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PHARMACOLOGICAL AND PHYTOCHEMICAL STUDIES OF DILLENIA INDICA: A REVIEW

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ABSTRACT

Dillenia indica, an evergreen tree commonly known as elephant apple. *Dillenia indica* is markedly disseminated in the seasonal tropics of many Asian countries. In India this evergreen deciduous tree fills in the damp wood of sub-Himalayan district to Assam. It is a significant therapeutic plant and has been commonly utilized in Indian conventional and Ayurvedic medication for relieving plenty of diseases. Different parts of *Dillenia indica* have been predominantly examined for the plenty of biological activities which includes anti-cancer, anti-diabetic, anti-hyperlipidemic, anti-leukemic, antioxidant, anti-mutagenic, antimicrobial, and anti-diarrheal. Different extract of *Dillenia indica* have been accounted for essentially to contain a wide range of flavonoids, triterpenoids (lupine-type), phytosteroids, phenolics, alcohols, ketones and anthraquinone. A few Phytochemical examination uncovered significant presence of different sorts of active constituents which includes β -sito sterol, stigmasterol, betulin, betulinic acid, myricetin, quercetin, dillenetin and rhamnيتين. Among these the significant chemical constituents are betulin and betulinic acid that show a wide range of pharmacological activities. The purpose of this review article is to provide a brief introduction, phytochemistry, medicinal and traditional uses of *Dillenia indica*. The review article likewise accentuation on reported pharmacological activities of *Dillenia indica*.

Keywords “*Dillenia indica*”, “phytochemistry”, “traditional uses”, “pharmacological activities”

1. INTRODUCTION

The utilization of medicinal plant is consistently valuable to the humankind from ancient times. Plants are viewed as the foundation of life on earth and taken as a crucial assists for people as well as for animals. In industrialized and developing countries, affirmations of the safety, quality and efficacy of restorative plants and natural items that are used by individuals has become the primary concern of interest. The therapeutic employments of a plant rely on the active principle present in it. There are numerous active compounds for example Glycosides, Vitamins, Flavonoids, Alkaloids, Tannins and coumarin compounds, and these are the compounds upon which the biological activity of a plant relies. From ancient times plants were the solitary assets accessible for the treatment of sickness in individuals [1] and numerous restorative plants are exceptional, endemic and discovered just in forest areas. There is neither biological information nor agreeable data that incited their rarity in the characteristic environmental factors [2]. Apart from this many species of plants which have been used by ancestral communities of various forest regions of India nonetheless; their restorative and furthermore pharmacological activity is yet dark as these plants are not really accessible. Among these there are few plants

belonging to family *Dilleniaceae* which have not acquired a lot of prominence yet have fascinating restorative values. The genus *Dillenia* has 60 species nonetheless only few of them reported to have important Phytochemical and show medicinal values. *Dillenia indica* and *Dillenia pentagyna* are the two species of genus *Dillenia* which are available in India and *Dillenia indica* is the species which has been extensively studies and commonly found in different parts of India [3]. *Dillenia indica* is commonly known as Elephant apple and apart from that this plant has several other names as shown in

Table 1.

Table 1: Common names of *Dillenia indica*

Language	Common Name
English	Elephant apple
Hindi	Chalta
Sanskrit	Avartaki, Bhavya
Assamese	Outenga
Bengali	Chalta
Gujarat	Karambel

2. Plant Description

Dillenia indica an evergreen enormous bush or small to medium sized plants, are found in the damp wood of sub-Himalayan district to Assam. *Dillenia indica* contain various restorative properties and separated from this the plant has been honored with consumable constituents as well. The main yield of the plant is its fruits yet because of absence of information and not knowing its restorative value the vast majority of the fruit and other parts of *Dillenia indica* are

wasted. Leaf, bark and fruits of *Dillenia indica* are used in the indigenous system of medicines. *Dillenia indica* has various therapeutic properties like relieving pain and controlling the body heat. It is likewise utilized as cooling refreshment in the treatment of fever [4]. Customarily they are utilized as diuretics and carminatives. It

likewise helps in alleviating fatulence [5]. Fruit juice of *Dillenia indica* is furthermore used as cardio tonic. Barks and leaves of the plants are utilized as purgative and astringent. Because of its various biological activities for example anti-diabetic, anticancer the plant is securing importance as a significant restorative plant [6, 7].



Figure 1: *Dillenia indica* Linn. Tree and Fruits

3. Chemical Constituents

Extraction of *Dillenia indica* shows the presence of significant classes of chemical constituents which includes flavonoids and triterpenoids (lupene type). The extraction also shows numerous other phytoconstituent for example: phytosteroids, diterpene, ionone, phenolics, anthraquinone, alcohols and ketones. Presence of these phytoconstituent

in *Dillenia indica* shows numerous health benefits.

3.1 Phytochemical constituents isolated from methanolic extract of *Dillenia indica*

Methanolic extract of *Dillenia indica* showed presence of phytoconstituent named as lupeol, betunaldehyde, betulinic acid and stigmasterol [6]. Methanolic

extract of the fruits of *Dillenia indica* showed the presence of about 34% phenolics and polysaccharides like arabinogalactan [8].

Fixed oils, coloring matter, Glycosides, free Amino Acid, steroids, Sugars, Protein free Amino Acid and Tannins are mainly present in the seeds of *Dillenia indica* [9]. Apart from this *Dillenia indica* linn also shows the presence of ash, eater soluble ash, acid insoluble ash, swelling index, foaming index, organoleptic value. Upon Phytochemical screening of the plant sample shows presence of numerous other phytoconstituent which includes alkaloids, terpenoids, glycosides, tannins etc. [10]. Apart from the fruits and seeds, Bark and wood of *Dillenia indica* also contain myricetinhydroxy-lactone, dihydroisorhamneti [11].

3.2 Phytochemical constituents isolated from ethanolic extract of *Dillenia indica*

Kaempferol glycosides and quercetin derivatives as well as triterpenoids are the

flavonoids obtained from the ethanolic extract of stem bark of *Dillenia indica* [10, 12].

3.3 Phytochemical constituents isolated from alcoholic extract of *Dillenia indica*

Numerous pharmacological activities like anti-cancer, anti-malarial and anti-inflammatory activities are shown by the alcoholic extract of *Dillenia indica* and these activities are shown due to the presence of significant amount of polyphenol in the alcoholic extract [13]. Alcoholic extract of *Dillenia indica* also shows the presence of carbohydrates, starch, proteins containing sulphur, saponin glycosides, alkaloids, tannins, flavonoids, cardiac glycosides and phenol compound [14, 15]. Literature review shows the presence of many primary and secondary metabolites in different parts of plant. Stem bark of *Dillenia indica* contain 10% tannins, dillenetin, betulinaldehyde, dipoloic acid, betulinic acid, quercetin, myricetin derivatives [3].

Table 2: isolated chemical constituents from *Dillenia indica* [6, 3, 12, 14]

S. No.	Isolated Chemical Constituents	Chemical Type	Part Of Plant Used
1	Kaempferol	Flavonol	Pericarp, Twig, Stem
2	Myricetin	Flavonol	Stem bark
3	Quercetin	Flavonol	Leaf
4	Dillenetin	Flavanol	Pericarp
5	Lupeol	Lupene	Stem bark, Leaf, Fruit
6	Betulin	lupene	Stem bark, leaf, Fruit
7	Betulinaldehyde	Lupene	Stem
8	Betulinic acid	Lupene	Stem bark
9	Stigmasterol	Phytosteroids	Stem, Leaf
10	Gallic acid	Phenolic	Twig

4. Medicinal and Traditional Uses

Traditionally all parts of *Dillenia indica* are exploited for therapeutic purposes.

- For the prevention of diarrhea and cancer a mixed juice of stem bark and leaves of *Dillenia indica* is used [16, 17].
- Stem bark and leaves of *Dillenia indica* are used as a laxative and astringent [18].
- Stem bark of *Dillenia indica* is also used for the production of charcoal
- For the treatment of diseases like Diabetes, wounds, diarrhea, cancer rheumatism, urinary problem, skin diseases, aches, fever, and cough, the fresh and dried material of various parts of *Dillenia indica* are used as juice, decoction, poultice and mucilage.
- Leaf, fruits and stem bark of *Dillenia indica* is also used to treat skin problems which include leukoderma, eczema, skin itches and skin rash [19, 20]
- Leaves as well as decoction and juice of the fruit and stem bark of *Dillenia indica* are used in daily practice to cure cancerous growth mainly breast and gastric cancer [21]
- Oral administration of the fruit juice of *Dillenia indica* is used to treat

fever and cough associated symptoms [22, 23]

- For the treatment of diabetes a mixed juice of the fruit and calyx of *Dillenia indica* is used in daily practices [24, 25]
- Roots of *Dillenia indica* are generally used for the purpose of abortion [26]
- Bark of the stem and roots of *Dillenia indica* are extensively used as a food poisoning neutralizer [27, 28].

5. Reported Pharmacological Activities

5.1 Anti-diabetic Activity

Data from various studies and folk tales proof expressed that *Dillenia indica* may be helpful in the treatment of diabetic mellitus. A study on Wistar rat's shows that at a dose of 250 and 500mg/kg body weight in streptozotocin induced diabetic model showed significant anti-diabetic activity. An increase in the level of serum insulin was reported after administration of methanolic extract of *Dillenia indica* [29, 30]. The methanolic extract treatment also showed an increase body weight of diabetic rats when compared with diabetic control group [29]. In another study alcoholic extract of *Dillenia indica* was exposed to column chromatography for the isolation of another compound named as chromane. In this examination diabetes was induced in experimental rats by the administration of

streptozotocin at a dose of 50mg/kg body weight. Results from the study shows that both *Dillenia indica* and chromane showed significant decrease in elevated fasting blood glucose, lipid levels as well as decrease oxidative stress. The examination concluded that *Dillenia indica* and its isolated chemical constituents proved to have a strong anti-diabetic effect [31].

5.2 Anti-oxidant Activity

There are numerous signaling molecules that maintain the cellular homeostasis among which Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) plays an important role in maintaining the cellular homeostasis. Production of excess amount of ROS and RNS is either act as a cause or act as a mediator in the pathogenesis and pathophysiology of several illnesses. Excess production of ROS and RNS leads to oxidative damage of numerous biological molecules which includes DNA, lipid, and many proteins, as a result of which there is restriction in the signaling pathways which end up by promoting cellular damage and death [32]. During the clinically silent prodromal period of Alzheimer's disease, expanded oxygen species (OS) has been over and over exhibited to represent pathological changes. Increased amount of lipid content and rapid metabolic rate incline the brain to the impending impact of oxygen species.

Presence of oxygen species in the hippocampus and cortex is detailed as a fundamental component of Alzheimer's disease [33]. Being a restorative plant *Dillenia indica* is known for its cell reinforcement activity. Fruits of *Dillenia indica* proved to show maximum antioxidant activity. Different extract of the fruit of *Dillenia indica* were prepared and the total phenolic content was determined in these extracts, apart from this numerous in vitro models are also used to determine the antioxidant activity. Results from the studies shows that the methanolic extract of *Dillenia indica* contain highest phenolic content (34%) and the lowest amount of was present in water extract. From this it was determined that the antioxidant activity is in accordance with the total phenolic present in *Dillenia indica* [34].

5.3 Anti-Inflammatory Activity

Anti-inflammatory activity was observed in the methanolic extract of *Dillenia indica* leaves. Carrageenan induced paw edema and acetic acid induced capillary permeability was used to observe the anti-inflammatory activity. At a dose of 200 mg/kg and 400 mg/kg the methanolic extract showed significant ($P<0.01$) anti-inflammatory activity in the paw edema test and acetic acid induced capillary permeability. Methanolic extract of *Dillenia indica* at a dose of 100mg/kg showed significant ($P<0.05$) activity in

acetic acid induced permeability. This research support the folklore uses of *Dillenia indica* in disease related to inflammatory conditions [35].

5.4 Anti-diarrhoeal Activity

Anti-diarrhoeal activity was analyzed in the ethanolic extract of the leaf and fruit of *Dillenia indica*. The activity was analyzed using two methods that is castor oil method and charcoal plug method. Administration of castor oil showed percentage of inhibition of wet feces and significantly decreases the total number of feces produced in 2nd hour (for leaf extract 6 for 200mg/kg dose and 4 at dose of 400mg/kg and for the fruit extract it is 5.33 for 200mg/kg dose and 4 at 400mg/kg dose). And 3rd hour (for leaf extract, 3 for 200mg/kg dose and 2 at a dose of 400mg/kg and for the fruit it is 4 for 200mg/kg dose and 3 at 400mg/kg dose). In charcoal plug method activity was measured with the help of distance travelled by the charcoal plug. The average distance travelled by leaf was 28.67cm and by fruit was 22.67cm which is lower when compared with the control that is 41cm and the standard loperamide showed the averaged travelled length of 16cm [36].

5.5 Anti-cancer activity

5.5.1 from Stem

Ethanolic and petroleum ether extracts of *Dillenia indica* stem barks demonstrated cytotoxic impact in saline solution Shrimp

lethality bioassay performed by noticing mortality rate of brackish water shrimp nauplii (*Artemia salina*). The LC50 values observed by probit analysis were 574.926 and 334.284µg/ml for ethanolic and petroleum ether extracts [37].

5.5.2 from Bark

Methanolic extract of *Dillenia indica* bark and its n-hexane and ethyl acetate fractions have strong cytotoxic principles with LC50 value 17.68µg/ml, 17.68µg/ml, 15.80µg/ml and LC90 value 486.61, 287.66, 148.82µg/ml, separately, compared with positive control vincristine sulphate (LC50 0.631mg/ml and LC90 value 13.51mg/ml) [38].

5.5.3 from Fruits

Methanolic extract of the fruit of *Dillenia indica* demonstrated significant anti-leukemic activity in human leukemic cell lines U937, HL60, and K562. Fractionation of the methanolic extract based on extremity indicated that ethyl acetic acid fraction had highest anti-leukemic activity. A significant compound, betulinic acid was confirmed from the ethyl acetic acid fraction by silica gel column chromatography, it was recognized and characterized. With the help of betulinic acid, the anti-leukemic activity of methanolic and ethyl acetic acid fraction could explained [39]. By inducing apoptosis mechanism it actuates cell death in U937, HL60 and K562 cell lines. Anti-

cancer drug works by destroying the cancer cell by stopping growth or multiplication sooner or later in their life cycles. The cytotoxicity of plant that down-regulate the anti-apoptotic genes for example: COX-2, Inos, TNF α , and Bcl-2 and up regulation of proapoptotic genes such as p53, p21, Bax, caspase and cytochromeC [40].

5.6 Anti-microbial Activity

Methanolic extract of the leaves of *Dillenia indica* were analyzed for the evaluation of anti-microbial and cytotoxic activities. Carbon tetrachloride, n-hexane and chloroform fractions of the methanolic extract of *Dillenia indica* and aqueous extract were screening for anti-microbial activity with the help of disc diffusion method. Among these fractions of the methanolic extract of *Dillenia indica* n-hexane, chloroform and carbon tetrachloride fractions showed moderate anti-bacterial and antifungal activity when compared with the standard antibiotics, kenamycin and the aqueous fraction was found to be insensitive to microbial growth. The average zone of inhibition was ranged from 6-8mm at a concentration of 400 μ g/ml disc. When the results were compared with vincristine sulfate (with LC50 of 0.52 μ g/ml), the n-hexane and chloroform fractions of *Dillenia indica* showed a significant cytotoxic activity (LC50 of 1.94 μ g/ml and 2.13 μ g/ml). The study confirms the moderate antimicrobial

and potent cytotoxic activities of methanolic extract of *Dillenia indica* leaves [41]. Data from another study shows that the methanolic extract including other organic fractions of the bark of *Dillenia indica* were tested against Gram (+) and Gram (-) bacteria and also against three pathogenic fungi. Among these fractions n-hexane fraction showed highest activity against *Shigella dysenteriae* and the zone of inhibition was found to be 15.51 \pm 0.75mm. The methanolic fraction of *Dillenia indica* showed highest activities against *Candida albicans* and the zone of inhibition was found to be 13.13 \pm 1.75mm. Lowest LC50 value 19.02 \pm 1.16mm of n-hexane fraction of *Dillenia indica* indicated the highest toxicity when compared with other fractions [42].

6. CONCLUSION

Natural drugs are the most widely utilized therapeutics around the world. To advance their legitimate use and to set up their potential as a source for new medications, it is important to contemplate restorative plants having folk tales notoriety in a superior and increase way. The broad writing overview and ongoing reports on investigation its activity uncovered that *Dillenia indica* is profoundly viewed as a potential and forthcoming candidate in the natural medicines. Many phytoconstituent like flavonoids, steroids, triterpenoids, phenolics, saponin, extracted from different

parts of this plant and are responsible for prevalent pharmacological activities performed on animal models. Major constituents like betulin and betulinic acid are present in almost all parts of *Dillenia indica* and responsible for the treatment of various human infections and diseases. Due to its good nutritional value the fruits of *Dillenia indica* are taken as energy drink. The review in general portrays the significance of *Dillenia indica* as a restorative plant by its different Phytochemical compounds and pharmacological activities. To explore the unknown effects, clinical application of *Dillenia indica* further evaluation needs to be carried out for the welfare of the mankind.

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8. Conflicts of Interest

The author declares that there is no conflict of interest.

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