A SYSTEMATIC REVIEW OF PHARMACOGNOSTIC PROFILES OF *BERGENIA CILIATA* AND *CAESALPINIA BONDUCELLA* AS PROMISING MEDICINAL HERBS

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ABSTRACT

Medicinal herbs play a very important role in today's life for prevention, treatment and management of any disease. Most of the world's population is nowadays relying on traditional medicines due to its fewer side effects. Based on this concept this review is focusing on two important plants namely *Bergenia ciliata* and *Caesalpinia bonducella* which are believed to be of much pharmacognostic value. These plants can turn out to be promising medicines for various diseases in the future which will contribute to the good health and well-being of individuals.

KEYWORDS: Bergenia ciliata, Caesalpinia bonducella, Phyto constituents, bergenin, isolation, good health & well being

BERGENIA CILIATA

Introduction:

From the ancient times medicinal herbs are used to treat various diseases. The tribal people rely more on traditional herbs and it has been found that these herbs can actually treat various ailments like various bacterial and viral infections, infertility, cardiac diseases and so on. 25% of current medication is derived from herbs. Medicinal plants are a rich source of drug discovery. In the market, medicinal plants are available as raw materials and processed final products. Due to health awareness, today's generation is focused more on plant-based health products.(1) *Bergenia ciliata* (Haw.) Sternb. of Saxifragaceae family is a perennial rhizomatous herb. The name Bergenia was coined by Conrad Moench in 1794 in the name of a Botanist and Physician Karl August von Bergen.

Vernacular names:

Gujarati: Pakhanbheda
Hindi: Silparo
Kannada: Pasanberu

Kashmiri: Pashanbhed
Malayalam: Kallorvanchi
Marathi: Pashanbheda
Punjabi: Batpia
Sanskrit: Ashmabheda
Tamil: Sirupilai
Telugu: Kondapindi
Urdu: Kachalu
English: Rockfoil[2]

Location:

Temperate Himalayan regions of India, Pakistan and Nepal [3]

Taxonomy:

Kingdom: Plantae
Subkingdom: Tracheobionta
Superdivision: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Dilleniidae
Order: Saxifragales
Family: Saxifragaceae
Genus: Bergenia
Species: Bergenia ciliata[4]

Morphology:

The height of *Bergenia ciliata* is 40 cm, it grows in moist, shady places between rocks. It has thick rhizomes and rosette succulent, broad, oval to obovate shaped leaves. It's flowering and fruiting season is from March to June.[5]

Phytochemistry:

The reported yield of water-soluble extract of *Bergenia ciliata* rhizome was 30.4%, alcohol soluble extract was 28.8%, 80% ethanol-aqueous extract was 20.98% and n-hexane extract was 0.29%. The 80% ethanol-aqueous extract contained phenolic compounds, alkaloids, saponins, mucilage, glycosides and carbohydrates.[6] A phyto constituent bergenin was isolated from methanol extract of rhizome. The dried powder of rhizome was subjected to cold maceration in methanol. After maceration it was filtered and concentrated to dryness. It was suspended in distilled water and ethyl acetate was added in separating funnel. The ethyl acetate fraction was collected and evaporated to dryness. The aqueous layer was extracted with n-butanol. The n-butanol layer was separated and evaporated to dryness. The aqueous

layer was concentrated to half the volume. The precipitates were separated from n-butanol and aqueous fraction and dissolved in methanol. The methanol was evaporated to get crystalline bergenin. The yield was 0.5% w/w of dry rhizome powder.[7] 100 mg bergenin also known as cuscutin was also isolated from aqueous extract of rhizomes (1 kg dried rhizomes) through column chromatography. The Mobile phase for thin-layer chromatography was Ethyl acetate: acetic acid: formic acid: water: 8:0.9:0.9:2.[8] The methanol extracts of rhizomes gave 19.4%, roots gave 9.2% and leaves gave 6.9% bergenin. It was detected at 275 nm. C18 column and isocratic solvent system; water: methanol: acetic acid; 62.5:37:0.5 v/v/v was used for separation of bergenin.[3] Phyto constituents which are isolated from *Bergenia ciliata* are phenols (bergenin, gallic acid, tannic acid), alcohols (3-pentanol, terpinen-4-ol, pentanol), flavonoids ((+)-afzelechin, Quercetin 3-o-α-L-arbinofuranoxide), fatty acids (2-methyl butanoic acid, decanoic acid, nonanoic acid), terpenoids (camphor, glucoside) and terpenes (linalool and β-phellandrene).[9] The methanol extract of flowers showed presence of hexanedioic acid, bis(2- ethylhexyl) ester (48.88%), γ-sitosterol (22.56%), cyclohexane, 1,3,5-triphenyl- (12.87%), n-hexadecanoic acid (4.97%), pentadecanoic acid, 14-methyl-, methyl ester (3.77%), 9,12-octadecadienoic acid, methyl ester, (Z,Z)- (2.94%) and 9,12,15-octadecatrienoic acid, methyl ester, (Z,Z,Z)- (2.92%).[10] The methanol extract of rhizomes had highest total phenolic content of 31.46 mg gallic acid equivalents per gram of dry extract of the sample.[11] The ethyl acetate fraction of methanol extract of rhizomes contained bio-actives like Fumaric acid, α-D-Glucopyranoside, O-α-D-glucopyranosyl-(fwdarw 3)-β-Dfructofuranosyl, 2-decenoic acid, 3-hydroxy-benzoic acid, 4-hydroxy-3,5-dimethoxy-benzoic acid, 3-methyl-2,5-Furandione.[12] Hydroquinones (benzoids) were isolated from ether extract of leaves. The rhizome also contains gallolyted leucoanthocyanidin-4-(2-galloyl) glucoside. Also important secondary metabolites like bergenin, gallic acid, catechin and arbutin were reported to be present in *Bergenia ciliata.*[13]

Pharmacological activities:

Antibacterial:

Root extracts of *Bergenia ciliata* at 1200 µg/well and its synthesized silver nanoparticles at 150 µg/well failed to inhibit the growth of *E. coli*, *Staphylococcus haemolyticus*, and *Bacillus cereus*.[14] The ethanolic and methanolic extract of rhizomes have activity against *E. coli, S. typhi, and S. aureus* (minimum inhibitory concentration = 6.25 µg/mL).[11] The ethanol extract of leaves showed highest antibacterial activity against gram positive: *Bacillus subtilis, Paenibacillus polymyxa and Lactobacillus brevis* except *Staphylococcus aureus* and gram negative: *E. coli, Serratia marcescens, Enterobacter aerogenes and Pseudomonos aeruginosa*.[15] The methanol extract of root showed highest antibacterial activity against multi drug resistant-carbapenem resistant organisms causing respiratory illness like *Pseudomonas aeruginosa, Klebsiella pneumonia, Acinetobacter baumannii* with maximum zone of inhibition but aqueous extract showed minimum antibacterial activity.[16]

Antioxidant:

The ethyl acetate extract of stem had high total phenolic content and total flavonoid content which was responsible for antioxidant activity.[17] The methanol leaf extract is a potent free-radical scavenger with median effective concentration of 36.24 μg/mL as reported through 2,2-diphenyl-1-picrylhydrazyl assay. The methanol extract of rhizomes had high antioxidant activity.[18]

Anti-diabetic:

The ethyl acetate extract of stem showed greater activity against α amylase than aqueous extract against α glucosidase.[17] The methanol extract of entire plant contained catechin which has a higher binding affinity towards α amylase and is considered to bind GLU233 and ASP 300 amino acid residues by hydrogen and hydrophobic bonds in an *in silico* study.[19]

Anticancer:

In silico study of components from *Bergenia ciliata* revealed that stigmasterol, β-sitosterol, paashaanolactone and afzelechin had high affinity towards breast cancer targets like estrogen receptor-α, progesterone receptor, human epidermal growth factor receptor-2 and epidermal growth factor receptor.[20]

Anti-thiamine activity:

Thiamine is the coenzyme of pyruvate dehydrogenase and transketolase enzymes. Anti-thiamine compound will decrease their activity leading to decreased energy production and nucleic acid synthesis. 100 mg of unknown compound isolated from ethanol extract of leaves inactivated 29.5 mg of thiamine hydrochloride in *in vitro* assay.[21]

In Parkinson's disease:

The ethanol extract of leaves showed excellent binding affinity towards α-synuclein and mono amino oxidase-B due to presence of Methyl 5-cyclopentyl-2-(4-methylbenzyl)-1,2,5-thiadiazepane-3-carboxylate 1,1-dioxide (-8.0 kcal/mol), (2S,3S,4S,5S)-5-Azido-3-methyl-2-phenyloxepan-4-ol (-8.3 kcal/mol) and 1-[[3's-Hydroxy-2'R-butoxy]methyl]thymine, 1'-ethyl hydrogenphosphate (-8.2kcal.mol).[22]

Anxiolytic:

The methanol extract of rhizome in a dose of 200mg/kg showed anxiolytic effect same as that of diazepam in Swiss albino mice when tested on animal models like elevated plus maze, staircase, social interaction, and light/dark model. It works on γ-amino butyric acid receptors as it contains β-sitosterol glucoside.[23]

Marketed formulations:

Asmarihara Kasaya Churna and Mutravirecaniya Kasaya Churna of *Bergenia ciliata* rhizomes.[5]

***CAESALPINIA BONDUCELLA* LINN.**

Introduction:

A traditional medicine treat more than 64% of the population, and among those 82% of the population is in developing countries. Traditional medicine includes plant parts like bark, roots, seeds, stems, fruits, and leaves. *Caesalpinia bonducella* is a prickly shrub or woody vine. The name bonducella is derived from Arabic word bonduce which means small ball which represents the round shape of the seed.[24]

Vernacular names:

Fever nut (English), bonduc nut, nicker nut, gray nicker, kantkaranja (Hindi)

Location:
Asia's tropical and subtropical regions like India, Sri Lanka, Bangladesh, Burma, Myanmar, China, Andaman and Nicobar islands and Vietnam.[25]

Taxonomy:

Kingdom: Plantae
Phylum: Magnoliophyta
Division: Magnoliopsida
Class: Angiospermae
Order: Fabales
Family: Fabaceae
Genus: Caesalpinia
Species: bonducella[26]

Morphology:

Stem bark is usually thin, double or compound quilled; 1-2 mm thick, scaly; externally blackish brown with intermittent cream brown patches; inner surface is smooth, pale brown; fracture uneven, splintery. It has hooks and straight yellow thorns on branches.

Microscopy:

The transverse section of stem bark shows, outer most cork 40-45 layered; cells rectangular, tangentially elongated, measuring 17.5 - 70 μm (31.5) long and 3.5 - 21μm (7) wide; walls

slightly thick, contents of golden yellow color with presence of stone cells isolated or in groups, mostly rectangular, measuring 21 - 42 μm (35) long and 7 - 17.5 μm (10.5) wide; walls thick and contents scanty.[27]

Phytochemistry:

Dichloromethane root extracts of *Caesalpinia bonducella* showed presence of alkaloids, flavonoids, cardiac glycosides and terpenoids. 15 cassane diterpenoids are present in the seed extract like phanginins A–F, H–J, K, and R–T; caesalpinilinn G, M, and N; and phangininoxy A.[28] *Caesalpinia bonducella* seed kernel contains Phytosterols- neutral saponins, heptocosane, sitosterol, bitter glycoside, non-crystalline Bonducin, its seed contains Neutral saponins, caesalpin, terpenoids, α- caesalpin, and β-caesalpin and leaves contain Pinitol, calcium, glucose, brazzillin.[29] The yield of seed extract in methanol was 55.35%, in n-hexane was 14.7% and in ethyl acetate was 31.7%. The flavonoid glycoside homoplantaginin isolated from ethyl acetate extract of seed reacted with ferric chloride to give yellow spots on thin layer chromatography.[30] Extraction in ethanol is preferred for phenolic compounds as it dissolves most polar and non-polar compounds.[31]

Pharmacological activities:

In reproductive health:

Ethanolic extract of seeds of *Caesalpinia bonducella* significantly down regulated the IGF-1 and IGF-2 (Insulin like Growth Factor) gene expression which is typically found to be high in females with Poly Cystic Ovarian Syndrome. The extract has shown to lower the circulating concentrations of free IGF proteins, and it makes the free IGF proteins combine with IGF-binding protein I to reduce the androgen produced in the ovarian cells.[32] The ethanolic seed extract at a dose of 400 mg/kg body weight decreased hyperinsulinemia, insulin resistance, and hyperandrogonism and increased ovulation. It reduced the luteinizing hormone and protected the ovaries from proliferation of theca cells.[33]

Anti-diabetic:

400mg/kg seed extract has shown to inverse the diabetic effects. The mechanism of action was believed to be the secretion of insulin from pancreatic β-cells or due to increased transport of blood glucose to peripheral tissue, decrease in hepatic glucose production and decrease in intestinal absorption of glucose.[34] Aqueous and ethanolic extracts of *Caesalpinia bonducella* increased insulin secretion in isolated islets in chronic type II diabetic model.[35]

Anti-malarial:

Dichloromethane root extracts of *Caesalpinia bonducella* showed anti plasmodial activity at 800mg/kg/day. The suppression rate of plasmodium was similar to chloroquine. It is also reported that the extract had minimum median effective dose (ED_{50}).[36] The activity was

mainly due to norcaesalpin D. The extract also showed anti plasmodial activity against chloroquine resistant and artemisinin resistant *Plasmodium falciparum.* The extract also showed activity against Mondolkiri parasites.(37)

In respiratory health and anti-cancer:

Caesalpinia bonducella is used to treat chronic cystic fibrosis caused by *Pseudomonas aeruginosa* in the lungs and it also showed anti-cancer activity.(38) The methanol extract of leaves decreased packed cell volume, tumor volume and viable cell count and it also increased life of Ehrlich Ascites Carcinoma affected mice.(39)

Antioxidant:

The ethyl acetate fraction of *Caesalpinia bonducella* seed extract showed the highest antioxidant activity.(40) However, aqueous extract of seed contained catalase which showed highest antioxidant activity in-vitro. The catalase protects living cells from oxidative stress. The seed has shown effective results in acetaminophen induced oxidative damage.(41) The ethanolic extract of seed kernels also shows antioxidant activity. The flavonoid glycoside homoplantaginin isolated from ethyl acetate extract of seed showed antioxidant activity.(30)

Anti-atherogenic:

The n-hexane, ethyl acetate and methanol fraction of seed extract showed cholesterol lowering activity.(40) The ethyl acetate and ethanol extracts of seed kernels show anti-atherogenic activity.(42) The triterpenoids, polyphenols, flavonoids and saponins present in ethanolic extract of seed kernels show decrease in all lipid parameters except high density lipoprotein.(39)

Anti-apoptotic and anti-inflammatory:

The glyceryl monostearate and 2-Palmitoylglycerol present in seeds showed in-silico anti-apoptotic and anti-inflammatory activity.(43) The aqueous extract of seed kernels showed high content of alkaloids other than carbohydrates and flavonoids of which quinolizidine was believed to give anti-inflammatory activity. The aqueous alkaloid fraction of seed kernels showed attenuation of pro-inflammatory mediators.(44)

Anti-bacterial:

Methanol leaf extract of *Caesalpinia bonducella* showed anti-bacterial activity against *Salmonella typhi.* The 800µg/disc shows 6 mm zone of inhibition.(45) Methanolic extracts of seeds showed presence of diterpenoid and quaternary alkaloid which showed antibacterial activity against *Staphylococcus aureus, E. coli, Vibrio cholare,* and Shigella dysentery.(46) The chloroform extract of leaf gave βSitosterol and stem bark gave methyl (4E)-5(2[(1-E)-buta-1,3-dien-1-yl]-4,6-dihydroxyphenyl) pent-4-enoate (SC-2)

as -bioactives- out of which SC-2 showed significant anti leptospiral activity against *Leptospira interrogans* than βSitosterol through inhibition of citrate synthase and outer membrane protein of leptospiral protein.[47]

Anti-viral:

Ethanolic extract of root and stem showed activity against the Vaccinia virus. The aqueous extract of leaf showed activity against Alzheimer's disease.[48]

Anti-pyretic:

The seed kernel extract showed anti pyretic activity against Brewer's yeast initiated pyrexia in rats.[48]

Antiurolithiatic:

The ethanolic extract of seed showed antiurolithiatic activity. It prevents oxidative stress, inflammation, pain and formation of intra papillary calcifications which in turn damages epithelial cells of nephron. It also reduces super saturation of calcium oxalate.[31]

CONCLUSION

Most of the people in the world are suffering from one or the other disease may be due to stress, modern lifestyle, lack of proper nutrition and lack of exercise. So, there is increase in need of effective medicines which can prevent, treat or manage such diseases. From this review, we have presented the medicinal value of two herbs: *Bergenia ciliata* and *Caesalpinia bonducella* which can be future promising medicines. Various Phyto constituents have been identified and isolated from both the plants. Also, both the plants have shown various pharmacological activities like antibacterial, antiviral, antilipidemic, anticancer, antidiabetic, antiurolithiatic and so on. The researchers can contribute to the good health and well-being of individuals by focusing on these plants for potent medicines.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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