Review Article

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MULTI FACETED *SAXIFRAGA LIGULATA*

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Received on: 12/05/13 Revised on: 19/06/13 Accepted on: 17/07/13

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DOI: 10.7897/2277-4343.04432
Published by Moksha Publishing House. Website www.mokshaph.com

ABSTRACT
Saxifraga ligulata belongs to family saxifragaceae, is an accepted source of ayurvedic medicine Pashanabheda. This plant has been already recognized for its role in dissolving kidney stone. This review supports all updated information on its chemical constituents, pharmacological activities, traditional uses and scientific approach. The chemical entities of this plant have been used as an Antibacterial, Antiviral, Antipyretic, Antidiabetic, Anti inflammatory, Diuretic, Antiurolithiatic, Antioxidant, Antitussive and Hepatoprotective. This review is studied for the further development of various formulations for their traditional use and Pharmacological activities.
Keywords: *Saxifraga ligulata*, Pashanabheda, Antiurolithiatic, Berginin.

INTRODUCTION

India has a rich culture of medicinal herbs and spices, which includes more than 2000 species and has a vast geographical area with high potential abilities for Ayurvedic, Unani and Siddha traditional medicines. Human beings have used plants for the treatment of diverse ailments for thousands of years. Herbal medicines are in huge demand in developed and developing countries as a source of primary health care owing to their attributes towards biological and medicinal activities, high safety margins and lesser costs[1-3]. *Saxifraga ligulata* is a perennial herb belongs to family saxifragaceae. This family contains 440 species of Holarctic perennial plants. *Saxifraga* is the largest genus in family saxifragaceae. The Latin word *Saxifrage* means stone breaker. It is popularly known as Pashanabheda in Indian system of medicine. *Saxifraga* are becoming more popular among the environmentally conscious because they are drought resistant and non toxic plants[4].

Taxonomical classification

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Saxifragales
Family: Saxifragaceae
Genus: Saxifraga
Species: Ligulata

Synonyms

Berginia ligulata (wall), *Megasea ciliate* (Haw), *Saxifraga ciliata* (Haw) Royle[5-6].

Vernacular names

Saxifraga have different names in different states such as Pakhanabheda (Gujarat), Pashanabheda (Maharashtra), Telanurupindi (Andhra Pradesh), Patharchur (Uttar Pradesh, Bihar), Sirupilai (Tamil nadu), Kachalu (Punjab) and Padamdawi (Mizoram).

Botanical Description

Saxifraga ligulata is a small plant. Stems are short, thick, and fleshy. The leaves typically have less or incised margin. Long leaves are about 2.5cm in diameter obviate to sub orbicular, hairy, mid green, tapering at base. Flowers have five petals and sepals and are usually white. Fruits are capsular. Seeds are numerous. Rhizomes are solid, barrel shaped and cylindrical with small roots. Rhizome is used for medicinal purpose. It has rich chemical constituents in its root, stems and leaves. It is having aromatic odour and astringent taste[7].

Distribution

It grows well in moist and shady areas of Afghanistan, Himalayas (Kumaon to Bhutan), South Tibet, Meghalaya, Lushai hills west Bengal (Darjeeling, Labha, Takdah, Rimbick, Kalimpong), Arunachal Pradesh (Nyam Jang Chu), Bhutan (Phuntsoling district, Deothang district, Ha district and Mongar district[8]).

Ethanomedical Information

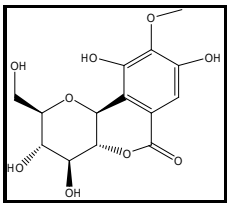
The very first mention of this drug appears in Charaka samhita (600BC), under the name "Pashanabheda" for painful micturition and breaking up calculi. Ayurveda mentioned leaf juice usage in urinary troubles, cold, hemorrhagic disease, distension of stomach and epilepsy. Unani suggests its usage in dissolving stones. Bhavaprakash mentioned it as an Astringent, bitter and sweet, purifies the urinary bladder[9].

Chemical constituents

Berginin

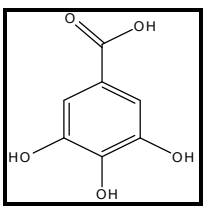
Berginin is most abundant in *Saxifraga ligulata*. It's IUPAC name is (2S,4R,5S,6S,7R)-5,6,12,14-tetrahydroxy-4-(hydroxymethyl)-13-methoxy-3,8-

dioxatricyclo[8.4.0.0^{2,7}]tetradeca-1(14),10,12-trien-9-one. Berginin possess hepato-protective, antipyretic and diuretic properties[10].



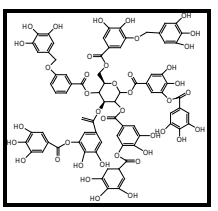
Gallic acid

Gallic acid is found in seed of *Saxifraga ligulata*. Gallic acid is also known as 3, 4, 5-Trihydroxybenzoic acid. It is used as standard to determine phenol content by Folin–Ciocalteu assay. It possesses antifungal and antiviral properties. It is used to treat psoriasis[11].



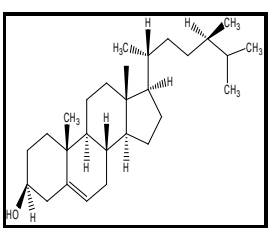
Tannic acid

Tannic acid is found in seeds of *Saxifraga ligulata*. It has a weak acidity because it has many phenol groups in their structure. The chemical formula for tannic acid is $C_{76}H_{52}O_{46}$. Tannic acid is used to produce albumin tannate which is used as antihistamines and antitussive to impart slow release property to active ingredient[12].



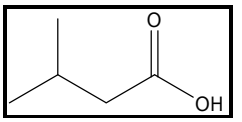
β-Sitosterol

It is found in *Saxifraga ligulata*. It is also known as 22, 23-Dihydrostigmasterol, Stigmast-5-en-3-ol, and β-Sitosterin. It reduces blood levels of cholesterol. It inhibits cholesterol absorption in intestine[13].



Isovaleric acid

It is found in root of *Saxifraga ligulata* in the form of volatile oil. It is also known as 3-Methylbutanoic acid, Delphinic acid, 3-methylbutyric acid and isopentanoic acid. It has been proposed that it is the anticonvulsant agent in valerian[14].



Paashanlactone

It is identified in *Bergenia ligulata* rhizome[15].

1, 8-Cineole

It is found in volatile oil of *Saxifraga ligulata* root. 1,8-cineole is also known by a variety of synonyms such as eucalyptol, limonene oxide, cajeputol, 1,8-epoxy-p-menthane. 1,8-cineole was found to control airway mucus hyper secretion and asthma, suppress arachidonic acid metabolism and cytokine production in human monocytes[16].

Pharmacological Activity

Antibacterial activity

Antibacterial activity was studied by disk diffusion method. Methanolic extract of *Berginia ciliata* rhizome was used in concentration of 200, 400, 800, 1000µg/discs against the Gram positive bacteria i.e. *Bacillus pumilis* and *Staphylococcus aureus* and Gram negative bacteria i.e. *Pseudomonas aeruginosa* and *Vibrio choleare*. Chloramphenicol was used as a standard in concentration of 10µg/disc. Methanolic extract exhibited a broad spectrum activity at all tested concentrations. The antibacterial efficacy of the extract was potent at 1000µg/disc, the maximum effect shown against *S. aureus* being also comparable to that of chloramphenicol 10µg/disc[17].

Antitussive activity

Antitussive effect against sulphur dioxide (SO_2)-induced cough was evaluated in mice by using method described by Miyagoshi *et al*. (1986). The animals were divided into five groups, each containing ten mice. One group served as control, three groups for methanol extract of *B. ciliata* (100, 200 and 300mg/kg body wt. p.o.) and the remaining group was used for the standard drug, codeine phosphate (10mg/kg body wt., p.o.). The antitussive activity of the extract was comparable to that of codeine phosphate (10mg/kg body wt.), a standard antitussive agent. The extract at doses of 100, 200 and 300mg/kg body wt., p.o. showed significant inhibition of cough reflex by 28.7, 33.9 and 44.2%, respectively, within 90min of the experiment. Both codeine phosphate and the extract of *B. ciliata* (at different doses), maximum inhibition of cough reflex occurred 90min after drug administration. The highest cough inhibition (44.2%) was produced by the extract at a dose of 300mg/kg body wt. (p.o.) 90min after the experiment, whereas codeine phosphate (10mg/kg) showed maximum 48.9% inhibition at the same time[18-19].

Diuretic activity

Diuretic activity was evaluated on Wistar albino rats, using Lipschitz model. The animals were deprived of food and water for 18hours prior to the experiment and

then divided in three groups of six each. Group I-Normal control group animals were treated with 2% gum acacia suspension only at a dose of 10ml/kg. Group II-Standard group animals were, treated with standard drug furosemide at a dose of dose 20mg/kg p.o. Group III-Test group animals were treated with Ethanolic extract of *Bergenia ligulata* in a 2% gum acacia at a dose of dose 500mg/kg p.o. On the day of the experiment, animals were given 25ml/kg of body weight normal saline orally. Immediately after dosing, the animals were placed in metabolic cages, specially designed to separate urine and faeces. The volume of urine collected was measured at the end of 5hour and during this period, no food and water was made available to animals. Na^+ and K^+ concentrations were determined by flame photometry and Cl^- was estimated by titration with silver nitrate solution using 3 drops of 5% potassium chromate solution as indicator. Result showed significant diuretic activity by Ethanolic extract.

Hepatoprotective activity

Hepatoprotective activity was evaluated on male albino rats. The Liv 52 syrup was used as standard and carbon tetra chloride was used to induce hepatotoxicity. The animals were divided in three groups of six each. Group I-Normal control (administered with 1% Gum acacia in distilled water), Group II- Negative control (CCl_4 intoxicated, 0.7ml/kg ip), Group III-administered with ethanolic extract of root (500mg/kg p.o./day). CCl_4 was given on 3rd, 6th and 10th day for all groups except Group I. On the 10th day one hour after the last dose of CCl_4 injection, blood was collected from carotid artery. SGPT, SGOT and total bilirubin levels were estimated. CCl_4 toxicant increased the level of SGPT, SGOT, and total bilirubin. Group III animals treated with *Bergenia ligulata* has shown significant decreased in the levels of SGOT, SGPT, ALP and Total Bilirubin as compared to negative control group. Hence the Ethanolic extract of roots of *Bergenia ligulata* can be used as Hepatoprotective.

Antipyretic activity

Antipyretic study was evaluated on Wistar rats. The animals were divided in three groups of six each. Group I-Normal **c**ontrol group animals; treated with 2% gum acacia suspension only at a dose of 10ml/kg. Group II-Standard group animals, treated with standard drug Paracetamol at a dose of dose 20mg/kg p.o. Group III-Test group animals; treated with ethanolic extract of *Bergenia ligulata* in a 2% gum acacia at a dose of dose 500mg/kg p.o. The normal body temperature of each animal was measured by thermister probe coated with the lubricant. Pyrexia was induced by subcutaneous injection of 2.0ml/kg, of 20% aqueous suspension of Brewer's yeast (*Saccharomyces cerevisiae*) in normal saline. After 18 hour of yeast injection the rectal temperature was recorded at a time interval of 0, 30 min, 1h, 2h and 3h after drug administration. Ethanolic extract of roots of *Bergenia ligulata* has shown the significant antipyretic activity, it had shown significant fall in body temperature up to the 4 hour following its administration. The response was comparable to that of antipyretic activity of Paracetamol-a standard antipyretic drug[20].

Antiurolithiatic activity

Crude powdered drug was extracted with petroleum ether, chloroform, n-butanol, ethyl acetate and finally with alcohol. Prepared extracts were subjected to qualitative chemical test to detect different phyto-constituents. The compound P1 obtained from column chromatography was taken up for pharmacological evaluation. All this extracts were evaluated for antiurolithiatic activity by an in vitro model using calcium oxalate and calcium phosphate stones. Formulation cystone was used as a reference standard. Weighed 1mg of calcium oxalate and 10mg of extract/compound/standard and packed in semi permeable membrane of egg by suturing. This is suspended in a conical flask containing 100ml tris buffer. One group served as negative control. Conical flasks of all groups were placed in an incubator and pre heated for 7-8 hours. Content is removed from semi permeable membrane and placed in test tube. 2ml of 1N sulphuric acid added and titrated with 0.9494N $KMnO_4$ until light pink end point was obtained. The amount of un-dissolved calcium oxalate subtracted from the total quantity used in the beginning. Phenolic compound P isolated from ethyl acetate fraction demonstrated highest dissolution of calcium oxalate by *in vitro* model[21-23].

Antioxidant effect

Antioxidant effect was estimated by free radical scavenging and lipid peroxidation inhibitory effect. 0.1mM solution of DPPH (Diphenylpicrylhydrazyl) radical in methanol was prepared and 1ml of this solution was added to 3ml of the test material at different concentrations prepared in methanol. Solutions were incubated for 30min at room temperature and then absorbance was measured at 517nm. Decreasing of the DPPH solution absorbance indicates an increase of the DPPH radical-scavenging activity. For lipid peroxidation inhibitory activity, the kidneys isolated from Wistar rats were homogenized with electric homogenizer in ice cold 50mM phosphate buffer adjusted to pH 7.4. The homogenate was centrifuged for 10min and the supernatant was incubated without (control) and with different concentrations of (50 and 150g/ml) the test material in the presence of 10M FeSO4 and 0.1mM ascorbic acid at 37^0C for 1 h. The reaction was stopped by the addition of 0.5ml TCA (Trichloroacetic acid) (28%) and 0.75ml TBA (Thiobarbituric acid) (1%) in succession. The solution was then heated at 90^0C for 20min. Pink coloured Malondialdehyde-TBA complex was extracted with n-butanol (3ml) and the colour intensity was measured at 532nm using spectrophotometer. The inhibition ratio was calculated using the formula given for free radical scavenging activity. BLR caused scavenging of DPPH free radical with IC_{50} value of 2.0 (1.25-2.94)g/ml and inhibited *in vitro* lipid peroxidation induced in rat kidney homogenate by 41.33±1.86 and 94.75±0.30% at 50 and 150g/ml[24-25].

Anti-inflammatory activity

Anti-inflammatory activity was evaluated by checking level of enzyme succinate dehydrogenase. Anti-inflammatory activity of aqueous and 50% Ethanolic extracts of the rhizomes of *Bergenia ligulata* are reported

to attenuate the inflammatory response as determined by pharmacological and biochemical measurements. The treatment significantly decreased the inflammation. The activity level of succinate dehydrogenase (SDH), which has been reported to rise in inflammation, decreased in rats receiving the extract treatment. The study reports the radical scavenging activity of the rhizomes of *B. ligulata* and establishes the therapeutic rationale of using *B. Ligulata*[26].

Antiviral activity

Methanol-water extract from rhizomes of *Bergenia ligulata* inhibited *in vitro* the replication of influenza virus in a dose dependent manner and did not show virucidal activity at effective concentration. Pre-treatment of cells with *B. ligulata* extract was shown to be most effective to prevent cell destruction. The extract inhibited viral RNA synthesis and reduced viral peptide synthesis at 10μ/ml. The principal chemical compound was condensed tannins in the extract[27.]

Antidiabetic activity

The 80% Ethanolic extract of *B. ligulata* rhizome was fractionated for α-glucosidase inhibiting or antidiabetic activity. Sample solution obtained from fractions was evaluated at dose levels of 5.0, 0.5, 0.05mg/ml to obtain dose response. The ethyl acetate extract exhibited an inhibitory effect of α-glucosidase activity. The α-glucosidase inhibitor was isolated by silica gel column chromatography with chloroform and methanol as eluents. This research suggests that the α-glucosidase inhibitor in *B. ligulata* was primarily (+)-Afzelechin[28].

CONCLUSION

It is quite evident from this review that *Saxifraga ligulata* contains a number of phyto-constituents, which reveals its uses for various therapeutic purposes. The plant or its individual parts can be used for the treatment of various disorders in human being such as diabetes, liver toxicity, bacterial infection, inflammation, pyrexia and to relieve pain. Still, much work is required to investigate the mechanism of actions with other therapeutic activities.

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Cite this article as:

Priyanka Kantivan Goswami, Mayuri Samant, Rashmi S. Srivastava. Multi faceted Saxifraga ligulata: A mini review. Int. J. Res. Ayurveda Pharm. 2013;4(4):608-611 http://dx.doi.org/10.7897/2277-4343.04432