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Dillenia indica: anethno-medicinal plant with high values inpharmaceutical industry

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ABSTRACT

Medicinal plants have been usedfor the welfare human being from immemorial time. During past, human beings are totally relyupon plants for the medicinesand also in the modern era many of the modern medicines are produced indirectly from plants. According to WHO, 80 per cent of the world's population depend on herbal medicine; especially the millions of people of developing countries.Dillenia indica is a flowering plant belongs to dilliniaceae family. It is a widely used medicinal plant inpharmaceutical industries. It has high medicinal values like Anti-inflammatory, Analgesic, Anti-diabetic, Antimicrobial and Antibacterial, Anticancer, Antioxidant, Antidiarrheal,wound healing indigestion, influenza, asthma, dysentery, weakness, jaundice and rheumatic pain etc. This review is about Dillenia indica and its application in pharmaceutical industry.

Keywords:Anti-diabetic, Anti-inflammatory, Medicinal Plants, prehistoric.

I. INTRODUCTION

India is an affluent source of biodiversity and habitat for more than 45000 distinct plant species [1].Out of these, about 15,000-20,000 plants have medicinal value. However, traditional communities used only 7,000-7,500 species for their different medicinal properties. Due to anthropogenic activity these plants are eliminating at alarming rate.

Plants are important part of universal sustainability because of their many ecosystem services like supply of fuel, food, medicine, shelter, condiments, aromas and perfumes [2]. Healthy ecosystems are essential for the welfare of all human beings. All living organisms are inter-dependent upon one another directly or indirectly. Therefore, we must take care of both animals and plants by raring them in eco-friendly environment to establish their continuity and conservation. In return the requirements like food, forage, shelter and protection etc. are met by both the flora and fauna residing in the same ecological niches [3]. Therefore, it is essential to keep the plant diversity indiscrete for the continuous running of the environment because local plants are important representatives of world biological diversity [4].

Plants are sources of many drugs that are used for the cure of many diseases in human history. During traditional times people completely depends on plants to cure diseases and continuous use of medicinal plants extended to several parts of the world. Thus, combination of magic, need, fault and art has generated knowledge of medicinal plants; which has formed the base of present medicine. These are used for health care in bothdeveloping countries and in developed countries where modern medicines are mostly used. The old

medicines are derived from medicinal plants, minerals and organic matter while the herbal drugs are prepared from medicinal plants only. India is being the largest medico-culturally diversified country in the world where the use of medicinal plants is part of a time-honoured culture that is valued even today by different primitive healthcare systems of medicine likeAyurveda and unani system

II. MORPHOLOGICAL DESCRIPTIONOF DILLENIA INDICA

Habit:It is an evergreen medium-sized tree growingup to length of about 6-15 m.Its bark is smooth, thick, red bearing tomentose branches and iscommonly used to make good firewood.

Leaves:The leaves are large lanceolate, with a noticeable grooved surface with impressed veins.

The flowers are large, solitary,terminal, bisexual, pedicellate,smooth,pentamerous containing many yellow stamens.Flowering season is June – July.

Fruit:the fruits are indehiscent, mucilaginous, covered by calyx, larger round in shape with huge number of seeds and are edible for flavouring food.Fruits are very watery because of 86.4% water, with 10% insoluble matter, very little of which is nutritious.

Seeds:seeds are small,thick, hairy and kidney shaped.

III. OCCURRENCE AND DISTRIBUTION

It occurs in countries like Bhutan, India, Indonesia, Nepal, Laos, Malaysia, Myanmar, Philippines, Sri Lanka, Thailand, and Vietnam. It is native to India. In India, scattered in sub Himalayan region of Assam, Bihar, North Bengal, Orissa, Madhya Pradesh andGujarat. [5-8]

IV. SCIENTIFIC CLASSIFICATION

Kingdom: Plantae
Subkingdom: Tracheobionta
Superdivision: Spermatophyta
Division: Phanerogamae
Class: Dicotyledonae
Subclass: Dilleniidae
Order: Dilleniales
Family: Dilleniaceae
Genus: *Dillenia*
Species: *indica*

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Fig 1; plant of *Dillenia indica*Fig 2; branch of *Dillenia indica* containing a Fruit

Fig 3; Showing Flower of *Dillenia indica* Fig 4; Showing leaves of *Dillenia indica*

V.VERNACULAR NAMES OF DILLENIA INDICA

English	**Elephant Apple,**
Hindi	**Chalta, Karambel**
Sanskrit	**Avartaki**
Assamese	**Outenga**
Bengali	**Chalta, Chalita**
Nepal	**Ramphal**
Burma	**Thabyu, thibuta, Zinbrun, Zinpyunnga**
Malyalam	**Chalitha, Punna, Syalitha, valapunna**
Tamil	**Akku, Ugakkay, uva, uvav, uvatteku**
Telugu	**Peddakalinga**

VI. PHYTOCHEMICAL CONSTITUENTS

Dillenia indica is rich in various chemical compounds, some of the phytochemical were identified from this medicinal plant such as Betulinic Acid (Dillenetin),Betulin, Betulinaldehyde, β- sitosterol, stigmasterol, Glycoside, Steroids, Flavonoids, Saponins, tanins, malic acid, arbinoglactan, and reducing sugar. [9],[10].

VII.APPLICATIONS

Dillenia isan ethno-medicinal plant with lots of medicinal properties in pharmaceutical industries.In spite of large number of chemical drugs available in modern times, medicinal herbs are being an important alternative source of medicines because of low cost, effectiveness and no side effects.Some of the applications of *Dillenia indica* in related to pharmaceutical companies are as given below:

7.1. AntimicrobialActivity

The extract prepared from the leavesof *D. indica* was checked for their antimicrobial action for both gram positive and gram-negative bacteria by Apu *et al*. (2010). The gram- positive bacteria were *Bacillus megaterium, B. cereus, B. subtilis, Sarcina lutea and Staphylococcus aureus* and the gram - negative bacteria were *E. coli, Salmonella paratyphi, Salmonella typhi, P. aeruginosa, Shigella dysenteriae, Shigella boydii, Vibrio parahemolyticus, and Vibrio mimicus*. The extract is also checked for antifungal activity and has showed antifungal activity against some of the fungi such as *Candida albicans, Aspergillus niger, and Saccharomyces cerevisiae.* [11]

Antimicrobial action of unsaponifiable matter and fixed oil of *D. indica* was checked. It was reported that fixed oil does not shown any activity against most of test bacteria accept*Vibrio cholera* and mild antifungal activity, while unsaponifiable matter showed good activity. Acetone and alcoholic extracts of seeds of *D. indica* showed good antimicrobial activity while chloroform extract found to have mild activity. [12]

The extracts prepared from the *Dillenia indica*bark were checked against four gram-positive, seven gram-negative bacteria and against three pathogenic fungi. N-Hexane and dichloromethane fractions showed significant activity against all the tested bacteria however, the highest activity against fungi was shown by n-hexane. [13]

7.2. Anticancer activity

Cancer, one of the most vulnerable diseases is a main cause of death in numbers of countries. Betulinic acid showed an inhibitory activity on the K562 tumour cell line and IC50 value was about 6.25 μg/ml and induced 35% apoptosis at 25 μg/ml. The results of cancer cell death by betulinic acid are by inducing apoptosis involving caspases. Moreover, it was found that betulinic acid up to 500 mg/kg was no toxic effects and is well tolerated in mice. The methanolic extract of fruits of *Dillenia indica* showed powerful antileukemic activity against U937, HL60 and K562 cell lines. The ethyl acetate and methyl fraction both showed antileukemic activity, but the highest activity was shown by the ethyl acetate fraction. The compound betulinic acid shows the antileukemic activity and was isolated, identified and characterised from ethyl acetate fraction. [14] – [19].

7.3. Antidiabetic activity

Diabetes is a metabolic disease cause increase sugar level in blood and affect carbohydrate,fat and protein metabolism. This disease increases day by day and it is estimated that its number may reach up to 366 million in coming 10-15 years. [20].

During traditional time,people usemedicinal plants or their extracts to cure diabetes. It has been also recommended by W. H. O. to evaluate medicinal plants to cure diabetes. [21].

Diabetes is regulated by oral administration of certain synthetic drugs; these synthetic drugs are expansive and cause side effects. Therefore, we are searching for hypoglycaemic agents which are effective, low in cost and having no side effects. [22].

The antidiabetic activity of methanolic extract of *Dillenia indica* was carried out by Sunil kumar *et al*., using experimental diabetic wistar rats and the molecules exhibit activity are β sitosterol, stigmasterol and stigmasterol palmitate. They induce type -I and type -II diabetes by intraperitoneal injection of Streptozocin (60 mg/kg body and Streptozocin (60 mg/kg body weight) followed by intraperitoneal injection of Nicotinamide (120 mg/kg body weight) after 15 mins. The rats were then treated with ethyl acetate fraction of methanolic extract for 21 days. The results show significant decrease in sugar level in diabetic rats due to increase in insulin secretion from pancreatic cells. [23] – [25].

7.4. Antidiarrheal activity

The methanol extract prepared from the leaves of *Dillenia indica* by using castor oil induced diarrhoea model were studied, from which it was concluded, that the inhibition of the diarrhoea is due to inhibition of inflammatory mediator release and phytoconstituents such as tannins and flavonoids are reason for the activity. [26] – [28].

7.5. Antioxidant Activity

The antioxidant activities of fruit extracts (methanol, EtOAc, and aqueous extract) of *D. indica* in in vitro models such as b-carotene-linoleate model system, 2,2-diphenyl-2-picrylhydrazyl radical (DPPH) scavenging assay, and phosphomolybdenum method was studied by Abdille *et al.* (2005). The highest activity was shown by methanol extract. The phenolics present in the extracts are believed to be responsible for the anti-oxidant activities. [29].

*Baikunthaet.al*carried out the antioxidant activity of fruit extract (50% aqueous methanol > methanol > ethyl acetate> hexane) of *Dillenia indica*. Antioxidant activity was determined by checkingthe visible absorbance of 2,2-diphenyl-1-picrylhydrazyl (DPPH) on addition of the plant extracts. The decrease in absorbance indicatesantioxidant activity. The nonlinear regression curve was used for the determination of mean inhibitory concentration (IC_{50}) values. The standard used in DPPH and TPC assay is L-Ascorbic acid and gallic acid. The antioxidant activity of *Dillenia indica* fruit extract is due to its phenolic content. The hexane extract of *Dillenia indica* fruit has low antioxidant activity because it contains very low content of phenolic content. The aqueous

methanol (50%), methanol and ethyl acetate extracts have bearable phenolic content as well as antioxidant property. [30].

The Methanol, petroleum ether and water extracts of dried fruits of *Dillenia indica* was checked for their antioxidant activity. The IC50 values of their DPPH, hydroxyl, oxygen and nitric oxide scavenging activitieswere estimated as well as their reductive ability, vitamin C and total phenolic content was evaluated.The IC50 values for the DPPH, hydroxyl, oxygen, nitric oxide and reductive ability of the methanolic extract of *Dillenia indica* were 31.25 ug/ml, 51.82 ug/ml, 51.44 ug/ml, 39.73 ug/ml and 40.18 ug/ml, respectively. These IC50 values for DPPH were superior in comparison to its petroleum ether and water extracts. [31].

The evaluation of Methanolic extract prepared from the bark of *Dillenia indica* Linn. (MDI) for its antioxidant activity. For Antioxidant potential, 1,1-diphenyl-2-picrylhydrazyl (DPPH) and radical Reactive Oxygen Species (ROS) were used. Good antioxidant activity was shown by (MDI)in DPPH and total ROS scavenging method, and the IC_{50} value of 12.32±0.16 and 34.72±0.48 μg mL^{-1}. This study suggested that MDI has strong antioxidant effects. [32].

7.6. Anti-inflammatory Activity

Inflammation is a complicated physiological process associated with secondary process such as pain, redness, swelling and fever 68. According to the latest research done by Preet *et al*. 2016, the extract from stem bark *Dillenia indica* at dose of 100 and 300 mg/kg possessed good central and peripheral analgesic activity. The extracts further showed good ($P<0.01$) anti-inflammation activity in formalin and carrageen an induced inflammation models. Due to presence of flavonoids like kaempferol, rhamnetin, dihydro-isorhamnetin, myricetin, naringenin and quercetin derivatives, *Dillenia indica* favoured anti-inflammatory and analgesic activity.

Carrageenan-induced enema and capillary permeability was observed for the anti-inflammation activity. The methanolic extract showed better ($P<0.01$) anti-inflammation activity in the acetic acid-induced capillary permeability and paw enema test at 200 mg/kg and 400 mg/kg. The extract at 100 mg/kg showed good ($P<0.05$) action in acid-induced permeability. These endings support the folkloric use of *Dillenia indica* in diseases related to inflammatory conditions.

The ethyl acetate extract from the bark of *D. indica* f. *elongata* (100 and 300 mg/kg) and *S. robusta* (100 and 300 mg/kg) may be responsible for its analgesic and anti-inflammation activity

Saowakhon *et al* studied anti-proliferation activities of Thai Lanna medicinal plant extracts in cancer cell lines by SRB assay including *D. indica* which found more powerful than doxorubicin compares to other medicinal plants. Anticancer potential of *D. indica* can be further analysed for treatment (Saowakhon *et al*., 2008). [33] – [35].

7.7. Hepatoprotective Activity

Liver diseases are the most serious diseases. They may be classified as acute or chronic hepatitis (inflammatory liver diseases), hepatitis (non- inflammatory diseases) and cirrhosis (degenerative disorder resulting in fibrosis

of the liver). Harmful chemicals (some antibiotics, aflatoxin, chemotherapeutics, carbon-tetrachloride,peroxidised oil, chlorinated hydrocarbons, etc.) infections, enormous consumption of alcohol, and autoimmune disorder are the main cause of liver diseases.Most of the chemicals that are toxic to liver harm cells of liver generally by promoting lipid peroxidation and other oxidative damages in liver. Hepatitis and Cirrhosis may result due to increase per-oxidation of lipids during the liver microsomal metabolism of ethanol (Kumar *et al*., 2011**)** [36].

As it is known, the production of reactive oxygen species (ROS) during metabolic processes by results oxidative stress and macromolecular damage, contributing to the pathogenesis of many diseases. Liver damage is very common because the liver is a key organ for the detoxification. Liver toxic chemicals damage liver cells mainly by the production ROS, some form covalent bonds with the lipid tissue. Excessive hazardous chemicals exposure of liver leads to generation of high percentage of free radicals that they overcome the natural defence system, leading to hepatic damage. [37].

Himakar *et.al*. studied the hepatoprotective effect of extract from the seeds of *Dillenia indica* n-hexane extract processed from the seeds of *Dillenia indica* showed powerful hepatoprotective activity in wistar rats by reducing the activity of bilirubin, serum enzymes, urea, lipid peroxidation creatinine and no toxic effects. [38]

7.8. Wound healing activity

A glycolic extract prepared from the fruits of *Dillenia indica* showed significant wound healing activity lonely or in mixture with micro current stimulation to skin wounds surgically produced on the back of Wistar rats. Moreover, because of presence of flavonoids*Dillenia indica* works well in healing of wounds as determined by Janick Paull *et al* 2008 [39].

7.9. Anti-HIV activity

Human immunodeficiency virus (HIV) is most serious infectious pathogens and it cause acquired immune deficiency syndrome (AIDS) in both developed and developing countries. [40].

*Dillenia indica*contain betulinic acid, because of occurance of betulinic acid,dillenia indica possess anti-HIV activity as remarked by Theo *et al*, 2009. [41].

7.10. Antiimplantation activity

Biological screening of 50% ethanolic extract of stem bark of *Dillenia indica* revealed Antiimplantation activity in rats. CNS effects were not favoured. Local dose (LD50) of the extract was >1000mg/kg intraperitoneal in mice and significant results for Antiimplantation activity was achieved. [42].

VIII. CONCLUSION

From the present review it is being concluded that the *Dillenia indica* is a most important ethnomedicinal plant having high medicinal values in pharmaceutical industry used for curing many diseases as discussed in this review**.**Therefore, more evaluation must be done for identification,isolation and purification of new compounds from this plant to cure fatal diseases**.**

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