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Review

PLUMERIA OBTUSA PHYTOCHEMISTRY AND PHARMACOLOGY: INSIGHTS INTO POTENTIAL THERAPEUTIC TARGETS

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Abstract:
Plumeria obtusa, a plant belonging to the Apocynaceae family, has attracted a lot of interest lately because of its rich phytochemical profile and variety of pharmacological effects. This review sheds light on Plumeria obtusa's possible therapeutic targets by offering insights into the phytochemistry and pharmacology of the plant. Numerous bioactive substances have been found and classified after being separated from various plant sections. These include flavonoids, iridoids, and pentacyclic triterpenoids. Numerous pharmacological activities, such as anti-inflammatory, antioxidant, antipyretic, antinociceptive, anticancer, and antiviral effects, are shown by these substances. Furthermore, Plumeria obtusa has been historically utilized in many cultures to cure a wide range of illnesses, such as cancer, fever, and skin conditions. The results of phytochemical and pharmacological investigations demonstrate Plumeria obtusa's medicinal potential and stress the need for further investigation to completely understand its modes of action and possible clinical uses.

Keywords: *Plumeria obtuse, Phytochemistry, Pharmacology, Therapeutic targets, Bioactive compounds, Traditional medicine*

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1. INTRODUCTION

Ayurveda, which is an old traditional Indian medical practice, is considered to be one of the most important complementary and alternative medicine systems. Throughout the course of recent years, there has been a significant expansion in the quantity of individuals keen on medicinal plants. In any case, westerners have likewise given this matter a lot of worry by dealing with various examinations that incorporate the utilization of drugs that are gotten from plants.

In the old Indian medicinal framework, plumeria species are in many cases utilized as a laxative, a medicine for looseness of the bowels, a treatment for tingle, bronchitis, hack, asthma, fever, dying, heaps, diarrhea, blood issues, and growths [1]. Plumeria species are likewise utilized as a laxative.

Tropical America is the natural territory of Plumeria L. It is feasible to find individuals from the Apocynaceae family anyplace from southern Mexico to northern South America, with India being the essential objective for their dispersal [2]. Then again, because of the simplicity with which it very well might be proliferated by cuttings, different species and half and halves of Plumeria are presently broadly developed and scattered over the hotter districts of the world [3].

The plumeria, which is often considered to be the most famous tropical flower, is sometimes referred to as frangipani in India. Although it is most often known as "kemboja" in Malaysia, other names for it, such as "pokok kubur" and "bunga kubur," have also been used to refer to a number of other species and hybrids of Plumeria. Plumeria acutifolia Poir was the variety of the tree that was first recognized by Burkill. There are at least three

primary species of the tree that are extensively dispersed in Malaysia, where they were introduced. once known as P. obtusa, P. rubra, and P. acuminata; however, this was eventually changed to P. ruhra (arma acutifolia (Poir.) [5]".

- **Domain:** Eukaryota
- **Kingdom:** Plantae
- **Subkingdom:** Viridaeplantae
- **Phylum:** Magnoliophyta
- **Subphylum:** Euphyllophytina
- **Infraphylum:** Radiatopses
- **Class:** Magnoliopsida
- **Subclass:** Lamiidae
- **Superorder:** Gentiananae
- **Order:** Apocynales
- **Family:** Apocynaceae
- **Genus:** Plumeria

In the old Indian medicinal framework, plumeria species are in many cases utilized as a The leaves of Plumeria obusta are polished, dull green, obovate, and obuste at the two closures. The white sprouts have a little, dazzling yellow community and may compare 9 cm in width. Trees might arrive at levels of 6 to 9 meters and show fractional deciduousness relying upon the season.

Then again, plumeria sharpen is an evergreen or somewhat deciduous tree that develops to a level of 6 cm. Its leaves have an elliptic structure with sharpen closes, and their variety might go from white to yellow [6].

All species are little trees that give a smooth liquid when their leaves or branches are cleaved. They have very thick, substantial, tough branches. The natural products are a couple of round and hollow, horn-molded natural products with various level seeds that are momentarily winged toward one side, and the leaves are spirally organized toward the finishes of the expanding branches. The blossoms of frangipani are large, fragrant, waxy, and organized in terminal or horizontal followed groups. The leaves are regularly green [7].

Conversely, Plumeria rubra has sprouts in an assortment of red, pink, orange, and yellow tints, as well as leaves that arrive in a variety of sizes, shapes, and tones [8]. This species is a deciduous tree that might develop to a level of north of 10 m in tropical districts however is probably not going to develop to a level of multiple m in subtropical locales [9].

It is said that the Spanish acquainted plumerias with the Far East, as improving trees as well as for their therapeutic characteristics. Native medicinal practices in Java and Madoera utilize a leaf decoction as a moisturizer for foot breaks and ejections, and a bark decoction for gonorrhea, dropsy, and physically communicated diseases. The smooth plastic and bark decoction are said to have laxative, emmenagogic, febrifugic, and diuretic impacts in the Philippine Islands and the West Indies. The plant is utilized in India to treat fevers, dispersed dropsies, skin conditions, and even ague [2].

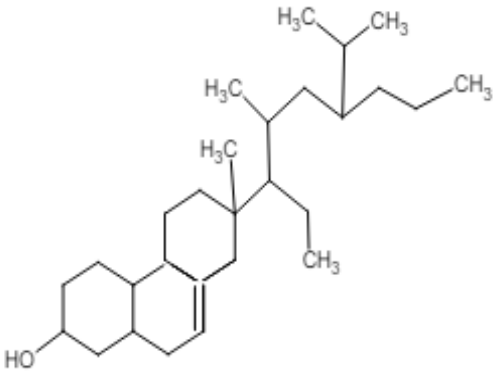
2. PHYTOCHEMISTRY

Preliminary phytochemical screening: -

A careful assessment of substances including steroids, alkaloids, glycosides, terpenoids, decreasing sugars, tannins, carbonyls, flavonoids, phlobatannins, and carbonylated synthetic compounds was important for the investigation into the sub-atomic cosmetics of various plumeria species. The goal of this investigation was to uncover these plants' shifted biochemical structure.

The investigation of plumeria phytochemistry traces all the way back to 1870, when Peckolt and Boorsma made significant revelations. Plumieride, a significant iridoid glucoside, was detached and detailed by them independently from the stem bark of two distinct types of plumeria, P. rubra and P. lancifolia, separately. This critical accomplishment set up for additional examination into the pharmacological and therapeutic capability of these Plumeria class synthetic compounds. [10].

The leaves of Plumeria acuminata were extracted with ethanol, and the phytochemical components Lupeol acetate (3), Stigmast-7-enol (1), Lupeol carboxylic acid (2), and Urosolic acid (4) were identified. These chemicals have also shown remarkable anti-mutagenic properties [11].



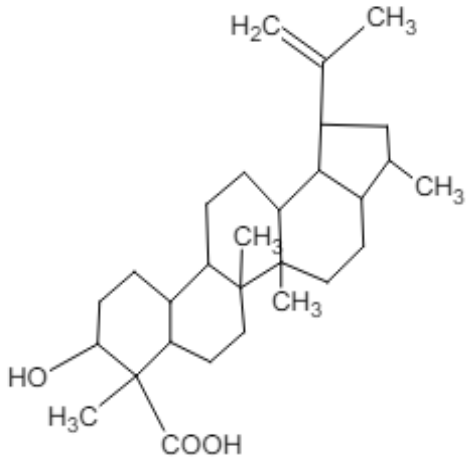
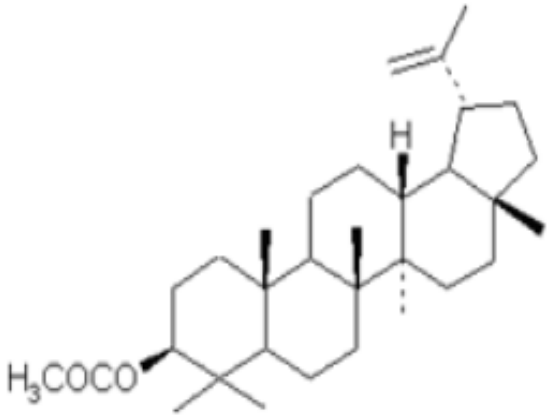


Fig 1 & 2: Lupeol carboxylic acid & Stigmast-7-enol



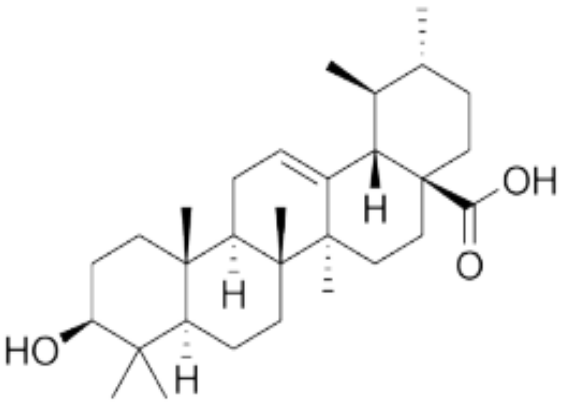


Fig 3 &4: Ursolic Acid & Lupeol Acetate

The ferulic acid derivatives 34-hydroxy tetratriacontanyl ferulate(5) and 34-O-acetyl tetratriacontanyl ferulate[6], the plumericin(7) and isoplumericin, were isolated from Plumeria bicolor stem bark (8) [12].

3. PHARMACOLGICAL ACTIVITY

1) Anti-inflammatory activity

In rat hind paw oedema models, inflammation caused by carrageenan, dextran, histamine, and serotonin is significantly reduced by a methanolic extract of Plumeia acuminata leaves.

The concentrated on exploratory creature models show imperative mitigating activity because of methanolic extricate, as per the outcomes. Following three hours, the concentrate showed the most mitigating impacts with carrageenan, dextran, receptor, and serotonin, separately. The administration of indomethacin significantly reduced the improvement of granuloma tissue created by the cotton pellet technique, at a rate of 51.57% and 45.06 percent, respectively [13].

2) Hypolipidemic, antioxidant, and free radical scavenging properties

Areas of strength for Plumeria acuminata methanolic separate have and free revolutionary rummaging agents. The results show that the various concentrations of Methanolic extract at 50, 100, 200, 300, 400, and 500 µg mL-1 had a portion-subordinate effect as a cancer preventive agent and individually inhibited lipid peroxidation of the linoleic acid framework by 46.01, 52.83, 57.43, 61.38, 68.27, and 73.14%. With 500 µg mL-1 of α-tocopherol, an 81.21 percent obstruction was seen simultaneously [14].

Plumeria rubra flavone glycoside has hypolipidemic and antioxidant properties. Comparing the hyperglycemic control mice with those that received an alloxan injection, the flavone glycoside

therapy resulted in a considerable decrease in serum triglyceride levels but no discernible change in blood glucose or serum total cholesterol [15].

2) Antipyretic and Antinociceptive Activity

Rodents that were given a solitary oral measurements of Methanolic extricate at 100, 250, and 500 mg kg-1 showed a critical decline in the hyperthermia brought about by brewer's yeast. In the antinociceptive test, mice's acidic corrosive actuated squirming response, hot plate, tail flick, and tail submersion reactions were all uniquely restrained by the methanolic extricate concentrate of Plumeria acuminata [16].

3) Antitumour and antcancer activity

The outcomes show that methanolic concentrate of Plumeria alba leaves serious areas of strength for has action against mice with dalton lymphoma ascites. It can likewise extensively build the host's future, decline the size of the growth, and improve its haemotological boundaries 17]

4) Antiviral activity

Reversing trancriptase of the human immunodeficiency virus type 1 (HIV) is inhibited by plueria rubra that contains fulvoplumierin [18].

Table 1: investigations on the pharmacological properties of plants belonging to the genus Plumeria

Scientist	**Contribution**	**Reference**
Garcia et. al. (2022)	According to research done on P. alba bark, 2% of the substance is non-toxic, non-irritating to the conjunctiva, and has no impact on breathing or circulation, even when administered intravenously. The glycoside is inefficient against genous Staphylococcus bacteria and has no direct impact on isolated uterine muscles. In humans, its purgative effects have been verified. More than 300 mg of it is linked to diuresis and purgation.	[19]
Hall and coworkers (2021)	It has been reported that high quantities of plumericin are bactericidal.	[20]
Little et. al. (2021)	shown that the activity of plumericin in fungus is somewhat higher than in bacteria.Micobacterium tuberculosis is inhibited by it.	[21]
Siddiquiet. al. (2020)	shared the results of a pharmacological investigation on P. acutifolia leaves. The water-soluble component had a potent relaxant effect on the smooth muscles of the separated guinea pidilium and rabbit duodenum. Additionally, it inhibited the oxytocin and acetylcholine-induced uterine contraction response and calmed the isolated rat uterus.	[22]

4. CHEMICAL CONSTITUENTS

The first physiologically significant substances to be identified from the Plumeria species were iridoid glycosides. Later, it was discovered that some of these species' latex and oil included other physiologically significant components such sterols, sugars, tannins, triterpenoids, and alkaloids. Subsequently, similar components were extracted in different concentrations from other extracts of the roots and several other plant sections. Here is a quick overview of some of the Plumeria species' bioactive chemical components:

1.1. Plumeria rubra: - Amyrin, fulvoplumierin, β-sitosterol, lupeol, plumieride, unpleasant glycosides, and plumeric corrosive. The plant's bark contains plumericin, isoplumericin, 4-hydroxy acetophenone, plumieride, coumarylplumieride, and protoplumericine. Natural balms are tracked down in blossoms. Fulvoplumierin, plumericin, and three newfound compounds — isoplumericin, β-dihydroplumericin, and βdihydroplumericinic corrosive — are completely tracked down in roots.

1.2. Plumeria alba:- Plumeria alba contains various bioactive parts, including triterpenoids, sterols, polysaccharides, tannins, and iridoid glycosides. Stems, flavonoids, and alkaloids have all been viewed as present in the plant's elevated parts [24]. A blend of amyrins, ß sitosterolscopotein, iriddoidsisoplumericin, plumeride, plumeridecoumerate, and plumeridecoumerateglucoside have been viewed as present in the plant [25] [26]. Rainieride, resinic corrosive, and fulvoplumierin — a mixture of terpenoids, sterols, and plumieride — are available in the new leaves and bark [23].

1.3. Plumeria acuminata: - Dynamic fixings like as tannins, alkaloids, steroids, flavanoids, and glycosides are found in plumeria taper [27]. While maintaining a phytochemical focus on the Plumeria family. The

chemicals stigmast-7-enol, lupeol carboxylic acid derivative, ursolic acid, and lupeol were isolated using leaf testing. The following chemicals have been isolated from Plumeria acuminata by Peckolt and Boorsma: isoplumericin, β-dihydroplumericin, and β-dihydroplumericinic acid, in addition to Fulvoplummierin and Plumericin. A little amount of aldehyde and ketones (6.8%), together with essential alcohols, citronellol, farnesol, phenylethyl liquor, and geraniol and citronellol, make up the medicinal balm (0.04-0.07%) obtained from the steam distillation of Plumeria acuminata. These oils have a saponification value of 123 and a corrosive value of 20.2. [28] [29].

1.4. Plumeria obtuse: - There has been no current reporting from this source on these findings. New, complete spring leaves of P. obtusa have produced two new iridoids and three more that have been observed. 6"-Oacetylplumieride p-E-coumarate is how the new iridoids are shown [30] [31]. Plummieride, plumieride p-Z-coumarate, and plumieride p-E-coumarate are the remaining synthetics, together with 6-0-acetylplumieride - p-Z-coumarate [32].

5. SOME RECENT PHARMACOLOGICAL ACTIVITIES

Stiffness, loose bowels, blennorhea, venereal illness, uncleanliness, psychosis, and diuresis are only a few of the many ailments that have found relief via the use of different Plumeria animal species. Researchers have also looked at plumeria species for irridoids and triterpenoids, which are known to have cytotoxic, antibacterial, and algicidal effects.

5.1 Anti-inflammatory activity

Plumeria acuminata methanolic extricate showed impressive calming impact on carrageenan-actuated edema in both intense and persistent test creature models (45). This peculiarity was seen in both the intense and ongoing models.

Utilizing the CH3)2CO precipitation method, a protease known as Plumerin-R was extricated from the plastic of the plant P.rubra. The calming adequacy of this protease was examined utilizing carrageenan-prompted paw edema in rodents. The abatement in carrageenan-prompted rodent paw edema by 20, 40, and 80 mg/kg body weight of Plumerin-R was 21.6, 33.8, and 48.8% correspondingly [36] [37]. This decrease happened four hours after treatment. In another examination, the saponin concentrate of P. rubra showed an extensive diminishing in how much irritation that was available in the paws of rodents.

It was concentrated on whether or whether the lupine alkaloid Plumerianine, which was detached from the root bark of P. acutifolia, has mitigating properties against the carrageenan-actuated edema and cotton pellet granuloma in pale skinned person rodents. The beginning stage and late stage provocative action might be liable for the noticed measurements subordinate calming reaction [38]. This response was demonstrated to be portion subordinate.

5.2 Antibacterial activity

The antimicrobial characteristics of the methanolic extract from P. sharper leaves were concentrated using the agar circle dispersion technique. Some of the gram-positive bacteria that the concentrate killed were Bacillus subtilis, Staphylococcus aureus, and micrococcus luteus [39]. Bacillus subtilis, Salmonella typhimurium, Pseudomonas aeruginosa, and Escherichia coli were among the gram-negative microbes.

The medicinal balms that were extricated from the blossoms of three unique types of Plumeria situated in Malaysia, specifically P. rubra L., P. acutifolia Poir, and P. obtusa L., were exposed to GC/MS examination, which brought about the ID of 27 unique parts. The plant P. rubra yielded seven parts that were secluded and recognized, while P. obtusa yielded fourteen parts, and P. acutifolia yielded nineteen parts. The two alkane hydrocarbons, nanodecane and heneicosane, as well as the 2-hydroxybenzoic corrosive phenylmethyl ester, are the essential parts that are available in each of the three structures. As per the agar dispersion technique, the antimicrobial properties of the natural oils were assessed by utilizing eight distinct kinds of microorganisms. These microorganisms included Escherichia coli, which is a Gram-negative microbes, Microscopic Gram-positive bacteria Staphylococcus aureus and Bacillus cereus, yeasts Candida albicans and C. humicola, and growths Trichophyton mentagrophytes, T. rubrum, and Microsporum canis. The presence of P. obtusa medicinal oil was determined to indicate broad range restraint. The concentrate inhibited the growth of all tested bacteria except E. coli. The highest inhibitory zone against C. humicola was seen in P. obtusa natural ointment [40]. This persisted throughout the evaluation. Also, it inhibited the growth of Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus marcescens to the greatest extent possible (91.53, 92.84, 94.69%, and 85.29 percent,

respectively) [41]. Medicinal ointment with broad-spectrum antibiotic action was developed by hydrodistilling airborne P. albaby segments using clavenger gear [42].

5.3 Antioxidant properties

To decide the cell reinforcement and hypolipidemic qualities of the flavone glycoside that was separated from P.rubra L., a diabetes model that was created by alloxan was utilized in rodents. Fatty oil levels in the blood were displayed to have fundamentally diminished because of the treatment, though glucose and cholesterol levels in the serum stayed unaltered. It was additionally shown that the prescription had cell reinforcement properties by means of the utilization of in vitro tests [43]. Moreover, the cancer prevention agent movement of the methanolic concentrate of Plumeria taper was explored in various examination, and the outcomes showed that the cell reinforcement action was measurement subordinate [44].

5.4 **Antipyretic Activity**

There was an examination on the antipyretic viability of an ethanolic concentrate of the leaf of P.rubra, which was led on creatures. The infusion of cooked milk through the intraperitoneal course at a dose of 0.5 milliliters per kilogram of body weight was utilized to deliver pyrexia in pale skinned person hares. Ensuing intraperitoneal infusion of an ethanolic concentrate of the leaf of P.rubra at a grouping of 200 mg/kg body weight brought about an extensive decrease in the raised internal heat level of the bunny. When contrasted with the results of the regular enemy of pyretic prescription anti-inflamatory medicine [45], the outcomes were comparable.

One more examination concentrate on that was led fully intent on analyzing the issue zeroed in on the antipyretic and antinociceptive properties of the substance. An extra exploration was embraced to investigate the antipyretic and antinociceptive properties of methanol concentrate of P.acuminata leaves utilizing various different exploratory models. At the point when rodents were given a solitary oral measurements of P.acuminata leaves separate at different portions (100, 250, and 500 mg kg-1), there was an impressive lessening in the hyperthermia that was created by brewer's yeast [46].

5.5 Antitumor activity

Following the seclusion of against growth compounds, specifically plumeric corrosive and methyl plumerate, from the leaves of P. accutifolia, the counter cancer action of Plumeria became found. An endophytic growth called Colletotrichum gloeosporioides was disconnected from P. acutifolia in 2009. This growth was displayed to create a diterpenoid synthetic called taxol, which is known to show anticancer impacts [47]. Moreover, the anticancer properties of the methanolic concentrate of P. alba leaves were analyzed involving in-vitro cytotoxicity and mean endurance time. The outcomes showed a decrease in the volume of the cancer as well as the quantity of reasonable cells in the DLA growth has. Following the organization of MPA to growth bearing mice, the creatures were accounted for to give indications of progress in their hematological boundaries. Also, it was noticed that the concentrate showed cytotoxicity in the in-vitro model. The concentrate showed its adequacy by prompting an expansion in the endurance time, the quantity of dead cells, hematological boundaries, and the greater part of the strong growth was additionally decisively diminished [48].

5.6 Gastroprotective activity

By involving pylorus ligation and indomethacin as models, the methanolic concentrate of Plumeria obtusa from the stem bark was inspected to decide if it has gastroprotective properties. The concentrate showed activity because of a diminishing in how much stomach corrosive discharge, gastric cytoprotection, and a system that successfully restrains the proton siphon [49]. The conventions of ulcer brought about by non-steroidal calming prescriptions, ethanol, and pylorus ligation were used to examine the antiulcerogenic properties of hydroalcoholic concentrate and parts got from the leaves of Plumeria alba L. In the indomethacin-prompted ulcer model, the hydroalcohol extricate (at portions of 200 and 400 mg/kg), the ethyl acetic acid derivation part, and the n-butanol division (at dosages of 100 and 200 mg/kg, orally) all shown a mending impact on the stomach ulcer. Both EAPA and BPA had a gastric cytroprotective impact in rodents with a pylorus ligation, and they likewise stifled gastric discharge in rodents with a gastric ulcer that was created by ethanol [50].

5.7 Miscellaneous

The bark of P. rubra contains Fulvoplumericin, which has becteriostatic, cardiotonic, and neighborhood sedative properties, separately [51]. Ursolic corrosive, which is gotten from the leaves, plumeric corrosive, which is gotten from the plastic and leaves, and fulvoplumericin all have these properties. P.rubra that contains fulvoplumierin has been displayed to hinder the compound revereasetranscriptase, which is delivered by the human immunodeficiency infection type 1 (92). Hepatoprotective impact was shown by the methylic concentrate of P.

alba against the liver harm that was produced by paracetamol [53]. Utilizing 96 well miniature titerplates, the counter parasitic movement of chloroform concentrate of P. bicolor, plumericin, and isoplumericin was considered in contrast to the promastigote and amastigote types of Leishmaniadonovani. The outcomes showed that the concentrate displayed movement, with the IC50 upsides of 21±2.2 and 14±1.6 μg/ml, individually. Plumericin had a huge degree of action, separately, against the promastigote and amastigote structures, individually [54]. Amelia P. what's more, partners directed an alternate examination in which they detached four different separates from the ethanolic concentrate of the green leaves of P.acuminata. These detaches included stigmast-7-enol lupeol carboxylic corrosive, ursolic corrosive, and two extra compounds whose designs were not totally made sense of. These four confines displayed enemy of mutagenic activity [55]. It was as of late found that the iridoid plumieride50, which was disengaged from P. bicolor, had antifertility activity [56].

Table 2: Plumerias phytoconstituents: an analysis of their pharmacological action

Phytoconstituents	**Pharmacological activity**	**Species**	**Part used**
The following substances are present: octanoic acid, 3-β-hydroxy-27-12 hours, and obstructin, which is (Z)-p-coumaryloxy. Obtusinidin, 27-[p-(E)-Coumaroyloxy] Obtusinin, Obtusilin (¼ 3b-hydroxy-11-oxours-12-en-28-oic acid), ursolic acid all belong to the same family of compounds. One stem, 12,20(22)-dien (3 β,20Z)-Dammara-12,20(22), and Dammara (20Z) are all related.trimethylbenzoic acid The foliage"Oleanolic acid," "Olean-12-ene-3," and "27-hydroxyolean-12-en-3-one" (¼champalinone) are the components. Obtusic acid and oleanonic acid found in leaves	Therapy for excessively proliferative tissue	P. obtusa	Leaves, Stem and Bark
(Kanerosid, Neriucoumaric acid, Obtusilinin, Oleandrin, Obtusol, and 3β)-3,27-Dihydroxylup-29-ene	antimicrobial action	P. obtusa	Leaves, Stem and Bark
(6a) 3α)-3,27-Dihydroxyolean-12-eneThree-epi-hydroxy-6-oleanolic acid	-	P.rubra	Bark
Rubrinol	-	P.rubra	Leaves, Stem and Bark

6. CONCLUSION

There is reason to believe that Plumeria obtusa might be a promising option for the development of novel therapeutic molecules [33]. The potential of this substance as a disease-treating agent is highlighted by the extensive pharmacological activity and the large variety of bioactive compounds that it contains. The fact that Plumeria obtusa has been used historically in a variety of different cultures lends more support to the herb's efficacy and safety. Even if the findings have been promising, further research is still required in order to fully appreciate the mechanisms that are responsible for its pharmacological activities, as well as to evaluate its safety and efficacy in clinical settings [34], [35]. As a result of future study into the molecular targets and synergistic interactions among its bioactive constituents, the door will be opened for the development of standardized herbal formulations or medications manufactured from Plumeria obtusa for the treatment of human illnesses.

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