A STUDY ON DIVERSE PHARMACOLOGICAL POTENTIAL OF PLUMERIA ALBA LINN (APOCYNACEAE)

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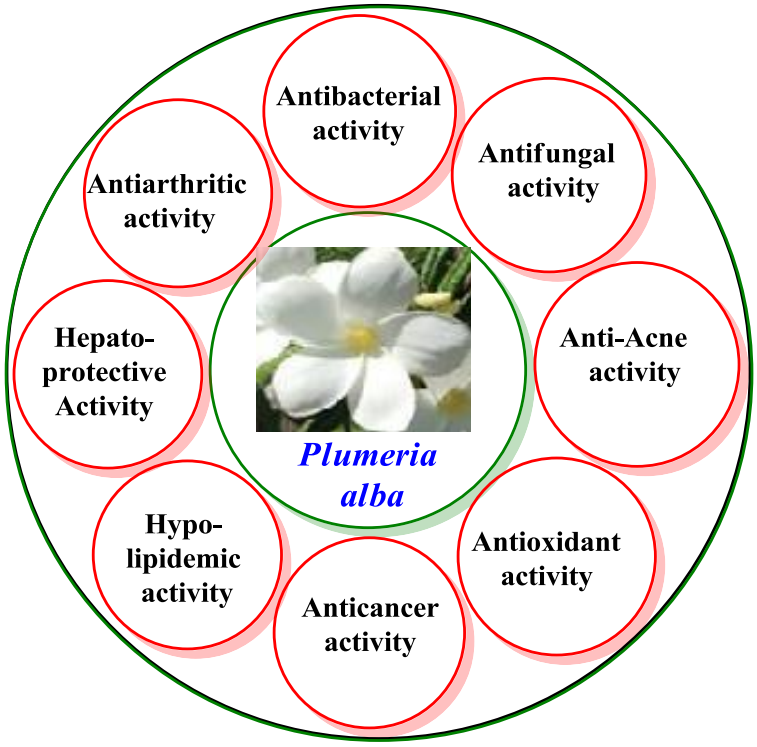
Graphical Abstract



Pharmacological Potential of *Plumeria alba*

Abstract

The present review aims to explore the pharmacological activities of Plumeria alba Linn. The medicinal value of Plumeria species in the treatment of various human ailments is mentioned in Ayurveda, Charaka Samhita, and Sushrita Samhita. Plumeria alba Linn. is widely used in perfumery and traditional medicinal systems for various diseases**.** Plants have a variety of compounds like glycosides, alkaloids, terpenoids, and steroids which possess important diverse pharmacological activities to alleviate various diseases and disorders. Extracts of various parts of this plant can be safely used as antifungal, antioxidant, antiacne, hypolipidemic, antiulcerogenic, antibacterial, cytotoxic, anti-inflammatory, hepatoprotective, etc activities. The present literature review has been envisaged to provide scientific information about the pharmacological profile**.** Plumeria alba has been scientifically validated by various researchers

all over the world. In the Indian system of medicine plants are a vital source of drugs from the ancient time. This alternative system of medicine is gaining increasing popularity worldwide. This paper enumerates the pharmacological importance of P. alba which may help the researchers to set their minds for approaching the usefulness, efficacy, and potency of the plant.

Keywords: Plumeria alba, antimicrobial, hepatoprotective, hypolipidemic, antioxidant, anti-inflammatory, pharmacological activities.

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1. INTRODUCTION

Medicinal herbs have been in use for thousands of years, under the indigenous systems of medicine like Ayurveda, Siddha, and Unani. On earth, about 3.6 lakh species of medicinal plants are present among these about 1.4 lakh species are present in India (Mehrola, 1990) and about 70000 plants are used in traditional systems of medicine. All over the world, plants were used as the main source of medicines by ancestors (Mukherjee, 2001; Jadhav, 2006). The workers have made valuable contributions towards the ethnobotanical knowledge of primitive men, tribes, and other folk healers of the state. The natural and traditional relationship between human societies and plants has been brought to light in various. Even today the rural and aboriginal folks are very much in harmony with nature and bioresources (Shah and Singh, 1990). An obvious advantage of the present study is to create awareness of the species and enumerate their traditional uses.Some interesting information on Plumeria alba. Plumeria or frangipani is a genus of flowering plants in, the family Apocynaceae.

Figure 1a. Flowers and tree of Plumeria alba.

Pharmacological Activities

A variety of extracts and chemical compounds of Plumeria alba have shown antifungal, antioxidant, antiacne, hypolipidemic, antiulcerogenic, antibacterial, cytotoxic, anti-inflammatory, and hepatoprotective activities. Methanolic extract showed antimicrobial activity against Bacillus anthracis, and Pseudomonas aeruginosa. Different parts of the P. alba were believed, to have been useful in a variety of diseases. The milky sap of the stem and leaf is applied to skin diseases such as herpes, scabies, and ulcers (Prajapati et al, 2004). The seeds are in hemostasis while the latex is used as purgative, cardiotonic, diuretic, and hypotensive (Rengaswami and Venkatarao, 1960). The bark is bruised as plaster over hard tumors (Raju, 2000). The essential oils from the flowers are used for perfumery and aromatherapy purposes. It is used in the treatment of syphilitic ulcers, blennorrhagia, dartre, and syphilis, and as a cure for itch. The fruit is edible to be eaten in West India and branches are used as abortifacient. Leaves are used in antipyretic, antifungal, stimulant, inflammation, rheumatism, antibacterial, bronchitis, cholera, cold, and cough.(Radha et al, 2009;Devprakash et al, 2012;Kirtikar et al., 1935).

Antibacterial Activity

Plumeria alba appears to have significant antimicrobial capacity resembling a broad spectrum antibiotic against the common uro-gastro pathogenic Escherichia coli, one of the common bacteria with pathogenic strains, and are relatively resistant towards synthetic drugs. This aromatic plant can be a potential source of evolving newer antimicrobial compounds and as a non-toxic antibiotic producer agent. The extracts of frangipani have the potential as a natural anti-toxic antibiotic producer, especially against E. coli (Zahid et al., 2010). Antibacterial activity of P. alba (Frangipani) petals methanolic extracts was evaluated against E. coli, Proteus vulgaris, Staphylococcus aureus, Klebsiella pneumoniae, P. aeruginosa, S. saprophyticus, Enterococcus faecalis, and Serratia marcescens using disk diffusion method. Frangipani extract also showed high antibacterial activity against S. saprophyticus, P. vulgaris, and S. marcescens, but not more than the zones of the positive control used (Radha et al., 2008; Syakira et al., 2010). In vitro antibacterial activity of Plumeria alba Linn. bark against Gram-positive Staphylococcus aureus, Bacillus subtilis, Gram-negative P. aeruginosa, Escherichia coli, and fungal species

Candida albicans was carried out and methanol extract showed significant results against pathogens than that of water extract of Plumeria alba Linn.(Goyal et al., 2012). Antibacterial compounds of ethyl acetate extract from P. alba stem bark and their antibacterial activities against E. coli and S. aureus were investigated (Mustanir Y et al., 2014). Antibacterial activity of silver nanoparticle of P. alba flower water extract against S. aureus, S. pneumoniae, P. mirabilis, and E. coli using the Agar-well diffusion method (Patil and Hooli, 2013).

Antifungal Activity

Antifungal activities of methanolic extract and the isolated fraction of the plant Plumeria alba were assessed. The zone of inhibition was compared with that of the Standard antibiotic ciprofloxacin (5 mg/disc) by disc diffusion method. The anti-fungal activity was assessed by standard dilution technique using Sabouraud dextrose agar medium. The results are compared with standard Clotrimazole (125µg/ml) (Radha et al, 2008; Kumari et al, 2012). The ointment formulated dosage form from ethanol extract of P. alba L leaves investigate its physical properties and its activity against C. albicans by agar diffusion method (Ningsih et al., 2018).

Anti-Acne Activity

Ethanolic leaves extract of Plumeria alba into the water-leached ointment base and evaluated the stability of the ointment included organoleptic, adhesion test, dispersive power test, determination of pH, and the antibacterial activity test. Optimal antibacterial activity at concentrations of 5 ppm provides a zone of inhibition of 24.00 mm (Ningsih et al., 2017).

Hepatoprotective Activity

The hepatoprotective activity of both the plants and also their combination. The methanolic extract of Plumeria alba and aqueous extract of Aloe vera were tested for their hepatoprotective activity against carbon tetrachloride (CCl_4) induced hepatotoxicity in adult male Wistar rats. The degree of protection was measured by using biochemical parameters like serum transaminases (SGOT and SGPT), alkaline phosphatase, total protein, and histopathological studies. The combination of both extracts showed significant hepatoprotective activity comparable with standard drug silymarin (Sudheer et al., 2011). The methanol extract (MLE) at different doses (100, 200, and 400 mg/kg, b.w.) of the plant P. alba for its efficacy against paracetamol-induced acute hepatic damage in Wistar rats. The rats were monitored for biochemical changes of

serum Glutamate Oxaloacetate Transaminase (GOT), serum Glutamate Pyruvate Transaminase (GPT), serum Alkaline Phosphatase (ALP), serum Gamma Glutamyl Transferase (GGT), and for histopathological changes (Chowdhur et al., 2012).

Antiarthritic Activity

The antiarthritic potential of fractions of hydroalcoholic extract from leaves of Plumeria alba. This extract was further fractionated with solvents ethyl acetate and n-butanol to obtain EAPA and BPA respectively. These fractions were tested against formaldehyde and Freund's complete adjuvant (FCA) induced arthritis. Arthritis assessment, paw volume, body weight, motor incoordination, and nociceptive threshold were measured. On day 21, the animals were sacrificed and histopathology was done. The present study suggests that P. alba has protective activity against arthritis and supports the traditional use of P. alba for rheumatism and other inflammatory diseases (Choudhary et al., 2014).

Hypolipidemic Activity

Methanolic flower extracts of Plumeria alba and P. rubra for in vitro antioxidant potential, cytotoxicity, and hypolipidemic activities. DPPH assay of the methanolic extract of Plumeria revealed 81% and 72% inhibition by P. alba and P. rubra respectively. Anti-cholesterol assay of the extracts demonstrated P. rubra has the highest hypolipidemic activity (60%) followed by P.alba (52%) (Rahman et al., 2014).

Antioxidant Activity

Methanolic (MeOH) extract and crude polysaccharides of Plumeria alba leaves were evaluated for in vitro antioxidant activity. Antioxidant activity was evaluated at different concentrations ranging from 0.25 to 3 mg/ml using three different in vitro antioxidant activity assays (Dawood et al, 2016). P. alba flowers were found as a potential source of antioxidant activity. Methanolic flower extracts of P. alba and P. rubra were used for biological assays. 2, 2'diphenyl-2-picrylhydrazyl (DPPH) assay of methanolic extract of Plumeria revealed 81% and 72% inhibition by P. alba and P. rubra respectively thereby confirming the presence of antioxidants. Total antioxidant potential was carried out using ascorbic acid and was determined as 1.74 mg/ ml and 1.67 mg/ml (Rahman et al, 2014). The in vitro antioxidant property of flowers and leaves of P. alba. aqueous and ethanolic extracts of both parts of P. alba were evaluated using total antioxidant capacity, reducing power assay, hydrogen peroxide scavenging activity, and nitric oxide scavenging activity. Among all the extracts, ethanolic flower extract showed the highest antioxidant activity than other extracts (Nisha and Prasanna, 2014**).** Antioxidant activities of different leaf extracts of P. alba using 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) free radical assay. The DPPH scavenging activity of the methanolic extract was 60.84±5.93 % which was comparable to 64.29±5.19% demonstrated by the control, Vitamin C (Chaudhuri et al., 2015).

Anticancer Activity

A cytotoxic assay using colon cancer cell lines (HCT 116) revealed the antiproliferative activity of Plumeria against HCT 116 cell lines. Plumeria alba has exhibited dose-dependent cytotoxicity whereas P. rubra completely failed to control the proliferation of colon cancer cells. Loss of viability of the dying cells as evidenced by the morphological changes was scrutinized by microscopy. Depending on the concentration, the extract exhibited different levels of cytotoxicity like cell shrinkage, aggregation, and cell death with an IC50 value of 259.9 µg ml-1 observed with P. alba. (Rahman et al., 2014). The anticancer activities of different extracts of leaves of P. albafor in vitro cytotoxicity by

the trypan blue exclusion method using DLA and L929 cell lines. The methanolic extract showed potent in vitro anticancer activity (Radha, 2009). The antitumor activity of the methanolic extract of P. alba leaves against EAC and DLA using in-vitro cytotoxic and mean survival time, a decrease in tumor volume, and viable cell count in the DLA tumor hosts. The animal was observed for improvement in the hematological parameters (e.g., hemoglobin content, red and white blood cells count, and differential cell count) following MPA treatment of the tumor-bearing mice (Ramalingam et al., 2008).

Hypoglycemic Activity

The total root extract and fractions of Plumeria alba exhibit significant antidiabetic properties in streptozotocin-induced diabetic animals. The hypoglycemic effect of the total extract, supernatant fractions (SF), ethyl acetate (EA), and the dregs of supernatant was evaluated on normal mouse hyperglycemia caused by an Oral glucose tolerance test (OGTT). The results of this test showed that the total extract, supernatant, and ethyl acetate fraction significantly reduced hyperglycemia in 30 min. A comparison of different fractions activities showed that mice treated with ethyl acetate fractions and supernatant fractions at a dose of 100 mg/kg had the highest hypoglycemic effect (Kadebe et al., 2016). The beneficial effects of three indigenous plants in lowering glucose and lipid levels. The aqueous ethanolic extracts of M. spicata (leaves), P. alba (leaves), and N. alba (flowers and rhizomes) were evaluated individually in 200mg/kg and 400mg/kg doses against alloxan (130mg/kg i.p.) induced hyperglycemic rats (Mushtaq et al., 2017). The effect of P. alba hydroalcoholic extract of root on some markers of metabolic syndrome in type 2 diabetes (hyperlipidemia, glucose intolerance, obesity) and atherogenic index. This syndrome was induced by high fructose and fat diet in male Wistar rats (Kadebe et al., 2014).

Larvicidal Activity

Dried extracts were used for larvicidal bioassay as per WHO standard method. Larvicidal activity (LC_{50} of 123 ppm) followed by Annona squamosa (LC_{50} 190.5 ppm), Bauhinia variegata (LC_{50} 204.2 ppm), Plumeria alba (LC50 218.8 ppm), Psidium guajava (LC50 223.9 ppm), Syzygium cumini (LC_{50} 223.9 ppm) and Alstonia scholaris (LC_{50} 239.9 ppm). Leaves extract of P. alba was found (LC_{50} 218.8 ppm) against Aedes aegypti mosquitoes (Kaushik and Saini, 2009).

Anti-inflammatory Activity

Comparison between the anti-inflammatory potential of methanolic extract of Plumeria alba leaves (MELPA) and T. divaricata Linn. leaves (MELTD) of the family Apocynaceae. Extracts showed a dose-dependent response for anti-inflammatory activity in carrageenan-induced paw edema. The methanolic extract of P. alba leaves was found to be more effectual in carrageenan-induced inflammation (Kumari et al., 2018).

Antiulcerogenic Property

The antiulcerogenic property of hydroalcoholic extract obtained from the leaves of Plumeria alba. Antiulcer assays were performed using the protocols of ulcers induced by NSAIDs, ethanol, and pylorus ligation. Hydroalcoholic extract (HAPA) and various fractions of HAPA like, n-hexane extract (HPA), ethyl acetate extract (EAPA), and n-butanol extract (BPA) were administered at doses of 200 and 400 mg/kg for HAPA and 100 and 200 mg/kg for fractions of extracts. Parameters of gastric secretion (volume, pH, total protein, free and total acidity) were determined by the pylorus ligation model. Parameters like aspartate aminotransferase and alanine aminotransferase were also determined in ethanol induced ulcer model.

To determine the mechanism of action, the role of nitric oxide was also evaluated (Choudhary et al., 2014).

Antifilarial Activity

The effect of aqueous bark extract of Plumeria alba on the spontaneous movements of the whole worm preparation and nerve-muscle complex of S. cervi a cattle filarial parasite and on the survival of microfilariae. The aqueous extract could inhibit the spontaneous movements of S. cervi, characterized by initial stimulation followed by reversible paralysis. The concentration required to produce a similar effect on the nerve-muscle complex was less as compared to the whole worm (Rizvi et al., 2009).

Antimalarial Activity

The antimalarial properties of Plumeria alba using aqueous (30-300 mg/kg) and dichloromethane/ methanol (30-300 mg/kg) extracts of the plant in imprinting control region mice infected with Plasmodium berghei. For the curative test, the extracts were administered to the infected mice 4 days post-infection. In the prophylactic test, the animals were pre-treated with the extracts for 3 days before challenging them with P. berghei infected erythrocytes (Boampong et al., 2013).

2. CONCLUSION

The Plumeria alba is an important medicinal plant with a diverse ethnomedical and pharmacological spectrum. The findings justify the varieties of extracts and chemical compounds of P. alba have shown antifungal, antioxidant, antiacne, hypolipidemic, antiulcerogenic, antibacterial, anti-inflammatory, anticancer, antimicrobial, antifungal, antiarthritic, hepatoprotective and larvicidal activities, etc. As the global scenario is now changing towards the use of nontoxic plant products, the development of modern drugs from P. alba should be emphasized. An evaluation needs to be carried out on P. alba to use and preparation of the plant in their practical clinical applications to combat the ever-increasing new human ailments and to save humanity from the clutches of such diseases.

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Conflict of Interest

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Ethical Considerations

Not Applicable

Author Contributions

All authors are contributed equally.

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Not Applicable

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