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Review Article

## Bridging Tradition and Modern Pharmacology of *Bergenia ciliata* (Haw.) Sternb: A Review

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### Abstract

*Bergenia ciliata*, a perennial rhizomatous herb holds a special place in the traditional herbal healthcare system due to its diverse therapeutic uses and potentials. Validation of its efficacy with scientific investigation is a prerequisite of any prospective herbal resource. The plant is a rich source of various bioactive chemical compounds. The present review is an attempt to consolidate comprehensive information sourced from 100 different literatures, exploring the plant's distribution, phytochemistry, traditional medicinal uses, and pharmacological activities specially focusing on some prevalent diseases of present day. The herb's antimicrobial, anticancer, antiulcer and antidiabetic properties signify its potential in modern pharmacology. The review underscores *B. ciliata*'s relevance in drug development and nutraceutical formulations, bridging age-old wisdom with contemporary healthcare solutions. Further exploration into its bioactive compounds and clinical applications promises innovative avenues in therapeutic intervention.

**Keywords:** *Bergenia ciliata*, perennial rhizomatous herb, traditional herbal healthcare, age-old wisdom

## Introduction

*Bergenia ciliata* (Haw.) Sternb. a perennial rhizomatous herb belonging to Saxifragaceae family holds significant ethno-medicinal importance. The name *Bergenia* was coined by Conrad Moench in 1794 in the name of a distinguished Botanist and Physician Karl August von Bergen<sup>1</sup>. The plant is known by various names such as Shailagarbhaja, Pashanbheda (Ayurveda), Pakhanabeda (Hindi), Pakhanbed (Unani) Pakhanbed (Nepali) is a cornerstone among medicinal plants. It is found growing extensively in the Himalayan region from Kashmir to Arunachal Pradesh<sup>1,2,3,4,5</sup> between 1000 – 3000 m above sea level. Its geographical extent reaches beyond the Indian Himalayas to neighboring countries like Nepal<sup>6,7,8</sup>, Bhutan<sup>2</sup>, Pakistan<sup>9,10,11</sup>, Afghanistan<sup>12</sup> up to South Tibet<sup>13</sup>, mostly growing at higher altitudes. The name 'Pashanbheda' (Pashan meaning rockstone 'bheda' meaning piercing) aptly describes its prolific growth on the rocky surfaces.

*Bergenia ciliata* is a highly versatile medicinal herb renowned for its wide-ranging therapeutic value. Because of their medicinal properties it is traded in large amount, particularly from Sikkim and Kumaon Himalaya and Nepal<sup>3,8,14</sup>. It is one of the most important folk medicines in Indian subcontinent including China<sup>13,15,16</sup>, with medicinal roots tracing back to vedic times. The rhizome of *Bergenia* have been used for centuries in Ayurvedic, Unani, Amchi and Jodi-buti formulation to dissolve kidney and gall bladder stones, piles, abnormal leucorrhea, and pulmonary affections<sup>17,18,19</sup>. It is also used in the treatment of many diseases like skin diseases,

gastrointestinal problems, heart diseases, ophthalmic problems, worm infection, diarrhoea, respiratory diseases, fever, oral infections, cancer, and gynaecological disorders<sup>1,12,16,20,21,22,23,24</sup>. Its historical remedial significance and broad applications highlight its enduring importance in the traditional practices and in modern drug development.

Herbal remedies hold significant value as a rich bioresource for preventing infections and diseases<sup>25,26</sup>. The traditional herbal remedies serve as the primary sources for bioprospecting. Researches worldwide have explored the therapeutic potential of *B. ciliata* on various ailments. The present review is an attempt to gather information on the traditional use of *Bergenia ciliata* its phytochemistry, and pharmacology and also discuss research findings particularly focusing on the plant's effectiveness against some prevalent disease like diabetes, ulcers, antimicrobial and anti-cancer that prevalent now-a-days.

## Methodology

The current review on *Bergenia ciliata* draws upon comprehensive collection of literature sources. A systematic approach was employed to meticulously review existing literature, aimed at consolidating pertinent information on the plant's distribution, phytochemical composition, traditional medicinal applications, and pharmacological activities, specifically focusing on its efficacy in addressing current prevalent diseases – microbial, cancer, diabetes and gastric ulcers afflicting the world populace. To achieve this, diverse bibliographic search engines and online databases (such as

Google Scholar, WoS, PubMed, CAB abstracts, INMEDPLAN, Scopus, NATTS, EMBASE, SciFinder, MEDLINE) were meticulously consulted, alongside pertinent websites, facilitating an in-depth and detail analysis.

## Botanical description

*Bergenia ciliata* is a perennial rhizomatous herb that reaches a height of up to 35 cm tall with stout rhizomatous rootstock with intermittent axillary buds. The Leaves are sparse, spreading and leathery, glabrous or hirsute, suborbicular to orbicular or broadly obovate up to 30 cm long; Leaf margin sparsely hairy, Petiole 1-2(-5) cm long, glabrous or hirsute. Inflorescence a terminal corymb, often subtended by an ovate leafy bract; bract glabrous or sparsely ciliate; scape and inflorescence greenish or pink tinged. Peduncle up to 10 cm long; flowers pink to purplish, pedicellate. Sepals c. 7 mm long, oblong. Petals 10 x 4 mm, unguiculate, limb orbicular. Filaments c. 1 cm long, pink to red. Carpels 2. Styles c. 7 mm long. Carpels and styles green or pinkish. Capsule 13 x 6 mm, including styles. Seeds elongated, c. 1 mm long, brown, minutely tuberculate.



Habit of *Bergenia ciliata*

## Traditional use:

*Bergenia ciliata* has a rich history in traditional medicine, maintaining a significant role in both Unani and Ayurvedic medicinal practices. Various plant parts including rhizomes, roots, leaves, stem, and entire plant have been integral in treating a diverse range of ailments from ancient times. These include kidney and gallbladder stone, lungs and liver disease, spleen enlargement, tumors, diarrhoea, dysentery, dysuria, eyesores, cough, fever, piles, gastro-intestinal disorders, fever<sup>20,27,28,29,30</sup>.

Ethnobotanical studies involving local herbal healers and knowledgeable elderly people have provided substantial information about the use of the *B. ciliata*. Choudhury et al.<sup>20</sup> recorded 30 uses of *B. ciliata* in the Kumaon Himalayan region. Similarly, Rafiq et al.<sup>16</sup> extensively documented 104 uses ranging from common to chronic ailments in the Kashmir Himalaya.

In Darjeeling and Sikkim Himalaya, local communities utilize *B. ciliata* in treating various conditions such as cuts and

wounds, diarrhoea, bone fractures, fever, cough, boils, and pulmonary infections<sup>31,32,33,34</sup>. Among the local tribal communities in Kumaon Himalayas including Bhotiya, Van Rawat and Buxa communities, rhizome usage is prevalent for treating asthma, chronic ulcers, skin infection, dysentery, diarrhoea, gastrointestinal problems, piles, rheumatism, cuts and burns, urine disease, anthelmintic, fever, in kidney, and gall bladder<sup>20</sup>. While in the Kashmir Himalaya, the Hakims and Bohris (herbal healers) treat 104 diseases and common ailments using *B. ciliata*<sup>16</sup>.

Traditional healers used rhizome, roots, leaves in diverse formulations to address various ailments. The decoction derived from the *B. ciliata* leaves serves as an effective remedy for eye infections, while crushed leaves serves as poultice for treating cuts and wounds<sup>20,24</sup>. Rhizome and root paste is applied in the burns, wounds, and for pain relief, setting dislocated bones, skin diseases<sup>16,35,36,37</sup>. Rhizome decoction mixed with honey is prepared to treat diarrhoea<sup>36,38,39</sup>. Additionally, post-partum women have historically used a combination of rhizome juice and honey as tonic and to treat digestive disorders<sup>16,40</sup>. Fresh juice of rhizome is used to treat intermittent fever<sup>20,41</sup>. Boiled roots and rhizomes, combined with salt, exhibited therapeutic effects in managing asthma<sup>12,20</sup>. Furthermore, reports suggest its use in treating piles and cancer-related symptoms<sup>4,12,20,42</sup>, an effective antipyretic and anthelmintic agent<sup>16,20,43</sup>. The powder of rhizome and roots mixed with mustard oil is used for arthritis, gout, urinary problems and rheumatism<sup>16</sup>, higher dosage exhibited anti-diuretic property<sup>16,20</sup>. The rhizome powder is aphrodisiac and is used to increase sperm count<sup>20</sup> in Kumaon Himalaya. Furthermore, crushed rhizome, roots, and leaves are administered to treat gastro-intestinal disorders like ulcers, colitis, indigestion etc<sup>16,20</sup>.

## Phytochemistry of *Bergenia ciliata*

Literature review reveals large number of phytochemical compounds in *Bergenia ciliata*. These phytochemicals include wide range of constituents such as flavonoids, terpenoids, sterols, saponins, glucosides, phenols, tannins, coumarins, fatty acids, carboxylic acids, and various others compounds<sup>44,45,46,47,48</sup>. Notably, among these phytochemicals, key bioactive compound identified in *B. ciliata* comprise bergenin, catechin, gallic acid  $\beta$ -sitosterol, tannic acid, (-)-3-O-galloylepicatechin, (-)-3-O-galloylcatechin, gallicin, afzelechin, paashanolactone, sitoindoside<sup>12,49,50,51</sup>. An ultra-high performance liquid chromatography coupled to hybrid linear ion trap triple quadrupole mass spectrometry study by Pandey et al<sup>52</sup> made a quantitative estimation of 8 major bio-active phenolic compounds from *Bergenia*. While, Gopane et al<sup>48</sup> identified 12 bioactive flavonoids belonging to hydrocarbon, alcohol, fatty acids, lactones etc. using gas chromatography-mass-spectrometry.

Bergenin a key bioactive compound exhibits hepatoprotective, immunomodulatory properties<sup>53</sup>, alongside antioxidant capabilities<sup>54,55</sup>. It is also effective in alleviating phlegm, cough inflammation<sup>54,56</sup>, and has also shown promise in treating gastric ulcer<sup>57</sup>. Gallic acid another constituent, displays antimicrobial activity<sup>58</sup>. (-)-3-O-galloylepicatechin and (-)-3-O-galloylcatechin have been identified for their effectiveness against type 2 diabetes<sup>59,60,61</sup>.

## Pharmacology Action of *Bergenia ciliata*

### Antimicrobial property

*B. ciliata* demonstrates strong antibacterial activity, as highlighted in various studies<sup>4,31,62,63,64</sup>. Pharmacognostic analysis of the rhizome of *B. ciliata* has unveiled its significant inhibitory effect on pathogenic bacteria such as *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and

*Staphylococcus aureus* infections<sup>31,63,64,65</sup>. Investigation into extracts derived from different parts of the plant and using various solvent<sup>4,58,65,66,67</sup> have been conducted against pathogenic bacteria. Among the diverse solvents and plant parts utilized for extract preparation, methanol extract from the rhizome emerged as the most effective in controlling these pathogenic bacteria<sup>4,66</sup>. The plant was also found to be effective in suppressing the malarial parasites - *Plasmodium falciparum* and *P. berghei*<sup>68,69</sup>. Leaf extract exhibited considerable antimalarial activity against *P. falciparum*<sup>70</sup>. Recent *in vivo* studies of the ethanol extract of rhizome exhibited considerable inhibition of schizont maturation of two strains of *P. falciparum*<sup>69</sup>. The efficacy of the rhizome extract was found to be comparatively higher than the chloroquine. Collectively, these studies strongly suggest that *B. ciliata* holds potential as a candidate for the treatment of various pathogenic microbes.

### Anticancer Activity

Cancer is one of the most prevalent life-threatening diseases in modern times. The scientific community's focus has shifted towards plant-based compounds for developing new clinical drugs due to their lower costs and fewer associated side effects as compared to traditional chemotherapy<sup>71</sup>. Numerous plant species have exhibited anti-cancerous properties and are currently utilized in the treatment of various types of cancer<sup>72</sup>. These researchers are primarily based on traditional herbal medicine practices, particularly in developing countries<sup>73,74,75</sup>. Investigation into the methanolic and aqueous extract derived from the rhizome of *Bergenia ciliata* on human breast, liver, and prostate cancer cell-lines have revealed concentration-dependent toxicity<sup>76</sup>. Recent studies conducted by Ozaira et al<sup>77</sup> used MTT assay on the methanolic extract of *B. ciliata* on MDA-MB-231 and C6-Glioma cancer cell-lines. Their immunoblotting and enzyme assay using spectrophotometric technique revealed promising anti-cancer properties of *B. ciliata* due to its ability to modulate Unfolded Protein Response (UPR) and Reactive Oxygen Species (ROS) pathways leading to UPR-induced apoptosis. Moreover, Zinc oxide Nanoparticle synthesised from the rhizome extract of *B. ciliata* have exhibited remarkable abilities in scavenge free radical and demonstrating selective cytotoxicity against cervical cancer (HeLa) and Human colon cancer (HT-29) cell line<sup>78</sup>. Consequently, *Bergenia* shows potential as an antineoplastic agent, suggesting potential clinical utility in preventive medicine.

### Antiulcer Activity

Across the globe, extensive research has delved into the anti-ulcer potential of various traditional medicinal herbs<sup>79,80,81</sup>. One such herbal remedy *B. ciliata* has gained attention for its reported efficacy in addressing stomach disorders and gastric ulcers<sup>82,83</sup> because of its traditional usage in the treatment of stomach disorder. In a notable investigation by Kakub & Gulfranz<sup>82</sup> and Pokhrel et al<sup>58</sup>, using aqueous and methanolic extract of *B. ciliata* administered at different doses (15, 30, and 60 mg/kg), were evaluated *in-vivo* on ulcer-induced rats to ascertain gastro-protective effect. Their findings highlighted that the aqueous extract showed remarkable reduction of stomach-ulcer lesion, indicating significant anti-ulcer properties attributed to the enhancement of the gastric mucosal barrier by the aqueous extract. Moreover, in a separate study conducted by Ali et al<sup>83</sup>, bergenin isolated from the methanolic extract of *B. ciliata* rhizome, exhibited substantial inhibition similar to the standard amoxicillin antibiotic against *Helicobacter pylori*, the bacteria responsible for gastric ulcers. This led to the conclusion that *B. ciliata*'s anti-ulcer activity primarily arises from its effective anti-*Helicobacter pylori* action.

**Antidiabetic Activity** (Insulin stimulated glucose uptake, enzyme dependent glucose transport and induces insulin production by pancreatic B-cell.)

Diabetes is one of the most prevalent lifestyle diseases worldwide, with the International Diabetes Federation (IDF) reporting approximately 537 million affected adults in 2021<sup>84</sup>. The disease's prevalence has been rising rapidly across all economic strata<sup>85,86</sup> exerting a significant burden on individuals, families, and nation alike. Ethnobotanical and pharmacological research through-out the developing countries, reveals a large number of plant species showing anti-diabetes potentials<sup>85,87,88,89,90,91,92</sup>. These plants contain diverse bio-active chemicals for combat diabetes. *B. ciliata* is one such promising herb used in the diabetes treatment by herbal healers in traditional communities throughout Asia<sup>50,59</sup>.

Recent studies have aimed to assess the efficacy and perform phytochemical characterization of the bioactive compounds within this herb<sup>50,57,60,61</sup>. investigated the anti-diabetic properties using an *in-vitro* model, and isolating two active compounds 3-O-galloylepicatechin and 3-O-galloylcatechin. These compounds exhibited significant dose-dependent enzyme inhibitory activity against rat intestinal  $\alpha$ -glucosidase and porcine pancreatic  $\alpha$ -amylase, showcasing *B. ciliata*'s anti-diabetic potential. Subsequent studies on the rhizome extract (ethyl acetate) revealed higher concentration of Total Phenolic Content (TPC) and Total Flavonoid Content (TFC), displaying significant inhibitory activity against  $\alpha$ -glucosidase and  $\alpha$ -amylase<sup>59,61</sup>. Docking analysis further unveiled that catechin, a major bioactive compound in the plant, exhibited a notably higher affinity for the enzyme. These findings offer valuable insights into potential preparations, nutraceutical, and functional foods aimed at diabetes management and treatment.

### Conclusion

*Bergenia ciliata*, a small perennial herb of the Himalayas exhibits profound therapeutic value, deeply rooted in traditional practices and validated through contemporary research. Its diverse medicinal uses ranging from the treatment of kidney and gall bladder stones, gastrointestinal issues, heart ailments, respiratory disorders, skin diseases, and gynecological problems among numerous others are well known. Historical relevance in Ayurveda, Unani, and other traditional medicinal systems resonates through its various formulations utilizing different parts such as rhizomes, roots, leaves, and their extracts, showcasing its efficacy against an array of ailments.

Pharmacological and toxicological studies on *Bergenia ciliata* has revealed a substantial antimicrobial efficacy against pathogenic bacteria and its anti-malarial potential. Exciting findings also emphasize its anticancer attributes, including its ability to induce apoptosis and exhibit selective cytotoxicity against cancer cell lines. Furthermore, its anti-ulcer properties, particularly against *Helicobacter pylori*, and its efficacy in managing diabetes through enzyme inhibition have shown promising therapeutic avenues.

The robust ethno-medicinal history coupled with contemporary scientific validation underscores *Bergenia ciliata*'s immense potential in modern pharmacology. Its varied therapeutic properties, demonstrated through various studies, offer promising prospects for the development of novel drugs, nutraceuticals, and functional foods, reinforcing its relevance in the realm of preventive and curative healthcare. Further research and exploration into its bioactive compounds and clinical applications may pave the way for innovative treatments, substantiating its position as a formidable candidate in the pursuit of enhanced healthcare solutions.

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