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Dillenia pentagyna Roxb.: A Review on Phytochemistry and Pharmacology

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ABSTRACT

Dillenia pentagyna often known as 'Karmal' is a member of Dilleniaceae. Different parts of the plant have been used by tribal communities to treat a broad spectrum of ailments. The plant reports the presence of some vital therapeutic compounds such as botulin, botulinic acid, morolic acid, lupeol, diploic acid, etc. Some of the major pharmaceutical properties of the plant are anti-cancerous, anti-fungal, anti-bacterial, and anti-diabetic. This plant has been recently classified as a critically endangered species in Madhya Pradesh state. Low germination rates are one of the major factors of being a critically endangered species. Despite being a potent curative plant species, it is yet to be fully explored. The objective of the present review to highlight the phytochemical investigations and pharmacology applications for several purposes like anti-diabetic, anti-cancerous, anti-microbial, anti-oxidant, etc of this plant species. In future studies, this knowledge can be applied to the safe and evidence-based use of traditional Indian medicinal plants in global Phyto pharmacotherapy and to the discovery of novel leads for the development of herbal formulations.

Keywords: *Dillenia Pentagyna*, Phytochemicals, Pharmacological Potential.

INTRODUCTION

Plants have been a keen subject of research for their medicinal properties since ancient times. The Asian countries especially China, India and Nepal possess an abundant diversity of plant species. These plant species have been studied to treat a large variety of ailments such as cholesterol, diabetes, peptic ulcer, bronchitis, cancer, etc. Recently several natural products of plant origin are being used in the drug formulation in the US that are in the late phase of clinical trials^[1].

Dilleniaceae is one such pharmaceutically important family with about 130 active compounds distributed amongst the varied species and in the varied parts of the plants. The *Dillenia* genus is represented by about 60 species of which *Dillenia indica* and *Dillenia pentagyna* are found in India. Of these two plants, *D. indica* has been widely studied for its pharmacogenetic values while *D. pentagyna* is less studied and needs further exploration.

D. pentagyna Roxb, is an important medicinal plant species commonly known as Karmal, Karkotta, Kallai, and Dog Teak. The fruit of the plant is one of the important constituents in the formulation of traditional medicine 'Malabar Nageswara', which has been reported to be effective against gastrointestinal tract (GIT), bleeding, and skin disorder^[2].

In addition to therapeutic purposes, it has some non-medicinal uses, such as green leaves being fed to the tussler silkworms and as green manure too. Also, dried leaves are used as a substitute for sandpaper. Wood and timber have been utilized for internal house support, planks, and rafters, as well as tool handles, boats, cupboards, and panelling. The bark of the plant produces fibre that is used to make cordage^[3].

Taxonomical Classification

According to the botanical scheme of Engler, the plant is classified as follows:

Kingdom :	Plantae
Division :	Phanerogamic
Sub-division :	Angiospermae
Class :	Dicotyledonae

Subclass : Polypetalous
 Order : Millennials
 Family : Dilleniaceae
 Genus : *Dillenia*
 Species : *pentagyna* Roxb. or *Hainanese* Merrill.

Occurrence And Distribution

D. pentagyna is distributed in rain forests, thickets as well as in the hills below 400 m. Hainan, Yunnan in Bhutan, India, Indonesia, Malaysia, Myanmar, Nepal, Thailand, Vietnam. In India, it is distributed in Himalayan terrain, also from Punjab to Assam, South India, Andamans, Gujarat, Mizoram and West Bengal. Predominantly found in various districts of Central India such as Ali Rajpur, Chinaware, Reiwa, Umari, Siddhi and Reiwa [4]. Its distribution in Madhya Pradesh state is depicted in Fig. 1.



Figure 1: Distribution of *D. pentagyna* in Madhya Pradesh state

Threat Status

D. pentagyna has been declared as critically endangered in central India. Some of the causative factors to this decline in population are limited availability of adequate amount of quality seeds/planting stocks, poor germination rate of the plant species and limitation in propagation [4].

Morphological Features

D. pentagyna is a moderate deciduous tree with an approximate height of 15-18m and a girth length ranging from 80-90cm (Fig 2(a)). The bark of the plant is an exfoliating, smooth, and greyish colour. The branches are ascending and drooping at the ends, when old they become scarred. The leaves are alternate, petiolate, globous, oblong to obovate with an approximate size of 20-60 x 10-25cm (Fig 2(b)). The leaf shows reticulate venation with about 20-50 secondary veins on either side. These secondary veins are parallel to each other. The margin of the leaf is slightly denticulate with the apex being obtuse - subacute. Flowers are bright yellow measuring 2-3cm in diameter, and pedicels (2-4cm) and bracts are deciduous (Fig 2(c)). They are found on leafless old branches. The sepals (5) are thick and ovate whereas the petals (5) are lanceolate and possess fragrance. The flower possesses multiple free stamens and is postcapillary. Fruit is yellow, sub-globose 1-2 seeded, and is enclosed by fleshy sepals (Fig 2(d)). The seeds are black, ovoid, and glaucous (Fig 2(e)) [4,5].



Figure 2: *Dillenia pentagyna*: a) Tree b) Leaf c) Flower d) Fruits e) Seeds

Traditional Uses

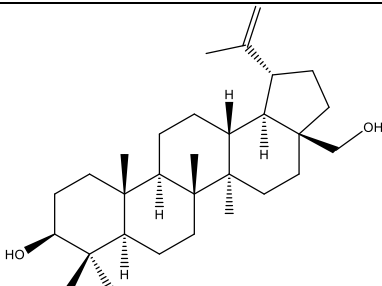
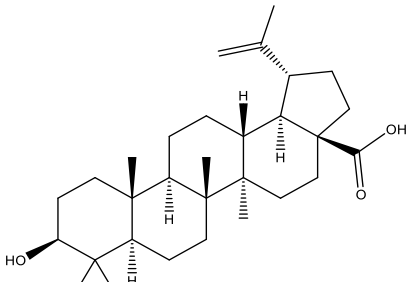
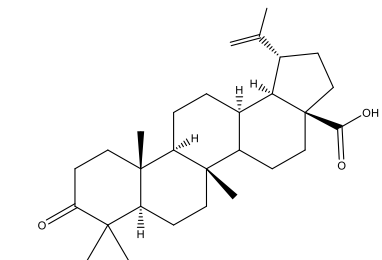
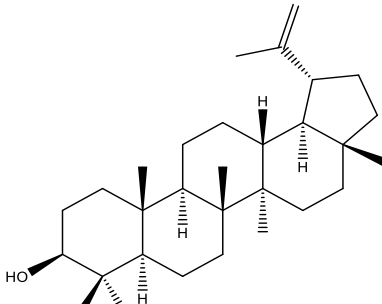
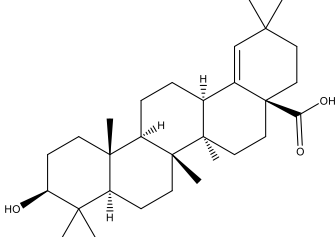
Various parts of this plant species have been reported to be used by tribals and many folklore communities. The bark of the plant is used for treating diabetes, diarrhoea, cuts, and burns [6]. The Koch-Rajbanshi people of the western Assam use the seed and the bark of the plant against cancer. The tonic from the bark is considered miraculous for postpartum care. Chest pain and wounds are treated by the leaves. Both leaves and bark are utilized for treating cancer [7]. The people of the Konkan region of Maharashtra use the bark of the plant that is levigated in water, followed by making a paste out of it. This paste is applied for 3-5 days to heal deep wounds [8]. The tribals of the Deogarh district use the fruit decoction of the plant along with *Zingiber montane*, thrice a day for about three days before food to treat blood dysentery [9]. For stimulating hair growth and preventing baldness the juice of the bark is applied to the head once a week. The paste of the leaf is applied twice a day to cure piles. The ripe fruits are consumed regularly to treat diabetes. One teaspoon of the bark powder with warm water thrice a day is used for diabetic patients for a period of three months. The tribal communities also worship the plant as a portrayal of Lord Laxmi on the occasion of Deepawali [10].

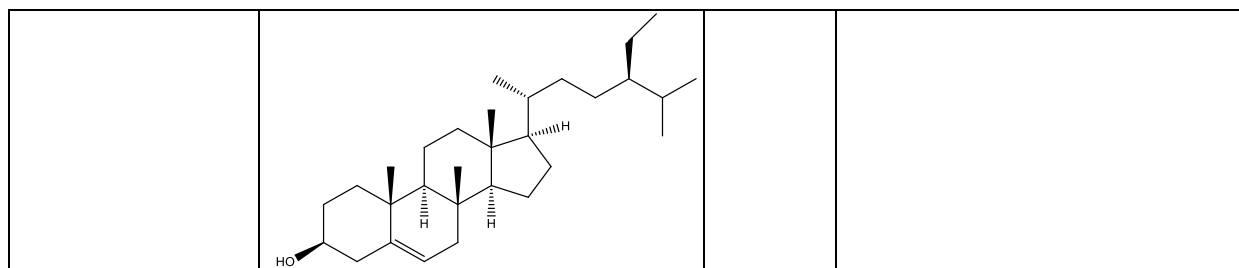
Phytochemicals And Their Analysis

Phytochemicals

The curative properties of the plant are attributed to its wide range of phytochemical constituents. A study on the plant reveals the presence of two major classes of compounds i.e., triterpenes and flavonoids. Some of the complex flavonoids reported are Rhamnetin 3-O-glucoside, Dill hydro quercetin 5-glucoside, Naringenin 7-galactosyl (1-4) glucoside and Naringenin-4'-O-[4-O-(β-D-glucopyranosyl)]-β-D-xylopyranoside [11,12]. Lupeol, botulin, botulinic acid, morolic acid, and botulinic acid are some of the triterpenes present in plant parts. Other than the flavonoids and triterpenes, some miscellaneous constituents are also reported such as β-sitosterol which is a Phyto steroid, and diploic acid which is a diterpene [13].

Table 1: Some widely distributed phytochemical constituents of *D. pentagyna*

Phytochemical compounds	Structures	Plant parts	Properties
Botulin			A highly effective triterpene, which has long been exploited for its pharmaceutical properties in folklore medicines. It possesses anti-inflammatory, anti-ulcer, anti-diabetic, anti-bacterial and anti-microbial, anti-malarial, anti-viral, anti-hyperlipidaemic, anti-cancer, anti-HIV, anti-leukaemia, antileishmanial, powerful prophylactic, choleric and immunomodulator activities [14,15].
Botulinic acid		Stem, Bark	Triterpene is widely distributed throughout the plant kingdom. It is effective against varied types of cancer such as Melanoma, Lung carcinoma, breast cancer, Medulloblastoma, Hepatocellular carcinoma, Rhabdomyosarcoma, Cervix carcinoma, etc [14]. Along with cancer, it has a wide range of medicinal activities such as inhibition of human immunodeficiency virus (HIV), anti-bacteria, anti-malarial, anti-inflammatory, anti-anthelmintic, and anti-HSV-1 [16].
Botulinic acid		Stem Bark	Prostatic cancer cell line PC3, breast cancer cell line MCF-7 and human gastric cancer cell line MGC-803 are some of the major cancer cells against which botulinic acid has reported to possess substantial antitumor activity [17,18]. The botulinic acid initiating the process of apoptosis through mitochondrial signalling involving the expression of caspases 9 and 3, protein p53 and Bax is the cause of the anti-cancerous activity of the compound [18].
Lupeol		Leaf	A triterpene that possesses an array of biological potency such as anti-malarial, anti-cancerous, anti-arthritic, anti-inflammatory, and analgesic [19]. Its anti-cancerous properties are due to its ability to reduce the transcript level of tumour necrosis factor- α (TNF- α) [19]. It has also been used to prove to be effective against cardiovascular diseases, kidney diseases, and diabetes [21].
Morolic acid		Stem Bark	Morolic acid is a plant-derived triterpenoid with cytotoxic, anti-HIV, anti-HSV, anti-inflammatory, and anti-diabetic activities [22].
β -Sitosterol		Stem	Possess numerous vital properties such as anti-inflammatory, induces apoptosis, angiogenic, hypocholesterolaemia, genotoxicity effect, and immunomodulatory activity. Due to its similarity in structure to cholesterol, it inhibits the absorption of cholesterol and therefore is an effective anti-hyperlipidaemic agent too [23,24].



Chromatographic Analysis

A validated HPTLC method has been devised for determination of botulinic acid from the parts of *D. pentagyna*. The highest concentration of botulinic acid was reported in the bark [25]. Another study was conducted to establish a simple, precise, and accurate method for simultaneous quantification of botulinic acid, β -sitosterol, and lupeol in the plant's fruit, leaves, stem, and bark. The highest concentrations of botulinic acid and lupeol were found in the stem bark, while the highest concentrations of β -sitosterol were found in the plant's leaf [26]. Botulin has also been quantified in fruit leaf, root bark, and stem bark of *D. pentagyna* using HPTLC. The maximum botulin was reported in stem bark whereas the minimum botulin was quantified from the leaf of the plant sample [27].

Pharmacological Studies

Anti-diabetic

According to a study, for a concentration of 2 μ g/ml, the leaf extract showed the greatest inhibition 74.6 percent but no such activity was reported with fruit extracts [28]. In induced diabetic rats, the hydroalcoholic extract of the fruit at 400 mg/kg showed significant antihyperglycemic effects compared to a low dose (200 mg/kg b.w.) in various biochemical parameters such as liver marker enzymes, liver tissue regeneration, and beneficial metabolic effects through augmenting ALP activity [29].

Anti-oxidant and Anti-cancerous

D. pentagyna has been evaluated scientifically both *in vivo* and *in vitro* for anti-cancerous properties. At doses of 50 and 100 mg/kg/day, the ethanolic extract of *D. pentagyna* demonstrated the most potent anticancerous properties, with ILS of 55% and 48 %, respectively. Lipid peroxidation in the tissues of the tumour mice has been reported to be mitigated by the extract of *D. pentagyna* which indicated a possibility of its protective function against the tissue damage caused by the oxidative stress [30]. When compared to butylated hydroxy toluene (BHT), aqueous methanol (20%) and acetone extracts of the fruit assayed employing FRAP and DPPH were found to have antioxidant activity with capacities of 13.19 and 5.03 mg ascorbic acid equivalent/g of dry fruit and IC₅₀s of 0.51 and 2.21 mg/dry fruit, respectively as compared to BHT [30]. Other studies suggest that the stem and bark extracts of *D. pentagyna* (Dilleniaceae family) are cytotoxic to DL, MCF-7, and HeLa cell lines (IC₅₀ values of 25.8, 41.6, and 76.8 g/mL, respectively). In *D. pentagyna*-treated animals, the amount of glutathione (GSH) was also likewise found to be reduced [32,33]. The treatment also lowered the amount of sialic acid content which is a tumour marker in the liver, kidney, spleen, and Dalton's lymphoma cells, as well as led to the reduction in the size of the ascites tumour [5]. In comparison to ascorbic acid (IC₅₀ of 394.56 μ l, the aqueous stem bark extract (90%) reported anti-oxidant activity of 416.90 μ l, when measured by DPPH assay [34]. At 0.5-50 mg/mL, the chloroform and butanol fractions of the fruit's 10% aqueous methanol extract scavenged the DPPH radical with percentage inhibition ranging from 6 to 61 percent and 12-65 percent, respectively. In comparison to ascorbic acid (0.5-50 mg/mL; 35-90 percent), the 10% aqueous methanol extract of the leaf scavenged DPPH radical with a proportion of 7-67%. At 100 mg/mL, the extracts and fractions significantly reduced the superoxide radical, with

percentage inhibition ranging from 5 to 73 percent, similar to BHA (10-27 percent) [35].

Anti-microbial

A study on the anti-microbial activity revealed that at 3 mg/disc with zones ranging from 10-23 mm, petroleum ether and ethyl acetate (Ea.) extracts of the sun-dried stem bark of *D. pentagyna*, inhibits the growth of *B. cereus*, *B. subtilis*, *B. polymyxin*, *B. megaterium*, *Shigella soni*, *S. auras*, *S. dysenteries* type-1, *S. basic*, *S. Flexner* type-1, *S. boydii*, *P. aeruginosa*, *Vibrio mimicus*, and *V. cholera* as compared to ampicillin (10 μ g/disc; 10-35 mm). In comparison to griseofulvin (25 μ g/disc; 12-18 mm), the ethanol extract (3 mg/disc) inhibited the fungi, *A. fumigates*, *A. Niger*, *C. albicans*, *C. arriza*, *C. krusei*, *R. Oryza*, *S. cerevisiae*, and *Trichoderma* sp. with zones ranging from 10 to 17 mm [36]. When compared to streptomycin (10 mg/disc; 15-20 mm), the methanol extract of the stem bark inhibited the growth of *B. subtilis*, *B. cereus*, *S. aureus*, *E. coli*, *P. aeruginosa*, and *Salmonella* sp. with zones ranging from 7 to 10 mm at 100 mg/disc. When compared to albendazole (10 mg/disc; 10-20 mm), the extract was also efficacious against fungus *T. varied*, *Penicillium* sp., and *A. Niger* with zones ranging from 6 to 10 mm at 1 mg/disc [37]. Also, when checked against the growth of municipal sewage microbes, it has been found that in comparison to ciprofloxacin (0.001-0.005 mg/disc; 8-26 mm), the chloroform, ethyl acetate, and butanol fractions of the defatted aqueous methanol extract of the fruit reduced the development of municipal sewage microbes with zones of 7-19 mm over a concentration range of 2-3 mg/disc [38].

Others

The astounding plant has also been reported to play a vital role in treating various other ailments. The fruit extract of the plant possesses the ability to inhibit the angiotensin-converting enzyme (ACE) [39]. According to a finding, the bioactive extract/fractions of the bark of *D. pentagyna* appeared to help in reducing Dox-induced cardiotoxicity. Polyphenolic antioxidant substances such as gallic acid, syringic acid, and synapic acid are considered to be responsible for the potent - cardioprotective impact, according to LC-QTOF-ESI-MS study of *D. pentagyna* and phenolic-rich fraction (F1) [40].

CONCLUSION

The detailed pharmacogenetic review of *D. pentagyna* reflects the therapeutical importance of the plant. It is effective against a broad spectrum of ailments. The extracts of the plant have been established to have extensive biological effects against some chronic diseases like cancer, diabetes etc. Hence, the plant species awaits more intensive research to manifest its properties for the discovery of drugs against these serious diseases. Moreover, looking to its myriad uses, the efforts should be made for its *in-situ* as well as *ex-situ* conservation.

Conflict of Interest

None declared.

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None declared.

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