



PASHANBHEDA A GOLDEN HERB OF HIMALAYA: A REVIEW

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ABSTRACT

Pashanbheda or stone breaker is a well known Indian drug referred to botanical name *Bergenia ligulata*. This plant already has been recognized for its role in dissolving kidney stone. Its pharmacological activity are antidiabetic, antipyretic, hepatoprotective, anticancer, antiprotozoal, diuretic, cardiovascular, antiscorbutic, antilithiatic, anti-inflammatory due to phytochemicals Bergenin, Pashaanolactone, β -Sitosterol, Stigmesterol, Tannic acid, Gallic acid, Parasorbic acid, Isovaleric acid, 1,8-cineole present in Pashanbheda.

Key words: Pashanbheda, Stone breaker, *Bergenia ligulata*, Pharmacological activity, Phytochemicals.

INTRODUCTION

Bergenia ligulata belongs to family saxifragaceae. Pashanbheda, Pashana, Zakhmehayat, Asmaribheda, Ashmabhid, Ashmabhed, Nagabhid, Upalbheda, Parwatbhed and Shilabhed are the common name of *Bergenia ligulata*. It is called Stone breaker because it dissolves slabs. Rhizome is the medicinal part used of this. The plant *Bergenia ligulata* is main botanical source of Pashanbheda drug which is used in indigenous system of medicine [1-5].

SCIENTIFIC CLASSIFICATION

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Saxifragales
Family: Saxifragaceae
Genus: *Bergenia*
Species: *ligulata*

DISTRIBUTION

Bergenia ligulata is a perennial climbing plant that 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). It is found in Kyongnosla,

Changu, Karponanag, Lachen to Thongu, Nathang, Prekchu -Tsokha, Pangolakha- Subaney Dara, Gangtok (domesticated) in Sikkim. The flowers are white, pink or purple [3,6,7].

Biodiversity and Traditional knowledge of *Bergenia Ligulata* in Kumaun Himalaya

Kumaun Himalaya is rich in biodiversity and home of several medicinal plants. Our ancestors were aware of the medicinal values of Pashanbheda and prove in our ancient literatures like Ayurveda, Charaka Samhita, Susrata Samhita and Vagbhata which were known as divine truth of this plant. *Bergenia ligulata* is a well known Indian drug referred to as Pashanbheda or Stone breaker. It is an important medicinal plant of temperate Himalaya between 4,000 - 12,000 feet. Hooker (1888) has reported three species of this plant from India in the Flora of British India. Wehmer (1948) reported three species of *Bergenia* from India in the Wealth of India. Pande (1984) has observed one species i.e. *Bergenia ligulata* from Almora district. Recently, Gaur (1999) reported only *Bergenia ligulata* from north-west Himalaya in the flora of the district Garhwal, north-west Himalaya. Sharma observed two species i.e. *Bergenia ligulata* and *Bergenia stracheyi* from India in medicinal plants of India. Recently, Pangtey (2005) reported two species *Bergenia ligulata* from lower altitude and *Bergenia stracheyi* from higher altitude from Kumaun Himalaya.

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Figure 1. *Bergenia ligulata* plants with different colour of flowers



The plant *Bergenia ligulata* is chief botanical source of 'Pashanbheda', drug in indigenous system of medicine. Already this plant has been recognized for its role in dissolving kidney stone. It is also effective in fever, eye ailments, dysentery and diarrhea, piles, inflammation, chronic ulcers etc. The traditional data of Pashanbheda is limited and more information will help in discovering new drugs for several diseases. Extensive survey in and around kumaun Himalaya revealed this plant found in mixed vegetation on rocky slopes in moist & shady habitats, predominantly on northern and western slopes [8].

Taking reference from various ayurvedic medicinal books *Bergenia ligulata* is used as a medicine in different diseases as described:

Ayurveda: Leaf juice in urinary troubles, cold, hemorrhagic disease, distension of stomach and epilepsy.

Sushruta Samhita : In stones and sugars.

Charak Samhita: Useful in urinary complaints and stones.

Unani: In dissolving stones.

Chakradatta: In urinary troubles and stones.

Rajnighantu: In urinary disease.

Bhavaprakash: Astringent, bitter and sweet, purifies the urinary bladder.

Bergenia ligulata root, rhizome, and whole plant is used for kidney and bladder stones, urinary problems [9-18]. Rhizome is the main part or source of drug. It is light, cool, bitter, have useful effect in cough and cold [19] flowers are also consume as a form of pickled. With honey *Bergenia ligulata* is applied to gums in teething of children to allay irritation [11]. *Bergenia ligulata* has been reported to exhibit various pharmacological activities and thus has several traditional uses. It is used as an antidiabetic, antipyretic, [11,20,21] and as a tonic [13,22,23]. Ethanobotanical study of upper siran velly in Pakistan show that *Bergenia ligulata* (*but pewa*) used as diuretic, [11,24-26] hepatoprotective, alcoholic extracts of *Bergenia ligulata* showed anticancer, antiprotozoal, diuretic, cardiovascular, antiscorbutic, antilithiatic [9,27,28], litholytic property, anti-inflammatory, activity in dose dependent manner in rats [29,30]. *Saxifraga ligulata* (*Bergenia ligulata*) is used in formulation of herbal composition. Its composition is usefull for caring the skin around the eyes [30-32]. The plant *Bergenia ligulata* showed in vitro, in vivo animals study for the activity of calcium oxalate monohydrate growth inhibition, decreases calcium phosphate nucleation, calcium oxalate inhibition, diuretic, hypermagneseuric and antioxidant effect [3,33,34].

PHYTOCHEMICALS AND ITS ACTIVITY

Phytochemicals of rhizome

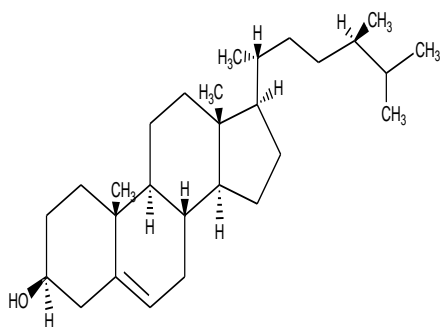
Bergenia ligulata rhizome has many bioactive chemical constituents such as Paashaanolactone Arbutin, (+)-Afzelechin² and Bergenin² Catechin and Minerals, Vitamins, Abumin (7.75%), Glucose (5.5%), Mucilage, Gallic acid etc. Starch (19%), Ash (mostly calcium oxalate) [35-38].

Table 1. Traditional uses of *Bergenia ligulata*

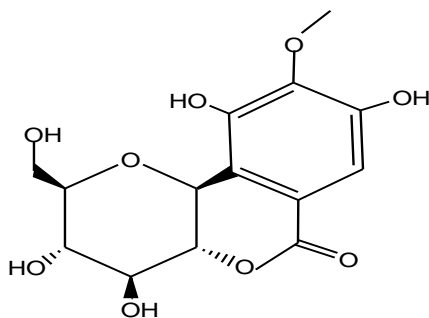
Location	Part used	Traditional Use
Tribes of Dharchula (UP)	Root	Boils, cuts, wounds, and ophthalmia, kidney stone, urinary complaints
Johari	Root	In asthma, urinary troubles
Kumaoni	Rhizome	In fever and thirst
Monpa(Arunachal Pradesh)	Leaf	In boils, cuts, wounds
Naga	Root	In lever complaints and TB
	Leaf	Boils, cuts and wounds
Central Himalaya Region	Plant	In dizziness, headache, vertigo
	Leaf	For dissolving kidney stones

Table 2. Traditional Knowledge of *Pashanbheda*

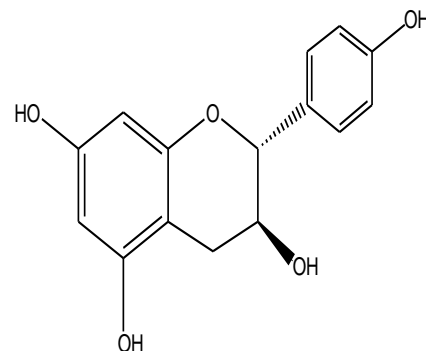
S.No	Ailments	Plant Parts Used	Method Used	Community Reported Used
1	Kidney and Gall bladder stone	Rhizome	Dried powder is used	Local knowledgeable person, Van Rawat, Bhotiya and Illiterate local people.
2	Wound / old wounds	Leaves and Rhizomes	Powder of dried leaves and rhizome are applied to heal old wounds	Local illiterate people, Buxa and Van Rawat
3	Septic	Rhizome	Paste of rhizome used as antiseptic	Locals and Van Rawat
4	Cough and cold	Leaves and Rhizome	Leaves and rhizome boiled with water and given in cold and cough.	Bhotiya
5	Cut and Burns	Rhizome	Crushed rhizome mixed with curd and applied on burns	Bhotiya and Van Rawat
6	Dysentery and Diarrhoea	Rhizome	Infusion of rhizome is taken orally for diarrhoea and dysentery	Locals, Van Rawat and Bhotiya
7	Fever	Rhizome	Dried powder is given in fever	Buxa
8	Asthama	Rhizome	Rhizome juice is given in acute asthma	Van Rawat and Buxa
9	Gasto-intestinal problems	Rhizome	All kinds of intestinal problems are cured by chewing fresh rhizome	Local literate and illiterate people
10	Eye ailments	Rhizome	Crushed rhizome sap is applied in eye diseases	Local knowledgeable people, Van Rawat and Bhotiya.
11	Septic pimples developed on the head of new born baby (Laizi)	Rhizome	Rhizome paste is applied	Local people, Bhotiya and Van Rawat
12	Chronic ulcers	Rhizome	The rhizome is crushed and used in all kinds of ulcers	Van Rawat and Bhotiya
13	Cutaneous infections	Rhizome	Rhizome paste is effective in cutaneous diseases	Local people
14	Inflammation	Rhizome	Paste of fresh rhizome is used	Local people
15	Rheumatic	Rhizome	Rhizome paste is anti rheumatic	Local people
16	Helmintic	Rhizome	Fresh & dried rhizome extract is used orally	Bhotiya
17	Piles	Rhizome	Fresh & dried rhizome extract is used orally	Buxa, Bhotiya and Local people
18	Tonsils	Leaves and Rhizome	Rhizome & leaves paste is applied externally	Bhotiya and Van Rawat
19	Cardiac problems	Rhizome	Rhizome powder is given	Bhotiya
20	Colitis	Rhizome	Rhizome paste cure internal wounds including colitis	Bhotiya
21	Aphrodisiac	Rhizome	Rhizome powder is given to increase spermatozoa	Bhotiya
22	Urinary diseases	Rhizome	Rhizome sap is taken orally in all kind of urinary problems	Locals, Van Rawat, Bhotiya and Buxa



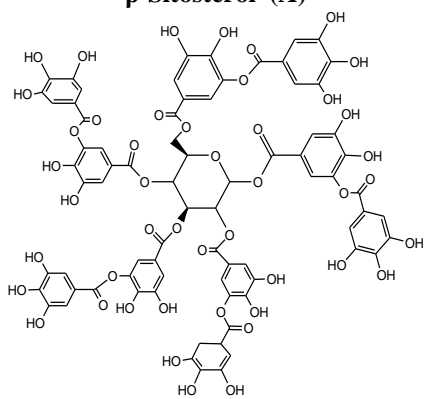
β -Sitosterol (A)



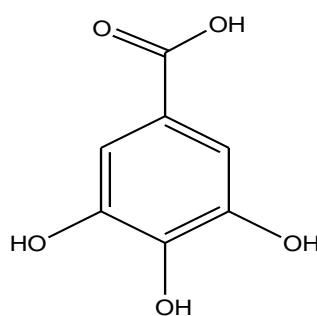
Bergenin (B)



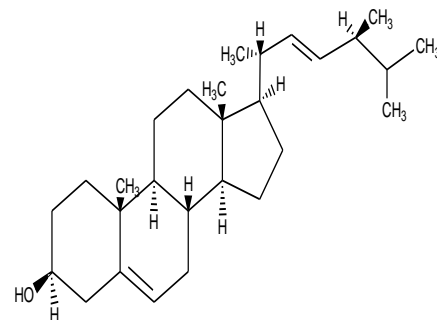
(+)- Afzelechin (C)



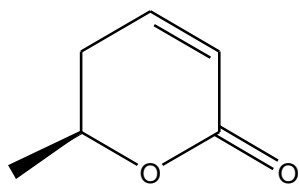
Tannic acid (D)



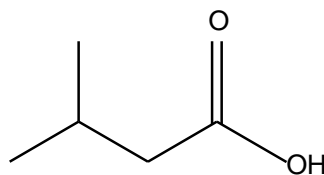
Gallic acid (E)



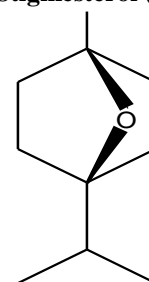
Stigmasterol (F)



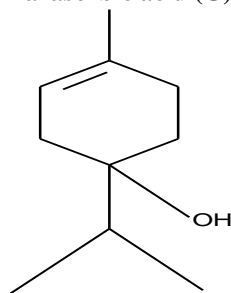
Parasorbic acid (G)



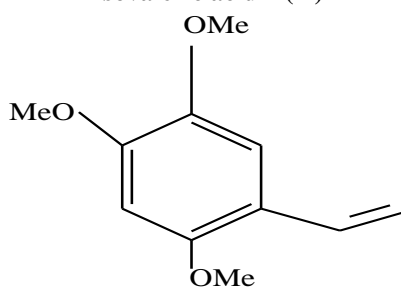
Isovaleric acid (H)



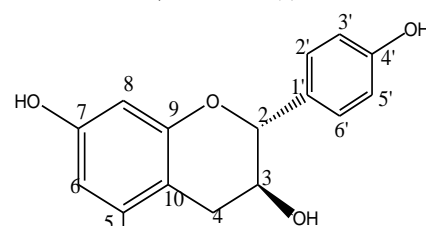
1,8-cineole (I)



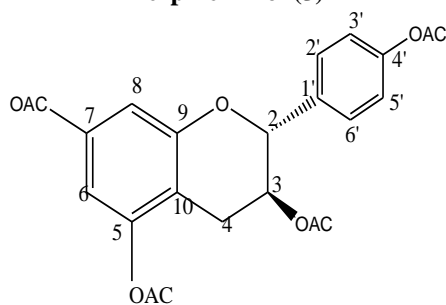
Terpinen-4-ol (J)



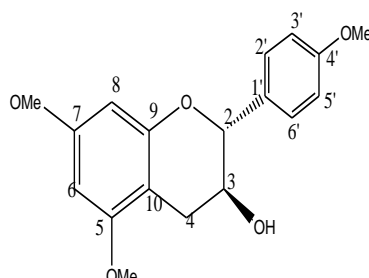
(Z)-asarone (K)



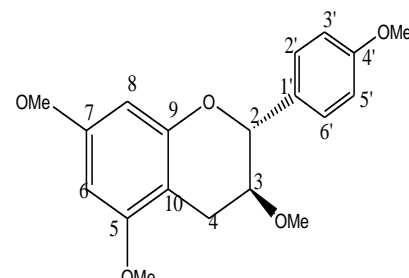
(+)- afzelechin(L)



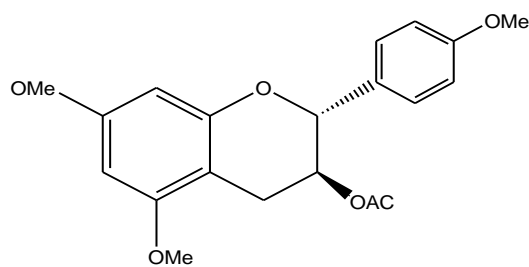
(+)-afzelechin tetracetate(M)



(+)-5,7,4'-trimethoxyafzelechin (N)



(+)-tetramethoxyafzelechin (O)



(+)-3-acetyl-5,7,4'-trimethoxyafzelechin (P)

Phytochemicals of seeds

Seeds of *Bergenia ligulata* contain Coumarin, Tannic acid, Gallic acid, Minerals and Wax [39].

Phytochemicals of root

The root of *Bergenia ligulata* showed the presence of alkaloids, steroids, flavonoids, terpenoids, tannins, glycosides, carbohydrates and saponins in preliminary investigation. β -Sitosterol, Stigmasterol, Tannic acid and Gallic acid were isolated by using thin layer and column chromatography [40].

In fact, the whole plant of *Bergenia* can be used in medicine, but its active ingredients were mainly focused on Polyphenols, among which Bergenin is studied and applied most frequently [41-44,66]. The volatile oil from roots of *Bergenia ligulata* was analyzed by GC-MS. (+)-(6S)-Parasorbic acid 47.45%, Isovaleric acid 6.25%, 1,8-Cineole 4.24%, (Z)-Asarone 3.50%, and Terpinen-4-ol 2.96% were the most prominent constituents. From the rhizomes of *B. ligulata* only Bergenin and β -sitosterol have been isolated.

Quantification of Bergenin and (+)-Afzelechin

Rhizome, petiole and leaf (1gm each) were extracted with methanol and analysed by HPLC for the estimation of Bergenin and (+)-Afzelechin. Extraction of the rhizome material using three reflux periods (60, 90, 120 min.) showed that a 90 min reflux periods time gave the highest yield of the two active constituents, Bergenin and (+) - Afzelechin. Thus a procedure involving two cycle of refluxes (90 min each) with methanol (50 ml) was found to be suitable for the complete quantification of Bergenin and (+)-Afzelechin in all the test samples. Bergenin was found to be the major component of *B. ligulata* rhizomes with the concentration being about 7 times greater than that of (+)-Afzelechin while the latter was not detected in the aerial parts (petiole, leaf). The content of Bergenin in the petiole and leaf was found to be less than 8 times of that found in the rhizomes. Therefore rhizomes from the major source of Bergenin and (+) - Afzelechin [45].

Antidiabetic activity

The 80% ethanolic extract of *B. ligulata* rhizome was fractionated to investigate for α -glucosidase or antidiabetic activity. Sample solution were evaluated at dose levels of 5.0, 0.5, 0.05 mg/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

and identified as (+)-Afzelechin (L) by EI-MS, IR, H^1 and C^{13} NMR spectroscopy. The inhibitory compound 12 was investigated in the inhibition of α -glucosidase activity at a concentration of 0.25 mm and the ID_{50} (50% Inhibition dose) value was 0.13 mm. For confirming the structure-activity relationship, compounds M-P were investigated in the inhibition of α -glucosidase activity test. Compound M-P inhibited 2.8%, 41.8%, 59.4% and 90.4% of α -glucosidase activity at a concentration of 0.25mm. The ID_{50} values of compound O and P were 0.14 and 0.05 mm respectively. Compound P had strongest inhibitory activity in this compound and IC_{50} value of P was 2-fold higher than those of L and O. Previously, α -glucosidase inhibitory activity of natural occurring flavan-3-ols has been reported. IC_{50} value of (+)-Catechin and (-)-Epicatechin were 12.8 and 0.18 mm respectively. Compound L, O and P showed more potent inhibitory activity than those of Catechins. This research suggests that the α -glucosidase inhibitor in *B. ligulata* was primarily (+)-Afzelechin [46-49,66].

MEDICINAL ACTIVITY OF RHIZOME

Anti-inflammatory activity

Evaluation of the 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* in Indian System of Medicine [50-52,66].

Antilithic activity

The alcoholic extract had no effect in preventing stone formation in rats (after the method of Lyon) but was of significant help in dissolving preformed stones. Low doses of Pashanabheda extract (0.5 mg/kg of alcoholic extract) promote diuresis in rats, but higher dose 100 mg/kg reduce the urine output and also reduce the diuresis produced by urea [30,54].

The crude aqueous-methanolic extract of *Bergenia ligulata* rhizome (BLR) was studied using in-vitro and in-vivo methods. The result was that BLR inhibited calcium oxalate (CaC_2O_4) crystal aggregation as well as crystal formation in the metastable solutions and exhibited antioxidant effect against 1,1-diphenyl-2-picrylhydrazyl free radical and lipid peroxidation in the in vitro. BLR caused diuresis in rats accompanied by a saluretic effect. In an animal model of urolithiasis, developed in male wistar rats by adding 0.75% ethylene glycol (EG) in drinking water, BLR (5-10 mg/kg) prevented CaC_2O_4 crystal deposition in the renal tubules. The lithogenic treatment caused polyuria, weight loss, impairment of renal function and oxidative stress, manifested as increased malondialdehyde and protein carbonyl contents, depleted reduced glutathione and

decreased antioxidant enzyme activities of the kidneys, which were prevented by BLR. Unlike the untreated animals, EG intake did not cause excessive hyperoxalurea and hypocalciurea in BLR treated groups and there was a significant increase in the urinary Mg^{2+} , instead of a slight decrease. These data indicate the antiurolithic activity in *Bergenia ligulata* mediated possibly through CaC_2O_4 crystal inhibition, diuretic, hypermagneseuric and antioxidant effects and this study rationalizes its medicinal use in urolithiasis. Garimella et.al studied urine or cell culture in vivo on *Bergenia ligulata* and the result was that the plant decreases calcium phosphate precipitation [55,66].

Anti-bradykinin activity

The alcoholic extract of *Bergenia ligulata* rhizome displays marked anti-bradykinin activity. Although it does not affect the action of 5-HT and acetylcholine on isolated guinea pig ileum. It has been shown to potentiate the action of adrenaline on guinea-pig trachea and ileum muscle. Its cardiotoxic, antidiuretic and CNS depressant action on experimental models have been reported with large doses. It is unlikely that these effects will be encountered with the doses in clinical use. In rats, the LD_{50} of the aqueous extract was 650 mg/kg intraperitoneally. It is widely used in the treatment of dysuria and renal failure, cystitis and crystalluria. Its anti-inflammatory property finds a use in the treatment of abscesses and cutaneous infections. It is also used in the treatment of dysentery and diarrhea [60].

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. Pretreatment 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 10 microg/ml. The principal chemical compound was condensed tannins in the extract [61,62].

Antibacterial activity

The antibacterial activity was tested using the disc diffusion method measured by 10, 25 and 50 mg/ml plant extract. The zone of inhibition was calculated by measuring the minimum dimension of the zone of no microbial growth around the well. Aqueous, 50% ethanolic and methanolic extracts of *B. ligulata* rhizomes were tested for their ability to inhibit the growth of *E. coli*, *B. subtilis*, and *S. aureus* at the dose levels of 10, 25 or 50 mg/ml for each extract. At a dose level of 50 mg/ml, the antibacterial effect was most significant. Incidentally, the antibacterial effect of the extracts at this level was comparable to ciprofloxacin (25 mg/ml). The results clearly suggest that *B. ligulata* possesses a strong antibacterial activity [63-65].

MEDICINAL ACTIVITY OF ROOT

Hepatoprotective activity

The ethanolic extracts of root of *Bergenia ligulata* were assessed for hepatoprotective activity in albino rats that was compared with standard drugs. Acute toxicity studies were carried out for ethanolic extract of *Bergenia ligulata* root on healthy Swiss albino mice of body weight 25- 35g by using Up and Down or Stair case method. Evaluation of the hepatoprotective activity was done by measuring the levels of serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT) serum alkaline phosphatase and total bilirubin levels. The ethanolic extract of the roots of *Bergenia ligulata* was found to produce significant activity.

Diuretic activity

The ethanolic extracts of root of *Bergenia ligulata* were assessed for diuretic activity in albino rats that was compared with standard drugs. For evaluation of the diuretic activity Lipschits method, was used. It was done by measuring the volume of urine collected at the end of 5 hrs and Na^+ , K^+ and Cl^- concentration in urine. The ethanolic extract of the roots of *Bergenia ligulata* was found to produce significant activity.

The extracts of *Bergenia ligulata* root were studied in the presence of artificial reference urine (ARU) and human urine (HU) the growth behaviours of CHPD crystals grew within the rings. The addition of aqueous extract of *B. ligulata* to the calcium chloride in the supernatant solution modified the diffusion process and hence the periodic precipitation and the number of Liesegang rings. The maximum length of the crystals was reduced due to inhibition produced by the addition of aqueous extract of *B. ligulata* the HU aqueous extract (AE) of *B. ligulata* contained a large number of salts and organic molecule. And their complex formation may have promoted the effect on growth of CHPD crystals. But when they are added separately to $CaCl_2$ they inhibit the growth of crystals. This suggests that these solutions separately inhibit the growth of crystals in in-vitro condition. But mixing with HU (humane urine) changes their behaviour markedly. The diuretic nature of AE/*B. ligulata* seems to be important in the remedy rather than their inhibitive nature [60-66].

MEDICINAL ACTIVITY OF COMBINED PLANT PART (ROOT, RHIZOME AND LEAVES)

Antipyretic activity

The ethanolic (95%) extracted of roots, rhizomes and leaves and aqueous extract of whole plant of *Bergenia ligulata* Wall in yeast induced fever in albino rats of wistar strain were assessed for antipyretic activity.⁵¹ The yield of semisolid mass (w/w) was obtained as ethanol extract of roots (13.36%), ethanol extract of rhizomes (15.12%), ethanol extract of leaves (11.02%) and aqueous extract of whole plant (09.21%). Acute toxicity studies were carried out for all the extracts of *Bergenia ligulata* Wall on healthy swiss albino mice of body weight 25-35g by using Up and Down or Stair case method. The suspension of all the extracts of *Bergenia ligulata* Wall was prepared in 5% gum acacia and employed for assessment of antipyretic

activity at the dose of (300 and 500mg/kg- body weight). The standard drug used was paracetamol (200mg/kg.p.o). Rectal temperature of experimental animals was recorded at a time interval of 1hr, 2hr, 3hr, 4hr and 5 hr after drug administration for evaluation of antipyretic activity. The ethanolic extract of roots and rhizomes of *Bergenia ligulata* Wall at a dose of 500mg/kg.p.o decreased the yeast induced fever in experimental animals [51,63].

The ethanolic extracts of root of *Bergenia*

ligulata were assessed for antipyretic activities in albino rats that were compared with standard drug. The assessment of Antipyretic activity was carried out using Brewer^{rs} Yeast induced pyrexia method in wistar rats. Rectal temperature was recorded at a time interval of 0, 30 min, 1 hr, 2 hr, 3 hr after drug administration for evaluation of antipyretic activity the ethanolic extract of the roots of *Bergenia ligulata* was found to produce significant antipyretic activity [64].

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