

## Phytopharmacological and Chemical Profile of *Bergenia ciliata*

Mohammad Yaseen Khan and Vimal Kumar\*

Department of Phytopharmaceuticals and Natural Products, Institute of Pharmacy, Nirma University of Science and Technology, S.G. highway, Ahmedabad- 382 481, India

### \*Correspondence Info:

Dr. Vimal Kumar

Department of Phytopharmaceuticals and Natural Products,  
Institute of Pharmacy, Nirma University of Science and Technology,  
S.G. highway, Ahmedabad- 382 481, India

E-mail: [cognosy@gmail.com](mailto:cognosy@gmail.com)

### Abstract

*Bergenia ciliata* (Haw.) Stern (Saxifragaceae) is very useful plant traditionally used to dissolve kidney stones, antihelmenthic, tonic, wound healer, fever, dysentery etc. Phytochemistry of the plant revealed compounds like bergenin, (+) afzelechin, (+) catechin,  $\beta$ -sitosterol. Plants have been investigated for many pharmacological activities like antipyretic, antidiabetic, anti inflammatory, antitussive, antiurolithic & antimalarial. In this review a report for its phytoconstitents along with their structure and pharmacological profile has been described. Little work has been done on its phytochemistry and pharmacology with so many traditional uses, so this plant can be the target for many research activities.

**Keywords:** *Bergenia ciliata*, Traditional uses, Phytochemistry, Bergenin, Pharmacology

### 1. Introduction

*Bergenia ciliata* (Haw.) Stern belongs to family Saxifragaceae consists of about about 30 genera and 580 species worldwide. The plant is known as Pashanbheda (Pashan = rock stone, bheda = piercing) in Hindi; and Rock-foil in English which itself indicates that the plant grows between rocks and appears to break them or that it possesses lithotriptic property.

#### Vernacular Names

English	Rock-foil
Sanskrit	Paashaanabheda
Hindi	Pashanbhed, Dakachru
Gujarati	Pashanbheda, Pakhanbheda
Bengali	Patharchuri
Marathi	Pasanbheda
Malayalam	Kallurvanchi
Oriya	Pasanbhedi
Tamil	Sirupilai
Telugu	Kondapindi
Urdu	Pakhanabeda, Zakhm-e-hayat
Arabic	Barghienia-mehdiyata

### Taxonomic hierarchy

- **Classification**-*Bergenia* Moench.
- **Kingdom**-Plantae-plants
- **Subkingdom**-Tracheobionta-vascular plants
- **Super division**-Spermatophyta-seed plants
- **Division**-Magnoliophyta
- **Class**-Manoliopsida-dicotyledons
- **Subclass**-Rosidae
- **Order**-Saxifragales
- **Family**-Saxifragaceae
- **Genera**- *Bergenia*
- **Species** - *ciliata f. ciliata*.

### Geographic distribution

It is mostly distributed in the cold and temperate regions. It is found throughout temperate Himalayas from Kashmir to Bhutan at an altitude of 900-3000m [1]. Very common on rocks in and around the Murree area, especially in the Galis. The Saxifragaceae is primarily north temperate, although it does have representatives in the southern hemisphere.

## 2. Botanical Description

The salient botanical features of the family Saxifragaceae are: leaves simple or compound, alternate, rarely opposite, usually exstipulate, inflorescence cymose or racemose, rarely flowers solitary flowers; bisexual or occasionally unisexual. Stamens are inserted with the petals, equaling or doubling their number rarely indefinite. Ovary consisted of 3-5 united carpels with axial placenta, occasionally celled with partial placentas, ovules numerous, erect or pendulous. Styles are as many as carpels, free or more or less connate. Stigma capitate or lateral and subcapitate. Fruits capsular or baccate. Seeds are usually numerous.

The *Bergenia* is a genus of 10 species of flowering plants in the family Saxifragaceae native to Central Asia, from Afghanistan to China and Himalayas. They are evergreen perennial plants with spirally arranged of rosette of leaves 6-35 cm long and 4-15 cm broad and pink flower produced in cyme. The leaves of *Bergenia* create wonderful foliage throughout the year. They can be described as leathery or somewhat rubbery. Leaf shape and texture of *Bergenia* has earned the plants with some interesting nicknames. In addition to elephant ear, *Bergenia* may be called heartleaf, pigsqueak, picnic plates, or leather cabbages. Leaf size may vary in length from 5.08-30.48 cm and in width from 2.54-15.24 cm. Plant spread is about 45.72-60.96 cm, so *Bergenia* should be planted about two feet apart from full ground cover. *Bergenia* are becoming more popular plants among the environmentally conscious because they are drought resistance. The leaves do tend to attract slugs and snails, though spreading coca beans around the plant can help naturally keep these pests away. *Bergenia* also make an excellent choice for families with young children, as the plants are non-toxic. Roots of the plant have been used in Ayurvedic medicine for centuries and we can find *Bergenia* in over the counter medicinal substance for weight loss and kidney [2,3].

### 2.1 *Bergenia ciliata*

*B. ciliata* (Haw.) Sternb. (Saxifragaceae) is a small perennial herb, in the autumn attaining 30 cm. or more, these herbs grow in moist and shady places, closely oppressed to rocks. Leaves few, spreading, 4-11×3-10 cm, glabrous or hirsute, suborbicular to orbicular broadly obovate, base cordate or sometimes rounded, apex round or sometimes abruptly acuminate; margin entire to occasionally denticulate at top, ciliate Figure 1. Petiole 1-2(-5) cm long, glabrous or hirsute. Inflorescence a one sided raceme or corymbose, often subtended by an ovate leafy bract; bractglabrous or sparsely ciliate; scape and inflorescence greenish or pink tinged. Peduncle up to 10 cm long; flowers pink to purplish, pedicellate Figure 2. Sepals 7mm long, pink to red. Styles 7 mm long. Carpels and styles green or pinkish. Capsule 13×6 mm, including styles. Seeds elongated 1 mm long, minutely tuberculate, usually numerous, albuminous. Stamens inserted with the petals, equaling or double their number, Ovary of 2 or 3-5 united carpels, usually 2 or 3-5 celled with axile placentas, occasionally 1-celled with parietal placentas ovules numerous, anatropous. Figure 3 shows the plate of *B. ciliata*



Figure 1: Leaves of *B. ciliata*



Figure 2: Flowers of *B. ciliata*

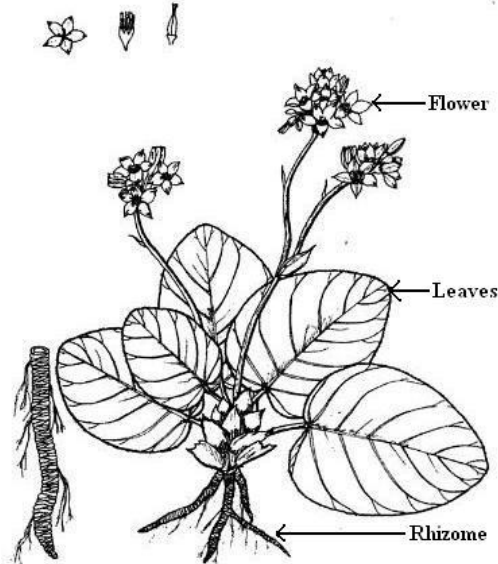


Figure 3: Plate of *B. ciliata*



Figure 4: Dried rhizome of *B. ciliata*

### 2.1.1 Rhizomes

The *B. ciliata* rhizomes are compact solid, somewhat cylindrical barrel shaped, 1.5 to 3.0 cm. long and 1.0 to 2.0 cm. in diameter with irregular, longitudinally wrinkled and ridged outer surface which is buff-brown outside and pinkish brown inside. Rhizomes are covered with root scars and possess a characteristic, slightly camphoraceous odour and pungent taste Figure 4[4].

### 2.2.2 Microscopical Observations

The histological examination of transverse sections of *B. ciliata* rhizomes stained with phloroglucinol and hydrochloric acid or iodine reagents has been reported. The transverse sections of *B. ciliata* rhizomes is reported to have cork, divided in two zones with wide cortex of thick parenchymatous cells containing light brown color and starch grains, few rosette crystals of calcium oxalate are also present in some cells of secondary cortex. The vascular bundles are found in a ring. They are conjoint, collateral and open. Xylem consists of tracheids vessel with simple pits, xylem parenchyma and xylem fibers. Pith cells are found in central portion of in *B. ciliata* rhizomes [4].

## 3. Traditional Uses

*B. ciliata* is used in traditional Ayurvedic medicine for the treatment of several diseases in Nepal, India, Pakistan, Bhutan and some other countries. All species of *Bergenia* are reported to dissolve gravel and stone in kidney and used as an anti-urolithiatic. Rhizomes of plant are reported to given in fever, cough, diarrhea, pulmonary affections and lungs diseases. The drug is also reported for the treatment of asthmatic disorders in traditional medicine in Jammu and Kashmir. In the traditional system of medicine, the rhizome is used fresh or in dried powdered form. It is used orally, simply chewed if fresh, for curing diarrhea and during vomiting. It is also reportedly used against fever, cough and pulmonary affections. In Swat and Kashmir areas *B. ciliata* (*Zakhnehayat*) has been reported to be used in fever, diarrhea and applied to bruises and boils. It is a very promising herb with many traditional uses. One teaspoonful of the juice of dried rhizome of *B. ciliata* along with an equal amount of honey has been taken orally 2-3 times a day by post-partum-women, against the digestive disorders as carminative, and tonic as well. This preparation however was prescribed at least a week or longer for bearing build up [5]. Rhizome of *B. ciliata* has been taken orally by human adults as an anthelmintic[6]. Juice of the rhizome of *B. ciliata* has been taken orally by human adult to relieve intermittent fever (Malaria)[7]. Juice of the rhizome of *B. ciliata* is administered orally by human adults, to treat low fever (hypothermia), and intermittent fever. Furthermore, the juice of the said plant has been used as tonic and carminative against the indigestion [8]. Bhattarai, in his studies has reported that a prescription when prepared by boiling the crushed rhizome of *B. ciliata* in water and approximately 10 to 15 ml juice of this resultant preparation is diluted with water and when given to human adults thrice a day for 3-5 days, it was found effective for the treatment of chronic dysentery The author further mentioned that its decoction is also taken orally by the human adults, as antipyretic [9]. In North West and trans-Himalayan region in Jammu and Kashmir State the roots of *B. ciliata* are boiled in water and table salt is added in the decoction. Traditionally this decoction is taken orally by human adults of this region for the treatment of asthma [10]. In Central Nepal, a multiple component prescription having ingredients; roots of *B. ciliata*, *Brassica mpus* var. *napus* and *Astilb rivularius* is utilized in veterinary medicines and when this is applied externally to the cattle it produces an astringent effect. The dried rhizomes of *B. ciliata* constitute the drug *Paashaanabheda* in *Ayurvedic system of medicine*. The name *Paashaanabheda* is attributed to about a dozen plants belonging to different genera, but the drug in the Indian markets mainly consists of two closely related herbs viz. (i) *B. ciliata* f: *ciliata* syn. *Saxifraga ligulata* auct, in part, non Wall.; *S. ligulata* Wall. Var. *ciliata* (Royle) Hook. F. & Thoms. and (ii) *B. ciliata* f: *ligulata* Yco syn. *S. ligulata* Wall; CB Clarke. The drug is reported to possess astringent, tonic, antiscorbutic, and laxative properties. It is reported to be given in pulmonary disorders, dysentery, ulcers, dysuria, spleen enlargement, cough and fever. The drug is utilized in folklore medicine in the Sudh-Mahadeo region of Himalayas against vertigo, and headache. It is reported to be helpful in dissolving kidney stones. The juice of the leaves of *B. ciliata* is used for earache [11]. All the species of *Bergenia* are reported to dissolve gravel and stones in the kidney. Root is used as a tonic, in fever, diarrhea, and pulmonary affections, and as an anti-scorbutic and in ophthalmia. It has also been used as a poultice, as it is regarded as a locally effective remedy for boils in Kashmir, here it is known as "Zakhnehayat"[12]. In lower doses, the extract is mildly diuretic but in higher it exhibits anti diuretic action. The bruised rhizomes are applied in the eye diseases, boils, cuts and burns. The juice of the rhizome of *B. ciliata* is used as an anti-tussive for cold and cough by the local people of the Sikkim and Darjeeling districts of West Bengal [13].

### 3.1 Other Uses

The juvenile leaves are fried with gram flour and served as 'pakora'. The broad leaves are used as plates in picnic, parties and agricultural fields. The children offer the flowers at the doors of their neighbours for a good luck in a local festival called 'Phool Sangran' in Utranchal. The people also grow this plant for its beautiful pinkish flowers in their garden.

### 3.2 National Status

This species has been included in the vulnerable category by a Conservation Assessment and Management Plan Workshop Process, WWF, India, ZOO/CBSG, India and Uttar Pradesh Forest Department in 1997. There is good demand for rhizomes of this plant species in various pharmaceutical companies. The villagers who are poor and do not care about degradation of plant resources, collect this plant for earning their livelihood. As a result the whole plant is dug out with very little chances of regeneration.

## 4. Conservation and cultivation

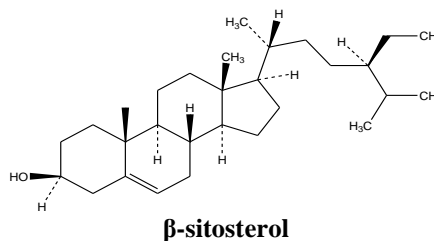
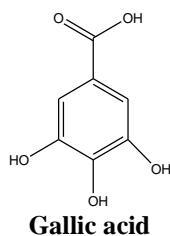
Possible reasons for rarity might be over-exploitation for medicinal value, beautiful flowers and its occurrence in select habitats. Keeping in view these reasons, its *in-situ* as well as *ex-situ* conservation is highly recommended. It has great potential for large scale cultivation. This plant can be grown in rocky-gravelly and sandy soil at elevations of 800-3000 m. It is recommended that the seeds should be sown from April-May and pieces of rhizome should be planted from January – February for getting maximum germination (92%) and maximum sprouting (96%). Due to its great potential for large-scale cultivations, the various State agencies and NGOs may initiate its cultivation in the Himalayan region. Farmers may grow the plant in their agricultural land for their economic upliftment as it has good market value in Ayurvedic and Unani systems of medicine.

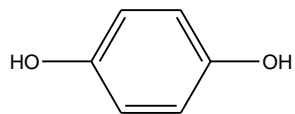
## 5. Phyto-Constituents

In a preliminary phytochemical screening, the root was shown to contain flavonoids, glycosides, sterols, terpenoids and saponins, while alkaloids were found to be absent. The literature search on *B. ciliata* has revealed that very little chemical work has been carried out on this plant. The phytochemical investigation on the aerial parts and on the leaves have resulted in the isolation of hydroquinone (benzenoids)[14] (+) afzelechin, (+) catechin, quercetin-3-O- $\beta$ -D-xylopyranoside, quercetin-3-O- $\alpha$ -L-arabinofuranoside, eryodictiol-7-O- $\beta$ -D-glucopyranoside, arbutin, 6'-O-p-hydroxybenzoylarbutin, bergenin, 4-O-galloylbergenin, 11-O-galloylbergenin, p-hydroxybenzoic acid and protocatechuic acid. 6'-O-protocatechuoylarbutin, 11-O-p-hydroxybenzoylbergenin, 11-O-protocatechuoylbergenin and 6'-O-p-hydroxybenzoylparasorboside [15]. (-)-3-O-galloylprocatechin and (-)-3-O-galloylprocatechin [16].

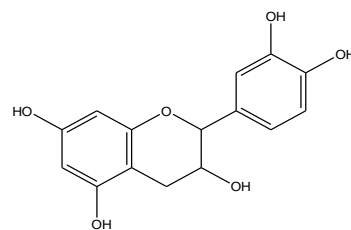
Aqueous extract of rhizomes were showed the presence of bergenin , phenolic compounds leucocyanidin, gallic acid, methyl gallate, catechin and polymeric tannin [17]. The rhizomes also yielded a new lactone compound Paashanolactone and confirmed the presence of (+)-catechin, (+)-catechin-3-gallate 11-O-galloyl bergenin and sterols viz., sitoindoside,  $\beta$ -sitosterol and  $\beta$ -sitosterol-d- glucoside[18]. Bergenin is major compound in the rhizome (0.6%). It is 4-methoxy-2-[(1S,2R,3S,4S,5R)-3,4,5,6-tetrahydro-3,4,5-trihydroxy-6-hydroxymethyl]-2H-pyran-2-yl]- $\alpha$ -resorcylic acid  $\delta$ -lactone monohydrate. It is a C-glucoside of 4-O-methylgallic acid. The molecule is composed of three six-membered rings: an aromatic ring, a glucopyranose ring and an annellated  $\delta$ -lactone ring. The glucopyranose ring exhibits only small deviations from an ideal chair conformation. The annellated  $\delta$ -lactone ring possesses the expected half-chair conformation. There is one intra- and six intermolecular hydrogen bonds which form an extensive hydrogen-bonding network within the crystal.

### Structure of isolated Phytoconstituents

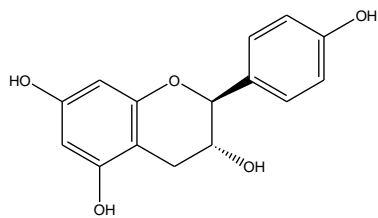




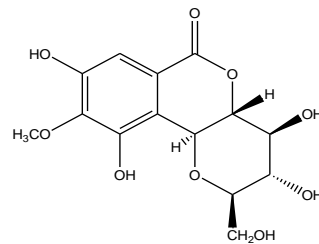
**Hydroquinone**



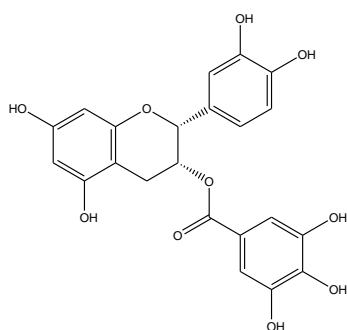
**Catechin**



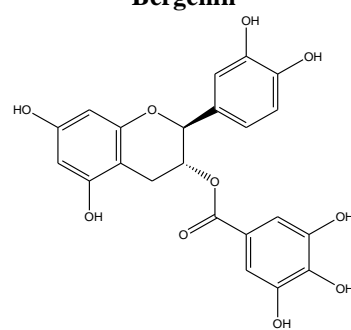
**(+) Afzelechin**



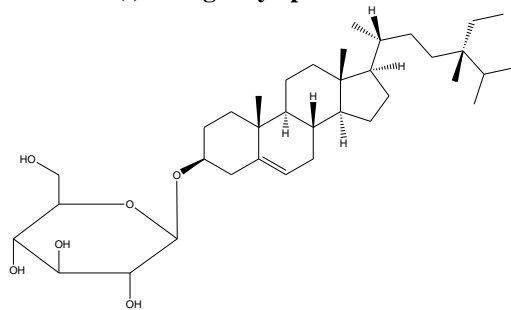
**Bergenin**



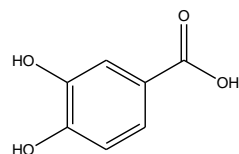
**(-)-3-O-galloylepicatechin**



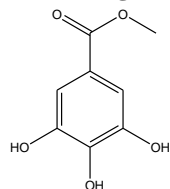
**(-)-3-O-galloycatechin**



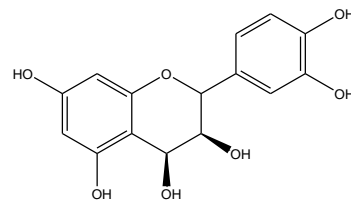
**$\beta$ -sitosterol-d-glucoside**



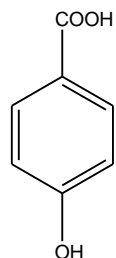
**Protocatechuic acid**



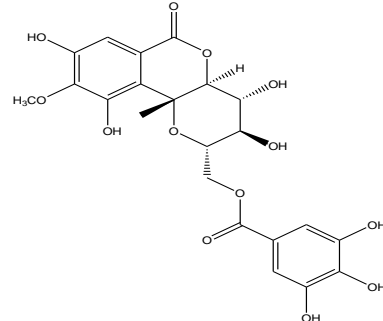
**Methyl gallate**



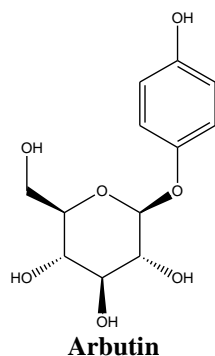
**Leucocyanidin**



**Para hydroxy benzoic acid**



**11-O-galloylbergenin**



## 6. Pharmacological Profile

### 6.1 Toxicology

The toxicological investigations of *B. ciliata* with particular reference to acute systematic toxicity and intracutaneous toxicity in experimental animals displayed that it elicit severe toxicity. The symptoms of toxicity in intracutaneous test showed erythema and edema whereas assessment of acute systemic toxicity frequently observed breathing problem and initiations of diarrhea with blood in stool of experimental model and caused gastro-intestinal syndrome. *B. ciliata* can produce toxicity suggesting a role in certain diseases [19]. In higher doses it is cardio-toxic, shows anti-diuretic action, and has depressant action on the central nervous system.

### 6.2 Anti-pyretic activity

The methanol extract of *B. ciliata* rhizome exhibited significant antipyretic effects on normal body temperature and yeast-induced pyrexia in rats. It in both models at oral doses of 100, 200 and 300mg/kg. *B. ciliata* extract, at 300 mg/kg significantly reduced the normal body temperature in rats for up to 5 h after its administration. In yeast-induced pyrexia, the extract significantly lowered body temperature for up to 4 h after its administration in a dose-dependent manner and the effect was comparable with that of paracetamol, a standard antipyretic agent [20].

### 6.3 Anti-diabetic activity

The hydroalcoholic extract of the *B. ciliata* exhibited significant anti-diabetic activity in an *in vitro* model. Extraction and fractionation of the extract lead to the isolation of two active compounds, (-)-3-O-galloylepicatechin and (-)-3-O-galloylcatechin. These isolated compounds demonstrated significant dose dependent enzyme inhibitory activities against rat intestinal  $\alpha$ -glucosidase and porcine pancreatic  $\alpha$ -amylase. IC<sub>50</sub> value for sucrose, maltase and  $\alpha$ -amylase were 560, 334 and 739  $\mu$ M, respectively for [(-)-3-O-galloylepicatechin] and 297, 150 and 401  $\mu$ M, respectively for [(-)-3-O-galloylcatechin][21].

### 6.4 Anti-inflammatory activity

Paashanolactone is a important constituents isolated from *Bergenia ligulata* rhizomes was showed significant anti-inflammatory activity[22] and the same activity of aqueous extract of *B. ciliata* rhizomes was confirmed in dose dependent manner on carrageenin induced paw oedema in rats[23]. The methanol extract of the rhizome of *B. ciliata* exhibited significant anti-inflammatory activity in acute rat models (carrageenan- and serotonin (5-HT)-induced rat paw oedema) and a chronic rat model (cotton pouch-induced granuloma). At 300 mg/kg the methanol extract exhibited maximum inhibition of  $32.4 \pm 2.89\%$  in carrageenan-induced rat paw oedema. In the serotonin-induced rat paw oedema model, 300 mg/kg methanol extracts suppressed oedema by  $45.33 \pm 2.09$ . In the cotton pouch granuloma model the methanol extract inhibited significantly the granuloma weight in a dose-dependent manner [24].

### 6.5 Anti-bacterial activity

The methanolic extract of *B. ciliata* rhizome showed a wide spectrum of concentration dependent antibacterial activity of methanolic extract of *B. ciliata* rhizomes at a concentration of 200-1000  $\mu$ g/disc [25]. The broad spectrum and concentration dependent antibacterial activity was also confirmed in aqueous extract of crude drug.

### 6.6 Anti-tussive activity

The methanolic extract of *B. ciliata* rhizome showed significant and dose dependent anti-tussive activity in mice using sulphur dioxide gas model. The extract exhibited significant anti-tussive activity in a dose-dependent manner, as compared with control. The anti-tussive activity of the extract was comparable to that of codeine

phosphate (10 mg/kg body wt.), a standard anti-tussive agent. The extract at doses of 100, 200 and 300 mg/kg body wt. (p.o.) showed significant inhibition of cough reflex by 28.7, 33.9 and 44.2%, respectively, within 90 min of the experiment [26].

### 6.7 Anti-ulcer activity

*B. ciliata* was evaluated for its gastroprotective effects on ethanol/HCl, indomethacin and pylorus ligation-induced gastric ulcers in rats. Doses of 15, 30 and 60 mg/kg b/w of the aqueous and methanol extracts of the rhizome exhibited anti-ulcer activity. The aqueous extract decreased the ulcer lesion ( $p < 0.05$ ) in all models to a greater extent than the methanol extract, but at the higher doses the effect was reduced. The antiulcer activity appears to be mediated via cytoprotective effects conferred by enhancement of the mucosal barrier, rather than by prevention of gastric acid secretion or the lowering of pH and acidity [27].

### 6.8 Antioxidant activity

The methanolic extract of *B. ciliata form a ligulata* rhizomes was also reported to have free radical scavenging property in superoxide radical and nitric oxide scavenging models. The methanolic extract was found to be a good scavenger of DPPH radical with an EC of 36.24  $\mu\text{g/ml}$ . The extract scavenged superoxide radical in a dose dependent manner with EC of 106.48  $\mu\text{g/ml}$ [28]. In another study antioxidant activity of methanolic and aqueous extracts of *B. ciliata* revealed that both extracts to be active radical scavengers. Reducing power and lipid peroxidation inhibition efficiency (TBARS assay) of both extracts showed promising activity in preventing lipid peroxidation and might prevent oxidative damages to biomolecules. the ability of the extracts to protect DNA (pBR322) against UV-induced photolysed oxidative damage was analysed. Both the extracts were able to protect DNA from oxidative damage [29].

### 6.9 Antimalarial activity

The leaf extract of the plant showed good in vitro antiplasmodial activity, with an  $\text{IC}_{50} < 10 \mu\text{g/ml}$ . When tested in vivo, different concentrations of the extract (250 to 1,000 mg/kg) exhibited considerable chemosuppression on day 7, in a dose-dependent manner. Maximum chemosuppression was observed to be 87.50 % at 1,000 mg/kg. Administration of (750 and 1,000 mg/kg) significantly ( $p < 0.0005$ ) enhanced the mean survival time of mice in comparison to infected control, which exhibited a mean survival time of  $8.6 \pm 1.5$  days [30].

### 9.10 Anti-Antiuro lithic activity

The crude aqueous-methanolic extract of *Bergenia ligulata* rhizome exhibited antiuro lithic activity in mediated possibly through  $\text{CaC}_2\text{O}_4$  crystal inhibition, diuretic, hypermagneseuric and antioxidant effects [31]. In an another study, the hydro-alcoholic extract of *Bergenia ciliate*/standard drug cystone were administrated simultaneously at a dose of 150 and 300 mg/kg body weight/day, p.o. along with ethylene glycol (0.75% v/v) for 28 days. Significant changes were observed in body weight and absolute organ weight of ethylene glycol treated rats. Histopathological results showed disrupted renal parenchyma, degenerative changes in glomeruli and focal calcification in glomerulo-tubular structures in ethylene glycol treated animals. Administration of *Bergenia ciliata* extract/cystone along with ethylene glycol showed significant protective effect in body weight and organ weight with few stray areas of calcifications in glomeruli. Moreover, *Bergenia ciliata* extract shows higher renoprotective index than cystone at the same dose level [32].

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