Indian Journal of Drugs, 2016, 4(2), 57-62 **ISSN: 2348-1684**

Review Article

A REVIEW ON *COCCULUS PENDULUS* (J. R. FORST. & G. FORST.) DIELS: TRADITIONAL USES, PHYTOCHEMISTRY AND PHARMACOLOGICAL PROPERTIES

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Received: 04.03.2016
Accepted: 22.06.2016

Access this article online

Website:
www.drugresearch.in

Quick Response Code:

ABSTRACT

The ethno pharmacy of Rajasthan represents a good example of a strongly interconnected integration between medicinal remedies, health, diet and traditional healing practices characterized by cultural specific symbolism. One such under-explored plant is an evergreen tropical tree Cocculus pendulus (J. R. Forst. & G. Forst.) Diels. The genus Cocculus belongs to the family Menispermaceae, comprises about 35 species, distributed throughout the tropical and subtropical countries of the world. Cocculus pendulus and Cocculus hirsutus mainly found in Rajasthan. Cocculus pendulus reported to have good medicinal values in traditional system such as used in biliousness, menstrual disorder, jaundice, leprosy, helminthic, syphilis, fever, malaria, inflammation and used in rheumatic pains. Leaves, roots, bark, stems have been reported for medicinal activity. Therefore, the present review aims to provide updated comprehensive information on the phytochemistry and pharmacological properties of different parts of Cocculus pendulus (J. R. Forst. & G. Forst.) Diels (Menispermaceae).

KEY WORDS: *Cocculus pendulus*, traditional uses and pharmacological properties.

INTRODUCTION

The genus *Cocculus* belongs to the family Menispermaceae. It comprises about 35 species, mainly two species of *Cocculus* are found in Rajasthan, *Cocculus pendulus* and *Cocculus hirsutus*. The plant *Cocculus pendulus* (synonym: *Cocculus leaeba*) family Menispermaceae has important medicinal properties. It is known by variety of varnecular name such as pilwan in Rajasthani, Villumbi in hindi, parwatti in Gujrati, Ullarbillar in sindi, Dusaratige in telugu and Ssag-el-ghorab in Arabi. It is found in most parts of the world, it occurs in India, Iran, Iraq, Pakistan, Saudi Arabia; Africa (northern, In tropical Africa it is distributed throughout the Sahara desert and its semi-desert edges, from Cape Verde east to Somalia and north-eastern Kenya). In India, it is found in Andhra Pradesh, Gujarat, Haryana, Jammu & Kashmir, Karnataka, Madhya Pradesh, Maharashtra, Punjab, Tamil Nadu, and Uttar Pradesh and grows abundantly in Rajasthan[1] to an altitude up to 300-1900m. *Cocculus pendulus* is a woody scandent shrub, climbing on e.g. *Acacia* and *Balanites* spp[2]. Cocculus pendulus has perennating summer shedding and it is non-succulent[3]. Juice of ripe fruits yields a durable purple dye which is used as ink and for dyeing the cloths by the tribals[4].

Habitats

Cocculus pendulus grows in a variety of habitats and has a very wide distribution, and therefore it does not seem to be in danger of genetic erosion. It grows on sandy and gravelly soils, and sometimes colonizes dry fallow land[2].

Taxonomical classification

Kingdom	:	Plantae
Subphylum	:	Euphyllophytina
Infraphylum	:	Radiatopses [5]
Phylum	:	TracheophytaMagnoliophytaCronquist, Takhtajan& W. Zimmermann, 1966 [6]
Subclass	:	Magnolidae
Class	:	Magnoliopsida
Superorder	:	Ranunculanae
Order	:	RanunculalesJuss. Ex Bercht. &J.Presl, 1820
Family	:	Menispermaceae Juss.
Tribe	:	Menispermeae
Genus	:	Cocculus dc
Species	:	*Cocculus pendulus* (J. R. Forst. & G. Forst.) Diels

Synonyms [5]

Epibaterium pendulum J. R. Forst. & G. Forst

Epibaterium pendulum J. R. Forst. & G. Forst.

Cocculus leoeba (Delile) DC.

Morphology [3,5, 8]

Flower: flowers are small and unisexual, consist 6 sepals, ovate-elliptical, fleshy to membranous, 3 outer ones (1–1.5 mm long) slightly hairy and 3 inner ones larger finely hairy to glabrous; 6 petals which are ovate-obovate, (0.5–2 mm × 0.5–1 mm) notched apex; and peduncles are 1.5 cm long; flowering period is almost throughout the year. Petal or tepal colour is green. Male flowers: Sessile or with short pedicel, 6–9 stamens (up to 1.5 mm long) free Female flowers: With pedicel (up to 1 cm long), staminodes (61 mm long), ovary superior, consisting of 3(–6) free, ovoid and laterally compressed carpels (1 mm long), stigma (0.5 mm long) [7].

Fruit: fruits are dark red, stone ribbed on lateral faces, 1-seeded. Drupes are ovoid to obovoid or reniform and flattened reddish, black when dry; endocarp ribbed on lateral faces, not crested, not perforated in middle, each drupe are of 4–7 mm × 4–5 mm.

Root: Roots are dark brown in colour extranally.

Leaf: Arranged Alternate (one leaf per node), simple, margin is smooth; stipules absent; petiole 2–10 mm long; blade oblong-lanceolate, in lower leaves sometimes ovate, 1.5–5 cm × 0.5–2 cm, base cuneate, rounded or sometimes spear-shaped, apex obtuse, with micro, sometimes notched, leathery, glabrous, basal veins 3, conspicuous.

Stems: Branches long, slender, terete, puberulous, up to 15 cm in diameter at base, striped, bark grayish brown to dark brown or dark grey.

Traditional uses

The flowers are added to food. The fruits are edible and used to make an intoxicating drink from the fruits [9]. Diluted leaf-juice with sugar is a good tonic, the juice contains mucilage which when mixed with water forms a jelly which is applied externally in skin diseases[5]. This is taken as a cooling medicine for gonorrhea. Leaves are mostly used in wound healing, nose bleeding, and fertility medicine for women, and to regulate the menstrual cycle. Decoction of leaves is used in constipation. The root has a great reputation against biliousness and menstrual problems and as a diuretic. Roots are part of medicines against constipation as laxative, helminthic, malaria and used as cholagougue. Roots decoction is used together with *Tinosporabakis* (A.Rich.) Miers, to prepare a stimulating tonic.

Roots and leaves are found to be used in jaundice, yellow fever, leprosy, syphilis, inflammation [6], in rheumatic pains [7] and of an aphrodisiac. Stem bark and root bark decoctions are used against intestinal parasites and gonorrhea[3]. An infusion of the plant is used to assist in removing thorns from the feet. Wood infusion is taken as an emetic. In the drier parts the plant is browsed by all livestock, especially camels and goats, but where more browse is available, few animals eat it [10].

Phytochemistry

The plants contain pedulin, cocculine, cocculidine, sinocculine and cocsulinine, while the root contains pelosine, sangoline and an amaroid columbin and many other alkaloids. Biscoclaurine alk. mp.192 °, penduline; and bisbenzulisoquinoline alk. mp.272°, cocsuline (Experientia 1970,26,241); alk. Cocsulinine, active against the cells derived from humen epidermoid carcinoma of nasopharynx, in vitro (Indian J Chem, 1974, 12, 517); biscoclaurine alks. Cocsuline, cocsoline, cocsulinine, pendulinine, pendine and penduline (Tetrahedron, 1975, 31, 2575) isolated and structure assigned form leaves and stems[11]. A great variety of siddiquine, penduline, tetradine, isotrilobine, siddiquamine, kohatine, telobine, pateline, kurramine, isotrilobine and tricordatine, and many derivatives of these are also found in leaves and stems[3]. Hentriacontanol, β-sitosterol, and choline, penduline and cocsuline isolated from leaves (Curr Sci,1978, 47, 768). Talreja T., *et al.* (2012) [12] isolated the flavonoids from medicinal plants such as *Aegle marmelos, Cocculus pendulus, Moringa oleifera* and *Tinospora cordifolia*. Plant parts as well as calli of all selected plant species were analyzed for antimicrobial activity. TLC, spectral studies data were used for qualitative and quantitative estimation of flavonoids. Rabari H., *et al.* (2010) [13] conducted pharmacognostical and phytochemical investigations of *Cocculus pendulus* (J.R & G. Forst.) Diels leaf. It was reported to have good medicinal values in traditional system of medicines. The study deals with pharmacognostical examination of morphological and microscopical characters and phytochemical investigations of *Cocculus pendulus* leaves including determination of loss on drying, ash values and extractive values. The preliminary phytochemical screening of powdered drug was also carried out. The qualitative chemical examinations revealed the presence of various phytoconstituents like alkaloids, carbohydrates, phytosterols, proteins and mucilages in the leaf extracts. Odedra and Nathabhai K., [14] (2009) reported that *Cocculus pendulus* stems and leaves contains bisbonzyliso quinolone alkaloids (including pendulin and cocsulin) and quercitolis. Rahman A.,*et al.* (2009) [15] isolated the bisbenzylisoquinoline alkaloids from *Cocculus pendulus*. A new bisbenzylisoquinoline alkaloid, 1, 2-dihydrokurramine and four known bisbenzylisoquinoline alkaloids 2-5, along with a morphine alkaloid were isolated from *Cocculus pendulus*. These alkaloids showed inhibitory activities against acetyl- and butyrylcholinesterases. Wahab A., (2007) [16] studied on the *Iris germanica*, *Cocculus pendulus* and related medicinal plants and reported various new and known isolated phytochemical constituents. Rahman A., *et al.* (2004)[17] isolated the new cholinesterase inhibiting bisbenzylisoquinoline alkaloids from *Cocculus pendulus*. The structures of the new alkaloids, kurramine-2'-beta-N-oxide (1) and kurramine-2'-alpha-N-oxide (2), was elucidated with the help of spectroscopic techniques. Ali M., *et al.,* (1998) [18] conducted the phytochemical investigation of cocculus pendulus stem and reported the two new sterols, *Cocculus pendulus* sterols A and B, and an unknown aliphatic hydrocarbon had been isolated along with two reported alkaloids, pendulinin and Cucsulininehexacosane from the stem of Cocculus pendulus. The structures of the new phytoconstituents had been established respectively as 7,8-seco-stigmast-11,20(22)-diene-3 beta-ol. stigmast-5,20(22)-diene-9 alfa-ol and 25-methyl tritriacont-21- -11-one-1-ol on the basis of spactral data analyses and chemical means. Jahan and Kishwar, (1998) [19] studied the isolation and structure elucidation of the new alkaloids from the leaves of *C. pendulus*. In addition to these all alkaloids, 1, 2-dehydrotelobine was isolated (12), which was previously not reported from *C.*

pendulus, along with the known alkaloids kohatine (13) and cocsoline. Bhakuni D.S.,*et al*. (1975) [20] reported six biscoclaurine alkaloids isolated from *Cocculus pendulus* (Forsk) Diels, of these cocsulin, cocsolin and pendulinin had been assigned structures and stereochemistry by a series of chemical transformations and spectral studies.

Pharmacological activity

Anti-inflammatory activity

Rabari H., *et al.* (2010) [21] studied the anti-inflammatory activity of leaf extracts of *Cocculus pendulus* (J.R. & G. Forst.) Diels. The chloroform and ethyl acetate extracts of leaves of *Cocculus pendulus,* was used for anti-inflammatory activity at the doses of 200 and 400 mg/kg body weight. The lower dose of chloroform and ethyl acetate extracts (200 mg/kg body weight) did not show significant inhibition of inflammation but the higher dose of chloroform and ethyl acetate extracts (400 mg/kg body weight) shown significant inhibition of carrageenan induced paw edema. The exhibited anti-inflammatory activity was comparable with the standard drug aspirin. The chloroform extract showed 42.10 % and 69.90 % inhibition of paw edema at the dose of 200 and 400 mg/kg body weight respectively, while ethyl acetate extract shown 39.20 %, and 67.00 % inhibition of paw edema at the dose of 200 and 400 mg/kg of body weight respectively, after 6 hours of drug administration as compared to the control group. The standard drug (Aspirin) shows 72.31 % inhibition of paw edema at the dose of 100 mg/kg body weight. The inhibition was less than that of the standard drug (Aspirin).

Wound healing activity

Rabari H., *et al.* (2010) [21] studied the wound healing activity of leaf extracts of *Cocculus pendulus* (J.R. & G. Forst.) Diels. The chloroform and ethyl acetate extracts of leaves of *Cocculus pendulus,* was tested for wound healing activity at the doses of 200 and 400 mg/kg body weight. The wound healing activity was evaluated in rats inflicted with excision wound. In this model, the extract treated animals showed a more rapid decrease in wound size, decreased time to epithelialization and reduction in scar area compared with the control rats which received simple ointment base. The percentage of wound contraction was found to be significant in animals treated with chloroform extract and ethyl acetate extract when compared to controls. Povidone was taken as a standard drug. The chloroform extract at a dose of 400 mg/kg shown increase in percent wound contraction from 39.80 % to 94.08 % from day 4th to 16th. While ethyl acetate extract at a dose of 400 mg/kg showed increase in percent wound contraction from 37.10 % to 90.64 % from day 4th to16th. Percentage closure of wound area was significantly high in standard drug treated group followed by chloroform extract treated group and then ethyl acetate extract treated group.

Spermicidal activity

Verma V., and Lall S. B., (2000) [22] evaluated the effect of leaf and stem extract of *Cocculus pendulus* on epididymal sperm of swiss albino mice. Cauda epididymal sperm of swiss albino mice was treated at a dose rate of 0.4 mg/kg body weight of ethanol soluble extract of stem and leaf of *Cocculus pendulus.* It caused reduction in sperm motility, increase in the number of dead sperm at day 7 post treatment. However, the cytoarchitecture of the sperm was remained unaffected. As such it may be considered as a potent ingredient of post-coital spermicidal jellies and creams used in family planning scheme.

Anti-oxidant and adsorbents effect in *Cocculus pendulus* callus cultures

Bhardwaj L., *et al.* (1993) [23] studied the effect of anti-oxidants and adsorbents on tissue browning associated metabolism in *Cocculus pendulus* callus cultures. Explants and callus of *C. pendulus* produced intense brown substances in the medium which caused necrosis. Various anti-oxidants

(ascorbic acid, cysteine and dithiothreitol) and adsorbents (activated charcoal and polyvinyl pyrrolidone) were used in different concentrations to prevent browning of the tissues. These in MS medium affected differently the growth, colour and texture of the tissues. It was concluded that both peroxidase and phenolase was involved in the browning. Increased peroxidase activity and decreased phenolase activity was probably due to more peroxidative oxidation of phenols and unavailability of substrate for phenolase activity. This resulted in faster growth of tissues, which further reduced the phenolase activity. Gaur A.,*et al.* (1993) [24] reported the changes in phospholipids, fatty acids, oxidative enzymes, phenolics and protein levels during growth of normal and habituated tissues of *Cocculus pendulus.* Cultures of *C. pendulus* was maintained on hormone free and hormone supplemented (NAA 1.0 mg/l and kinetin 0.5 mg/l) Murashige and Skoog medium. During the growth period, hormone free cultures had higher phenolic content, polyphenol oxidase activity and less protein content, peroxidase and IAA oxidase activity. Activity of all the three oxidising enzymes and phenolic content will high at 16 days growth. Total lipid content was higher (2.7-folds at 15 days) in hormone free cultures. Phospholipid content of both cultures were not markedly dissimilar accepts PC and DGDG contents. Thus it is evidenced that both the tissues were similar metabolically.

Toxicity studies[21]

An acute toxicity study was conducted by Rabri H., Pandya S. *et al.* 2010 on methanol and aqueous extract by the stair-case method. The healthy Wistar rats of either sex were fed with plant extracts in increasing doses of 250, 500, 1000, 2000 and 4000 mg/kg body weight respectively. The toxicity level was assessed by mortality and behavior changes of the animals. The doses up to 4000 mg/kg body weight did not produce any signs of toxicity and mortality. The animals were physically active and were consuming food and water in a regular way. These findings support the observation of safety of the plant extracts.

CONCLUSION

It is seen from the literature that *Cocculus pendulus* is a very important plant for its large number of medicinal properties as well as medicinally important chemicals like Dehydrokohatine, 12-O-Methyl-dehydrokohatine, 5-Hydroxyapateline, 5-Hydroxytelobine, 12-O-Methylkohatine, Cocsupendine, bisbenzylisoquinolinedioxine alkaloids, including cocsuline, cocsoline, cocsulinin, siddiquine, penduline, tetradine etc. The plant has many traditional uses in intermittent fever, biliousness, menstrual disorder, jaundice, leprosy, helmintic, syphilis, cholagougue, malaria, nose bleeding, inflammation, pain and in rheumatic pains etc. Many pharmacological activities are like wound healing, anti-inflammatory, anti-oxidant and reduction in sperm motility, which is being studied till today. Thus, as folk medicine *Cocculus pendulus* has many uses as a multipurpose medicinal agent so further clinical trials should be performed to prove its efficacy. Because of their wide utilization, the plant deserves special research attention of these uses and compounds.

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