

# Endangered Medicinal Plant *Coscinium fenestratum* (Gaertn.) Colebr. - A Review

Vijay Danapur\*, Haleshi C, Sringswara AN

Vijay Danapur\*, Haleshi C,  
Sringswara AN

Vriksha Vijnan Private Limited, #520,  
Brundavana, 10th Main, 3rd Cross, BHCS  
Layout, Chikkallasandra, Bangalore-560061,  
INDIA.

## Correspondence

Vijay Danapur

CEO, Vriksha Vijnan Private Limited, #520,  
Brundavana, 10th Main, 3rd Cross, BHCS  
Layout, Chikkallasandra, Bangalore-560061  
(Karnataka), INDIA.

E-mail: vijay.danapur@vrikshavijnan.com

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## ABSTRACT

*Coscinium fenestratum* (Gaertn.) Colebr. (Menispermaceae), is a large woody liana found in moist deciduous to the evergreen forest at an altitude of 350-1200m. It is well suited to wet evergreen, semi evergreen, deciduous and dry deciduous forest types. Stem and root of this species are highly medicinal and is sold in the drug sales of India as Maramanjil and Europe as False Calumba or tree turmeric. The stem is bitter, anti-inflammatory, antiseptic, febrifuge and tonic and is useful in vitiated conditions of kapha and vata, ophthalmopathy, wounds, ulcers, diabetes, fever, and general debility. Due to destructive collection, overexploitation and habitat loss, the plant is on the verge of extinction in the wild. It is categorized as critically endangered in India, Vulnerable in Vietnam, and Indeterminate in Sri Lanka and Malaysia<sup>1-47</sup>. Therefore an overview of this plant on pharmacognosy, pharmacology, safety and toxicity is presented below along with HPLC details of Berberine the active ingredient in the stem and root of the plant.

**Key words:** *Coscinium fenestratum* Menispermaceae, Berberine Pharmacognosy.

## INTRODUCTION

*Coscinium fenestratum* (Gaertn.) Colebr. is commonly known as, 'tree turmeric'. It belongs to the plant family *Menispermaceae*. The wood of *Coscinium fenestratum* has been used in traditional fabric dyeing. Yellow is the most typical color produced by this plant. *Coscinium fenestratum* is used in Malaysia for dyeing. Most populations of this species have been exploited on a substantial scale in its natural habitats and it has not been cultivated<sup>1</sup>. It is a woody climbing shrub with cylindrical stem, externally yellowish-brown and internally yellowish in color. Its stem has often been used as a substitute for berberis. However, it can be readily distinguished by the presence of large vessels in the wood, absence of annual rings and the crenate ring of sclerenchyma beneath the cortex. The stem yields a yellow dye, which is used either alone or in combination with turmeric and other coloring materials. The roots of *Coscinium fenestratum* contain alkaloids berberine, dihydroberberine, 12, 13-dihydro-8-oxo berberine, tetrahydroberberine, oxyberberine and noroxy hydrastinine<sup>2</sup>.

## Morphology

A large woody climber dioecious with distinct male and female plants. Young stem and branches covered with fuscous-cinereous bark, terete, distantly nodose, striated; bark yellow, corky, fissured and lenticellate, densely pubescent, very rarely with slender tendrillar branchlets. Leaves simple, alternate, thick, peltate, deltoid, exstipulate; petiole up to 10cm long, angular, thickened both at base and apex, densely adpressed, rusty pubescent; lamina thick, broadly ovate, acute or acuminate

at apex, rounded or truncate at base, margin entire 13-30 x 12-23cm, chartaceous, green, densely white, silky pubescent on both surfaces when young, green and glabrous above and silky pubescent below when mature, 5-7 nerved from the base, nerves divergent, often forked and reticulation raised and prominent below. Inflorescence supraaxillary, finely tomentose, divaricating branches 2cm. long, the male heads globose, densely flowered, 6-mm diameter; petals yellow, the outer 6-8 rotund, 1.5mm. long and broad, the inner 3 longer, spatulate, 2 mm. long, 1 mm. the broad, patent at the apex. Synandrium 1 mm. long. Carpels of female flower pilose; styles reflexed, filiform. Female fruiting peduncles 2-3 cm. long; drupes 1-3, very shortly stiptate, suberiform- globose, slightly tomentose, fuscous, about 2-2.5cm. diam.; endocarp 1.3cm. long, 1.9-cm. broad, bony, smooth, with an obsolete dorsal line testa hard and stony greyish, glabrous with a waxy coating, endospermous, endosperm white and ruminant<sup>3,4</sup>.

## Distribution

*Coscinium fenestratum* is an Indo-Malaysian species that occurs at an altitude of around 350-1200m<sup>4</sup>. It occurs in India, Sri Lanka, Malaysia, Cambodia, and Vietnam<sup>45</sup>. In India, it is restricted to the Western Ghats. It occurs sparingly in the evergreen forests in central and southern zones along the western slopes of the Western Ghats, mostly along watercourses. It is also found in crevices of rocks and trees<sup>4</sup>. In Karnataka occurs in dense evergreen forests of Coorg, Udipi, Dakshina Kannada & Uttara Kannada districts<sup>5</sup>. In Kerala it is found in Thiruvananthapuram district; Thirunelli of Wayanad

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district; Nilambur of Malappuram district and in Chimini dam area of Thrissur district<sup>4,5</sup>. In Tamil Nadu occurs in Kanyakumari, Tirunelveli and Nilgiri districts<sup>5</sup>.

### Threat status

The threat status of this species has been assessed as critically endangered for Karnataka, Kerala and Tamil Nadu in India<sup>5,6</sup>. It is also recorded in the red data book of Vietnam as vulnerable<sup>7</sup>.

### Pharmacognostic features

#### Stem

Physicochemical and Organoleptic Parameters

#### TLC finger printing profile

TLC Fingerprint profile of *Coscinium fenestratum* stem shows one band derivatized with sulphuric acid, two bands with anisaldehyde, two bands observed under long UV radiation and no bands under short UV radiation.

#### Macroscopic identification of stem

15 to 30 cm. or more in length, 2 to 8 cm. in diameter, straight or occasionally slightly twisted, pale grey or greyish yellow with a fairly smooth surface, marked with longitudinal striations spaced about a mm apart, cut surface yellowish-green to yellow in colour showing wedge-shaped areas, fissured with shallow vertical slits of varying length; texture, hard; acrid in taste<sup>46</sup>.

#### Anatomy of stem

Transverse section of the stem is circular in outline. The outermost zone is cork, which is composed of 15 or more rows of thick-walled cells. Cortex is seen below this cork layer. It is composed of rectangular and polyhedral, comparatively thin-walled cells. Most of the cells contain oil droplets. The inner boundary of the cortex forms a wavy band of several arches, which is composed of yellow coloured elongated stone cells, which form the major portion of the band and few short sclerenchymatous cells. These sclerenchymatous cells are seen in definite patches opposite to phloem. Below these arches, some crushed primary phloem cells are seen. Secondary phloem forms a cup-like structure above the secondary xylem. The wood consists of large-sized vessels, very little parenchymatous elements and thick-walled fibers. Medullary rays alternate the conductive tissues, which is composed of multiseriate radially elongated thick walled cells. In addition to the broad primary medullary rays, the narrow band of secondary medullary rays is seen. Pith is very prominent; the cells towards the center of the pith are large, polyhedral and fairly thick walled. The outermost cells of the pith are smaller with more thickened walls. Starch grains are smaller with more thickened walls and are present throughout the pith and medullary rays<sup>4</sup>.

#### Macroscopic identification of root

5 to 30 cm or more in length, 2 to 5 cm. in diameter, somewhat longitudinally grooved, transversely cut surface smooth, yellow; texture rough and fibrous; acrid in taste; no particular odour<sup>46</sup>.

#### Microscopic identification of root

In the transverse section, the root is more or less circular in outline. The outermost zone is the cork layer, which is composed of 10-13 rows of thick-walled cells. Below this cork layer is the cortex, which is composed of rectangular and comparatively thin-walled cells. In certain cells, oil drops are seen. The inner boundary of the cortex forms a wavy band of several arches, which is composed of yellow colored thick-walled cells. The tissue is composed of longer, elongated stone cells, which form the

major portion of the band, and besides a few short sclerenchymatous cells. Below these arches, some crushed primary phloem cells are seen. This is followed by secondary phloem tissues. The wood consists of large-sized vessels, parenchymatous elements, and thick-walled fibers. Medullary rays consist of multiseriate radially elongated thick-walled cells. In addition to the broad primary medullary rays narrow band of secondary medullary rays are seen. Pith is not discriminable in old roots<sup>4</sup>.

#### Microscopic identification of petiole

T.S. of the petiole is somewhat circular in outline. Epidermis is single-layered with thin cuticle and has multicellular, uniseriate trichomes. Cortical region is parenchymatous. Vascular bundles are seen in a ring and a sclerenchymatous bundle cap is seen above each bundle. In the center of the petiole parenchymatous cells are large and loosely arranged<sup>4</sup>.

#### Microscopic identification of leaf

T.S. of the leaf shows common dicotyledonous characters. In T.S. midrib portion appears in the shape of an inverted cone. Epidermis is single-layered. Lower epidermis possesses a large number of multicellular, uniseriate trichomes. Mesophyll consists of a single-layered palisade and multilayered spongy tissue with abundant intercellular spaces. In midrib portion, collenchyma is very prominent just beneath the lower and upper epidermis. Vascular bundle is encircled by a wavy ring of sclerenchymatous tissue. Stomata are of Ranunculaceae type<sup>4</sup>.

#### Organoleptic properties

The drug has no odour, but a bitter taste<sup>8</sup>.

#### Phytochemistry

The chief constituent of *Coscinium* is the yellow crystalline alkaloid, berberine; it also contains a saponin. Stems of *Coscinium fenestratum* from Thailand furnished the new protoberberine alkaloids oxypalmatine, (-)-8-oxotetrahydrothalifendine, (-)-8-oxoisocorypalmine and either (-)-8-oxothaicanine or (-)-8-oxo-3-hydroxy-2,4,9,10-tetramethoxyberberine in addition to berberine, the major alkaloid and (-)-8-oxocanadine<sup>9</sup>. The roots of *Coscinium fenestratum* contain alkaloids berlambine, dihydroberlambine, 12, 13-dihydro-8-oxo berberine, tetrahydroberberine, oxyberberine, and noroxyhydrastinine<sup>10,11</sup>.

TLC densitometry determination with 80% ethanol was done on ten different dried stem samples from different drug stores of Vietnam. The crude extracts were in the range of 9.87-16.38% dry weight while berberine contents in the dried powder and in the crude extract were in the range of 1.71-2.89% w/w and 11.84-18.45% dry weight, respectively. TLC fingerprints of each extract showed a similar pattern with bands of berberine as the major alkaloid and other minor alkaloids<sup>12,13</sup>.

Deevanhay *et al.*,<sup>14</sup> developed a microwave-assisted extraction of berberine, jatrorrhizine, palmatine from *Coscinium fenestratum* at atmospheric pressure (boiling point 83<sup>o</sup> C) and pressurized condition (160<sup>o</sup> C) under optimum conditions for 15 min were higher than those obtained using Soxhlet extraction for 8 h and extraction with 0.2% sulfuric acid for 24 h. jatrorrhizine(2.36 mg/g) and palmatine (0.73 mg/g) extraction yields were observed to be the highest at 170<sup>o</sup>C for 15 min. Microwave assisted extraction is more effective than conventional extraction methods concerning the extraction time and extraction yield for extracting protoberberine alkaloids from *C. fenestratum*.

Simultaneous characterization of quaternary alkaloids, 8-oxoprotoberberine alkaloids, and a steroid compound in *Coscinium fenestratum* was successfully performed by liquid chromatography hybrid ion trap time-of-flight mass spectrometry (LC/IT-TOF MS)



Figure 1: Habit: *Coscinium fenestratum*.



Figure 2: Flowering.



Figure 3: Leaves.

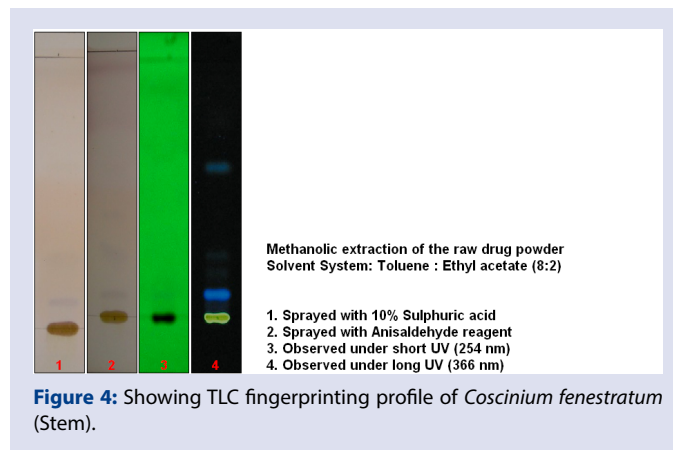


Figure 4: Showing TLC fingerprinting profile of *Coscinium fenestratum* (Stem).



Figure 5: Stem.

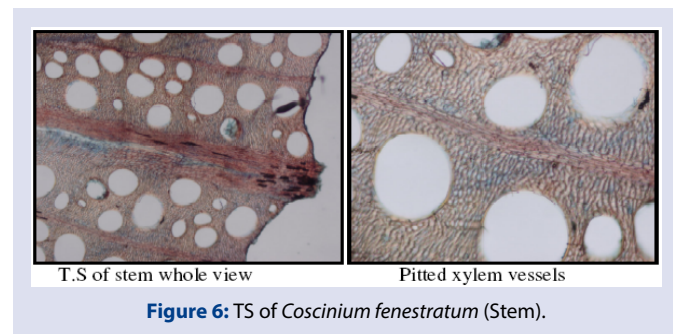


Figure 6: TS of *Coscinium fenestratum* (Stem).

Table 1: showing Physicochemical and Organoleptic Values.

Physicochemical Constants			Organoleptic Characters	
Parameters	Values	Limit	Parameters	Properties
TA	6.1%	NMT 3%	Taste	Bitter
AIA	4.3%	NMT 2%	Color	Yellowish
ASE	2.6%	NLT 3%	Odour	Mild
WSE	2.2%	NLT 8%	Texture	Fibrous

(TA - Total Ash; AIA - Acid Insoluble Ash; ASE - Alcohol Soluble Extractive; WSE - Water Soluble Extractive; Limit as per Ayurvedic Pharmacopoeia of India).

**Table 2: showing Rf values of bands with different detective reagents and UV light.**

<b>Under Visible Light</b>									
Rf Values	-	-	-	-	-	-	-	-	-
<b>Sprayed with 10% H<sub>2</sub>SO<sub>4</sub></b>									
Rf Values	0.09	-	-	-	-	-	-	-	-
<b>Sprayed with Anisaldehyde</b>									
Rf Values	0.09	0.95	-	-	-	-	-	-	-
<b>Under Short UV (254 nm)</b>									
Rf Values	-	-	-	-	-	-	-	-	-
<b>Under Long UV (366 nm)</b>									
Rf Values	0.09	0.56	-	-	-	-	-	-	-

was carried out by Deevanhxay *et al.*,<sup>15</sup>. Total of 32 compounds, including 2 benzyloquinoline alkaloids, 3 aporphine alkaloids, 12 quaternary protoberberine alkaloids, 10 8-oxoprotoberberine alkaloids, 3 tetrahydroprotoberberine alkaloids, and a steroid compound were simultaneously separated and characterized by matching the empirical molecular formulae with those published in the literature and the multi-stage mass spectrometry (MS(n)) data obtained using structural information from IT, an accurate mass measurement obtained from TOF MS, and HPLC separation. A total of 20 compounds, including 4 novel natural products were identified or tentatively identified for the first time from *Coscinium fenestratum*. The method can be applied for the analysis of 8-oxoberberine and other alkaloids in other herbal medicines.

### Substitute/ adulterants

The stems are used in South India as a substitute for *Berberis* (Daaruharidraa); also as an Indian substitute for True Calumba (*Jateorhiza palmate* Miers)<sup>16,43,44</sup>.

### Uses

#### Folk uses

Root—stomachic, diuretic, hypotensive, anti-dysenteric, antibacterial, antifungal, bitter tonic in dyspepsia and debility. The plant is also used against fractures; for dressing wounds and ulcers and in cutaneous leishmaniasis<sup>16</sup>. The plant is used in the treatment of skeletal fractures in Sri Lanka<sup>43</sup>.

It is widely used as a traditional medicine in the Northeastern part of Thailand, particularly along the border of the Lao People's Democratic Republic for many purposes including the treatment of high blood cholesterol, hyperglycemia as well as hypertension<sup>17</sup>.

The product of this plant in Sri Lanka is used as a therapeutic agent for various conditions including ophthalmopathy, inflammation, ulcers, skin disease, abdominal disorders, jaundice, fever, and general debility<sup>18</sup>.

The rural people of Kanyakumari District, Tamil Nadu, India use the decoction of the stem for the treatment of diabetes<sup>2</sup>. a paste of the root is applied to the head as a cooling application and also to bruises and contusions<sup>44</sup>.

The root is used in Sri Lanka as an efficient bitter tonic. It has antiseptic properties due to which it can be used for dressing wounds and ulcers. It is used as a cure for tetanus. The decoction of the bark is used against malarial fever<sup>3</sup>.

Crude alcoholic extracts of the stem are prescribed in Vietnam for colic and stomachache. A formulation along with other anti-inflammatory agents makes a good topical application for arthritis, rheumatism, gout, and fibromyalgia<sup>6</sup>.

#### Ayurvedic uses

The stem is bitter, thermogenic, ophthalmic, anodyne, anti-inflammatory, vulnerary, depurative, stomachic, antiseptic, febrifuge, sudorific and tonic and is useful in vitiated conditions of kapha and vata, ophthalmopathy, inflammations, wounds, ulcers, skin diseases, abdominal disorders, jaundice, diabetes, fever and general debility<sup>4,19</sup>.

The plant is mainly used for treating diabetes mellitus in traditional Ayurvedic and Siddha systems of medicine<sup>20</sup>. The infusion and tincture preparation of stem is widely used in the traditional Ayurvedic system for the treatment of diabetes mellitus<sup>2</sup>.

#### Siddha uses

In the Siddha system of medicine, the powdered stems are dissolved in milk and given to the diabetic patients<sup>2</sup>.

### Medicinal uses

*Coscinium fenestratum* has been reported to possess various pharmacological actions such as antioxidant, laxative, antiproliferative, antidiabetic, anti-hypotensive, anti-plasmodial and antibacterial activities. Various parts of the plant is used for fever, muscle pain, stomach pain, malaria, diarrhea, ulcers and infection of the eyes<sup>17,18</sup>. The stem is anti-inflammatory and antiseptic. Used to treat tastelessness, bleeding piles, cough, wounds, ulcers, skin diseases, abdominal disorders, jaundice, liver disorders, intrinsic hemorrhage, diabetes, fever, and general debility<sup>5</sup>. It also has antifungal and anti-yeast activities<sup>13</sup>.

The stem is useful in ophthalmopathy, wounds, ulcers, skin diseases, abdominal disorders, jaundice, diabetes, tetanus, fever and general debility<sup>21</sup>. It is used for dyspepsia, and as a febrifuge<sup>20</sup>. It is known to treat influenza and eye diseases. It is used to treat bleeding piles and excessive bleeding during menstruation. The bark is also used in the treatment of leucorrhoea and other gynecological problems<sup>6</sup>. It could protect against hepatotoxicity induced by carbon tetrachloride and also exhibited strong anti-feeding<sup>18</sup>.

### General uses

The dye obtained from the wood has been used in traditional fabric dyeing either alone or in combination with turmeric or other coloring matters<sup>19,43</sup>. It is used as hair shampoo and soap in Sri Lanka to enhance the skin complexion; it is also used in ayurvedic bath soap and bath oil. It is used as a tea extract with other herbals as an immunity booster. The dried root is insect resistant. Berberine has a fluorescent property, which is used to conserve the old documents like Dunhuang Diamond Sutra in China<sup>6</sup>. Birds and animals consume edible fruits<sup>43</sup>.

### Pharmacology

#### Anti-diabetic activity

The antidiabetic potential of the alcoholic stem extract of *Coscinium fenestratum* Colebr. (Menispermaceae), was evaluated in the STZ-nicotinamide induced type 2 diabetic model. Graded doses of the alcoholic stem extract were administered to normal and experimental diabetic rats for 12 days. Significant reduction in fasting blood glucose along with serum triglyceride, and cholesterol levels were observed in the normal as well as in the treated diabetic animals. Significant results were observed, thereby justifying the use of the plant in the indigenous system of medicine<sup>2,22</sup>.

*Coscinium fenestratum* (Gaertn.) Colebr. Or "Hamm" has been widely used as traditional medicine. The anti-hyperglycemic effects of *Coscinium fenestratum* on plasma glucose levels were studied in both normal and streptozotocin-induced diabetic rats by performing OGTT with several kinds of sugar, glucose, maltose, and sucrose. In normal rats, *Coscinium fenestratum* inhibited the increase of plasma glucose levels in all three kinds of sugar-loaded rats in a dose-dependent manner. In diabetic rats, *Coscinium fenestratum* significantly decreased plasma glucose levels in glucose and maltose loaded rats. The further stimulatory effect on insulin secretion from perfused rat pancreas and its inhibitory activity on rat intestinal alpha-glucosidase, maltase and sucrase was investigated. The result showed that the plant significantly increased insulin secretion in a biphasic pattern and gradually stimulated insulin secretion in a monophasic pattern, indicating that the in vivo hypoglycemic effect was due to stimulation of insulin secretion from pancreatic beta-cells. Also, it inhibited in vitro activities of maltase better than sucrase, which was similar to acarbose. Taken together, it is concluded that the crude ethanol extract of *C. fenestratum* had anti-hyperglycemic action in both normal and STZ-induced diabetic rats. The mechanisms underlying hypoglycemic activity were at least partly due to stimulation of insulin secretion and inhibition of intestinal alpha-glucosidase, maltase, and sucrase<sup>41</sup>.

Oral administration of alcoholic extract of the stems of *Coscinium fenestratum* caused a significant increase in enzymatic antioxidants such as catalase, superoxide dismutase, glutathione synthetase, peroxidase, and glutathione peroxidase and the nonenzymatic antioxidants ascorbic acid, ceruloplasmin, and tocopherol. The significant increase was seen in glycolytic enzymes such as glucose-6-phosphate dehydrogenase, lactate dehydrogenase, and hexokinase, whereas a significant decrease was observed in the levels of gluconeogenic enzyme, glucose-6-phosphatase and alanine aminotransferase in treated diabetic rats along with serum creatinine and urea. Thus demonstrating the significance of *C. fenestratum* as antidiabetic<sup>20</sup>.

The effect of *Coscinium fenestratum* ethanolic extract on plasma glucose concentrations in normal and streptozotocin (STZ)-induced diabetic rats, the stimulatory effect on insulin secretion from perfused rat pancreas and the inhibitory effects on rat intestinal  $\alpha$ -glucosidase enzymes, maltase and sucrase was carried out by Yibchok-anun *et al.*,<sup>23</sup>. In oral glucose, maltose and sucrose loading tests, the extract significantly decreased plasma glucose concentrations in a dose-dependent manner. The extract was most effective in decreasing plasma glucose concentrations and was closed to those of glibenclamide and acarbose. In perfused rat pancreas, the extract stimulated insulin secretion in a biphasic pattern. However, the berberine at the same dose as the extract slightly increased insulin secretion by 1.33-fold over the basal control group. In addition, the extract inhibited the activities of both maltase and sucrase with the  $IC_{50}$  value of 3.89 and 11.22 mg/ml, respectively. Suggesting that the *C. fenestratum* ethanolic extract exerted anti-hyperglycemic activity by stimulating insulin secretion and  $\alpha$ -glucosidase inhibition.

### Formulation anti-diabetic activity

Evaluation of the anti-hyperglycemic effect of 'Ilogen-Excel' in streptozotocin-induced diabetic rats was carried out which contains *Coscinium fenestratum* as one of the 8 plants present in the drug. Oral administration for 60 days resulted in significantly lowered levels of blood glucose and significantly increased levels of plasma insulin, hepatic glycogen, and total hemoglobin. The drug also decreased the levels of glycosylated hemoglobin, plasma thiobarbituric acid reactive substances, hydroperoxides, ceruloplasmin and vitamin E in diabetic rats. Plasma reduced glutathione and vitamin C were significantly elevated. Administration of insulin normalized all the biochemical parameters studied in diabetic rats. A dose of 100 mg/kg was more

effective than 50 mg/kg and brought back all the parameters to near normal levels<sup>24</sup>.

### Anti-hypertensive activity

A 50% ethanol extract of *Coscinium fenestratum* stem material (AECF) has been found to possess hypotensive action in anaesthetised dogs, rats and guinea pigs in a dose-related pattern. The effect was more pronounced in spinal-transected animals. It non-specifically inhibited the pressor responses to epinephrine, norepinephrine, DMPP and depressor responses to acetylcholine and histamine. It failed to exhibit any hypotension when administered via a cannula into the lateral cerebral ventricle. When treated orally it did not exhibit grossly observable central nervous effects up to doses of 800 mg/kg<sup>25</sup>.

Hypotensive and vasorelaxant effect of *Coscinium fenestratum* water extract was tested on rats. The extract showed an endothelium-dependent and independent vasorelaxant activity in isolated aortic rings precontracted with phenylephrine and KCl. The capacity of L-NAME, an inhibitor of nitric oxide synthase, to reduce the vasorelaxant action of the extract indicates the involvement of nitric oxide<sup>17</sup>.

### Toxicity

In the acute toxicity test, an oral dose of 5000 mg/kg of water extract of *Coscinium fenestratum* did not produce mortality or significant changes in the general behavior of animals and the gross appearance of internal organs of rats. Further, in the sub-chronic toxicity test, an oral dose of 2500 mg/kg/day of the *Coscinium fenestratum* extract given to rats for 90 days did not cause any significant change of any of the parameters observed when compared with those of the control animals. Moreover, the extract did not produce any effect on the central nervous system when spontaneous motor activity in rats was assessed. However, some hematological and blood chemistry values were found to be statistically different, further studies, including chronic toxicity test, should be done to confirm the safety when it is used over a long period of time<sup>17</sup>.

### Antioxidant activity

Antioxidant effect of methanol extract of *Coscinium fenestratum* stem powder was examined using carbon tetrachloride-intoxicated rat liver as the experimental model. Rats were treated with the methanol extract for 90 days orally at the dose of 60-mg/kg body weight. Rats co-administered with the methanol extract retained an almost normal level of thiobarbituric acid reactive substances and diene conjugates, and also a profound diminution in glutathione content in the liver. The decreased activities of antioxidant enzymes, such as superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase in rats were retrieved towards normalcy in the extract co-administered animals. Thus confirming the effectiveness of *Coscinium fenestratum* in combating oxidative stress due to hepatic damage<sup>26</sup>.

Antioxidant status in STZ-nicotinamide induced type 2 diabetic rats at two dosage levels (250 mg/kg and 500 mg/kg) of aqueous extract of *Coscinium fenestratum* was carried out by Punitha *et al.*,<sup>28</sup>, diabetic rats showed a significant increase in the levels of enzymatic antioxidants such as glutathione peroxidase, glutathione synthetase, peroxidase, superoxide dismutase and catalase as compared to the untreated control. A significant increase was also observed in levels of the non-enzymatic antioxidants ceruloplasmin, ascorbic acid, and tocopherol. Thus suggesting that the aqueous stem extract prevents type 2 diabetes-induced oxidative stress.

*In vitro* scavenging activity of methanolic extract of *Coscinium fenestratum* in DPPH scavenging, nitric oxide scavenging, iron chelation activity, superoxide scavenging, ABTS radical scavenging and lipid peroxidation was carried out by Shirwaikar *et al.*,<sup>27</sup>. In all the methods, the extract showed its ability to scavenge free radicals

in a concentration-dependent manner. The results indicate that *C. fenestratum* has potent antioxidant activity.

*Coscinium fenestratum* had 54.60mg/g phenols, 20.00mg/g of flavonoids when tried with Folin Ciocalteu reagent method for phenols and Aluminium chloride colorimetric method for flavonoids. Methanol extract of *Coscinium fenestratum* stem exhibited free radical scavenging activity of 0.5mg- 64.00%; 1mg- 83.01% quite lesser when compared with *Nardostachys jatamansi* and *Drypetes roxburghii*<sup>42</sup>.

### CNS depressant activity

A study was conducted by Prashith Kekuda *et al.*,<sup>29</sup> to investigate the analgesic and CNS depressant property of methanol extracts of *Coscinium fenestratum* Colebr. in an animal model. In analgesic activity, the reaction time increased significantly for the extract and standard groups when compared to the pre-drug treatment. The locomotor activity count in the extract and standard drug-treated group was significantly reduced when compared to the control group. The analgesic and CNS depressant activity of extracts was found to be more than that of the standard drug.

### Antiproliferative activity

Methanol and methanol-water extracts of *Coscinium fenestratum* exhibited antiproliferative activities in a concentration-dependent manner against human HT-1080 fibrosarcoma cells among the seventy-seven Vietnamese medicinal plants. It also showed selective activity against lung carcinoma and/or lung metastatic cell lines, A549, LLC and B16-BL6. Characteristic morphological change and DNA fragmentation indicated the antiproliferative activity to be due to the induction of apoptosis<sup>30</sup>.

In a trial to determine the molecular mechanism of beneficial effects of *Coscinium fenestratum* 80% ethanolic extract, aqueous extract and dichloromethane fraction was investigated. 80% ethanolic extract, aqueous extract and dichloromethane fraction showed anti-proliferative activity as assessed by cell growth assay. Further, the pro-apoptotic proteins NAG-1 and ATF3 were increased and the cell cycle protein cyclin D1 was decreased. The results indicate that the extract from the plant has anti-proliferative activity through the activation of pro-apoptotic proteins and PPAR $\gamma$ , and have potential as a preventive regimen in the treatment of cancer<sup>31</sup>.

### Cytotoxicity

Thai edible plant *Coscinium fenestratum* was extracted with 95% ethanol and tested with cytotoxic effects using Hep2 cells. The results showed that *C. fenestratum*, exhibited high cytotoxic activity against the Hep2 cell lines at a minimum concentration of 0.05% in ethanol extract. In addition, it demonstrated the most potent cytotoxic extract based on its lowest IC<sub>50</sub> (5 mg/mL)<sup>32</sup>.

### Anti-nociceptive activity

In a study by Chitra *et al.*,<sup>33</sup> the effect of *Coscinium fenestratum* on inflammatory pain induced by formalin in mice was conducted. The extract and its polar and non-polar fractions were administered intraperitoneally 30 minutes before formalin injection. The extract induced a significant reduction in response as compared to control. Fraction I (water phase) in doses (mg/kg) of 40, 80 and 160 in an early phase and 40, 80, 160 in the late phase induced antinociception when compared to controls. It is concluded that the polar ingredients of the extracts are responsible for the analgesic and anti-inflammatory properties of *Coscinium fenestratum* (Gaertn.).

### Hepatoprotective activity

Hepatotoxic rats were treated with methanol extract of *Coscinium fenestratum* stem for 90 days. Serum marker enzymes like aspartate

aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase, lactate dehydrogenase, etc. and glucose-6-phosphate dehydrogenase in liver registered a significant elevation in carbon tetrachloride-treated rats, which were significantly recovered towards an almost normal level in animals co-administered with methanol extract of *Coscinium fenestratum* stem. Other biochemical changes induced by carbon tetrachloride too showed reliable signs of retrieving towards the normalcy. Histopathological analysis confirmed the biochemical investigations. This study unravels the anti-hepatotoxic activity of methanol extract of *Coscinium fenestratum* stem<sup>34</sup>.

### Anti-gonococcal activity

*Coscinium fenestratum* (Gaertn.) Colebr. the extract showed the most effective activity against *Neisseria gonorrhoeae* ATCC 49226 with MIC value of 47.39  $\mu$ g/ml. When compared with other 21 Thai folk medicine for relieving STD. Bioautographic assay revealed that berberine was the active compound of *Coscinium fenestratum* against *Neisseria gonorrhoeae*. The average MIC values of purified berberine against *Neisseria gonorrhoeae* ATCC 49226 and 11 clinical isolates were 13.51 and 17.66  $\mu$ g/ml, respectively while average MIC value of the crude extract of *Coscinium fenestratum* against all clinical isolates was about 56.39  $\mu$ g/ml. There was no acute toxicity detected at the dose of 5g of *Coscinium fenestratum* crude extract per kilogram. The above results provide theoretical support for the ethnopharmacological relevance of anti-gonococcal activity of *Coscinium fenestratum* and its active compound<sup>35</sup>.

### Antibacterial activity

The antibacterial activity of *Coscinium fenestratum* is mainly due to the presence of berberine<sup>21</sup>.

Aqueous extracts of *Coscinium fenestratum* and its major alkaloid, berberine, inhibited the in vitro growth of *Clostridium tetani*. Thus, the traditional use of *C. fenestratum* as a prophylactic against tetanus must be based on its antibacterial activity rather than any inhibitory effect on the production or activity of toxin<sup>36</sup>.

Ethanolic extract of *Coscinium fenestratum* stem had strong inhibitory effects against *Propionibacterium acnes* and *Staphylococcus epidermidis*. Based on a broth dilution method, the *Coscinium fenestratum* extract had the greatest antimicrobial effect. In the bioautography assay, the *Coscinium fenestratum* extract produced strong inhibition zones against *Propionibacterium acnes*. Phytochemical screening revealed the presence of alkaloids, which could be responsible for the activity. Taken together, the data indicate that *Coscinium fenestratum* had a strong inhibitory effect on *Propionibacterium acnes* and *Staphylococcus epidermidis*<sup>37</sup>.

According to Kumar *et al.*,<sup>38</sup> berberine alkaloidal fraction of *Coscinium fenestratum* stem showed potent antiacne activity. It showed maximum anti-acne activity and the Minimum Bactericidal Concentration against both *Propionibacterium acnes*, and *Staphylococcus epidermidis*. The mechanism of action of highly aromatic planar quaternary alkaloids such as berberine is attributed to their ability to intercalate with DNA. Thus berberine could be of interest for further development as an alternative treatment for acne.

### Antifungal activity

Berberine extracted from *Coscinium fenestratum* showed anti-phytopathogenic fungal activity against various fungi like *Phytophthora parasitica*, *Phytium* spp., *Colletotrichum gloeosporioides*, *Cercospora* spp., *Fusarium oxysporum*, and *Alternaria porri*<sup>39</sup>.

### Antiplasmodial activity

The methanol extract of *Coscinium fenestratum* had the strongest antiplasmodial activity with EC<sub>(50)</sub> value of 0.5- $\mu$ g/ml of the 42 extracts

from 14 medicinal plants used in Vietnamese traditional medicine to treat malaria. the activity guided fractionation led to identification of berberine as the major active constituent<sup>40</sup>.

### Negative study (Neurotoxicity)

Oral administration of *Coscinium fenestratum* alcoholic extract at dosages of 5, 10 and 20 mg/kg body weight for 14 days increased the rats body weight and decreased the neuron density in the cerebral cortex, hippocampus and striatum. The plant extract significantly increased stereotyped behavior in licking but did not cause anxiolytic activity, anti-depression, sensory motor co-ordination impairment and ataxia. Thus it is concluded that *Coscinium fenestratum* possesses neurotoxicity and can induce neurobehavioral changes in rats<sup>18</sup>.

### ACKNOWLEDGEMENT

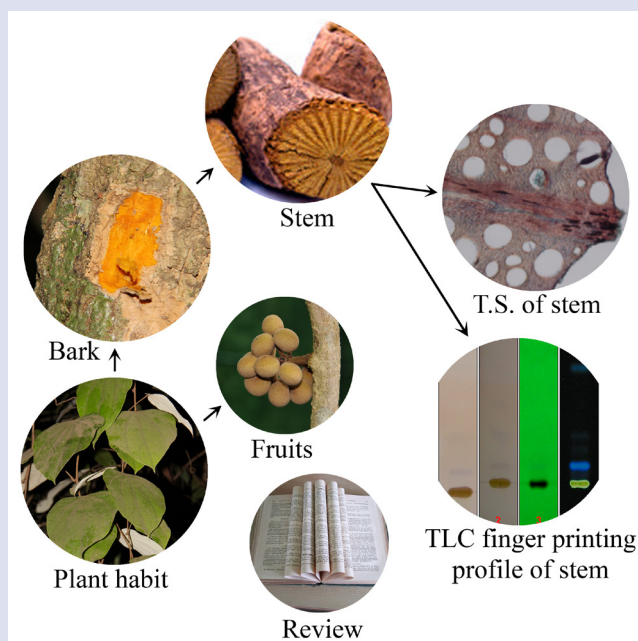
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## GRAPHICAL ABSTRACT



## ABOUT AUTHORS



**Dr. A. N. Sringeswara**, Curator of Mahatma Gandhi Botanical Garden, University of Agricultural Sciences, GKVK Campus, Bangalore is specialised in the field of taxonomy of Angiosperms and application of Remote Sensing and GIS in forestry and vegetation studies. He has obtained his Postgraduate and doctoral degrees from Kuvempu University, Shivamogga, Karnataka in Applied Botany. Published several papers in national and international journal on angiosperm taxonomy, remote sensing in vegetation studies, pharmacognostic studies important medicinal plants, besides contributed for books such as Flora of Karnataka – A checklist (Vol. 2) and for online database on Digital Flora of Karnataka housed at IISc., Bangalore.



**Dr. Haleshi C** is Ph.D in Floristic and Ecological studies of dry deciduous forests of Ballari and Bidar Districts. Receipt of Young Scientist Fellowship from DST in 2005. Working in the area of Taxonomy and Medicinal plant research for the past 15 years. Authored 8 books. Published papers in many national and international journals. Presently working as Assistant Professor at Davangere University, Karnataka.





**Dr. Vijay Danapur** is a medicinal plant scientist and has experience in the field of Medicinal plants for more than 15 years. Worked in the capacity of Research fellow, Scientist, Head of R&D Department and General Manager. pursued his doctoral studies in the area of Phytochemistry and Pharmacology. Awarded Doctorate from Gulbarga University, Gulbarga in the year 2002. Also worked as a Asst. Professor in the Academia. Published many papers in National and International journals, attended many conferences and presented papers and Authored 5 books on Medicinal plants. Delivered many invited lectures in Various institutions and Govt. Science Programs. Expertise in Dossier Preparation, Pharmacognosy and Ethnobotany. Was instrumental in setting up state of art labs for carrying out high end R & D for developing new herbal medicines for life style related health issues like CVD, Diabetes, Skin diseases etc. Has trained many Engineering, MSc and Ph.D. Students in devising suitable training and project material. Acted as BoS member of many educational institutes.

Recently published books entitled

1. Flora of Bidar District (2018).
2. Plants of Thimmalapur and Siddharabetta forests, Tumkur District (2018). (In Collaboration with Dept. Of Forests, Tumkur Division, Govt of Karnataka)
3. Kishkindha Kanda- A book on medicinal plants. (In Anegundi Utsava 2020 by District Administration Koppal, Govt of Karnataka).

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