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Review Article

Comprehensive Analysis of the Genus *Plumeria*: Phytochemistry, Traditional Uses, and Therapeutic Potential

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ABSTRACT

Natural products remain an important source of therapeutic agents due to their chemical diversity and biological activity. The genus *Plumeria* (Apocynaceae), widely distributed in tropical regions, is traditionally used for the management of inflammatory, infectious, and metabolic disorders. This review summarizes and critically evaluates current knowledge on the taxonomy, ethnomedicinal uses, phytochemistry, pharmacological activities, and safety profile of *Plumeria* species. Phytochemical investigations reveal the presence of iridoid glycosides, triterpenoids, flavonoids, sterols, and volatile compounds, which are associated with antioxidant, anti-inflammatory, antimicrobial, antidiabetic, and cytotoxic activities. Most pharmacological evidence is derived from in vitro and in vivo studies, with limited clinical validation. Mechanistic insights indicate modulation of oxidative stress and inflammatory pathways. Toxicological data suggest that leaf extracts are relatively safe, whereas latex and bark may exhibit irritant and cytotoxic effects. Pharmacokinetic information remains scarce. Overall, *Plumeria* species show significant therapeutic potential; however, further studies focusing on molecular mechanisms, pharmacokinetics, and clinical evaluation are required to support their development into standardized phytopharmaceuticals.

Key words: *Plumeria*, Apocynaceae, Ethnomedicine, Phytochemistry, Pharmacological Activities.

INTRODUCTION

Natural products continue to serve as a critical foundation for modern drug discovery, even with the development of advanced synthetic methodologies such as combinatorial chemistry and high-throughput screening. A significant proportion of approved drugs are either directly derived from plants or inspired by natural molecular frameworks, as these compounds frequently possess structural complexity and biological specificity that are difficult to reproduce synthetically. Consequently, medicinal plants remain indispensable in the search for novel therapeutic agents. [1]

Traditional medical systems, including Ayurveda, Traditional Chinese Medicine, and indigenous healing practices of the Americas, have historically relied on plant-based remedies to manage chronic and infectious diseases. These systems represent accumulated empirical knowledge that requires scientific validation through systematic phytochemical and pharmacological investigations to enable integration into contemporary healthcare practices. [2]

The genus *Plumeria* L. belongs to the family Apocynaceae and is native to tropical regions extending from southern Mexico to northern South America and the Caribbean. Owing to its adaptability, the genus is now widely cultivated across tropical and subtropical regions, including India and the Pacific islands. [3] Although earlier botanical records reported more than 100 species, current taxonomic evaluations recognize only 11 accepted species, among which *Plumeria rubra*, *Plumeria alba*, and *Plumeria obtusa* are the most prominent. [4]

The genus was named after the French botanist Charles Plumier; however, medicinal use of *Plumeria* predates formal botanical classification. Historical records document its use in Aztec medicine as early as 1522. [5] In India, *Plumeria* species are referenced in classical Ayurvedic texts such as the *Charaka Samhita* and *Sushruta Samhita* for treating fever, inflammation, and swellings. [6] Although widely cultivated for their ornamental and aromatic flowers, *Plumeria* species also possess a diverse range of bioactive secondary metabolites, including iridoids, triterpenoids, and flavonoids, which exhibit antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. [7,8]

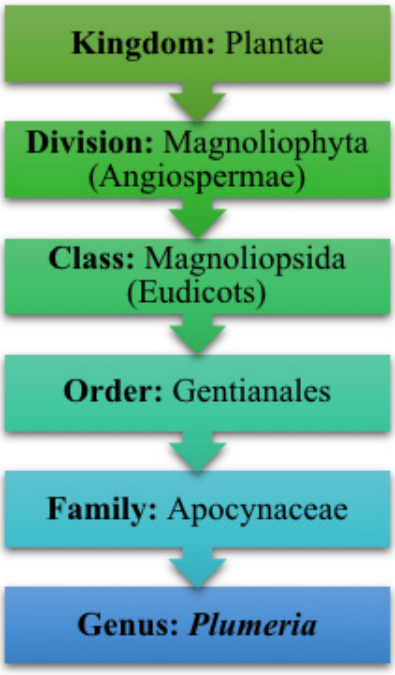
This review consolidates existing knowledge on the taxonomy, ethnomedicinal uses, phytochemistry, pharmacological activities, and safety aspects of the genus *Plumeria* to link traditional knowledge to contemporary scientific evidence.

TAXONOMY AND MORPHOLOGY

Taxonomic Classification

The genus *Plumeria* L. belongs to the family Apocynaceae, a group of angiosperms commonly distributed in tropical and subtropical climates and known for the presence of milky latex and diverse bioactive constituents. Within the botanical hierarchy, *Plumeria* is classified in the order Gentianales and is an important genus with both ornamental and medicinal significance. [4,9]

Contemporary taxonomic resources, including Plants of the World Online (POWO), recognize approximately 11 accepted species within the genus. Earlier reports described a much larger number of species; however, subsequent revisions have consolidated many of these names into synonyms based on improved botanical understanding. A notable example is *Plumeria acuminata*, which is now widely treated as a synonym of *Plumeria rubra*. Such revisions highlight the importance of adhering to updated nomenclature to ensure accuracy in phytochemical and pharmacological research. [4,9] The taxonomic position of the genus *Plumeria* can be summarized as follows:



Species within this genus display significant morphological diversity, particularly in floral characteristics, leaf morphology, and growth patterns. These variations previously contributed to taxonomic confusion, but recent classification systems, supported by morphological evaluation and modern phylogenetic insights, have improved clarity in species identification and classification. [4,9]

Species Descriptions (Table 1)

TRADITIONAL USES

Plumeria species have a long history of use in traditional medicine across multiple regions (**Table 2**). [10]

Table 1: Morphological characteristics of *Plumeria* species.

Species	Key morphological characteristics	Reference
Plumeria alba	Small to medium-sized deciduous tree; narrow oblanceolate leaves clustered at branch tips; highly fragrant white flowers with yellow center; smooth grey bark	[6]
Plumeria rubra	Medium-sized deciduous tree; leaves elliptic to oblong, variable in size; flowers highly diverse in color (red, pink, yellow, white) with strong fragrance; thick succulent branches with latex	[5]
Plumeria obtuse	Evergreen small tree; glossy, dark green obovate leaves with rounded apex; white flowers with yellow throat and overlapping rounded petals; dense canopy	[10]
Plumeria pudica	Small ornamental tree; distinctive spatulate (spoon-shaped) leaves; profuse clusters of non-fragrant white flowers; prolonged flowering period	[11]
Plumeria acuminata (synonym of *P. rubra*)	A notable example is the name P. acuminata, which appears in earlier literature but is currently treated as a synonym of *Plumeria rubra* under updated taxonomic classification.	[4]

Table 2: Detailed traditional uses/indications of *Plumeria* species.

Region	Plant part used	Traditional uses/indications	Reference
India	Roots, leaves	Treatment of fever, edema, bronchitis, cough, asthma, rheumatism, and dysentery; root decoctions used as mild laxatives and anthelmintics; leaf poultices applied to relieve chest congestion	[12,13]
Southeast Asia	Bark, latex	Used as purgatives, diuretics, febrifuges, and emmenagogues; abortifacient use reported in the Philippines	[14,15]
Latin America	Latex, leaves	Management of skin infections, fungal diseases, diabetes, and ear disorders; treatment of sores, itching, and fistulas	[16–18]

PHYTOCHEMICAL EXTRACTION AND SCREENING METHODOLOGIES

Plant Material Collection and Processing

Fresh plant materials, including roots, leaves, and bark, are collected from natural habitats and authenticated by botanists, with voucher specimens deposited in herbaria. [19,20] The materials are washed, shade-dried to prevent degradation of heat-sensitive compounds, and subsequently pulverized. [21]

Extraction Techniques

Methanolic extraction using a Soxhlet apparatus or cold maceration for approximately 72 hours is commonly employed to obtain a broad range of phytoconstituents. [21] Ethanol or hydroalcoholic solvents are also used, followed by concentration under reduced pressure at temperatures below 40°C. [22]

Phytochemical Screening

Preliminary qualitative analyses are conducted to detect alkaloids, iridoids, triterpenoids, and flavonoids using standard chemical tests such as Dragendorff's, Salkowski's, and Shinoda reactions. [19,23]

PHYTOCHEMICAL CONSTITUENTS (TABLE 3)

PHARMACOLOGICAL AND THERAPEUTIC ACTIVITIES

Antioxidant Activity

Reactive oxygen species are critically involved in the progression of numerous chronic disorders, including diabetes, cardiovascular diseases, neurodegenerative conditions, and cancer. These reactive molecules arise during normal metabolic processes but become harmful when their production exceeds the capacity of endogenous antioxidant systems. Natural products have gained attention for their role in restoring this balance.

Extracts from *Plumeria* species have demonstrated considerable antioxidant activity in both in vitro and in vivo studies. [33] Methanolic leaf extracts, in particular, exhibit strong scavenging effects against radicals such as DPPH, superoxide, and hydroxyl species. This activity is largely attributed to phenolic and flavonoid constituents, including quercetin and kaempferol derivatives, which stabilize reactive species through electron or hydrogen donation mechanisms. [29,33]

Animal-based investigations further reinforce these findings. In alloxan-induced diabetic models, administration of *Plumeria rubra* extracts resulted in reduced lipid peroxidation, as indicated by decreased thiobarbituric acid reactive substances (TBARS), alongside improved activity of antioxidant enzymes such as superoxide dismutase and catalase. [34] These results suggest that the plant's phytochemicals contribute to cellular protection by mitigating oxidative damage and modulating redox-sensitive pathways.

Anti-Inflammatory and Analgesic Activity

Inflammation is a multifaceted biological response regulated by mediators such as cytokines, prostaglandins, and transcription factors. While essential for defense, dysregulated inflammation contributes to various chronic diseases.

Evidence from experimental models indicates that *Plumeria* extracts possess significant anti-inflammatory properties.

Table 3: Detailed phytochemical profile of *Plumeria* species.

Chemical class	Key active compounds	Plant part	Biological/pharmacological activity	Reference
Iridoid glycosides	Plumieride	Roots, bark	Plant growth inhibition	[24]
	Isoplumericin	Bark (*P. alba*)	Cytotoxic, anti-inflammatory	[9]
	6″-*O*-acetylplumieride	Leaves (*P. obtusa*)	Cytotoxic, antiproliferative	[25]
Triterpenoids	Lupeol	Leaves	Anti-inflammatory, wound healing	[8]
	Ursolic acid	Leaves	Hepatoprotective, anti-inflammatory	[8]
	Rubrinol	Stem bark	Antimicrobial	[27]
	α/β-Amyrin	Bark, Leaves	Anti-inflammatory	[9]
Flavonoids	Kaempferol	Flowers	Antioxidant	[28]
	Quercetin derivatives	Leaves	Free radical scavenging	[29]
Coumarins	Scopoletin	Bark	Cardiotonic, diuretic	[30]
Sterols	β-Sitosterol	Bark	Hypocholesterolemic	[8]
Fatty acids	Lauric acid, myristic acid	Flowers	Antimicrobial	[31]
Volatile oils	Linalool, geraniol	Flowers	Antimicrobial, sedative	[32]

[19] In carrageenan-induced paw edema studies, methanolic leaf extracts have been shown to reduce inflammation effectively, suggesting inhibition of acute inflammatory responses. This effect is associated with decreased levels of pro-inflammatory mediators, including tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), as well as suppression of cyclooxygenase-2 (COX-2) activity. [19,35] Additionally, modulation of NF-κB signaling is believed to play a central role in regulating inflammatory gene expression.

Analgesic effects have also been demonstrated in both central and peripheral pain models, such as hot plate and acetic acid–induced writhing tests. Treated subjects showed reduced pain perception, indicating involvement of multiple mechanisms. These effects are likely linked to bioactive compounds such as triterpenoids, including lupeol and amyrins, which are known to influence inflammatory mediators and nociceptive pathways. [8,35]

Antimicrobial Activity

The antimicrobial potential of *Plumeria* species has been widely investigated against a range of pathogenic microorganisms. Extracts from leaves and bark have shown inhibitory effects against both Gram-positive and Gram-negative bacteria, as well as fungal species. [21]

These antimicrobial properties are primarily attributed to phytochemicals such as flavonoids, terpenoids, and iridoid glycosides. Their mechanisms of action include disruption of microbial membrane integrity, inhibition of essential enzymatic processes, and interference with nucleic acid synthesis. [21,32] In addition, essential oils derived from *Plumeria* flowers, containing compounds such as linalool and geraniol, enhance antimicrobial efficacy by increasing membrane permeability and causing leakage of intracellular contents. [32]

Some studies have also reported antiviral activity, including inhibition of enzymes like HIV-1 reverse transcriptase. However, these findings remain preliminary and require further experimental validation. [37] Earlier studies have also reported antimicrobial activity of essential oils derived from *Plumeria* flowers. [42,43]

Antidiabetic and Hypolipidemic Activity

Metabolic disorders such as diabetes mellitus and dyslipidemia are closely associated with oxidative stress and disruptions in glucose and lipid metabolism. Plant-derived compounds are increasingly being explored for their therapeutic potential in managing these conditions.

Extracts of *Plumeria rubra* have demonstrated significant hypoglycemic effects in experimental models. [34] In alloxan-induced diabetic rats, treatment resulted in reduced fasting blood glucose levels. This effect may be attributed to multiple mechanisms, including protection of pancreatic β-cells, enhanced insulin secretion, and improved peripheral glucose utilization. [34] Flavonoid constituents may also contribute by modulating enzymes involved in carbohydrate metabolism.

In addition to glycemic control, these extracts have shown lipid-lowering effects, including reductions in total cholesterol, triglycerides, and low-density lipoprotein (LDL) levels. These outcomes are likely associated with the regulation of lipid metabolism pathways and the inhibition of lipid peroxidation. [34] Such combined effects support the traditional use of *Plumeria* species in managing metabolic disorders.

Cytotoxic, Antimutagenic, and Neuroprotective Potential

Recent studies have highlighted the potential anticancer properties of *Plumeria* species. Methanolic extracts of *Plumeria alba* leaves have demonstrated antitumor activity in experimental models, including prolonged survival in mice with Dalton's Lymphoma Ascites tumors. [36]

These cytotoxic effects are linked to bioactive compounds such as iridoid glycosides and triterpenoids, which can induce apoptosis in cancer cells. The underlying mechanisms involve activation of caspase-dependent pathways, disruption of mitochondrial function, and inhibition of cell proliferation signaling. [8] Additionally, certain constituents have shown the ability to reduce mutagen-induced DNA damage, suggesting antimutagenic potential. [26]

Although direct evidence of neuroprotective activity remains limited, the antioxidant and anti-inflammatory properties of *Plumeria* phytochemicals indicate possible benefits in neurodegenerative conditions. These effects may involve attenuation of oxidative stress and modulation of neuronal signaling pathways, though further research is necessary to confirm these roles. [39]

TOXICOLOGY, SAFETY, AND PHARMACOKINETIC CONSIDERATIONS

Toxicological Profile and Safety

Although *Plumeria* species are widely recognized for their therapeutic applications, their safety characteristics differ based on the specific plant part utilized, preparation technique, and administered dose. Evidence from ethnobotanical sources and experimental investigations indicates that certain parts, particularly the latex and bark, may exhibit irritant or toxic effects, whereas leaf-derived extracts are generally associated with better tolerability. [14,40]

The latex contains biologically active compounds capable of inducing skin irritation, inflammatory reactions, and discomfort upon contact with mucosal surfaces. Oral exposure to latex or crude bark preparations has been linked to digestive tract irritation and laxative effects, and traditional accounts also describe potential abortifacient properties. Such findings suggest the presence of potent constituents that necessitate cautious use and appropriate dose control. [14] These observations align with earlier toxicological classifications that identify *Plumeria* among plants capable of causing adverse effects when used improperly. [40]

In contrast, studies conducted under controlled conditions suggest that leaf extracts present a comparatively favorable safety profile. Acute toxicity assessments of hydroalcoholic extracts from *Plumeria alba* leaves have reported good tolerance in animal models, with no marked alterations in behavior, biochemical markers, or tissue structure within therapeutic dose ranges. Furthermore, these extracts have demonstrated protective effects on the gastric mucosa, indicating a lack of ulcer-inducing potential and supporting their safer pharmacological use. [19,22]

Bark-derived constituents, however, require more careful consideration. While pharmacologically active, compounds isolated from *Plumeria rubra* bark have shown notable cytotoxic effects in vitro. Although this property may be advantageous in anticancer research, it also raises concerns regarding potential toxicity to healthy cells in the absence of proper standardization and dose regulation. [41] This highlights the importance of distinguishing between plant parts when assessing safety, as variations in phytochemical composition directly influence biological effects.

In summary, *Plumeria* species offer significant medicinal benefits, but their safe application depends on careful selection of plant material, appropriate extraction procedures, and controlled dosing to minimize potential adverse outcomes**.**

Pharmacokinetic Considerations of Isolated *Plumeria* Constituents

Information regarding the pharmacokinetic behavior of individual bioactive compounds derived from *Plumeria* species is currently insufficient and largely based on indirect evidence rather than dedicated pharmacokinetic analyses. Existing studies suggest that certain phytochemicals, particularly flavonoids and iridoid glycosides, are absorbed after oral administration, as inferred from observable systemic effects in experimental models. [34,35]

Observed pharmacological responses—such as reductions in blood glucose levels and alterations in pain perception following administration of *Plumeria* extracts—indicate that active constituents are capable of entering systemic circulation at biologically effective concentrations. [34,35] Nevertheless, critical pharmacokinetic parameters, including absorption rates, bioavailability, tissue distribution, metabolic fate, and routes of elimination, have not yet been thoroughly investigated for isolated compounds.

Flavonoid constituents identified in *Plumeria*, including derivatives of quercetin and kaempferol, are generally subject to extensive metabolic modification following absorption. These transformations commonly involve conjugation processes such as glucuronidation and sulfation, which may alter their bioavailability and influence pharmacological activity. [33] Likewise, iridoid glycosides are likely to undergo enzymatic breakdown followed by further metabolic conversion, potentially affecting their biological effects. [9]

Given these gaps, current knowledge of the pharmacokinetics of *Plumeria*-derived compounds should be regarded as preliminary. Comprehensive investigations employing advanced analytical methodologies are required to clarify their absorption, distribution, metabolism, and excretion profiles. Such data will be critical for ensuring proper standardization, optimizing therapeutic efficacy, and supporting the clinical development of *Plumeria*-based formulations (**Table 4**).

CONCLUSIONS

The genus *Plumeria* comprises a group of medicinal plants with notable pharmacological relevance, supported by longstanding traditional applications and increasing scientific investigation. Phytochemical analyses have revealed a diverse spectrum of constituents, including iridoid glycosides, triterpenoids, flavonoids, sterols, and volatile compounds, which are collectively associated with a broad range of biological effects such as antioxidant, anti-inflammatory, antimicrobial, metabolic regulatory, and cytotoxic activities.

Findings from experimental studies, largely based on in vitro systems and animal models, provide meaningful insight into the therapeutic potential of *Plumeria* species. However, the level of evidence is not uniform across all reported activities, and clinical confirmation remains limited. Furthermore, differences in chemical composition arising from species variation, plant parts, and extraction techniques emphasize

Table 4: Summary of major phytoconstituents, plant parts, pharmacological activities, and evidence level in *Plumeria* species.

Compound/class	Plant part	Reported activity	Study type	Reference
Plumieride (iridoid)	Roots, bark	Growth inhibition, anti-inflammatory	In vitro	[24]
Isoplumericin (iridoid)	Bark	Cytotoxic, anti-inflammatory	In vitro	[9]
Lupeol (triterpenoid)	Leaves	Anti-inflammatory, wound healing	In vivo/in vitro	[8]
Ursolic acid (triterpenoid)	Leaves	Hepatoprotective, anti-inflammatory	In vivo	[8]
α/β-Amyrin (triterpenoid)	Bark, leaves	Anti-inflammatory	In vivo	[9]
Kaempferol (flavonoid)	Flowers	Antioxidant	In vitro	[28]
Quercetin derivatives	Leaves	Antioxidant	In vitro	[29]
Scopoletin (coumarin)	Bark	Cardiotonic, diuretic	In vitro/traditional	[30]
β-Sitosterol (sterol)	Bark	Hypocholesterolemic	In vivo	[8]
Linalool, Geraniol	Flowers	Antimicrobial	In vitro	[33]
Methanolic leaf extract	Leaves	Antioxidant	In vitro	[33]
Methanolic leaf extract	Leaves	Anti-inflammatory	In vivo	[20]
Leaf extract (*P. rubra*)	Leaves	Antidiabetic, hypolipidemic	In vivo	[34]
Leaf extract (*P. alba*)	Leaves	Antitumor	In vivo	[36]
Bark extract	Bark	Cytotoxic	In vitro	[41]
Isolated compounds	Various parts	Antimutagenic	In vitro	[26]
Essential oil	Flowers	Antimicrobial	In vitro	[21,32]
Extracts (general)	Various	Antiviral (HIV-1 RT inhibition)	In vitro	[37]

the necessity for standardization to ensure consistency and reproducibility in research outcomes.

Safety considerations vary depending on the plant material used. While leaf-derived preparations have demonstrated relatively favorable safety profiles under controlled conditions, latex and bark extracts are associated with irritant and cytotoxic effects. This highlights the importance of appropriate selection, processing, and dosage in therapeutic applications.

Although the pharmacological prospects of *Plumeria* are promising, important gaps persist in areas such as detailed mechanistic understanding, pharmacokinetic characterization, and human clinical evaluation. Addressing these limitations through well-structured experimental and clinical studies will be critical for advancing the development of standardized and evidence-based therapeutic products derived from *Plumeria* species.

AUTHORS' CONTRIBUTION

All authors have significantly contributed to the work, whether by conducting literature searches, drafting, revising, or critically reviewing the article. They have given their final approval of the version to be published, have agreed with the journal to which the article has been submitted, and agree to be accountable for all aspects of the work."

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CONFLICT OF INTEREST

None.

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