of *Lallemantia royleana* seed. The zone of inhibition was 6 mm, 8 mm, 12 mm and 14 mm at 100, 200, 300 and 500 μg concentrations of methanolic seed extract respectively. The antibacterial study of the methanolic seed extract of *Lallemantia royleana* showed that *Bacillus cereus, Bacillus subtilis, Salmonella typhimurium* and *Staphylococcus epidermidis* were the most susceptible pathogens (MIC₅₀≤ 2μg/ ml), followed by *Staphylococcus aureus, Proteus vulgaris, Klebsiella pneumonia, Pseudomonas aeruginosa* and *Escherichia coli* respectively[49].

The essential oils from *Lallemantia royleana* were screened for their inhibitory effect against herpes simplex virus type 1 (HSV-1) in vitro on Vero cell line CCL-81-ATCC using a plaque reduction assay. Results showed that the inhibitory concentration (IC₅₀) was determined at 0.011% for *Lallemantia royleana* oil with a high selectivity index (6.45)[50].

**Antioxidant effect:**

The antioxidant effect of the methanolic extract of seeds of *Lallemantia royleana* was investigated using in vitro methods. The crude methanolic extract of *Lallemantia royleana* seeds showed IC₅₀ value of 140.53 ± 4.22 μg/ml by DPPH method and 576.5 ± 0.00 μg/ml by hydrogen peroxide method, while, the standard BHT showed an IC₅₀ value of 43.40 ± 1.30 μg/ml by DPPH method and IC₅₀ value of 26.16 ± 0.35μg/ml by hydrogen peroxide method[40].

The antioxidant activity of *Lallemantia royleana* seeds hydro-alcoholic extract was estimated by 2,2-diphenyl-1-picrylhydrazyl (DPPH) and ferric reducing antioxidant power (FRAP) assays. *Lallemantia royleana*
In studying of antioxidant effects of Lallemantia royleana, the methanolic seed extracts exhibited 61.30 ± 0.234 and 3.44 ± 0.376 percent inhibition, at the concentration of 1000 μg/ml and 1.95 μg/ml respectively, by hydrogen peroxide anti-oxidant method. The IC₅₀ value of Lallemantia royleana seed extract was 576.50 ± 0.00 μg/ml and the IC₅₀ value of BHT was 26.16 ± 0.351 μg/ml. By DPPH radical scavenging assay, the crude methanolic extracts of Lallemantia royleana seed extract gave percent inhibition of 68.72 ± 0.236 and 0.57 ± 0.197 at 1000 and 1.95 μg/ml respectively. The IC₅₀ value of Lallemantia royleana seed extract was 140.53 ± 4.22 μg/ml and the IC₅₀ value of BHT was 43.40 ± 1.307 μg/ml. The total anti-oxidant capacity of the methanolic crude plant extracts and BHT determined by phosphor-molybdenum method revealed that the percentage inhibition values of the Lallemantia royleana crude methanolic seed extracts ranged between 66.66 ± 2.309 and 1.33 ± 2.309 percent, at the concentration of 1000 μg/ml and 1.95 μg/ml respectively. IC₅₀ value of Lallemantia royleana was 187.46 ± 0.55 μg/ml and the IC₅₀ value of BHT was 124.25 ± 3.04 μg/ml.

Antidepressant effect:

The antidepressant effect of methanolic extract of Lallemantia royleana seeds (25, 50, 75 mg/kg, orally) was investigated in mice with acute mild stress model of depression using modified forced swimming test. All doses of the methanolic extract of Lallemantia royleana seeds produced significant reduction in % immobility. However, the percentage of immobility time was significantly reduced at 50 mg/kg, (56.67%, p<0.01).

Anxiolytic and sedative effects:

The anxiolytic and sedative like effects of methanolic extract of Lallemantia royleana seeds (75, 100, 250 and 500 mg/kg, orally) was studied in male mice. Behavioral tests such as open field, hole-board, elevated plus maze, light-dark box and staircase paradigm were used to screen anxiolytic activity. Diazepam (1 mg/kg, ip) was employed as standard. Behavioral tests for anxiety showed maximum increase in anxiolytic parameters at the dose of 250 mg/kg (p<0.01) without altering exploratory behavior i.e. number of head-dips 54 ± 3.1, time spent in open arm percent 70± 2.8, entries in open arm percent 67.3±1.2, percent time spent in light box 62± 1.5 and number of stairs ascend 16 ±2.1.

Hypolipidemic activity:

The hypolipidemic activities of Lallemantia royleana was studied in rabbits fed diets supplemented with cholesterol (0.5%) for 12 weeks to evoke hypercholesterolemia. Hypercholesterolemic rabbits were treated with different doses of whole Lallemantia royleana seeds (0, 5, 10, and 20%) for 12 weeks. The serum total cholesterol and triglyceride decreased in all groups treated with Lallemantia royleana seeds (p<0.05), however, Lallemantia royleana seeds increase of atherogenic index in all treated groups.

Antiemetic activity:

The antiemetic activity of ten aromatic medicinal plants including Lallemantia royleana leaves ethanol extracts was studied using chick emetic model at a dose of 150 mg/kg bw, orally. The extracts decreased in retches induced by copper sulphate pentahydrate given orally at a dose of 50 mg/kg bw and showed comparable antiemetic activity to domperidone (mean number of retches 11.16 ± 1.17 compared with 13.5±1.02 for domperidone and inhibition of emesis 83.61% compared with 80.18 for domperidone).

The protective activity:

The protective efficiency of Khamira (a Unani formulation contained Lallemantia royleana) was studied using isoproterenol (ISO) induce toxicity in simian virus derived murine endothelial cell line (SVEC) cells. Khamira was nontoxic to SVEC cells up to a concentration of 20 mg/ml, after this concentration cells were unable to survive. 150 μM concentration of isoproterenol induces mild lethality and higher concentrations leading to increased toxicity and induced death. Khamira co-treatment but not pre-treatment was able to maintain the sufficient endogenous antioxidant status that was useful to rescue cells from ROS or free radicals. Khamira might be acting either on signalling events prior to ROS or after ROS generation.

Mucilage in pharmaceutical formulations and as food additives:

Natural gums and mucilage have been widely explored as pharmaceutical excipients such as thickeners, suspending agents, emulsifying agents, and binders. Mucilage isolated from the seeds of Lallemantia royleana showed a great swelling property and was non irritating to the mucosal membrane and can act as a potential good candidate for various pharmaceutical formulations for its high swellability on coming in contact with water. It can be used as a thickening agent, suspending agent or as a super-disintegrant in formulations.
Lallemantia royleana seed gum solution was compared with Tragacanth gum, CMC, Na-alginate and Arabic gum at 0.4 % (w/w) concentration. The highest consistency coefficients were recorded for both Lallemantia royleana seed gum and Tragacanth gum. It was evident that the apparent viscosity of all samples decreased with increasing shear. Lallemantia royleana seed gum created solutions with a viscosity similar to CMC and Tragacanth gum and higher than Na-alginate and Arabic gum. Accordingly, Lallemantia royleana seed gum could be suitable for application as a thickening agent\(^{(58)}\).

The mucilage from the seeds of Lallemantia royleana was extracted and subjected to pre-formulation study for evaluation of its suitability for use as suspending agent. The suspension of furomamide prepared with 1.5 w/v of the extracted mucilage was found to be ideal and comparable with the other two preparations of xanthan gum 0.35% w/v and chitosan 1.5% w/v. The mucilage was white in color and the average yield of dried mucilage obtained from Lallemantia royleana nutlets was 14% w/w of the seeds used. It was sparingly soluble in water but swells in contact with it, giving a highly viscous solution. It was slightly acidic to neutral. It exhibited high viscosity profile and exhibited better mucoadhesive properties\(^{(58)}\).

Balangu mucilage was also used as a gel supplement, and natural matrix for sustained release of drugs. The anesthetic action of gel prepared from Balangu mucilage alone and its mixture with lidocaine hydrochloride were compared with the effect of commercial 2% lidocaine gel using rat tail flick test. The duration and potency of anesthesia induced by gel containing mucilage alone (0.01 g/ml) were identical to commercial 2% lidocaine gel. But, local anesthetic potency and duration of gel made from 2% lidocaine-mucilage gel mixture was significantly higher than commercial 2% lidocaine gel\(^{(49)}\).

The powdered seeds and the polymer obtained from aqueous extraction of the seeds were evaluated for use as a super disintegrant in tablet formulation. The powders were evaluated for various properties like swelling index, particle size, their micromeritic properties, density and viscosity. The results revealed that the aqueous acetone extract of the seeds had better swelling characteristics and the tablets prepared from the polymer showed considerably lesser disintegration times than those prepared using powdered seeds\(^{(60)}\).

The effect of the gum of Lallemantia royleana seed on some physicochemical and sensory characteristics of a typical soft ice cream was investigated. In comparison with carboxymethyl cellulose, Lallemantia royleana seed gum did not make a significant difference (p > 0.05) to most characteristics and could be used as a suitable stabilizer\(^{(61)}\).

Lallemantia royleana seeds was also introduced as yogurt stabilizer instead of gelatin. The yogurt was prepared by the standard method. The tukhm-e-balangu (Lallemantia royleana) in the powder form (0.15%, 0.2% and 0.25%), was added to the milk after pasteurization. The yogurt was stored at 4±2°C for 20 days and analyzed for different physiochemical (pH, titratable acidity, synersis, water holding capacity, total solids, viscosity, hardness, fat, protein and ash) and microbiological and sensory attributes at specified day intervals. The utilization of stabilizer and its rate of incorporation affected the given attributes. Among different concentrations of Lallemantia royleana, yogurt with 0.25% Lallemantia royleana gave best results for physical and chemical parameters but yogurt with 0.20% Lallemantia royleana attained highest score for overall sensory acceptability throughout the storage period. Microbiological results were almost comparable with yogurt containing gelatin\(^{(62)}\).

**Safety and side effects:**
The methanolic Lallemantia royleana seeds extract was found to be non-toxic at LD\(_{50}>5\) g/kg in mice\(^{(53)}\).

**III. CONCLUSION**

*Lallemantia royleana* possessed many pharmacological effects included antimicrobial, antioxidant, antidepressant, anxiolytic, sedative, antiemetic, hypolipidemic, protective and many other pharmacological effects. The current review discussed the *Lallemantia royleana* as a beneficial medicinal plant.

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