ETHNOBOTANICAL AND PHYTOPHARMACOLOGICAL UPDATES ON DIDYMOCARPUS PEDICELLATA

Parveen Kumar Goyal¹, Santosh Kumar Verma², Ikshit Sharma³, Anil Sharma⁴, Anil Kumar Sharma*²

¹Hindu College of Pharmacy, Sonepat (Haryana), India. 
²CT Institute of Pharmaceutical Sciences, Jalandhar (Punjab), India. 
³R&D Deptt., Aimil Pharmaceuticals (India) Ltd., New Delhi, India. 
⁴Shri Krishna Govt. Ayurvedic College & Hospital, Kurukshetra (Haryana), India.

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ABSTRACT
From the beginning of time, treatment using herbal drugs has been a favourite tool of naturopathically inspired practitioners; and medical history is filled with descriptions of persons who used herbs as medicine for wellbeing of society. According to World Health Organization, traditional medicines are the synthesis of therapeutic experiences of generations of practicing physicians of indigenous systems of medicine for over hundreds of years before the development and spread of modern medicine. Herbs are the major and common element in many indigenous, traditional and alternative systems of medicine like Ayurvedic, Siddha, Unani, Homeopathic, Naturopathic etc. Herbs, since the dawn of mankind to till date, are being used as potent medicine but except than a handful, most of are not scientifically substantiated and well explored. One such herbal drug Didymocarpus pedicellata (Family: Gesneriaceae), traditionally used in renal disorders chiefly urolithiasis and having not so much scientific substantiations, is selected for study and hereby reviewed. This review is aimed to focus and compile the research work of various researchers on this drug and other data including vernacular names, taxonomy, botanical descriptions, traditional uses, pharmacological activities, chemical constituents, marketed formulation etc. This manuscript shall be of immense help to researchers interested in any aspects of research on this plant.

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INTRODUCTION

Herbal medicines are as old as human history. The earliest recorded evidences of use of herbal drugs in Indian, Chinese, Egyptian, Greek, Roman and Syrian texts dates back to about 5000 years \[1\]. Approximately 75% of the global population including most of the developing world depends on herbal medicines for their basic healthcare needs. Herbal medicines are not only inexpensive but better compatible with human body and have fewer side effects also, in comparison to allopathic synthetic medicines. Now a day, use of herbal drugs is not limited to indigenous and traditional systems of medicines only but the modern system of medicine also has derived many of its drugs from plant sources. Substances first isolated from plants account for approximately 25% of the western pharmacopoeias, with another 25% derived from modification of chemicals first found in natural products. A 2012 survey reported that 1 in 3 Americans use herbal medicines, estimating the size of the annual herbal market at $5.6 billion \[2\]. Many of globally marketed herbal formulations are with good scientific substantiations as per modern sophisticated technical methodology, pre-clinical and clinical studies but still plethora of herbal drugs and their formulations are lacking the same and restricted as a part of traditional knowledge and/or specific native medical practitioners. For wellbeing of society, as many as of herbal drugs should be explored and scientifically evaluated for their therapeutic effectiveness using modern methodology.

In light of the above text, *Didymocarpus pedicellata* (Fig. 1a) \[3\] belonging to family Gesneriaceae traditionally used in treatment of renal disorders particularly kidney stones and not scientifically explored so much is selected for study and hereby reviewed. It is highly valuable though a lesser known medicinal plant and popularly known as stone flower. It is an annual herb growing on rocky surface in shady and moist localities of temperate zone \[4\]. In Ayurveda it is known as shilapushpa, shantapushpi and sometimes pashanbheda \[5\]. Pashanbheda is an ayurvedic drug used in the treatment of urinary calculi, polyuria, dysuria, fever, piles, dysentery and uterine disorders \[6\]. Different botanical sources used in name of pashanbheda in different parts of country are *Avera lanata*, *A. Persica* (both of family Amaranthaceae), *Ammania baccifera* (Lythraceae), *Bauhinia racemosa* (Caesalpiniaecae), *Bergenia ciliata*, *B. stracheyi* (both of Saxifragaceae), *Bridelia crenulata*, *B. Retusa*, *B. stipularis*, *Homonoia riparia* (all of Euphorbiaceae), *Didymocarpus pedicelleta* (Gesneriaceae), *Gentiana kurroo*, *G. lutea* (both of Gentianaceaee), *Iris pseudacorus* (Iridaceae), *Kalanchoe pinnata*, *K. integra* (both of Crassulaceae), *Lepidagathis trinervis* (Acanthaceae), *Notthosarva brachiiata* (Amaranthaceae), *Ocimumtenuiflorus*, *Plectranthus amboinicus* (both of Lamiaceae), *Rotula aquatic* (Boraginaceae) and *Trianthema triqueta* (Aizoaceae) \[7-9\]. Of these, *A.lanata*, *B. crenulata*, *B. stipularis*, *H. riparia*, *N. brachiata* and *R. aquatic* are used as pashanbheda in South India while *B. ciliata*, *D. pedicellata*, *I. pseudacorus*, *K. pinnata* and *O. Tenuiflorum* are used in North India \[10, 11\]. *B. ciliata* is the accepted source of pashanbheda \[12\]. In common language *D. pedicellata* is also called charela or patharphori (Unani name) \[13\]. The name Stone Flower, and various local names, probably come from its believed efficacy in curing kidney stones, or probably because it occurs on rocks. According to a hypothesis the plant is supposed to regulate calcium absorption in the body. The plant is known for its diuretic effect and in maintaining healthy urinary tract \[14, 15\]. It is a major constituent (32.6%, w/w) of cystone (Himalaya Drug Company), a formulation used to cure renal ailments such as urolithiasis \[16\], neuro-ureterolithiasis \[17\], burning micturition \[18\] and several other renal disorders \[19\].

The prime objective of this manuscript is to describe the various unexplored and scientifically explored aspects like taxonomical classification, morphology, microscopic characteristics, traditional uses, phytochemical constituents, pharmacological activities of *D. pedicellata* as this plant has not been reviewed in recent past and non-availability of compiled data is a major hurdle in starting the research on it.

**Figure 1:** (a) Leaves and (b) Morphology of *D. pedicellata*.

**Synonyms**

*D. macrophylla* auct. non-Wall. ex D. Don \[20\]
*Roettlera pedicellata* (R.Brown) Kuntze \[21\]

**Vernacular Names**

English: Black stone flower, Stone flower \[15\]
Sanskrit: Shilapushpa, \[22, 23\] Shantapushpi, Pathar Chatta \[4, 24\]
Tamil: Kalpas \[25\]
Hindi: Charel, Patharphori \[23\], Pasanphori \[26\]
Nepali: Kumkum, Kum \[4\]
**Taxonomic classification** [21]

Kingdom: Plantae  
Subkingdom: Iridiplantae  
Infrakingdom: Streptophyta  
Division: Tracheophyta  
Subdivision: Spermatophytina  
Class: Magnoliopsida  
Super order: Asteranae  
Order: Lamiales  
Family: Gesneriaceae  
Subfamily: Cyrtandroideae  
Tribus: Disymocarpeae  
Genus: Didymocarpus  
Species: Pedicellata

**Habitat**

Temperate region of Western Himalayas from Chamba to Kumaon at an altitude between 1000 to 2200m. Also grows in subtropical Himalaya from Himachal Pradesh to Arunachal Pradesh [3, 20].

**Morphological characteristics** (Fig. 1b)[3]

**Rhizomes**

These are short (0.5 to 3.0 cm in length and 0.3 to 0.8 cm in diameter), horizontally creeping, tortuous and cylindrical. The lower and lateral sides of rhizomes are fully covered with 0.1 to 0.3 mm thick roots which are slender and wiry. The upper surface of rhizome has aerial stem (about 0.5 to 1.5 cm long and 0.5 to 0.8 cm thick). Adjacent to the vertically grown aerial stem, at upper surface of rhizome, there are small (1.5 to 3.0 cm long) young leaves which are somewhat triangular in shape, curly and orange in colour. The top of rhizome, from where the aerial stem grows, is encircled by leaf scar.

**Leaves**

Leaves are simple, petiolated (5.0 to 8.0 cm), ovate or cordate having unequal base and serrate margin. Mature leaves are about 8.0 to 10.0 cm in length and 5.0 to 8.0 cm in width. The upper surface is green and glabrous while the lower surface is rough and whitish with small orange coloured dots and prominent veins.

**Flowers**

Flowers are shortly conate, pedicellate having ovate bracts, funnel shaped calyx which is dividing nearly 1/3rd way down with rounded lobes and purple corolla. Peduncle is slender, oval, trichotomously branched, 5.0 to 10.0 cm long and 0.5 to 1.0 mm thick.

**Fruits**

The fruits are pedicellate, filliform capsule with persistent calyx. These are longitudinally dehiscing having minute ellipsoid seeds.

**Microscopic characteristics** [3]

**Stem**

T.S. of stem shows a layer of epidermis followed by cortex which consist of 20 to 30 rows of oval to tangentially elongated, somewhat shrivelled parenchymatous cells which are filled with brownish contents, oil globules and occasional calcium oxalate prisms. Endodermis is distinct encircling the ring of pericyclic fibres, narrow phloem, xylem and wide pith. The xylem consists of radially arranged vessels, tracheids, parenchyma and uniseriate to multiseriate medullary rays. The pith contains cells of different sizes and shapes having oleoresin canals and calcium oxalate prisms and clusters. The pith cells are reticulately thickened with pitted or wheel like striated walls (Fig. 2a).

**Rhizome**

T.S. of rhizome is irregularly circular with well developed suberized cork, parenchymatous cortex, traversed with secretory canals and oil globules. It also contains a layer of stellar tissue with bundles of lateral root traces and central parenchymatous pith (Fig. 2b).

**Root**

T.S. of root is circular having irregularly running outer brownish cork tissue, cortex, narrow phloem and wide central porous wood (Fig. 2d). It showed 5-8 rows of cork cells followed by 3 to 4 rows of parenchymatous cortex and 5 to 6 rows of phloem tissues having oil globules encircling the central wide xylem. The xylem tissues are composed of radially arranged isolated or groups of 2-4 vessels, thick walled fibres and few parenchymatous cells traversed with uniseriate to multiseriate medullary rays in continuation with phloem tissues (Fig. 2c).
Leaf

T.S. of young curly leaves and matured leaves through midrib differs in certain aspects. Young leaves (Fig. 3b) are deeply grooved on upper side and both surfaces are covered with many glandular, orange coloured, globular trichomes and simple covering trichomes with inflated basal cells and conical apex. It contains 1 to 3 centrally located conjoint, collateral meristel in midrib. In mature leaves (Fig. 3d), these are many and distantly arranged; one located at bottom which is semilunar, bigger in size that one which is facing to it at its upper side, other is subsidiary, laterally located and smaller in size. The surrounding parenchymatous cells are filled with cluster and rosette calcium oxalate crystals. The young leaves contain prismatic crystals. In mature leaves, cells of upper epidermis are elongated, broad, squarish and bigger in size and followed by 2 to 3 rows of very small sized compactly arranged cells of palisade layer continuous over the midrib followed by spongy parenchyma which is loosely arranged. In young leaves, epidermal cells are smaller in size and palisade cells are smaller and compactly arranged (Fig. 3a).

Fruits

The diagrammatic view of T.S. of fruit (Fig.3c) is circular in outline having 4 equidistantly located shallow notches, representing the 4 inner compartments each containing 1 to 3 seeds. A horizontal cleft lies in the centre. Each loculi has a layer of epidermis, narrow parenchymatous mesocarp and sclerenchymatous coiled endocarp reaching up to the centre of loculi.
**Peduncle (Scape)**

The diagrammatic view (Fig. 4b) of peduncle T.S. is oval having undulating outline and wide central pith encircled by a ring of xylem and narrow phloem. T.S. shows a layer of epidermis covered with cuticle followed by 5 to 6 rows of parenchymatous cortex which sometimes consist of isolated calcium oxalate prisms followed by narrow phloem. Xylem is wide having isolated or groups of 2 to 3 vessels associated with trachieds and fibres. Pith is lignified (Fig. 4a).

**Petiole**

The diagrammatic view (Fig. 4c) of T.S. of petiole is highly irregular in outline having two prominent winged projections on upper side (each placed on either sides of central convex elevation) and irregularly scattered vascular bundles traversing throughout the ground tissue.

T.S. shows a layer of epidermis having many simple covering trichomes differing in size, shape and thickness. Some trichomes are straight, bent and filled with dark orange colouring material while others are short and thick having 3 to 4 basal pedestal cells followed by 2 to 3 warty terminal cells. Underneath this, there are 4 to 7 layers of collenchymatous hypodermis. The remaining ground tissue is parenchymatous traversed with few secretory cells and conjoint, collateral vascular bundles of various sizes and shapes usually arranged in semilunar fashion especially near the lower side of petiole. The parenchymatous cells are embedded with cluster of calcium oxalate plenty at lower side and very few at upper side of petiole (Fig. 4d).

**Figure 4:** (a) T.S. of Peduncle, (b) Diagrammatic view of T.S. of Peduncle, (c) T.S. of Petiole, (d) Diagrammatic view of T.S. of Petiole.

**Powder**

The microscopy of powder (Fig. 5) shows lamina fragments with epidermal cells, trichomes and underlined palisade cells, epidermal cells with actinocytic stomata, sessile glandular trichomes with 5-6 celled heads, glandular trichomes with short unicellular stalk and unicellular head attached to epidermal cells or scattered as such throughout. It also shows rosette and cluster of calcium oxalate, longitudinally cut xylem vessels of midrib of leaf, reticulately thickened cells of pith embedded with few calcium oxalate prisms and clusters, thick-walled fibres running longitudinally and transversely (crossing each others) from endocarp of fruit, oleoresin cells with brownish contents and testa of seeds with striated cuticle.
Chemical constituents

The leaves contain a number of chalcones, quinochalcons and flavanones. Pediflavone has also been isolated from young leaves \(^\text{[20]}\). The main constituents isolated from leaves are Pedicellin (Fig. 6) \(^\text{[27, 28]}\), 2',4',5,6'-trimethoxychalcone \(^\text{[29]}\), 5,8-dihydroxy-7-methoxyflavon and Didymocarpin \(^\text{[30]}\). Some other major constituents are Pedicin \(^\text{[31, 32]}\), Pedicinin \(^\text{[27, 31, 33]}\), Pedicellin \(^\text{[29, 31, 33, 34]}\), Pediflavone \(^\text{[43]}\), \(D.\ pedicellata\) also contain 2-Hydroxy-3,4,6-trimethoxychalcone \(^\text{[32]}\), 5,6,7,8-tetramethoxyflavanone \(^\text{[29]}\), 8-hydroxy-5,6,7-trimethoxyflavanone \(^\text{[29]}\), Didymocarpene \(^\text{[36]}\), (7-hydroxy-5,6,8-trimethoxyflavanone), Didymocarpin-A \(^\text{[37, 38]}\), Didymocarpol, didymocaprenol \(^\text{[36]}\), Isodidymocarpin \(^\text{[19]}\), Isopedicine \(^\text{[31]}\), Methylpedicin \(^\text{[29, 32, 40]}\), Methylpedicinin \(^\text{[41]}\), Pashanone \(^\text{[40, 42]}\), Pediflavone \(^\text{[43]}\), Pseudoisopedicine \(^\text{[44]}\), \(\beta\)-sitosterol, Behenic acid, lignoceric acid, palmitic acid, stearic acid \(^\text{[36]}\).

Figure 5: Powder Microscopy.

Figure 6: Structure of Phytoconstituents
Traditional uses
It is traditionally used in the treatment of renal diseases particularly stones of kidney [8] and bladder [20]. The leaves are lithontriptic [45] and two spoonful pastes of fresh leaves for two weeks are potent remedies for discharging the stone from kidney [24]. It also regulates calcium absorption in the body. The plant is known for its diuretic effect and in maintaining healthy urinary tract [14]. Roots are also used as substitute of Bergenia ligulata (Family: Saxifragaceae) for its therapeutic use in stones [46].

Pharmacological profile

Antiurolithiatic activity
The hydro-alcoholic extract of whole plant of D. pedicellata (100 and 200 mg/kg) showed antiurolithiatic potential against calcium oxalate stones when tested against ethylene glycol induced urolithiasis in rats [47].

Nephro-protective activity
Ethanolic extract of aerial parts of D. pedicellata showed significant nephroprotective activity when tested against ferric nitritriacetate (Fe-NTA) mediated renal oxidative stress and nephrotoxicity in mice. The extract was found to possess high contents of total polyphenolics, exhibit potent reducing power and significantly scavenge free radicals including several reactive oxygen species and reactive nitrogen species [48].

Spasmolytic activity
Aqueous extract of D. pedicellata and isolated pedicellin from it showed papaverine-like spasmolytic activity on isolated ileum and uterus of guinea pig and ascending colon of rabbit. The extract also inhibited the carbamoylcholine produced intestinal hypermototy in cats and prostigmine produced intestinal hypermototy in rats [44].

Antimicrobial activity
Flavones (didymocarpin, didymocarpin-A), chalcones (isodidymocarpin, pedicellin), quinochalcones (pedicinin, methylpedicinin) and their derivatives isolated from D. pedicellata showed some deleterious effects against plant pathogenic fungi and bacteria [49]. Essential oil from this plant also showed antibacterial and antifungal potential [50].

CONCLUSION
In the present manuscript, thorough literature revealed that D. pedicellata, among practitioners of different systems of medicines, is a very popular remedy for renal disorders. It is also a vital constituents of herbal formulations used for kidney stones, even in modern system of medicine. This plant is not so much explored scientifically with evidences for various therapeutic uses. It recommended that further studies should be carried out on D. pedicellata regarding its various pharmacological and therapeutic effects, diverse chemical constituents responsible for the same. The present article can serve as a good compilation to start such studies on this plant in future.

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Conflict of Interest
None
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