

Bergenia ciliata (Haw.) Sternb.: A Comprehensive Review on Ethnomedicinal Significance, Phytochemistry, Pharmacological Activities and Therapeutic Potential

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ABSTRACT

Bergenia ciliata (Haw.) Sternb. is generally known as Pashanbhedha, is a perennial medicinal herb commonly found in Himalayan region. Traditionally the plant has been used in the treatment of urolithiasis (kidney stones), urinary tract disorders, inflammation, cough, wound healing, fever, and various gastrointestinal disorders. Phytochemical investigation has identified various bioactive phytochemicals such as bergenin, gallic acid, catechin, tannins, arbutin, β -sitosterol, flavonoids, polyphenolic metabolite, sterols, which promote its diverse pharmacological potential. The overview study analyses show scientific investigation which identified various bioactive phytoconstituents with is responsible for its biological activities and highlight it as a valuable source for novel therapeutic agents. Google Scholar, Science Direct, Pub Med or Research Gate are the scientific research database which are used for gathering information for the study of *B. ciliata*. Relevant peer-reviewed articles, books and published reports are used for screening and analysis of information on ethnomedicinal, phytochemistry, pharmacology and therapeutic potential. Pharmacological studies demonstrate diverse therapeutic potential such as free radical scavenging, inflammation inhibition, antibacterial/antifungal, antiurolithiatic, antiulcer, antiviral, antidiabetic, neuroprotective as well as cardioprotective effects. Recent evidence also supports its immunomodulatory and anticancer potential. Despite promising preclinical evaluation, comprehensive clinical validation and toxicity profiling remain limited. This review aims to collect and critically analyze the available literature on the phytochemical profile, ethnomedicinal uses, pharmacological activities and therapeutic potential of *B. ciliata*, and emphasizing its significance as a natural source for future drug development.

Keywords: Bergenin, Ethnomedicine, Pharmacological activity, Phytochemistry, Therapeutic Potential.

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Received: 11-08-2026;

Revised: 03-09-2026;

Accepted: 21-10-2026.

INTRODUCTION

The medicinal use of plant has developed over thousands of years and the Emperor Chin Nong in China thought to have composed an herbal in 2700BC.^[1] Currently, about 70-80% of world population uses herbal plant-based medicine directly or indirectly for curing diseases.^[2] According to the World Health Organization (WHO), traditional/herbal medicine refers to the sum of total of the knowledge, skills, and practices based on the theories, beliefs, and experiences of different cultures, whether explicable or not, used in the maintenance of health as well in the prevention, diagnosis, improvement or treatment of physical and

mental illness.^[3] Growing health challenges, such as antibiotic resistance and cancer require an innovative approach to drug development. Natural products offer a rich source of structurally complex molecules that have evolved to interact with multiple biological target systems, making them valuable candidates for drug discovery.^[4]

A perennial rhizomatous medicinal herb, *B. ciliata* is belonging to the Saxifragaceae family.^[5] There are over 580 species and 30 genera in the family Saxifragaceae worldwide.^[6] *B. ciliata* (Haw.) sternb. is widely known as “winter begonia”.^[7] The plant is popularly known as “Pashanbhedha”, a Sanskrit term meaning “stone breaker”, indicating traditional use in dissolving kidney stones.^[8] In English it is called “Rock foil” that demonstrate that the plant has lithotriptic potential and grows between the rocks. The major phytochemical constituents of *B. ciliata* including tannin constituents such as tannic acid, phenolic acid including gallic acid, bergenin, albuten, catechin, methyl gallate, metarbin and polymeric tannin.^[9]



DOI: 10.5530/phrev.20270067

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Geographical distribution and habitat

B. ciliata is widely found in cold and temperate climate regions. It is widely found at altitude between 900 to 2700 meters above sea level in the temperate Himalayan areas, from Arunachal Pradesh to Kashmir. *B. ciliata* generally flowers during the late winter to early summer, typically from February to May depending on climate conditions.^[10]

Botanical description

A perennial herb *B. ciliata* that grows up to about 35 cm in height. These herbs mostly found in moist and shady places. The leaves few, spreading, and vary in shape from nearly round to broadly ovate. The rhizomes are solid, dark brown, cylindrical and barrel shaped. It has a hard texture, aromatic odour, and an astringent taste. Seeds elongated about 1 mm long, brown, and tuberculate in shape.^[9,11]

Ethno-medical Importance of *B. ciliata*

B. ciliata has been widely used into traditional healthcare systems for the treatment of various diseases across Nepal, India, Pakistan, Bhutan and several other countries.^[12] The plant rhizomes were traditionally utilized for centuries as a therapeutic approach for kidney stones and rheumatoid arthritis in addition to its various therapeutic and nutraceutical application within ethnomedicine, and traditional system such as Ayurveda and Unani medicine system (Table 1).^[13]

Phytochemical Profile of *B. ciliata*

Phytochemical screening is an essential step in the identification and isolation of biologically active phytoconstituents from medicinal plants. Secondary metabolites were identified with the help of phytochemical screening, secondary metabolites like steroid, terpenoids, saponins, flavonoids, and anthraquinones.^[14] The pharmacological activity of *B. ciliata* is linked to the presence of diverse phytochemical constituents including, bergenin, tannic acid, gallic acid, (-)-3-O-galloylepicatechin, (-)-3-O-galloylcatechin, (+)-catechin, and gallicin, Paashanolactone, sitoindoside, quercetin, afzelechin.^[15,16] Phytochemical examination of *B. ciliata* leaf and aerial parts have led to the isolation of various important bioactive phytochemicals. These include hydroquinone (benzenoid compound), (+)-afzelechin, (+)-catechin, quercetin-3-O- β -D-xylopyranoside, quercetin-3-O- α -L-arabinofuranoside, eriodictyol-7-O- β -D-glucopyranoside, arbutin, 6-O-p-hydroxybenzoylarbutin, bergenin, 4-O-galloylbergenin, 11-O-galloylbergenin, p-hydroxybenzoic acid (Tables 2 and 3).^[9,17]

Pharmacological Profile of *B. ciliata*

Anti-cancer activity

B. ciliata methanol extract was studied for determining its anticancer potential underlying molecular mechanisms using

MTT assay in MDA-MB-231 and C6 glioma cell lines. The study evaluated UPR markers, ATF4 gene expression, and ROS levels through immunoblotting, RT-PCR and spectrophotometric assays. This study showed that methanol extract of *B. ciliata* induce apoptosis by suppressing the cytoprotective IRE1-XBP1 and ATF6 pathways while activating the PERK-ATF4-CHOP pathways, other side increasing ROS accumulation and inhibiting antioxidant enzymes. The finding of this study observed that *B. ciliata* methanol extract is a potent anticancer compound/agent targeting UPR and ROS pathways.^[18]

Antioxidant activity

This study demonstrates the antioxidant and anticholinesterase activities of crude extracts, subfractions, and isolated compounds from *B. ciliata*. DPPH and ABTS assay were used to determine free radical scavenging abilities. Anticholinesterase activity was evaluated against acetylcholine esterase and butyryl esterase enzyme. The crude extract showed maximum anticholinesterase and free radical scavenging against DPPH and ABTS potential. In ethyl acetate fraction total phenolic content was higher while flavonoid contents were higher in n-butanol fraction followed by crude extract. The obtained phytochemicals are pyrogallol, rutin, and morin were found active against ABTS and DPPH free radicals and pyrogallol also exhibited notable anticholinesterase activity.^[19]

Anti-inflammatory activity

The methanol extract of the rhizome of *B. ciliata* has been determined for its anti-inflammatory activity using two rat models (acute rat models and chronic rat models). In acute inflammation models, methanol extract displayed maximum reduction in carrageenan-induced rat paw oedema while the standard phenylbutazone showed inhibition after 3 h of drug treatment, and in chronic inflammation model/cotton pouch granuloma, the extract show inhibition considerably in dose dependant manner. In this model extract produced maximum inhibition in granuloma weight compared with standard. Methanol extract of *B. ciliata* showed significantly anti-inflammatory potential at dose levels examination.^[20]

Antibacterial activity

The ethyl acetate extract exhibits the highest antibacterial activity, which shows a strong inhibitory effect against *Streptococcus mutans* at required concentration. TLC-bioautography analysis revealed two active fractions (F1 and F2), which showed clear zone of inhibition. Kaempferol was identified as F1 fraction. This study shows the first time describing the antibacterial activity of *B. ciliata* flowers against oral pathogen. The mechanism of F1 shows its ability to compromise bacterial membrane integrity, reducing and damaging the biofilm formation and it also induced the generation of Reactive Oxygen Species (ROS) within the

bacterial cells, resulting in lipid peroxidation and leading to bacterial cell death.^[21]

Anti-ulcer activity

B. ciliata was investigated for gastroprotective activity against ethanol/HCl, indomethacin, and pylorus ligation-induced gastric ulcer model in rats. The extract of *B. ciliata* was given at different doses such as 15, 30, and 60 mg/kg body weight, which shows a potential anti-ulcer activity. The gastroprotective activity mainly attributed to cytoprotective mechanisms, which involved the enhancement of the gastric mucosal barrier rather than lowering the pH and gastric acidity.^[22]

Antiviral activity

In this study *B. ciliata* was evaluated as a host-directed antiviral agent against dengue virus by targeting ER- α -glucosidase II (a host enzymes), which was involved in dengue viral pathogenesis. *In silico* docking and molecular dynamics studies was done which confirmed the stable binding of both compounds to ER- α -glucosidase II, and ADMET studies was conducted which indicated the favourable drug like properties. The finding of this study suggests that, in *B. ciliata* particularly bergenin as well as gallic acid holds the significant potential as a broad-spectrum antiviral agent against dengue virus (Figure 1).^[23]

Anti-urolithiatic activity

Hydroalcoholic extract of *B. ciliata* was used to evaluate the antiurolithiatic property in ethyl glycol-induced urolithiasis using adult female rats (Wistar rats). Treat ethylene glycol (0.75% v/v) for 28 days to induce kidney stone formation, also with *B. ciliata* extract (150-300 mg/kg) or with standard drug cystone. Ethylene glycol treatment causes some alteration in body weight, organ weight and some major histopathological changes (disrupted renal parenchyma, glomerular degeneration). *B. ciliata* extract showed significant protection against these changes. This study exhibits more renoprotective index than cystone at same dose level, which indicate a potent anti-urolithiatic activity.^[24]

Formulation of *B. ciliata* (pashanbheda)

B. ciliata is recognized for its high medicinal value which is mentioned in ancient Ayurvedic literature (Vedas, Charaka Samhita, and Sushruta Samhita). Different parts of the plant show distinct therapeutic activities. In ancient Ayurvedic practice, the rhizomes commonly used for the treatment of bladder stones and urinary tract infection which is included in Ayurvedic formulation such as *Asmarihara Kasaya Curna* (urolithiasis) and *Mutravirecaniya Kasaya Curna* (dysuria).^[25]

Therapeutic Formulation of *B. ciliata*

IIIM-160 (capsule)

It is a botanical formulation developed by Indian Institute of integrative medicine (IIIM). It is a bergenin-rich extract of *B.*

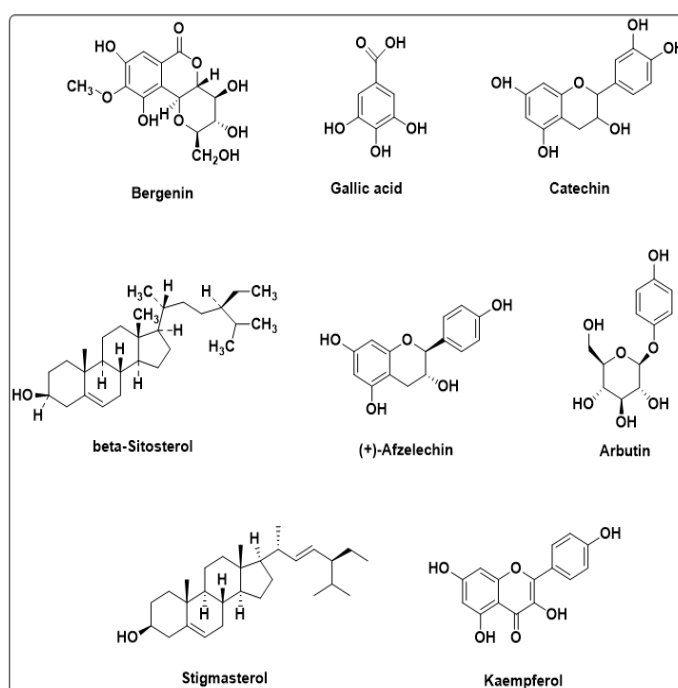


Figure 1: Structures of Active Phytochemical constituents present in *B. ciliata*.^[9,33,35,36,37]

Table 1: Ethnomedical uses of *Bergenia ciliata*, part used, formulation, diseases treated and area.

Plant part used and formulation	Traditional uses	Area	References
Rhizomes (Powder/paste)	Kidney stones, urinary disorder, gastrointestinal diseases, ulcers, respiratory diseases	India, Nepal, Pakistan	[28]
Roots (powder/decoction)	Rheumatism, gout, stomach ache, diuretic, burns, ophthalmia, skin disease	India, Bhutan	[29]
Leaves (Paste/juice/decoction)	Cough, sore throat, diarrhoea, Indigestion, boils and burns	Jammu & Kashmir	[28]
Flowers (Powder/paste)	Skin inflammation, headache	Ladakh	[31]
Whole plant (Paste/juice/decoction)	Skin sores, joint pains, Fracture	India, Arunachal Pradesh	[30]
Latex (Paste)	Warts	India, Bhutan	[29]
Stem (Paste)	Joint pain	India, Bhutan	[28]

Table 2: Phytochemicals of *B. ciliata* with their class and activities.

Phytoconstituent	Class	Activity/Pharmacological effect	References
Bergenin	Phenol	Antioxidant activity	[17]
Tannic acid	Phenol	Antioxidant, antiurolithiatic, antimicrobial	[32]
Gallic acid	Phenolic acid	Antifungal, antiviral	[17]
Catechin	Phenol	Antimicrobial, cardioprotective potential, antidiabetic activity	[17]
(-)-3-O-galloylecatechin	Phenolic acid	Anti-urolithiatic, hepatoprotective	[34]
(-)-3-O-galloylepicatechin	Phenolic acid	Hepatoprotective, cytoprotective	[32]
β -sitosterol	Sterol	Hypocholesterolemic, antidiabetic, anti-obesity	[33]
Arbutin	Glycoside	Anti-urolithiatic, antimicrobial, Skin diseases	[34]
(+)-afzelechin	Flavonoid	Antimicrobial, astringent activity	[32]
Kaempferol	Flavonoid	Antimicrobial and neuroprotective, anti-inflammatory, anti-anxiety	[34]

Table 3: Distribution of phytoconstituents in different parts of *B. ciliata*.

Phytoconstituent	Plant part (Source)	References
Bergenin	Rhizomes	[9]
Gallic acid	Rhizomes (also reported in roots and leaves)	[35]
Catechin	Rhizomes	[9]
β -Sitosterol	Rhizomes (also reported in leaves)	[36]
(+)-Afzelechin	Rhizomes	[37]
Arbutin	Rhizome Leaves	[9]
Stigmasterol	Rhizome	[33]
Kaempferol	Leaves	[33]

Table 4: Formulation of *B. ciliata* (Pashanbheda).

Formulation Name	Indication (uses)	References
Pashanabheda Churna	Ashmari (urolithiasis), Mutrakrichra (dysuria)	[38]
Pashanabhedadi Kwatha	Urinary calculi, urinary disorders	[38]
Cystone	Renal calculi	[39]
Neeri (Tablet/syrup)	Urinary tract infection	[40]
Zenex <i>Bergenia ciliata</i> (powder)	Dissolve kidney stones, and act as diuretic and anti-inflammatory agent	[41]

ciliata which is used as an anti-inflammatory and anti-arthritis drug IIM-160 (9.1% w/w), with dual activity of IL-6 inhibition and antinociception, which make it suitable for treatment of rheumatoid arthritis (Table 4).^[26]

Gastro-retentive swellable oral formulation

Gastro retentive sustained release formulation was prepared using *B. ciliata* for treating inflammatory diseases.^[27]

CONCLUSION

B. ciliata is a medicinal plant of significant ethnomedicinal importance, exhibiting various pharmacological activities. The occurrence of major phytoconstituents include gallic acid, bergenin, catechin and various other phenolic compounds, which underline its large therapeutic potential, particularly in treatment of urolithiasis (kidney stones), Inflammatory disorders, and gastrointestinal disorders. Even though many *in vivo* and *in vitro* studies support its traditional uses, but still there is a need for well-established clinical trials, detailed mechanism-based studies, standardized extract formulations and long-term safety evaluations. Overall, *B. ciliata* holds significant potential for the development of safe and effective herbal plant-based medicine and further more scientific investigation.

ACKNOWLEDGEMENT

The author truly thanks to the School of Pharmaceutical Sciences, Bahra University, Solan for their support and guidance in the preparation of this review article.

ABBREVIATIONS

WHO: World Health Organization; **DPPH:** 2,2-diphenyl-1-picrylhydrazyl; **ABTS:** 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid); **MTT:** 3-[4,5-dimethyl-2-thiazolyl]-2,5-diphenyl tetrazolium bromide; **UPR:** Unfolded Protein Response; **ROS:** Reactive

Oxygen Species; **IRE1**: Inositol-Requiring Enzyme 1; **ATF4**: Activating Transcription Factor 4; **CHOP**: Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisone; **PERK**: Protein kinase RNA-like endoplasmic reticulum kinase; **TLC**: Thin-layer Chromatography; **ADMET**: Absorption, Distribution, Metabolism, Excretion, and Toxicity.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

Anshika Thakur: Conceptualization, literature survey and drafting. **Ms. Shruti Thakur**: Conceptual guidance, supervision, critical revision and final approval of manuscript. **Vishnu Das, Vandana Sharma and Arun Thakur**: Literature survey, editing, and assistance in manuscript preparation.

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Cite this article: Thakur A, Thakur S, Das V, Sharma V, Thakur A. *Bergenia ciliata* (Haw.) Sternb.: A Comprehensive Review on Ethnomedicinal Significance, Phytochemistry, Pharmacological Activities and Therapeutic Potential. Pharmacog Rev. 2026;21(41):21-6.