



## A SHORT GLIMPSE ON PROMISING PHARMACOLOGICAL EFFECTS OF *BEGENIA CILIATA*

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*Bergenia ciliata* is a potent indigenous folk medicine that has been proved fruitful in the treatment of various adverse conditions of the body. The major chemical constituents of plant include tannic acid, gallic acid, glucose, metarbin, albumen, bergenin, (+)-catechin, gallicin. *Bergenia ciliata* was subjected to bioactivity analysis. The plant has antitussive, antiulcer, antioxidant, antibacterial, hypoglycemic, toxicological activity. It was observed that root and leaves extract were promising as antifungal agent. The root and leaves extract were effective against *Microsporum canis*, *Pleuroetus oustreatus* and *Candida albicans*. All the extracts except chloroform extract of root and leaves of *Bergenia ciliata* were found to possess hypoglycemic activity in Streptozotocin (STZ) treated rats. The methanolic extract exhibited significant anti-tussive activity in a dose-dependent manner. *B. ciliata* bear potent anti-neoplastic activities that may have prospective clinical use as precursor for preventive medicine. 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. *Bergenia ciliata* extracts exhibit a narrow spectrum antibacterial activity. The results obtained thus suggest that extracts of *B. ciliata* have promising therapeutic potential and could be considered as potential source for drug development by pharmaceutical industries.

**Key words:** antitussive, antioxidant, antibacterial, antifungal hypoglycemic, toxicological, antineoplastic

### INTRODUCTION

Nature is an extremely rich source of highly diverse and innovative chemical structures<sup>1</sup>. The relationship existing between plants and humans is as old as mankind, dating back to the origin of human civilization<sup>2</sup>. Traditional medicine (TM) is widely used and is rapidly growing health system with economic importance. Many factors are contributing to wide spread use of traditional medicines/ complementary and alternative medicines (TM/CAM)<sup>3</sup>. Some of the old remedies are recognized, today, as "official" drugs by the Federal Food and Drug Administration. Others are listed but classified as "unofficial," because they have proven unsatisfactory<sup>4</sup>. The earliest written account of herbal remedies was the Pen Ts'ao by Shen Nung of China and dates back to 2800 BC<sup>5</sup>. Several of the drugs used today are simple synthetic modifications or copies of the naturally obtained substances<sup>5</sup>. The therapeutic properties of medicinal plants offer a practically unexploited reservoir of potentially useful sources of

drugs<sup>6</sup>. The past decade has witnessed a tremendous resurgence in the interest and use of medicinal plant products. Plants have been found to have use in pharmaceuticals, cosmetics and food supplements<sup>7</sup>.

*Bergenia ciliata* (Haw.) Sternb., is commonly called winter bergonia. It is an evergreen perennial herb growing to 0.3 m by 0.5 m. *B. ciliata* rhizome extracts is proved to have anti-bacterial and anti-tussive properties<sup>8,9</sup>. It is reported to be helpful in dissolving kidney stones<sup>10</sup>. *Bergenia ciliata* (How. Sternb.) belongs to family Saxifragaceae. This family comprises of 30 genera and 580 species, mostly distributed in the cold and temperate regions. The genus *Bergenia* comprises of 6 species distributed in the temperate Himalays and Central and East Asia<sup>11</sup>. *Bergenia ciliata* is used in the traditional medicine of Asian as well as other countries. In Nepal, one tea spoonful 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 healthy build up. It is also used orally for anthelmintic. The

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plant is also used as demulcent and deobstruent, relieves pain in ribs and chest due to excessive cold humours, acts as effective diuretic and emmenagogue. Get-rid of kidney's and bladder stones and obstructions or toxic waste products, which remain in the alimentary canal, and urinary excretory system. The infusion is considered to be more active than root in asthma, bronchitis, epilepsy and spasmodic infections and to relieve flatulent colic in children. Root is effective to combat chronic venereal diseases



#### Anti-tussive activity

The anti tussive activity has been evaluated through the methanol extract of the rhizome of *Bergenia ciliata* Sternb (Saxifragaceae) in a cough model induced by sulphur dioxide gas in mice. 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.), taken as a standard anti-tussive 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<sup>15</sup>. The methanolic extract of *Bergenia ciliata* rhizome was screened for their antiviral activity against herpes simplex virus and influenza virus A by dye uptake assay. The methanolic extracts of *Bergenia ciliata* rhizome were found to be highly active against antiviral activity against HSV-1 (IC<sub>50</sub> value 6.25µgml<sup>-1</sup>) and influenza virus A (IC<sub>50</sub> values from 8 to 10µgml<sup>-1</sup>)<sup>12</sup>.

#### Antiulcer activity

*Bergenia ciliata* has been used for the treatment of stomach disorders as the folk medicine in some areas of South East Asia. This study was designed to evaluate its gastroprotective effects on ethanol/HCl, indomethacin and pylorus ligation-induced gastric ulcers in rats. Doses of 15, 30 and 60 mg/kg between of the aqueous and methanol extracts of the rhizome were administered 1 h after ulcerogenic treatment. The animals were killed 3 h later, their stomachs were removed and the mean area of ulcer lesion was determined. The weight of mucus and gastric acidity were also measured. 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<sup>13</sup>.

#### Anti-neoplastic activity

The methanolic and aqueous extract of *Bergenia ciliata* rhizome were found to have promising potential towards the development of drug that might be used to target tumours for chemoprevention or chemotherapy to check neoplastic growth and malignancy. Both extracts showed concentration-dependent cytotoxicity in each of the three cell lines. According to the American national cancer institute, the IC<sub>50</sub> value to consider a crude

extract promising for development of anticancer drugs is lower than a limit threshold (30µg/ml).<sup>81</sup> IC<sub>50</sub> value of both the extracts falls well within this prescribed threshold in all cell lines (except the aqueous extract with higher IC<sub>50</sub> in help 3B cell lines) *B.ciliata* bear potent anti-neoplastic activities that may have prospective clinical use as precursor for preventive medicine<sup>14,21</sup>.

#### Antioxidant 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. It is, however, interesting to note that the aqueous extract demonstrated considerably higher DNA protection, albeit lagging behind its methanolic counterpart as an antioxidant<sup>14,21</sup>.

#### Antibacterial activity

The roots as well as leaves extract viz ethanol, hexane, ethyl acetate, chloroform, butanol and aqueous (5mg/ml) aliquots of *Bergenia ciliata* were used to test of antibacterial activity. *Bergenia ciliata* root extract was found to inhibit the growth of gram positive bacteria as compared to gram negative strain. Therefore in a way it can be inferred that *Bergenia ciliata* extracts exhibit rather a narrow spectrum antibacterial activity. The screening result of various leaves extract of *Bergenia ciliata* exhibited activity against the gram positive *Staphylococcus aureus* (zone of inhibition 8-12 mm) whereas chloroform butanol and aqueous extracts were found active against *Bacillus subtilis*, *Bacillus megalerium* and micrococcus, (zone of inhibition 10-20). Consequently it can be suggested that the activity of root extract is much higher as compared to the leaves extract of *Bergenia ciliata*. The roots and leaves extract viz., ethanol, hexane, ethyl acetate, chloroform, butanol and aqueous of *Bergenia ciliata* were used to test of hypoglycemic activity. All the extracts except chloroform extract of root and leaves of

*Bergenia ciliata* were found to possess hypoglycemic activity in Streptozotocin (STZ) treated rats. Therefore the plant can be classified as hypoglycemic activity in experimental diabetes ranging from 40-70% of its onset to reduce blood glucose level<sup>15</sup>.

#### Antifungal activity

The ethanol, hexane, ethyl acetate, chloroform, butanol and aqueous root extracts of *Bergenia ciliata* is reported to exhibit antifungal activity against *Pleuroetus oustreatus*, *Microsporrmnt canis* and *Candida albicans* (zone of inhibition range 6mm-14mm). Whereas only ethanol extract exhibited activity against *Aspergillus niger*, *Penicillium funiculosiunt* and *Alternaria solani* (zone of inhibition 6mm-12mm). The hexane, ethyl acetate, butanol and aqueous extracts was found inactive against the subjected nine fungi. The results indicated that all the extracts found inactive against *Fusarium solani*, *Nigrospora oryza* and *Curvularia lunta*. The screening results of *Bergenia ciliata* leaves extract that exhibited no response against *Aspergillus niger*, *Alternaria solani*, *Pusarium solani* and *Nigrospora aryza*. Whereas ethanol extract has exhibited antifungal activity against *Penicillium fiticulosiutn*, *Microsporunt canis*, *Curvularia lunta* and *Pleuroeras oustreatus* (zone of inhibition 10mm-22mm). Hexane extract did not exhibit positive activity against any of the subjected fungi. Ethyl acetate extract has shown activity against *Microsporunt canis* (zone of inhibition (16mm). Chloroform extract has shown activity against *Penicillium funiculosiunt* and *Currularia Junta* (10mm-16mm). Butanol extract has shown activity against *Penicillium firniculosiunt*, *Plcuroetus oustreatus* and *Candida albums* (zone of inhibition range 10mm-20mm). Aqueous extract exhibited activity against *Penicillium funiculosium*, *Plenroetus oustreatus* and *candida albicans* (zone of inhibition range IOmm-20mm)<sup>11</sup>.

#### Hypoglycemic activity

The hypoglycemic activity of the extracts of *Bergenia ciliata* was tested through determination of the blood

sugar lowering effects in rats. Streptozotocins (STZ) induced diabetic rats were prepared by inducing hypoglycemia with a single intravenous dose of 50mg/kg. After 4 days of STZ administration, blood glucose level was examined and on the fifth day of STZ administration, the solution of root and leaves extracts were administered to the animals intraperitoneally. A dose of 200 mg/kg body weight twice a day for 5 times was given to the animals. Each group comprised of 6 rats after five doses the blood glucose level of the animals were analyzed and compared with the control. The results exhibited that animals suffered with severe hypoglycemic upto 6 hours after the administration of STZ through intravenous route. The blood glucose level remained constantly high after 24 hours of STZ-administrations by all doses for 30-mg to 70mg. The experiment led to conclude that STZ by the dose of 60 and 70mg produces a severe diabetic model while 30 and 40 mg/kg produces comparatively mild diabetes in rats. The effects of various *Bergenia ciliata* leaves extract on blood glucose revealed that the ethanol extract has significantly lowered 70.13% the blood glucose level (i.e. from 428.8±2.0 mg/dl to 137.8±6 mg/dl). The blood sugar level was reduced from 436.6±20.0 mg/dl to 134.8±13.8 mg/dl (71.34% reduction) in aqueous extract treated rats. In chloroform extract treated rats blood sugar level reduced from 455.2±283.7±21.9 mg/dl (i.e. 42.13% decreases). Ethyl acetate extract treated rats have shown the decrease in blood glucose level from 443.0±22.3 mg/dl. Whereas hexane and butanol treated extract have not shown any hypoglycemic activity and no significant reduction in the glucose level has been observed in the animals treated with these extracts<sup>10</sup>.

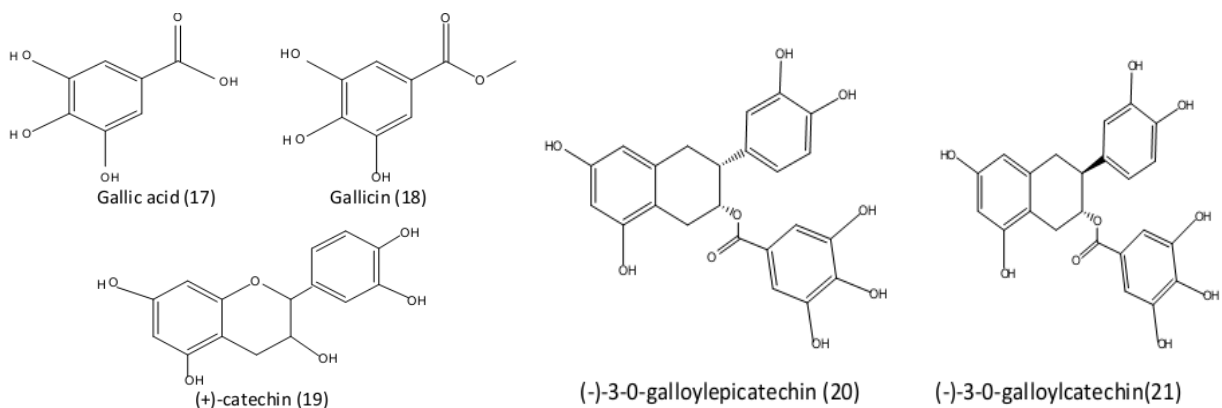
### Toxicological investigation

The toxicological investigations of *Bergenia 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. *Bergenia ciliata* can produce toxicity suggesting a role in certain diseases. It is therefore, premature to speculate about mechanism of effect until toxin is unequivocally identified<sup>16</sup>. The hemolysis test on the extract of *Bergenia ciliata* was almost devoid of activity<sup>16,21</sup>.

### Chemical constituents

The plant contains tannic acid, gallic acid, glucose, mucilage, wax, metarbin, albumen and mineral Salts<sup>99</sup> Bergenin, (+)-Catechin, Gallicin and Gallic acid quantified by using solvent System of Toluene: Ethyl acetate: Formic acid (6: 6: 1, v/v/v) by HPTLC. Developed method permitted simultaneous quantification of Bergenin, (+)- Catechin, Gallicin and Gallic acid, and showed good resolution and separation from other constituents of extract and was found to be simple, precise, specific, sensitive and accurate. It can be adopted for routine quality control of herbal material and formulations containing *Bergenia ciliata*<sup>17</sup>. Tinctures were prepared by macerating the rhizomes of *B. ciliata* in different strengths of alcohol (30, 40, 50, 60, 70, 80, 90 and 100%, v/v) for 7, 14 and 21 days. After maceration, the pH, specific gravity and total solid matter, chemical contents were determined. The pH of the tinctures decreased with increase in alcohol strength, as well as with the number of days of maceration. Results showed that the tinctures prepared with 50% alcohol had the highest specific gravity of 0.9907 and yield (total solid content) of 9.11% (w/v) when macerated for 21 days. The chemical components of the tinctures irrespective of alcohol strengths were steroid, triterpenoid, flavonoid, tannins, carbohydrates and saponins<sup>18</sup> The rhizome of *B. ciliata* yield galloylyted leucoanthocyanidin-4-(2-galloyl) glucoside as well<sup>19</sup>.



### Specific compound activity

50% aqueous-methanol extract of *Bergenia ciliata* rhizome 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-Ogalloylepicatechin] and 297, 150 and 401  $\mu$ M, respectively for [(-)-3-O-galloylcatechin]. The anti-diabetic potential of Pakhanbhed could be helpful to develop medicinal preparations or nutraceutical and functional foods for diabetes and related symptoms<sup>20</sup>.

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