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NOVEL LAMBADI, VENIVEL, AND PASHANBHED POLYHERBAL FORMULATION FOR THE TREATMENT OF UROLITHIASIS DISEASE: A COMPREHENSIVE REVIEW

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ABSTRACT

Kidney stone, a urological disorder, involves crystal concretion formed usually in the kidneys. The major symptoms of this disease are muscle cramps, loss of appetite, fever, swelling via feet as well as ankles, nausea and vomiting. In severe cases, it may cause severe pain, chills and blood in the urine. As kidney stone disease is having much more severe symptoms that are hazardous to human health, hence, it is necessary thing to treat this disease in an early stage. Several herbal drugs are available that shows remarkable effects on this disease. This involves Punarnava, Kantkari, Gokharu fruit. Still, due to development of recurrence and various side effects like dizziness, headaches, dehydration, muscle cramp, joint disorders; it is necessary thing to develop some potential drug or formulation that can well treat kidney stone disease. Some potential drugs like lambadi, Venivel, and Pashanbhed are available and it can be aimed that these should exhibit Antiurolithiatic activity. Therefore, it will be a research area to manage urolithiasis formulation of lambadi, Venivel, and Pashanbhed drugs.

Keywords: Kidney stone, Urolithiasis, Lambadi, Venivel, Pashanbhed

INTRODUCTION

Kidney stone is a severe health disease that involves formation of cluster of crystals together to form hard lump in the kidneys. They can vary in size from a few millimeters to several centimeters **(Figure 1, 2)**. The majority of stones will pass out of the body in the urine without any help, but some will require intervention to remove them. The Urinary stone have been developed with the crystals of phosphate, uric acid, magnesium ammonium phosphate with apatite and struvite. Among the urinary stones, calcium- containing stones have been found to about 75% of all urinary calculi, which may be present in the form of crystals of pure calcium oxalate (50%), calcium phosphate (5%) and a mixture of both compounds (45%). The diet can affect the concentration of certain substances in the urine and can affect the acidity of urine. If in the 24 hour urine collection found high level of calcium, oxalate, uric acid, or citrate then the conditions are known as hypercalciuria, hyperoxaluria, hyperuricaemia, or hypocitraturia accordingly **[1]**.

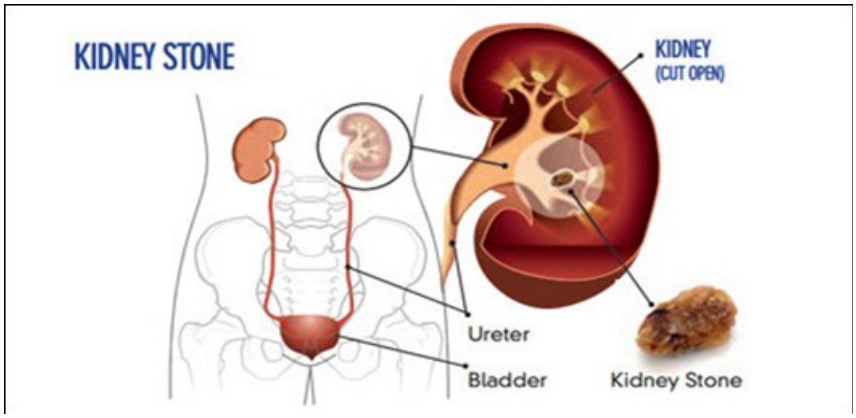


Figure 1: Structured Diagram and Location of Kidney Stone

There are total four different types of kidney stones that have been reported till date. This includes calcium (75 to 85%), struvite (2 to 15%), uric acid (6 to10%) and stones of cystine (1 to 2%). **Calcium stones** involve stones of calcium oxalate, calcium urate and calcium phosphate and associated with hypercalciuria which is caused by hyperparathyroidism. **Struvite stones** composed of magnesium ammonium phosphate stones which grow to fill the collecting system. **Uric acid stones** involve formation of uric acid stones that depend upon high purine intake drugs or high cell turnover (e.g. malignancy) which are mostly found in patients with gout. **Cystine stones** occur due to having hereditary intrinsic metabolic disorder called cystinuria which involve re-absorption of cysteine.

Sign and symptoms of kidney stone disease involve an acute, sudden, sharp and wavy pain in the back; a feeling of sudden urinates, burning feeling at urination, feeling of nausea and vomiting. Male patients may feel pain at the tip of their penis **[2]**.

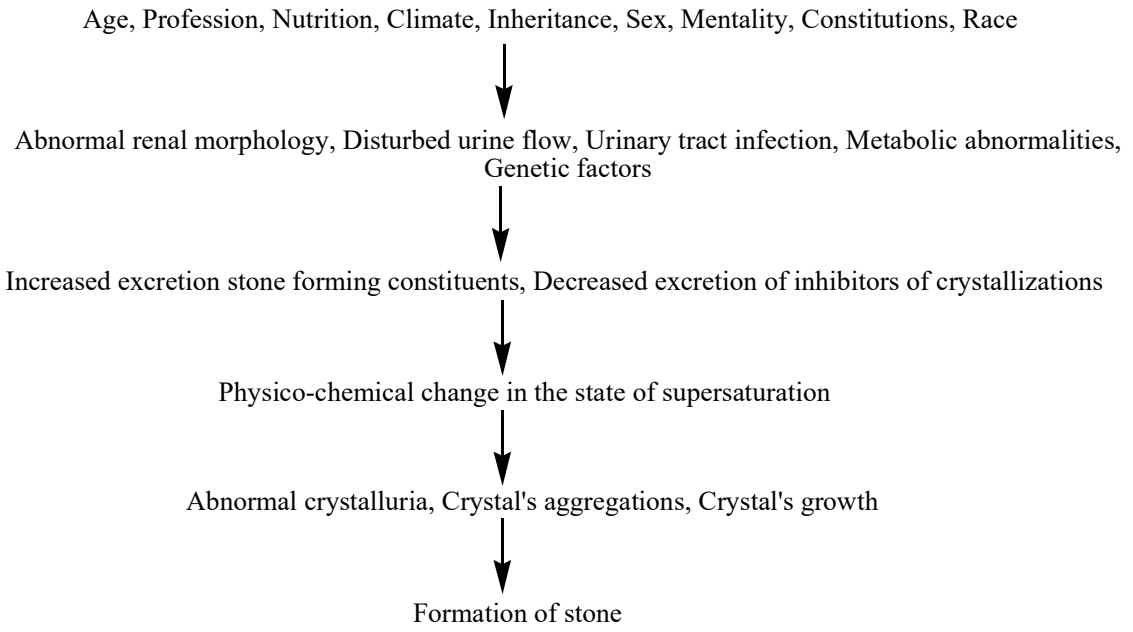


Figure 2: Mechanism of Formation of Stone in Kidney

Comprehensive Review on Lambadi, Venivel, and Pashanbhed

1) Lambadi

Biological Source: It consists of seeds of *Celosia argentea* Linn

Family: Amaranthaceae

Part used: Seed

Figure 3.1: ***Celosia argentea***

Figure 3.2: ***Celosia argentea*** **seed**

Vernacular names of Lambadi

Bengali: sushunimaak, Shushunishaak

English: Silver Spiked cock's comb

Guajarati: Laannpadi, Lonpadi

Hindi: Siriyaari, Suravali, Siravaari

Kannada: Alepgaya, Pahanbhedi, Hittaga, Pasanaberu, Hittulaka

Marathi: kuradu, karadu, Surali

Oriya: Pasanbhedi, Pashanabheda

Punjabi: Suravali

Tamil: pannaikkeerai

Taxonomical classification

Kingdom: Plantae

Order: Caryophyllales

Family: Amaranthaceae

Genus: Celosia

Species: argentea

Morphology

Annual erect herbs, simple or with many ascending branches. Leaves 2-15 x 0.1-3.2 cm, lanceolate-oblong to narrowly linear, acute to obtuse, shortly mucronate with the excurrent midrib, glabrous; lamina of the leaves from the centre of the main stem tapering below into an indistinctly demarcated, slender petiole, to 2 cm long; upper and branch leaves smaller, markedly reducing. Inflorescence a dense many-flowered spike, 2.5-20 x 1.5-2.2 cm, white to pink, terminal on the stem and branches, peduncle up to c. 20 cm long; bracts and bracteoles lanceolate or the lower deltoid, 3-5 mm, hyaline, more or less aristate with the excurrent midrib, persistent. Perianth segments 6-10 mm, narrowly elliptic-oblong, acute to rather blunt, shortly mucronate, margins hyaline. Filaments very delicate, free part sub-sequalling or exceeding the staminal sheath, sinuses rounded with very minute intermediate teeth; anthers and filaments creamy to magenta. Ovary 4-8-ovulate, style filiform.5-7 mm long; stigmas 2-3, very short. Capsule 3-4 mm, ovoid to globose; seeds c. 1.25-1.5 mm, lenticular, black, shining, very finely reticulate **[3]**.

Celosia species have been designated as a quantitative short-day plant, alternate entire or rarely lobed leaves. *C. argenta* is an erect, coarse, simple, branched, smooth annual herb, normally about 0.5 to 1.5 m in height but sometimes much taller. It has few branches, at least until it approaches the time for flowering. The leaves are alternate entire or rarely lobed, light green. They are typically 2 X 6cm, although those on flowering shoots are slightly longer. Even the green foliage may contain large amounts of betala in pigments. The often brilliantly colored flowers are borne in dense heads. Most occur in spikes, and stand like spears in the garden bed. But certain cultivated forms have compact or feathery clusters due to fasciation. *C. argentea* flowers yield large numbers of seeds that are about 1 mm in diameter and are normally black in colour. The Cock's comb flower blooms from late summer

through late fall. *C. argentea* plant is an annual dicotyledonous **[4]**.

Microscopy

Testa is made of 4 layers the outer layer of epidermis covered with thin cuticle, consisting of compactly arranged radially elongated, isodiametric dark brown coloured cells with thick outer walls and rod like thickening over the central region; bigger sized thick walled dome shaped cells; a narrow, brown coloured collapsed celled layer and an inner epidermis with spiral thickening at the edges of the cells. Perisperm is very wide parenchymatous zone of big sized angular cells compactly loaded with minute starch grains and prismatic crystals. Endosperm is embedded with aleurone grains. Cotyledons consist of upper and lower layer of epidermis enclosing mesophyll tissue embedded with starch grains and oil globules **[3, 4]**.

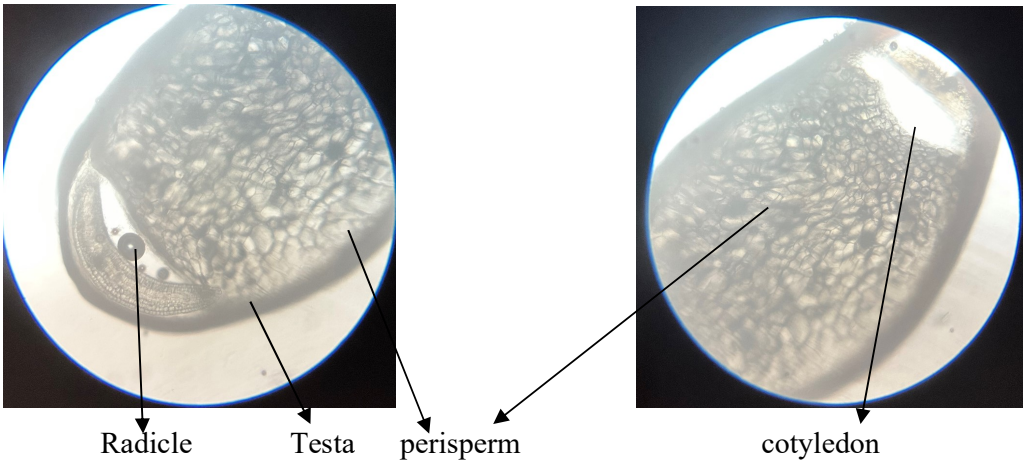
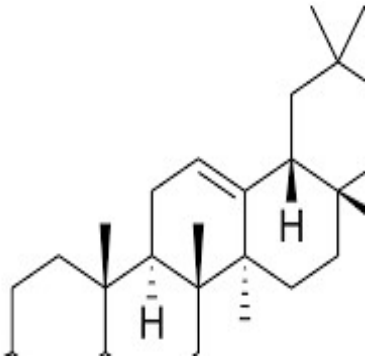
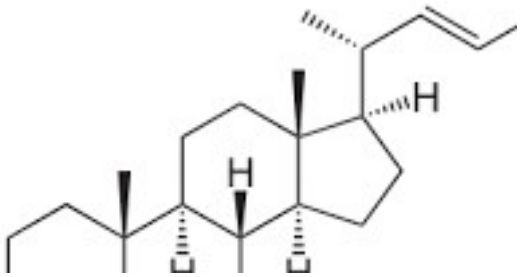


Figure 4: Transverse section of Lambadi seed

Chemical Constituents include Oleanolic acid, Stigmasterol, β- Sitosterol, Palmitic acid, Steric acid, Oleic acid, Heptadecenoic, Celosian etc. The plant contains tetracosanoic, hyaluronic, stearic, palmitic, betulinic and octacosanoic acids. Presence of tinosporin, ß-sitosterol, n-hentriacontane, petulin, lupeol, cetyl alcohol, ancistrocladine, rapanone, stigmasterol, luteolin, mannitol, hordenine, proteins, vitamins and minerals have also been reported in the plant. Two rare isoflavones have been isolated from the aerial parts. Seeds contain a fixed oil.



Oleanolic acid



stigmasterol

2-descarboxy-betanidin; 3-methoxytyramine;4-O-β-D_apifuranosy(l--2)- β-D-glucopyranosyl-2-hydroxy-6-methoxyacetophenone;amaranthin;betalimi c acid; celogenamide A, celogentin A-D,H,J and K, celosian; celosin E, F,G; cristatain dopaminelyciumin A methylate; lyciumin C methylate; moroidin; nicotinic acid; (S)-tryptophan.22

A variety of interesting but limited compounds have been isolated and identified from the plants of C.argentea which includes phenolics, steroids, diterpenes, and flavonoids. The recent investigations shows that, three novel triterpenoidsaponins, celosin E, celosin F and celosin G together with a known compound cristatain, were isolated from the seeds and characterized using extensive nuclear magnetic resonance (NMR) and mass spectroscopy (MS) technique. These three novel triterpenoid saponins and cristatain shows the antitumor and anti-inflammatory activities by in vitro screenings **[5]**.

Use: Calculus and dysuria. The seed is hypotensive and ophthalmic. It also has an antibacterial action, inhibiting the growth of pseudomonas. It is also used in the treatment of blood-shot eyes, blurring of vision, cataracts and hypertension **[6]**.

Dose: Churn (Powder): 3 to 6 g. **[5]**

2) Venivel

Synonym: kalipat, Patha

Biological Source: it consists of dried roots of *Cissampelos pareira*.

Family: Menispermacea

Part used: Root **[7]**

Figure 4.1: *Cissampelos pareira*

Figure 4.2: *Cissampelos pareira* root

Vernacular names [8]

English – False pareira brava, Velvet – leaf

Hindi – Akauadi, Harjeuri, Pari, Parh, Padh

Kannada – Hade balli

Malayalam – Kattuvalli, Pattuvalli

Bengali – Akanadi, Ekleja, Nemuka, Tejomalla.

Tamil – Appatta, Punaittitta,.

Telugu – Adivihankatige, Pata, Visaboddi.

Bombay – Pahadmul, Pahadvel, Venivel.

Gujarati – Venivel, Kari Path,

Marathi – Padavali, Padavel,

Punjab – Bat, BatidupathGoa – Parayet.

Taxonomic position [8, 9]

Kingdom – Plantae

Division – Magnoliophyta

Class – Magnoliopsida

Order – Ranunculales

Family – Menispermaceae

Genus – Cissampelos

Species – *Cissampelos pareira*

Morphology

C. pareira is an erect, perennial, climbing herb/shrub that twines. It grows to a height of 2 to 5 metres above the ground and is typically found near watercourses on hilly terrain. The roots are light brown, cylindrical, and have a rough surface from transverse clefts and wrinkles. They taste bitter and have a faintly aromatic smell. The stem is flexible and thin; it can twine around accessible supports or creep on the ground. Its greatest diameter is one centimetre. The leaf blades are ovate to cordate, membranous, simple, alternate, petiolate, basifixed, and veined palmately. Velvetleaf refers to the highly hairy surface beneath the light green, light green, and dark green lamina of a fully grown leaf. The dioecious, unisexual, small, green flowers have segments on their pedicel that can grow up to 2 mm in length **[10]**.

Microscopy

Transverse section of root showed non-lignified cork, composed of 7 to 15 layers of tangentially elongated, rectangular cells, outermost layer was obliterated. Cortex parenchymatous 3 to 10 cells wide;

pericycle characterized by 1 to 3 celled thick continuous ring of stone cells embedded with group of lignified fibres. vascular zone was composed of radially arranged discrete vascular strands with 6 to 8 narrow streaks of xylem with some reaching up to the center, externally capped with semi- circular patch of phloem on the outer side, alternating with medullary rays. Xylem was composed of vessels, tracheids, fibers and parenchyma; phloem was separated from xylem by 2 to 3 layers of cambium; sieve tubes and parenchyma were distinct but got obliterated towards the peripheral zone of cap; medullary rays parenchymatous; rod shaped prismatic crystals of calcium oxalate and simple and compound starch grains were present throughout the parenchymatous cells **[11]**.

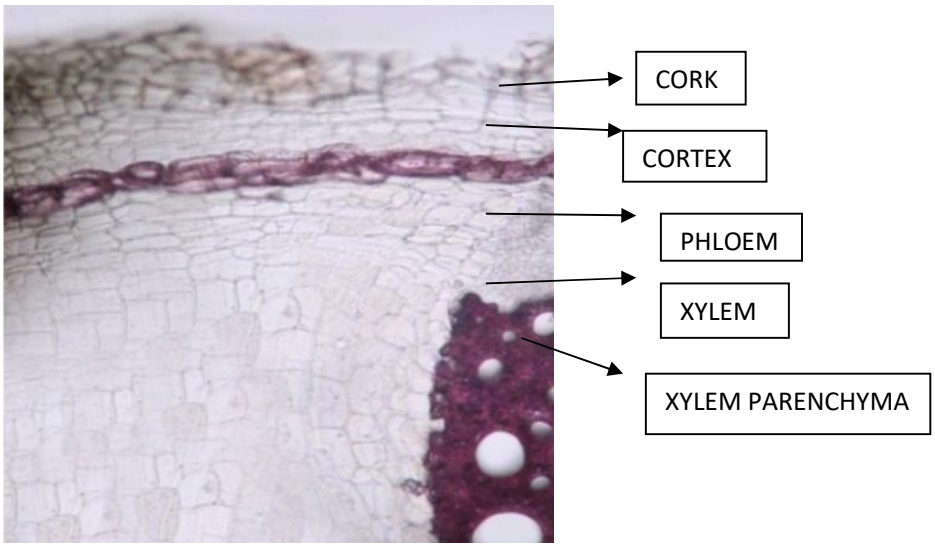
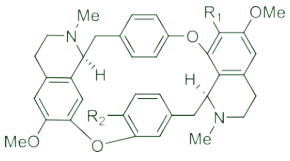


Figure 4: Transverse section of Venivel root

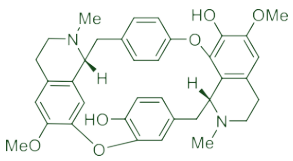
Chemical Constituents: Mainly isoquinoline alkaloids are major constituents of *C. pareira*. The different types of isoquinoline alkaloids i.e. benzylisoquinoline, bisbenzylisoquinoline, tropoloisoquinoline, aporphine, protoberberine, and azafluoranthene have been reported from *C. pareira.* The alkaloids isolated from the root are bisbenzylisoquinolines: pelosine, hayatine (also known as l-curine or l-bebeerine), hayatinine(or (++)-4″ -O-methylcurine), hayatidine (also known as (-)-O-methylcurine or (-)-4″-O-methylbebeerine), d-isochondrodendrine, cissampareine, tetrandrine, cycleanine, (-)-nor-N′ -chondrocurine, sepeerine, (+)-obaberine, (+)-obamegine, (+)-homoaromoline. Benzylisoquinolines: 1-(4-formyloxy)-3-methoxybenzyl)-6,7-

dimethoxy-2,2-dimethyl-1,2,3, 4-tetrahydroisoquinolin-2-ium, pareirarine, (-)oblongine, magnocurarine, (+)-coclaurine. Tropoloisoquinolines: pareirubrine A, pareirubrine B, isoimerubrine, grandirubrine and Pareitropone. Aporphines: dicentrine, dehydrodicentrine, magnoflorin. Azafluoranthenes: norruffscine and norimeluteine **[12, 13]**.

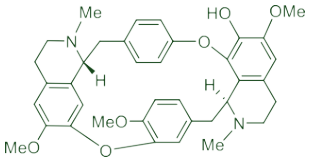
Bisbenzylisoquinoline



Pelosine: R_1=R_2=OH
Hayatinine: R_1=OH R_2=OMe

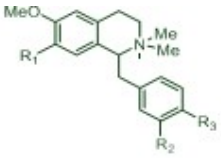


Hayatine

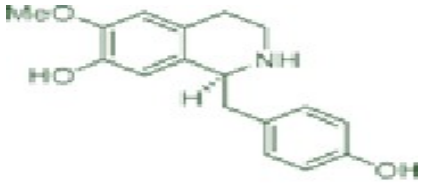


Hayatidine

Benzylisoquinoline

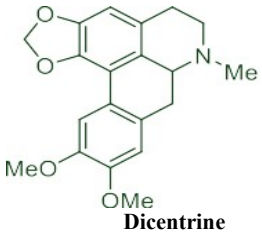


1-(4-formyloxy)-3-methoxybenzyl)-6,7-dimethoxy -2,2-dimethyl-1,2,3, 4-tetrahydroisoquinolin-2-ium, R_1=R_2=OMe , R_3=OCHO

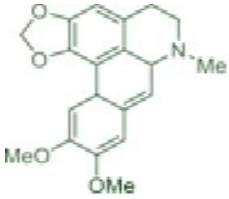


(+)-coclaurine

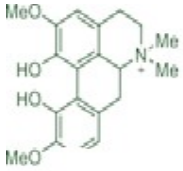
Aporphines



Dicentrine



Dehydrodicentrine



Magnoflorin

Uses: ulcer, wound, rheumatism, fever, asthma, cholera, diarrhoea, inflammation, snakebite, malaria, rabies, anti-arthritic, anti-fertility, anti-cancer, antiplasmodial activity and also recommended for blood purification **[12, 13]**.

3) Pashanbhed

Biological source: consists of rhizomes of *Bergenia ligulata* (Wall.)

Family: Saxifragaceae **[14]**

Figure 5.1: ***Bergenia ligulata***

Figure 5.2: ***Bergenia ligulata*** **rhizome**

Vernacular names [15]

Sanskrit: Asmabhedaka, Silabheda

Assamese: Patharkuchi

Bengali: Patharkuchi, Himasagara, Patrankur

English: Winter Begonia

Guajarati: Pashanbheda, Pakhanbheda

Hindi: Pakhanabheda, Silphara, Patharcua, Pakhanabhed, Silpbheda

Kannada: Alepgaya, Pahanbhedi, Hittaga, Pasanaberu, Hittulaka

Kashmiri: Pashanbhed

Malayalam: Kallurvanchi, Kallurvanni, Kallorvanchi

Marathi: Pashanbheda

Oriya: Pasanbhedi, Pashanabheda

Punjabi: Kachalu, Pashanbhed

Tamil: Sirupilai

Telugu: Kondapindi

Taxonomical classification [15]

Classification Category

Kingdom Plantae- Plants

Subkingdom Tracheobionta-Vascular plants

Supervision Spermatophyta- Seed plants

Class Magnoliopsida- Dicotyledons

Subclass Rosidae

Order Rosales

Family Saxifragaceae- Saxifrage family

Genus Bergenia moench- elephant ear

Species *Bergenia ligulata* (Wall)

Botanical description

It is a small perennial climbing plant that grows well in moist and shady hilly areas, especially in the foothills of the Himalayas and the Khasi hills of Assam. The stems are shortened thick and the leaves ovate and bright red seasonally. The flowers are white, pink or purple. Bergenia(s) are evergreen, perennial, drought-resistant, herbaceous plants that bear pink flowers produced in a cyme. Due to the leaf shape and leathery texture such as “pigsqueak”, “elephant-ear”, “heartleaf”, “leather cabbage **[16]**.

3.2.3 Microscopy

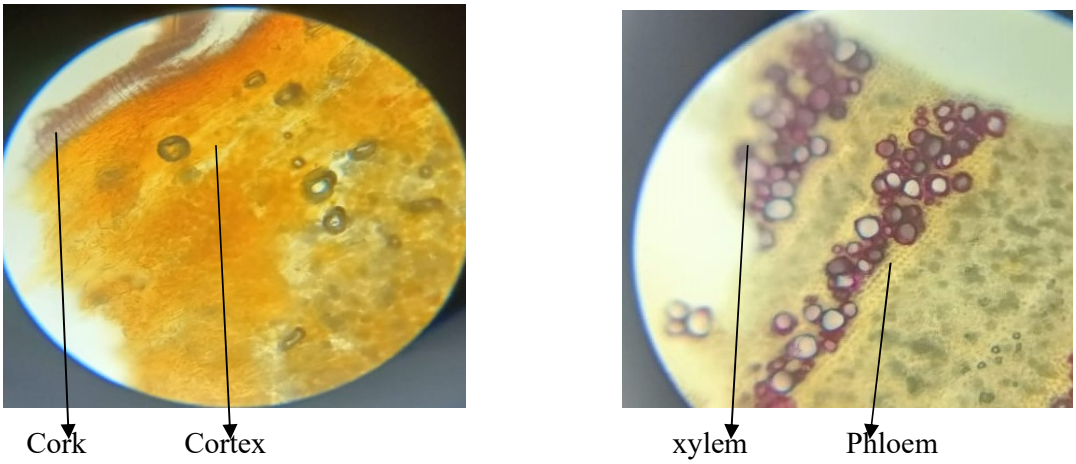


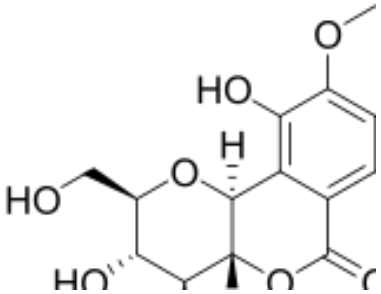
Figure 6: Transeverse section of *Bergenia ligulata* rhizome

Transverse section of rhizome shows cork divided into two zones; outer and inner. Outer zone is with few layers of slightly compressed and brown colored cells whereas inner zone is multilayered consisting of thin walled, tangentially elongated and colorless cells. Cork is followed by single layered cambium and two to three layers of secondary cortex. Cortex consists of a narrow zone of parenchymatous cells containing a number of simple starch grains whereas most of cortical cells contain large rosette Crystals of calcium oxalate and starch grains. Endodermis and pericycle are absent whereas vascular bundles arranged on a ring. Cambium is present as continuous ring composed of two to three layers of thin walled, tangentially elongated cells. Xylem consists of fibres, tracheids, vessels and parenchyma. Centre is occupied by large pith composed of circular to oval parenchymatous cells containing starch grains with CaC_2O_4 crystals similar to those found in cortical region. Vessels with simple pits have perforation plates on one end or at both ends and tracheids have helical thickenings **[17]**.

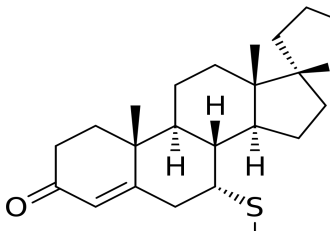
Chemical constituents: It consists of major phenolic compound 'bergenin' (nearly 0.9%) and other phenolic compounds in minor amount Phenolic compounds includes (+)- afzelechin, leucocyanidin, gallic acid, tannic acid, methyl gallate, (+)-catechin, (+)-catechin -7-O-ß-D-glucopyranoside, 11-O-galloyl bergenin, a lactone- Paashaanolactone . It also contains sterols viz., sitoindoside I, ß-sitosterol and ß-sitosterol-D-glucoside, glucose (5.6 %), tannin (14.2-16.3 %), mucilage and wax. Rhizomes of B. ligulata showed a presence of different chemical entities like

Coumarins: bergenin, 11-0-galloyl

bergenin, 11-O-P-hydroxy-benzoyl bergenin; 11-O-brotocatechuoyl bergenin, 4-0-galloyl bergenin; **Flavonoids:** (+) afzelechin, avicularin, catechin, eriodictyol-7-O-β-D-glucopyranoside, reynoutrin; **Benzenoids:** arbutin, 6-O-P-hydroxy-benzoyl arbutin, 6-O-protocatechuoyl arbutin; 4-hydroxy benzoic acid; **Lactone:** Idehcxan-5-olide, 3-(6'-O-P-hydroxy) **[18, 19]**.



Bergenin



Paashaanolactone

Uses: Calculus (Asmari), Excessive flow of urine, and Dysuria. Bergenia has been reported to dissolve gravel and stones in the kidney and is used as an anti-urolithiatic in all of it species. Fever, cough, diarrhoea, pulmonary affections and lungs diseases **[20]**.

CONCLUSION

Kidney stone difficulties are more likely in individuals with medical conditions such high fat diets, undernutrition, eating foods high in oxalate crystals, high protein diets, and post-surgical abnormalities. Treatment of kidney stone such as allopathic treatment removal of stones through surgery is now in trends. Herbal therapy is available for removal of kidney stones. Herbal treatment is the safest and inexpensive treatment. The main objective is to introduce Lambadi, Venivel and Pashanbhed as a kidney stones agents as it had not been introduced yet for the same purpose. The active phytochemical constituents of individual plants are insufficient to achieve the desirable therapeutic effects. When combining the multiple herbs in a particular ratio, it will give a better therapeutic effect. So it is necessary thing to develop polyherbal formulation of kidney stones so that this kind of drug resistance as well as side effects can be overcome and to handover such potential candidates to the society.

Human and animal rights

No animals or humans were utilized for the study of this review.

Conflict of interest

The authors asserted no conflict of interest.

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