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Berginia ciliata (Haw.) Sternb: A Miracle In Between the Stone Menace to Kidney Stone Its Vital Uses and Important Chemicals- A Review

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ABSTRACT

Medicinal plants have been known for millennia. The primitive man must have used medicinal plants as therapautical agents and remedial measures, which he was able to procure most easily. There is no authentic record of medicines used by man. Plants have been used as traditional healthcare system from the centuries. Today the WHO reported that 80% of global countries depend on the medicinal plants. In India around 20,000 medicinal plants species have been recorded, but around 500 traditional communities use 800 plant species for curing the diseases. A medicinal plant B. ciliata *is being used to cure 104 different types of ailments and high potential in the treatment of gastrointestinal disorders but it is well known for the treatment of kidney disorders particularly kidney stones. Moreover,* B. ciliata *was reported to possess high antifungal, antiviral, anti plasmodial and antibacterial activities. Urolithiasis is a complex process that occurs from series of several physicochemical event including aggregation, nucleation, super-saturation, growth, and retention within the kidneys. There are several types of renal stones having composition and pathogenesis.*

Key words: *Berginia ciliata, Antifungal, Antiviral, Anti-plasmodial, Urolithiasis and Antibacterial*

INTRODUCTION

Pashanbheda {*B. ciliata* (haw.) Sternb: Saxifragaceae} commonly known as hairy *Bergenia* is a perennial herb found between the height of 800–3000 m throughout the temperate Himalayas from Afghanistan to Southeast Tibet[1,2,3]. In Bhutan it is found in Deothang, Phuntsoling, Mongar and Ha districts. In India it is reported from Lushai hills, West Bengal, Arunachal Pradesh, Meghalaya, Himalayas (Kumaon), Kyongnosla, Karponanag, Gangtok in Sikkim, district Almora in Uttarakhand. In Nepal it occurs in Makanwanpur district, Karepalanchwok district and Dolakha district[4, 5, 6]. *B. ciliata* contains number of important phytochemicals such as bergenin, gallic acid, catechin, Paashanolactone, sitoindoside, quercitin, afzelechin etc[5,6,30]. Presence of tannic acid, albumen, mucilage, glucose, wax, metarbin and mineral salts is also reported[3].

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Biological analysis of *B. ciliata* revealed that this plant showed antioxidant, anti-inflammatory, antitussive, antiviral, antiulcer, hypoglycemic and toxicological activities. Rhizome of *B. ciliata was* found to show narrow spectrum of antibacterial activity, leaves and roots show antifungal activity.[24,25]

For century's rhizome of *B. ciliata* has been used for curing pulmonary infections, leucorrhea, piles and for dissolving bladder and kidney stones. In Ayurveda system of medicine it is commonly used as tonic, astringent, antiscorbutic, laxative, spleen enlargement, dysuria and ulcers. Local people of West Bengal use rhizome juice as an anti-tussive for cough and cold. It is being widely used against cough, cold, fever, pulmonary infections, heart diseases, ophthalmic, hemorrhoids and stomach disorders. Biological analysis of *B. ciliata* revealed that this plant showed antioxidant, anti-inflammatory, antitussive, antiviral, antiulcer, hypoglycemic and toxicological activities. Rhizome of *B. ciliata* was found to show narrow spectrum of antibacterial activity, leaves and roots show antifungal activity[5, 6, 7, 8].

Urolithiasis:

Urolithiasis affects around 5-15% of the population worldwide[9,] with recurring chance upto 50%[10]. The likelihood of developing kidney stones in one's lifetime is about 13% for men and 7% for women.[11] According to some epidemiological studies, kidney stone composition has changed from predominantly urate and phosphate to calcium oxalate, and now approximately 80% of stones are composed of calcium oxalate monohydrate (COM) and calcium phosphate (CaP), 10% are struvite (magnesium ammonium phosphate produced during infection with bacteria that possess the enzyme urease), 9% are uric acid (UA), and the remaining 1% are composed of cystine or ammonium acid urate or are diagnosed as drug-related stones[12]. Heredity, geographical location, diet and medications play vital role in forming kidney stone[13].

Types of Renal calculi: *Simple renal calculi* are those with a stone burden of <2 cm (aggregate diameter) and normal renal anatomy. Most simple renal calculi (80-85%) can be treated successfully with shock wave lithotripsy[14]. *Complex renal calculi* include stones >2 cm, such as staghorn calculi; stones occurring in kidneys with abnormal anatomy; and stones resistant to fragmentation. Recently published guidelines of the American Urologic Association recommend that staghorn calculi should not be treated with lithotripsy because of relatively poor stone-free rates[15].

Anti urolithiatic activity

Crude phenolic compound produced highest dissolution of both calcium oxalate & phosphate stones in comparison to alcoholic extract, butanol & ethyl acetate fractions. However, it was more effective in dissolving calcium phosphate stone (67.74 %) than oxalate (67.74 %). The dissolution capacity of phenolic compound can be further enhanced by purification[16]. In another experiment *B. ciliata* extract showed a significant dose dependent inhibition of the aggregation, with percentage inhibitions of 58–97%. The inhibitory concentration (IC50) of the plant extract was 0.9 mg/mL. However, Cystone also showed inhibitory activity on crystal aggregation, but was less potent than the plant extract at the same concentration range, with a percentage inhibition of 35–71% and an IC50 of 2.92 mg/mL, and in a concentration-dependent manner.[17] The crude aqueous-methanolic extract of *B. ciliata* rhizome exhibited antiurolithic activity inmediated possibly through CaC_2O_4 crystal inhibition, diuretic, hypermagneseuric and antioxidant effects.[18] In an another study, the hydro-alcoholic extract of *B. ciliata* (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 *B. 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[19].

Antitussives activity

The methanol extract of the rhizome of *B. ciliata* has been evaluated for its potential in a cough model induced by sulphur dioxide gas in mice. The extract exhibited significant antitussive activity in a dose dependent manner, as compared with control. The antitussive activity of the extract was comparable to that of codeine phosphate (10 mg/kg body wt.), a standard antitussive agent. The extract at doses of 100, 200 and 300 mg/kg body wt. showed significant inhibition of cough reflex by 28.7, 33.9 and 44.2%, respectively, within 90 min of the experiment.[9] The methanolic extract of *B. ciliata* rhizome was screened for their antiviral activity against herpes simplex virus and influenza virus A by dye uptake assay. The methanolic extracts of *B. ciliata* rhizome were found to be highly active against antiviral activity against HSV-1 (IC_{50}-6.25μgml^{-1}) and influenza virus A (IC_{50}-8to 10μgml^{-1}).[20]

Anti-ulcer activity

The experiment for antiulcer activity of *B. ciliata* evaluated indomethacin and pylorus ligation-induced gastric ulcers in rats and gastro protective effects on HCl or ethanol. The doses of aqueous and methanolic extracts of rhizome of *B. ciliata* of 15, 30 and 60 mg/kg were given after ulcer genic treatment. After 3 h animals were killed and stomachs were reduced and the area for ulcer lesion was determined. The measurements included mucus and gastric acidity also. Rather than methanoalic extract 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. In addition, 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[2, 3, 21].

Antioxident activity

Methanolic and aqueous *B. ciliata* rhizome extracts were found to possess antioxidant activity, including reducing power, free radical scavenging activity and lipid peroxidation inhibition potential. The methanolic extract displayed greater potential in all antioxidant assays[22].

Anti diabetic activity

The effects of different extracts of *B. ciliata* leaves on blood glucose showed that ethanolic extract lowered 70.13% the blood glucose level. Aqueous extract reduced 71.34% blood sugar level, Chloroform extract showed 42.23% reduction in blood glucose level while Ethyl acetate extract showed reduction in blood glucose level from 443.0 ± 22.3 mg/dl. Rats treated with Hexane and butanol extracts have not shown significant decrease in blood glucose level and any hypoglycemic activity[3].

Anti neoplanstic activity:

The study was aimed in evaluating the anti-neoplastic efficacies of the methanol and aqueous extracts of *Bergenia ciliata* (Haw.) Sternb. Rhizome. The extracts were tested for their cytotoxicity on MDA-MB-435S (human breast carcinoma), Hep3B (human hepatocellular carcinoma) and PC-3 (human prostate cancer) cell lines by the XTT assay. Furthermore, the apoptotic inducing abilities of the extracts were analyzed by the cellular DNA fragmentation ELISA. The results obtained suggest that the extracts bear anti-cancer metabolites and could be considered as a potential source for anti-cancer drug development[23].

Anti Bacterial Activity:

Methanolic extract from the rhizome with concentration 200–1000 μg was used for thesting of Antibacterial activity by disc diffusion method using both gram positive and gram negative bacteria such as *Bacillus pumilis*, *Bacillus subtilis*, Staphylococcus *aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Shigella dysenteriae*, *Vibrio cholera*. The antibacterial efficacy of the extract, concentration dependent against all tested strains, was potent at 1000 μg/disc, the

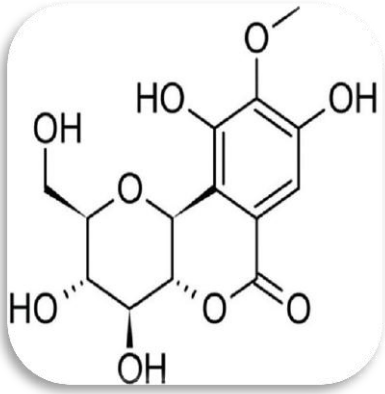
maximum effect shown against *S. aureus*[24]. Ethanol, hexane, ethyl acetate, chloroform, butanol and aqueous extract from leaves and roots was tested against Gram positive and gram negative bacteria viz. *Bacillus subtilis*, *Bacillus megaterium* and *Pseudomonas aeruginosa* and Root extract found antibacterial activity against *Pseudomonos aeruginosa* (zone of inhibition 12mm–20 mm) and *Escherichia coli* (zone of inhibition 6mm–8 mm) leave extract found activity against *Staphylococcus auereus* (zone of inhibition range, 8mm–12 mm), *Bacillus subtilis*, *Bacillus megaterium* and *micrococus* (zone of inhibition range 10mm–20 mm)[25].

Antiviral activity

In literature some workers used 20 extracts of different plants to find antiviral activity against influenza virus. IC_{50} of these extracts ranged from <6.25 to 97 mg/ml. Among them highest activity was shown by extract of *A. filicinus. B. ciliata* also showed high activity with IC_{50} values from 8 to 10 mg/ml and it was highly active against both viruses. Methnolic extract of *B. ciliata* inhibited the influenza virus A and HSV-1, which indicates that *B. ciliata*, could be one of the potent sources of antiviral drug[26].

Important chemicals and uses

Bergenin: Bergenin exhibits anti hepatotoxic, anti ulcerogenic, anti-HIV, antifungal, hepatoprotective, antiarrhythmic, neuroprotective, antiinflammatory, immunomodulatory and burn wound healing properties [27].



Gallic acid: (3, 4, 5-trihydroxybenzoic acid): inhibit lipids peroxidation, induces apoptosis, ROS scavenger, metal chelation, interfere cell signaling pathway[28].

Beta-sitosterol: used for heart disease and high cholesterol. It is also used for boosting the immune system and for preventing colon cancer as well as for gallstones, the common cold and flu (influenza). It is also used for enhancing sexual activity[29].

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