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Review Article

Phytopharmacological Review of *Plumeria species*

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Abstract: The various species of *Plumeria* are known to have medicinal properties and have a long history of use by indigenous and tribal people in India. The medicinal value of this *Plumeria* species in the treatment of a large number of human ailments is mentioned in *Ayurveda, Charaka Samhita, and Sushrita Samhita*. For millennia, the Indian population has depended mainly upon plant based crude drugs for a variety of ailments. This alternative system of medicine is gaining increasing popularity worldwide. *Plumeria* species are widely used as a purgative, remedy for diarrhea, cure of itch, bronchitis, cough, asthma, fever bleeding piles, dysentery, blood disorders and tumors etc. Today it is a challenge for scientists to provide efficient, safe and cheap medications. In this scenario *Plumeria* can be an exclusive medicine which is widely available throughout our country. The present review gives an account of updated information of the botanical, phytochemical and pharmacology aspects of *Plumeria* species.
Keywords: *Plumeria* species, phytochemistry, pharmacological activity.

INTRODUCTION

India is sitting on a gold mine of well-recorded and traditionally well-practiced knowledge of herbal medicines, therefore, any scientific data on such plant derivatives could be of clinical importance. The major merits of herbal medicines seem to be their efficacy, low incidence of side effects and low cost [1].Genus *Plumeria* belongs to the Apocynaceae family and is native to the new world. The plants from this genus are widely cultivated in the tropical and subtropical regions throughout the world. *Plumeria* L. (Family: Apocynaceae) is indigenous to tropical America and is found from southern Mexico to northern South America and also most abundant in India. They are recognized as excellent ornamental plants and often seen in the graveyards [2]. *Plumeria* plants are famous for their attractiveness and fragrant flowers. The essential oils from the flowers are used for perfumery and aromatherapy purposes [3]. According to the World Health Organization, 2003 about 80 % of the population of developing countries being unable to afford pharmaceutical drugs rely on traditional medicines, mainly plant based, to sustain their primary health care needs [4]. Herbal medicines are in great demand in the developed as well as developing countries for primary healthcare because of their wide biological and medicinal activities, higher safety margins and lesser costs [5].

The present attempt is to review and compile updated information on various aspects of different species of *Plumeria* Linn. used all over the world. This plant is commonly known as chafa, champa, temple tree and abundantly available in tropical and subtropical areas. Ancient history of India describes its diverse uses and also plays appreciable role in Ayurvedic or natural herbal medicines.

Taxonomical classification of *Plumeria*

Kingdom: Plantae - Plants
Subkingdom: Tracheobionta - Vascular plants
Superdivision: Spermatophyta - Seed plants
Division: Magnoliophyta - Flowering plants
Class: Magnoliopsida - Dicotyledons
Subclass: Asteridae
Order: Gentianales
Family: Apocynacea

Plumeria acuminata is used as medicinal plant native to Mexico, Central America, the Caribbean and South America spreaded throughout the tropics. They are commonly known as "Temple tree" or "Champa" in India. It is small tree, 3 to 7 m high; stem smooth and shinning succulent with abundant white latex easily breaks. The leaves crowed at the terminal end of the branch, commonly oblong in shape, reaching a length of 40cm and a width of 7cm.It is simple, opposite, rarely whorled or alternate, stipules absent or rarely present. The inflorescence is cymose, terminal or axillary, with

bracteoles. The stamens are inserted on the inside of the corolla tube. The flowers are bisexual, fragrant, the upper portion whitish, while the inner lower portion yellow, 5-6cm long. The fruits are linear oblong or ellipsoid follicles. These are brownish black in colour, seeds are oblong [6, 7].

Plumeria rubra grows as a spreading shrub or small tree to a height of 2–8 m (20–25 ft) and similar width. It has a thick succulent trunk and sausage-like blunt branches covered with a thin grey bark. The branches are somewhat brittle and when broken, ooze a white latex, or sap, which can be irritating to the skin and mucous membranes. The large green leaves can reach 30 to 50 cm (12–20 in) long and are arranged alternately and clustered at the end of the branches. They are deciduous, falling in the cooler months of the year. The flowers are terminal, appearing at the ends of branches over the summer. Often profuse and very prominent, they are strongly fragrant, and have five petals. The colors range from the common pink to white with shades of yellow in the centre of the flower [8,9]. Initially tubular before opening out, the flowers are 5-7.5 cm (2–3 in) in diameter, and only rarely go on to produce seed - 20-60 winged seeds [10].

Plumeria alba Linn (Apocynaceae) commonly called White Champa, a small laticiferous tree or shrub, native of tropical America. It is 4.5m high, occasionally grown in the gardens. The plant is mainly grown for its ornamental and fragrant flowers. Leaves are lanceolate. The flower of the plant is white with yellow centers. Fragrant in corymbose fascicles Frangipani is well-known for its intensely fragrance and spiral-shaped blooms [11]. *Plumeria alba* is a small tree known for is pungently fragrant, spiral shaped blooms typically produced from June through November. This tree has a thin bark and milky sap. The narrowly strap-like leaves stay on the tree for most of the year. The white flowers with a yellow center have an almost waxy feel. After flowering narrowly cylindrical pods borne in pairs attached at the base and filled with winged seeds are sometimes produced.

Plumeria obtusa can grow as either a small shrub or tree ranging in height from 0.9-6.1 meters with widely spaced thick succulent branches that are often covered with "knobby" protuberances. The leaves are found in clusters near the tips of the branches. They are large (6-22 cm long and 2-7 cm wide) and have a characteristic oblong shape and the tip of the leaf is obtuse (rounded) rather than pointed as it is in other species. The leaves are dark and leathery and tend to be shiny on the upper surface with conspicuous parallel secondary veins that run from the mid vein to the margins of the leaves.

The flowers of this species are borne in inflorescences (clusters) that form at the ends of the branches on a long thick stalk. Each inflorescence contains many white flowers with a small yellow center creating splashes of color throughout the tree. The well known and characteristic Plumeria flowers contain five petals that are fused at the base in a short funnel-shaped tube which gradually widens as the lobes of the petals are spread out. The fruit of this species is a dry follicle which splits along one side to release the winged seeds [12]. *Plumeria obtusa* is native to the Bahamas and the Greater Antilles in Central America. It is widely cultivated in tropical climates including eastern Africa, Asia, and Hawaii.

Fig. 1: *Plumeria acuminate* L.

Fig. 2: *Plumeria rubra* L. acutifolia

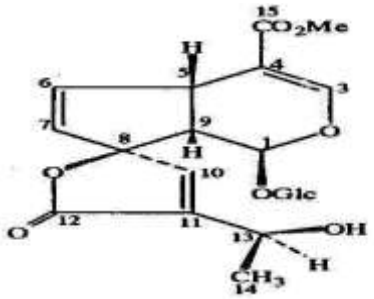
Fig. 3: *Plumeria alba*

Fig. 4: *Plumeria obtuse*

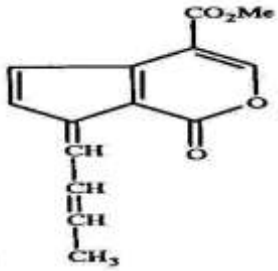
Phytochemical constituents

The stigmast-7-enol, lupeol carboxylic acid, lupeol acetate and ursolic acid had been isolated from *P. acuminate* leaves. The researchers have successfully isolated Fulvoplummierin, Plumericin along with three new compounds isoplumericin, β-dihydroplumericin and β- dihydroplumericinic acid from roots of *P. acuminata*. The steam distillate of *P. acuminata* yields an essential oil (0.04-0.07 %) which mainly consist of primary alcohols, geraniol, citronellol, farnesol and phenylethyl alchol with little amount of aldehyde and ketones (6.8 %). These oils have acid value (20.2) and saponification value (123) [13, 14].

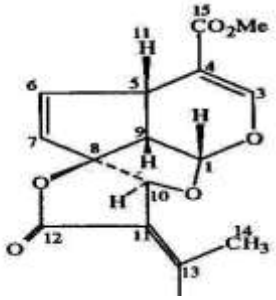
*P. rubr*a containing β-sitosterol-β-D- glucoside, lupeol nanoate, lupeol heptanoate, rubrinol glucoside, plumeiride coumarate, three irroides, fulvoplumierin, allamcin, and allamandin , as well as 2,5-dimethoxy-p-benzoquinone,(2R,3s)-3,4'dihdroxy-7,3',5'-trimethoxyflavan-5-O-β-*D*-glucopyranoside as Flavan3-Ol Glycoside [15]. Scopoletin, β-sitosterol, plumieride, fulvoplumerin, The root contains plumericine, β-dihydroplumericin, isoplumericin, β-dihydroplumericinic acid, fulvoplumerin and plumeride. Rubrinol; an antibacterial tritripenoid. together with teraxasteryl acetate, lupeol, stigmasterol, oleanolic acid had isolated from Bark [16]. The flower of *P .rubra* consist, 1-diethoxyethane, benzaldehyde, geraniol, citral, methylbenzoate, nerolidols, naphathalene, linalool, banzylbenzoate, methyl salicylate [17-19]. *Plumeria alba* bark containing alkaloids, carbohydrates, flavonoids, phenolic compounds and tannins [20]. The plant is reported as medicinal which contains amyrin acetate, mixture of amyrins, ß-sitosterol, scopotetin, the iriddoids isoplumericin, plumieride, plumieride coumerate and plumieride coumerate glucoside [21]. The flower oil mainly consists of primary alcohol, viz. geraniol, citronellol, farnesol and phenyl ethyl alcohol and some linalool. The flowers contain quercetin and kaempferol [22]. Two new and three known iridoids had isolated from the fresh, whole spring leaves of *Plumeria obtusa.* The new iridoids have been characterized as 6''-O-acetylplumieride p-E-coumarate (9) and 6"-0-acetylplumieride -p-Z-coumarate, while the remaining compounds have been identified as plumieride, plumieride p-Z-coumarate and plumieride p-E-coumarate through spectral studies. The oil of *P. obtusa* was found to be rich in benzyl salicylate (45.4%) and benzyl benzoate (17.2%), but also minute concentrations of alkanoic acids [23] (Fig. 5).



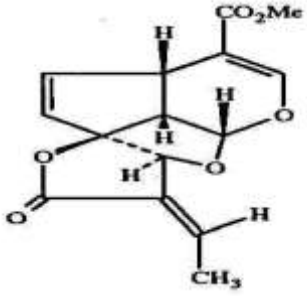
Plumerides



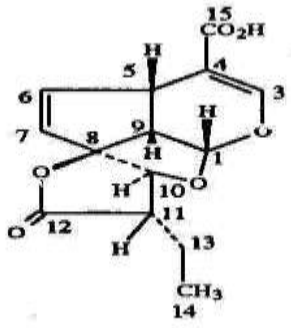
Fulvoplumierin



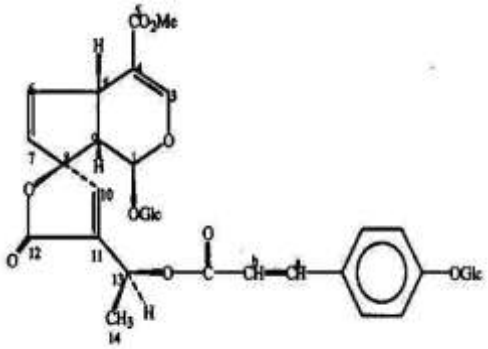
Plumericine



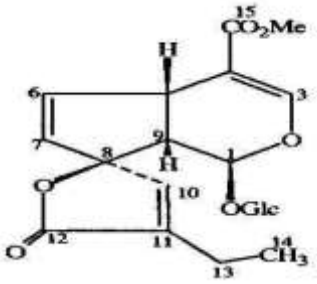
Isoplumericin



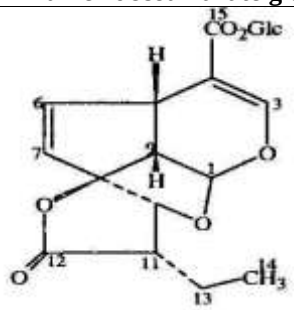
β-dihyroplumericinic acid



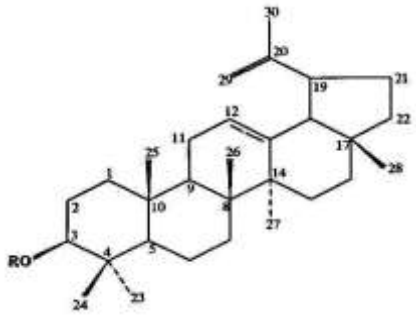
Plumeridecoumarate glucoside



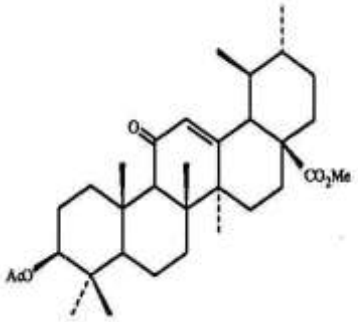
13-deoxyplumieride



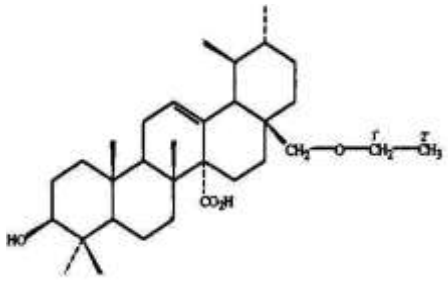
Plumenoside(β-dihyroplumericinic acid glucosylester)



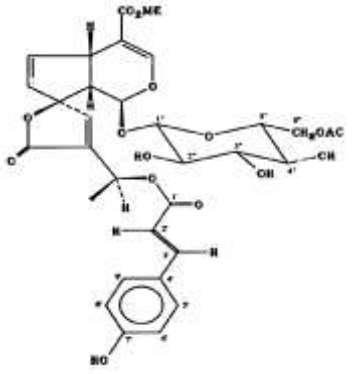
Lupeol fatty ester



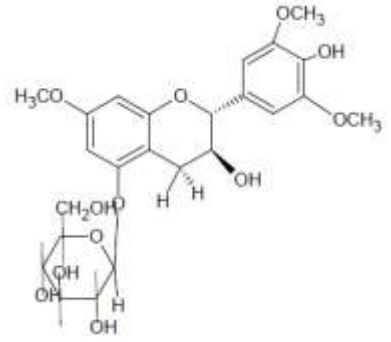
Acetylmethyl obtusilin



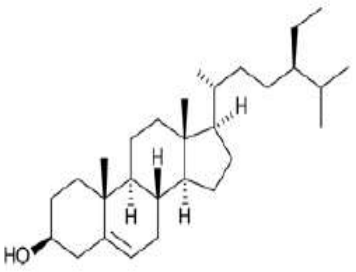
Obtusilinic acid



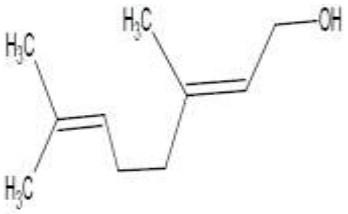
6”-O Acetyl plumieride p-E-coumarate



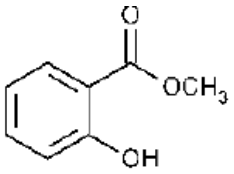
(2R, 3s)-3,4' dihydroxy-7, 3',5'- trimethoxyflavan-5-O-β-D glucopyranoside



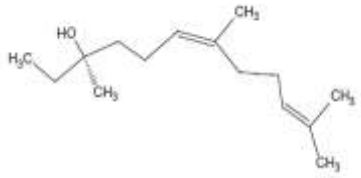
β-sitosterol



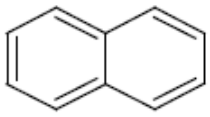
Geranial



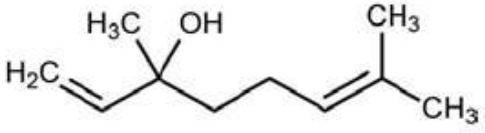
Methyl benzoate



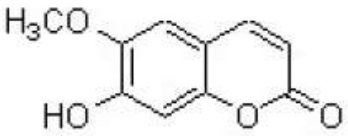
Nerolidols



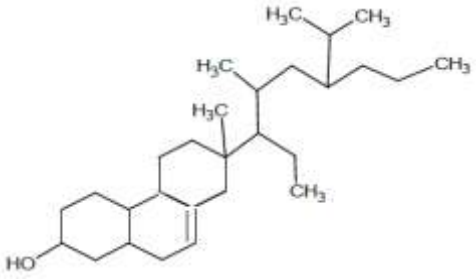
Naphthalene



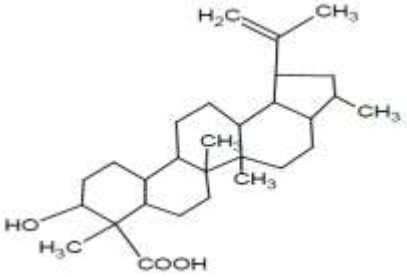
Linalool



Scopoletin



Stigmast-7-enol



Lupeol carboxylic acid

Fig-5: Phytochemical structures of Genus *Plumeria* [24-25]

TRADITIONAL USES

The leaves, bark, flower and oil of *P. acuminata* are used in many countries. Decoction of bark is used as purgative and febrifuge. The material may be taken as cooling tea for prevention for heart stroke.12 to 24 gm of dried material is used as decoction for controlling dysentery & diarrhea during summer season [24]. The latex is mixed with coconut oil warmed and applied to affected area to treat arthritis, rheumatism, pruritic skin lesion. Decoction of the bark is used as counter irritant on the gum for tooth ache. The juice is rubifecient in rheumatic pain [25]. Decoction of leaves is applied for cracks and eruptions of the soles of the feet. Infusion or extract from leaves is used to control asthma [26]. The decoction of the bark and roots of *P. rubra* is traditionally used to treat asthma, constipation, promote menstruation and reduce fever. The latex is used to soothe irritation [27]. The fruit is reported to be eaten in

West Indies. In India, however, it has been used as an abortifacient [28]. The flowers are aromatic and bechic and widely used in pectoral syrups. The flowers decoction of *P. rubra* was reported to use in Mexico for control of diabetes mellitus. The leaves of are used in ulcers, leprosy, inflammations and rubifecient [29]. Different part of the *P. alba* was believed, have been useful in variety of diseases namely the diseases of Malaria, Leprosy, Rheumatism and abdominal tumors. The milky sap of the stem and leaf is applied to skin diseases such as herpes, scabies and ulcers [30, 31]. Its bark is used as plaster over hard tumors, the seeds in hemostasis while the latex is used as purgative, cardiotonic, diuretic and hypotensive [7].

PHARMACOLOGICAL ACTIVITIES

Anti-inflammatory activity

The methanolic extract of *Plumeria acuminata* exhibited significant anti-inflammatory activity on the tested experimental animal models. The extract (500 mg) exhibited maximum anti-inflammatory effect. Carrageenan-induced oedema has been commonly used as an experimental animal model for acute inflammation and is believed to be biphasic. The cotton pellet method is widely used to evaluate the transudative and proliferative components of the chronic inflammation. The results obtained in this study indicated that the methanol extract of *P. acuminata* possess potent anti-inflammatory activity in both acute and chronic models [32].

Antiinflamatory and anthelmintic activity

The saponin extract was used for testing antiinflammatory and anthelmintic activity of *P. rubra* leaves. The anti inflammatory activity was evaluated by determining the reduction in carrageenan induced hind paw edema in albino mice. The result of the maximum dose of 200mg/kg *P. rubra* extract exhibited a significant reduction in the volume of inflammation. The anthelmintic effect of *P. rubra* extract of 25mg/ml concentration is comparable with that of the effect produced by reference standards piperazine citrate on Indian adult earthworms (*Pheretima posthuma*) [33].

Antioxidant activity

The laboratory experimental study on animal models exhibited that the antioxidant activity of methanolic extract of *P. acuminata* (MEPA) increases in a dose dependent manner 50, 100, 200, 300, 400, and 500µg. Like antioxidant activity, the effect of MEPA on reducing power increases in a dose dependent manner. In DPPH radical and nitric oxide radical scavenging assays, MEPA exhibited maximum activity at the concentration of 125µg/ml. The methanol extracts of leaves of *P. acuminata* possesses potent antioxidant and free radical scavenging properties [34].

The Anti-oxidative and proteolytic activities and protein profile of laticifer cells of *Cryptostegia grandiflora*, *Plumeria rubra* and *Euphorbia tirucalli*: Strong antioxidative activity of superoxide dismutase was detected in *P. rubra* and *C. grandiflora* latices, and to a lesser extent ascorbate peroxidase and isoforms of peroxidase were seen. Catalase was detected only in laticifer cells of *C. grandiflora*. Chitinase was the sole activity found in laticifer cells of *E. tirucalli*, but was also detected in the other latices. The strong proteolytic activity of *C. grandiflora* was shown to be shared [35].

The antioxidant and hypolipidemic effect of *Plumeria rubra* L. in alloxan induced hyperglycemic rats: Flavone glycoside isolated from *P. rubra* produced a significant reduction of serum triglycerides in alloxan-induced hyperglycemic rats and Antioxidant activity was confirmed through in vitro studies [36].

Antipyretic / Antinociceptive activity

A single oral administration of methanolic extract of at different doses (100, 250 and 500 mg/kg) showed significant reduction in brewer's yeast induced hyperthermia in rats. MEPA also showed inhibitory effect on acetic acid induced writhing response, hot plate, tail flick, tail immersion responses in mice in the antinociceptive activity. MEPA showed significant decreases in rectal temperature similar to that of paracetamol (100mg/kg). These results suggested that the plant has some influence on prostaglandin biosynthesis because prostaglandin is believed to be regulator of body temperature. The antinociceptive effect of the extract may be due to its anti-inflammatory action in case with salicylates which are particularly effective in relieving the type of pain associated with inflammation. The extract possesses potent antipyretic and antinociceptive properties which are mediated via peripheral and central inhibitory mechanism [37].

The effects of an aqueous extract (FX) of *Plumeira acuminata* (Frangipani) leaves on various isolated tissue preparations were tested. FX relaxed guinea-pig taenia caeci and contracted rat vas deferens. Phentolamine but not propranolol antagonized these responses. FX alone increased spontaneous activity of rabbit ileum. In the presence of atropine, FX decreased spontaneous activity, a response which was antagonized by phentolamine but not by propranolol. FX decreased the force of spontaneous contractions of rat atria. Atropine antagonized this response [38].

Antipyretic effect of ethanolic extract of the leaf of *Plumeria rubra* was investigated. The antipyretic activity exhibited that the ethanol extract of leaf possess a significant antipyretic effect in maintaining normal body temperature and reducing boiled milk induced elevated rectal temperature in rabbits and their effect are comparable to that of standard antipyretic drug aspirin. Such reduction of rectal temperature of tested animals by the extract at 200 mg/kg appears to be due to the presence of a single bioactive principles or mixture of compounds in them [39].

Antimicrobial activity

Methanol extracts of leaves of *Plumeria acuminata* (MEPA) was investigated for their *in vitro* antimicrobial properties by agar disc diffusion method. The methanolic extracts of MEPA inhibited the growth of both Gram positive bacteria (*Bacillus subtilis*, *Staphylococcus aureus* and *Micrococcus luteus*) and Gram negative bacteria (*Escherichia coli, Pseudomonas aeruginosa* and *Salmonella typhimurium*). The Gram positive bacteria tested appeared to be more susceptible to the extracts than the Gram negative bacteria. MEPA was found neutral against *M. luteus*, *E.coli*, *P. aeruginosa* and *S. typhimurium*. It is concluded that the plant possesses potent antimicrobial activity [40].

The Minor secondary metabolic products of the stem bark of *Plumeria rubra* Linn. displaying antimicrobial activities. Four new iridoids viz., plumeridoids A, B, and C and epiplumeridoid C were isolated from the stem bark of *Plumeria rubra* Linn. compounds exhibited antifungal, antialgal, and antibacterial activities [41].

The in vitro antibacterial activity of ethanol, chloroform, ethyl acetate and aqueous extract of leaves of *Plumeria rubra* has been evaluated using disc diffusion method against bacterial strains. The comparative study of extract with specific standard (Ciprofloxacin) showed significant antibacterial activity [42]. The crude ethanolic extract of *Plumeria rubra* showed antioxidant activity and it may possess moderate antimicrobial activity. The antimicrobial activity of *Plumeria rubra* was tested by using the disc diffusion method. The antimicrobial activity was assessed against a panel of 6 pathogenic bacterial strains (both gram positive and gram negative). Leaves extract exhibited significant antibacterial activity against *Salmonella typhe* and moderate activity against *Enterococcus coli*, *Streptococcus saprophyticus* and *Streptococcus agalactin.*

The anti-bacterial and anti-fungal activities of methanolic extract and the isolated fraction of the plant *Plumeria alba* was assessed by standard dilution test using Mueller Hinton agar (MH) medium. The zone of inhibition was compared with that of Standard antibiotic ciprofloxacin (5mg/disc) by disc diffusion method. The Anti fungal activity was assessed by standard dilution technique using Sabouraud dextrose agar medium (SDA). The results are compared with standard Clotrimazole (125mcg/ml). An attempt was made to isolate the fraction responsible for the antimicrobial property of the extract. The methanol extract showed potential anti-bacterial and anti-fungal properties comparable with standard Ciprofloxacin and Clotrimazole respectively against the organism examined. The minimum inhibitory concentration (MIC) of the extract for antibacterial activity was 200mcg/ml. The isolated fraction was also found to possess antimicrobial properties similar to that of the crude extract. The MIC of the fraction was 133.33mcg/ml and the thin layer chromatographic study of the fraction showed it as triterpenes. The study suggests that the plant is promising for development of phytomedicine for antimicrobial properties [43]**.**

Petroleum ether extract of leaves and flower exhibited significant activity against blue green molds and *P. digitatum* which was isolated from *Citrus sinesis* (sweet orange).Phytochemical analysis suggests the presence of biologically active compounds in the petroleum extracts of the sample could be correlated to antifungal activities [44].

Essential oils from flowers of *Plumeria alba* were tested against set of microorganisms in order to estimate their antimicrobial potentials. Result shows that Gram negative bacteria appear to be least sensitive to the action of many other plants essential oils. The volatile oils of *P. alba* flower part were more active against *S. aureus* and *B. subtilis* presenting an important growth inhibition at lower concentrations [45].

MIC values of the essential oil of the flower of *Plumeria alba* Linn. against various tested fungal pathogens. Essential oil is highly active against *Aspergillus niger*, *Candida albicans* and *Penicillium chrysogenum*. Whereas, it is moderately effective against *Candida albicans* and *Phaenorochaete chrysporium.* The essential oil is found to be very less active against *Ralstonia entropha*. The observation suggests that antifungal principles in the essential oil have a broad spectrum of activity which is quite comparable with that of griseofulvin [46].

Antibacterial activity of *Plumeria alba* (Frangipani) petals methanolic extracts were evaluated against *Escherichia coli, Proteus vulgaris ,Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus saprophyticus, Enterococcus faecalis* and *Serratia marcescens* by using disk diffusion method. Frangipani extract also showed high antibacterial activity *against Staphylococcus saprophyticus, Proteus vulgaris* and *Serratia marcescens*, but not more than the zones of the positive control used. Frangipani extracts showed no bacterial activity towards *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Enterococcus faecalis*. *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[47].

Ethanolic extract of *Plumeria acutifolia* Poir. (Apocynaceae) stem bark was tested for antimicrobial activity against Gram-positive bacteria (*Bacillus subtilis, Enterococcus faecalis, Staphylococcus aureus*), Gram-negative bacteria (*Escherichia coli, Klebsiella Pnumoniae, Psuedomonas aeruginosa, Salmonella*

typhimurium) and fungi (*Aspergillus niger* and *candida albicans*) by disc diffusion method. The ethanol extract showed the strong *in vitro* antimicrobial activity against *E. faecalis, B. subtilis, S. aureus, P. aeruginosa, S. typhimurium, A. niger* and *C. albicans* [48].

Mutagenic activity

The ethanolic extract of the green leaves of showed ant mutagenic activity. Four isolates A1, C1, D3, and F2 from the bioactive hexane and carbon tetrachloride fraction of the ethanolic extract of leaves of *Plumeria acuminata*. The structure elucidation studies indicated that C1 was stigmast-7-enol, D3 was lupeol carboxylic acid and F2 was ursolic acid. The structure of A1 not fully elucidated but MS data suggested that it contained a long hydrocarbon chain. These fractions were proved to possess ant mutagenic effect [49].

Toxicity study

The chronic toxicity of methanolic extract of *P. acuminata* was studied by single the long-term oral administration in mice at the doses of 100 and 250 mg/kg did not alter the hematological parameters, liver and kidney functions significantly. The results of chronic toxicity showed no abnormalities in the test groups as compared to the controls. Hematological and blood chemical values in treated groups were normal in comparison with the control group. Non-toxicity effects of MEPA were present as no changes in body weight, internal organ weight, and general behaviors. Macroscopic or microscopic of internal organs or tissues in treated rats showed no changes. MEPA at the doses of 100 and 250 mg/kg did not alter the hematological parameters, liver and kidney functions significantly [50].

Antitumor activity

The cytotoxic constituents of the bark of *Plumeria rubra* collected in Indonesia. Three iridoids (fulvoplumierin, allamcin and allamandin) and 2,5-dimethoxy-*p*-benzoquinone were active constituents of the petroleum-ether- and $CHCl_3$- soluble extracts whereas the iridoid plumericin and the lignan liriodendrin were isolated from the aqueous extract of the bark which showed cytotoxic effect [51].

The ethanolic extract of leaves of *Plumeria rubra (Linn)* were evaluated for their anti cancer activity against Ehrlich Ascites Carcinoma (EAC) in Swiss albino mice. The extract of *Plumeria rubra (Linn)* at the dose of 200 mg/kg body and 400 mg/kg body weight were administered orally. Anti tumor efficacy of plant extracts were compared with 5-Fluorouracil (20 mg/kg/day i.p) for 9 days. The anticancer activity of *Plumeria rubra* (Linn) was examined by determining the tumor volume, tumor cell count, viable tumor cell count, non viable tumor cell count, mean survival time and increase in life span in experimental animal models. Ethanolic extract of *Plumeria rubra* increased the life span of EAC treated mice and restored the hematological parameters as compared with the EAC bearing mice. increase in packed tumor cell volume, and number of viable tumor cells were found to be significantly less than the tumor control animals, mean while increase significantly in non viable tumor cell count, indicating the anticancer nature of the extracts. The reversal of Hb content, RBC, WBC and differential count of WBC by the ethanol extract treatment towards the normal values clearly indicates that ethanol extract of leaves of *Plumeria rubra* possessed protective action on the haemopoietic system [52].

Methanolic extract of *P. alba* leaves possesses significant antitumor activity against dalton lymphoma ascites in mice result shows that methanolic extract of *P. alba* can significantly prolong the life span, reduce tumour volume and improve the hematological parameters of the host (mice) [53].

Abortifacient activity

The aqueous, ethanol, chloroform and ethyl acetate extract Pods of *P. rubra* shows abortifacient potential in female albino rats. The extracts significantly reduced the number of live fetuses during post- implantation period, whereas the resorption index and post implantation losses increased significantly. The presences of alkaloids, phenolic, steroids and saponins in the extract of pods, which act either alone or in combination, may be partly responsible for observed pregnancy terminating effects in present study [54].

The effect of ethanol extracts of *Mitragyna parvifolia* bark (EEMP), *Plumeria rubra* flowers (EEPR), and *Zizyphus xylopyrus* fruits (EEZX) at two different dose levels were studied on the onset of reproductive maturity and the ovarian steroidogenesis on bred albino female mice. All three plants caused remarkably ($P<0.01$) a dose-dependent delay in sexual maturation in as evidenced by the age at vaginal opening and appearance of first estrus. The depressed ovarian steroidogenic activity and hypo functioning of the gland was evident by increase in ascorbic acid level after treatment with extracts of selected plants. In the present study, tested extracts inhibited the activity of two key steroidogenic enzymes significantly when compared with control groups. Therefore, in the present investigation a fall of G-6-PDH and Δ5-3β-HSD after treatment with EEMP, EEPR, and EEZX suggests a diminution of ovarian steroidogenesis and which may be the possible mechanism of action of this these plants in reducing fertility [55].

Antiulcer activity

The chloroform and ethanolic extract of *P .rubra* leaves shows antiulcer activity in albino rats. In pylorus ligation induced ulcer model various parameters were studied. The EEPR and CEPR are significantly capable of increasing mucous secretion. The significant effectiveness of extract in protecting against mucosal damage caused by alcohol is an indication of its effect

on prostaglandin synthesis and on the free radical scavenging activity. Thus it could be assumed that the existence of cytoprotective effect of compound present in ethanol and chloroform extract of *Plumeria rubra* because it showed the significantly less ulcer index in the observation when compared with control group[56].

The stem bark of *Plumeria obtusa* showed antiulcer effect by ulcer induced pylorus ligation. The methanolic extract stem bark and pantaprazole showed a significant reduction in pH, free acidity, ulcer index and percent protection compared to control this is suggested that it is having antisecretory effect. This study suggested that antiulcer effects due to reduction in gastric acid and gastric cytoprotection. The plant extract heal Indomethacin induced stomach ulceration by their triterpenoids action and inhibition was observed 62.26%, 33.96% and 54.72% in the animal treated with MEPO 250 mg/kg, MEPO 500 mg/kg and standard drug respectively[57].

Analgesic activity

Analgesic activity of *Plumeria rubra* was tested by acetic acid induced writhing model in mice. The extract produced significant writhing inhibition at the dose of 500mg/kg-body weight. Ethanolic extracts may possess centrally- and peripherally-mediated analgesic properties. The peripheral analgesic effect of the plant's extract may be mediated via inhibition of cyclooxygenases and/or lipoxygenases (and other inflammatory mediators), while the central analgesic action of the extract may be mediated through inhibition of central pain receptors. The crude extract of experimental plant showed analgesic activity [33].

Larvicidal activity

Leaves extract of *P .alba* found (LC50 218.8 ppm) against *Aedes aegypti* mosquitoes [58].

Hepatoprotective activity

Hepatoprotective activity of *Plumeria alba* extract against paracetamol induced-hepatotoxicity in rats. The methanol extract (MLE) at different doses (100, 200 and 400 mg/kg) of the plant *Plumeria alba* Lam. syn. *Plumeria acutifolia*. Poir were tested for its efficacy against paracetamol induced acute hepatic damage in Wistar rats. Methanolic extract of *Plumeria alba* did not produce any toxic symptoms or mortality upto the dose level of 2000 mg/kg body weight in mice, and hence the extract was considered to be safe and non-toxic for further pharmacological screening. biochemical parameters i.e. GOT, GPT, ALP and GGT after administration of the given dose of Pcml. The concurrent treatment of MLE (400 mg/Kg) significantly decreased ($P<0.05$) the elevation of enzymes by the toxin and thus provide satisfactory hepatoprotection in a dose dependent manner which was comparable to the effect of the reference drug Silymarin. Histological studies also provided supportive evidence for the biochemical analysis. Normal control group showed a normal liver architecture, hepatocytes very well arranged, central vein without alterations [59].

CONCLUSION

The literature survey revealed that the various species of *Plumeria* is an important source of many pharmacologically and medicinally important chemicals such as plumeride, isoplumeride, fluvoplumericin, irriod glycoside and other various minor secondary metabolites. Study of pharmacological activities with different extracts obtained from different parts of the plant with different in vitro and in vivo model, which show that the compounds have beneficial effects against a number of diseases. The plant has been widely studied for its pharmacological activities and regarded as universal panacea in Ayurvedic medicines and find its position as a versatile plant having a wide spectrum of medicinal activities. As the global scenario is now changing towards the use of non toxic plant products, development of modern drugs from *Plumeria* species should be emphasized. Clinical trials should be conducted to support its therapeutic use. It is also important to recognize that its extracts may be effective not only isolation, but may actually have a modulating effect when given in combination with others.

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