

Plumeria pudica Jacq. (Apocynaceae): An Updated Review of Bioactive Latex Proteins, Phytochemical Diversity and Pharmacological Potential

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Abstract

Plumeria pudica Jacq. is an ornamental lactiferous shrub of the family Apocynaceae, native to Colombia, Venezuela and Panama, whose leaves, flowers, roots, stems and latex are used in traditional medicine for inflammatory, gastrointestinal and infectious conditions. Although earlier reviews summarized its ethnomedicine and general phytochemistry, the species remains underexplored relative to other *Plumeria* members, and the rapidly growing evidence on its latex protein fraction (LPPp) has never been systematically and critically integrated. The present review provides a species-focused, evidence-graded synthesis of the botany, ethnomedicinal context, phytochemical composition, bioactive latex proteins, pharmacological activities and nanotechnological applications of *P. pudica*, with a preferred publication window of 2015 to 2026 and inclusion of seminal older studies. The evidence indicates that LPPp, a mixture of cysteine, serine and metalloproteinases, proteinase inhibitors and chitinases, exerts reproducible anti-inflammatory, antinociceptive, antidiarrhoeal, intestinal, periodontal and hepatoprotective effects in experimental models, predominantly through coordinated suppression of myeloperoxidase activity, leukocyte migration, pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6, IFN- γ , CXCL1) and oxidative tissue damage. Leaf, stem and root extracts rich in phenolics and flavonoids demonstrate antioxidant and antibacterial activities that vary substantially with solvent polarity, whereas silver nanoparticles green-synthesized using *P. pudica* floral and leaf extracts show larvicidal, antibacterial and cytotoxic properties that should not be conflated with direct extract activity. Major challenges include the absence of bioassay-guided isolation, unexplored molecular targets, scarce pharmacokinetic and toxicological data, and no clinical translation. Future work should integrate proteomic and metabolomic profiling, standardized extracts, mechanistic and in vivo validation, and safety assessment. *P. pudica* is a credible multi-target candidate for phytopharmaceutical and green-nanomedicine development, but current evidence remains preclinical.

Keywords: *Plumeria pudica*, Latex Proteins, LPPp, Antioxidant, Anti-Inflammatory, Antimicrobial, Silver Nanoparticles, Ethnopharmacology.

1. Introduction

Medicinal plants continue to serve as a productive source of structurally diverse secondary metabolites and bioactive macromolecules for modern drug discovery, particularly where conventional therapies for chronic inflammation, infectious disease and cancer remain inadequate or poorly tolerated (Balunas and Kinghorn, 2005) [1]. The genus *Plumeria* (Apocynaceae) comprises lactiferous tropical trees and shrubs that are well recognized for their ornamental, cultural and medicinal value, and genus-level reviews have documented antioxidant, antimicrobial, anti-inflammatory and cytotoxic properties across several of its approximately eight accepted species (Souza et al., 2024) [2]. Among them, *Plumeria pudica* Jacq., commonly called bridal bouquet or white frangipani, has attracted increasing scientific attention because of its unusual fiddle-shaped leaves, white flowers with a yellow centre, and a milky latex whose protein fraction exhibits reproducible pharmacological activity in experimental models (Chamakuri et al., 2020) [3].

The scientific literature on *P. pudica* has expanded considerably since the first characterization of its laticifer proteins, yet the evidence remains fragmented across phytochemical screening studies, latex-protein pharmacology, antioxidant and antimicrobial assays, and green-nanoparticle reports (Shrivastava et al., 2022) [5]. Several limitations characterize the existing review landscape. First, evidence from *P. alba*, *P. rubra* and *P. obtusa* is frequently presented together with, or in place of, *P. pudica*-specific data, although phytochemistry and bioactivity can differ substantially between congeners (Souza et al., 2024) [2]. Second, previous reviews have been predominantly descriptive and have not graded the strength of evidence, distinguished in vitro from in vivo findings, or separated nanoparticle-associated effects from the direct pharmacology of the plant (Kumawat et al., 2019; Chamakuri et al., 2020) [3, 4]. Third, important interpretive problems have persisted in the primary literature itself, including duplicated reporting of the same experimental dataset under different citations and conflation of extract effects with nanoparticle effects (Fernandes et al., 2015; Oliveira et al., 2022) [6, 7].

The latex protein fraction of *P. pudica* (LPPp) is the most distinctive feature of this species from a pharmacological standpoint. LPPp has been shown to inhibit inflammatory and nociceptive responses, protect the intestine in models of secretory diarrhoea, acetic-acid colitis and 5-fluorouracil-induced mucositis, reduce ligature-induced periodontitis, and attenuate acetaminophen-induced acute liver injury (Fernandes et al., 2015; Santana et al., 2018; Oliveira et al., 2019; Andrade et al., 2025; Souza et al., 2026) [6-11]. In parallel, metabolomic and chromatographic studies have substantially expanded the phytochemical profile of the leaves, stems and roots, linking phenolic and flavonoid content to antioxidant and antibacterial activities (Shukla et al., 2025, 2026) [12-14]. Green synthesis of silver nanoparticles using *P. pudica* floral and leaf extracts constitutes a further emerging application with larvicidal, antibacterial and cytotoxic outcomes (Suriyakala et al., 2021; Shrivastava et al., 2023) [15, 16].

Against this background, the present review aims to: (i) provide a species-focused, systematically searched synthesis of *P. pudica* for the period 2015-2026, retaining seminal older studies where relevant; (ii) critically evaluate agreements, contradictions and methodological differences among studies; (iii) articulate the key theories, models and concepts that explain the multi-target pharmacology of the species, and develop a conceptual framework supported by logical and theoretical justification; (iv)

correct inconsistencies in data reporting and interpretation, including duplicated citations; and (v) identify unresolved questions and priorities for future research. This review deliberately excludes genus-level findings unless they provide essential conceptual context, and it treats traditional claims as hypotheses for experimental testing rather than evidence of efficacy.

2. Botanical Description, Distribution and Ethnomedicinal Context

Plumeria pudica Jacq. is an evergreen to semi-evergreen shrub or small tree, commonly reaching 3-4 m in height, with one or two slender trunks that branch close to the ground to form a dense crown. It is native to Colombia, Venezuela and Panama and is now widely cultivated across tropical and subtropical regions of Asia, Africa and the Americas as an ornamental and landscape plant (Chamakuri et al., 2020) [3]. The species is readily distinguished from other *Plumeria* members by its leaf morphology: the leaves are elongated, broadened toward the apex and fiddle-shaped or spoon-shaped, with a cuneate base, caudate apex, pinnate-reticulate venation and smooth texture (Shukla et al., 2025) [12]. The flowers are white with a yellow centre, arranged in terminal clusters, and are essentially without fragrance. As in other members of the Apocynaceae, the plant produces a milky latex from laticifers, a tissue specialization that is central to the pharmacology reviewed here.

Ethnomedicinal reports attribute to *P. pudica* a range of applications, including inflammatory conditions, pain, diarrhoea and dysentery, helminthic infections, ulcerative colitis, respiratory complaints such as cough, asthma and bronchitis, fever, gynaecological disorders, neurodegenerative disorders, leishmaniasis and tumours (Kumawat et al., 2019; Chamakuri et al., 2020; Shrivastava et al., 2022) [3-5]. From an ethnopharmacological perspective, these claims are best regarded as a prioritization tool: traditional use identifies plausible bioactivities, but only experimental validation can establish them. Table 1 maps each reported traditional use against its current level of experimental validation, revealing a striking pattern in which the uses supported by the latex-protein studies (inflammation, pain, diarrhoea, colitis) show the strongest evidence, while uses such as anthelmintic, antileishmanial, antidiabetic and anticancer activity remain preliminary or inferred. This correspondence between ethnomedicine and experimentally tractable models strengthens the pharmacological rationale for the species, but it should not be read as clinical validation, for which no studies currently exist.

Table 1: Reported Ethnomedicinal Uses of *Plumeria pudica* and Their Current Level of Experimental Validation

Traditional Use	Plant Part	Level of Experimental Validation	Representative Evidence
Inflammatory conditions and pain	Latex (LPPp); flowers	Strong (multiple in vivo models)	[6, 18]
Diarrhoea and dysentery	Latex (LPPp)	Strong (in vivo models)	[19]
Ulcerative colitis / intestinal injury	Latex (LPPp)	Strong (in vivo model)	[8]
Periodontal inflammation	Latex (LPPp)	Moderate (in vivo model)	[9]

Chemotherapy-induced intestinal mucositis	Latex (LPPp)	Moderate (in vivo models; one duplicated review record)	[10, 20]
Liver injury / hepatoprotection	Latex (LPPp)	Moderate (in vivo model; docking-supported)	[11]
Helminthic infections	Leaves	Weak (in vitro worm model)	[5]
Diabetes (post-prandial glucose control)	Flowers	Preliminary (in vitro enzyme assay)	[21]
Neurodegenerative disorders	Leaves	Preliminary (in vitro enzyme assay)	[5]
Leishmaniasis	Leaves	Preliminary (in vitro promastigote assay)	[5]
Gynaecological disorders	Leaves	Preliminary (in vitro anti-Candida data)	[4]
Tumours	Leaves (nanoparticle-mediated)	Weak; nanoparticle-associated cytotoxicity only	[14, 15]

3. Phytochemical Profile and Analytical Advances

The phytochemistry of *Plumeria pudica* has been investigated through qualitative screening, quantitative spectrophotometric assays, Fourier-transform infrared (FT-IR) spectroscopy, gas chromatography-mass spectrometry (GC-MS), and, most recently, high-resolution liquid chromatography coupled to quadrupole time-of-flight mass spectrometry (LC-MS-QTOF). Early screening of methanolic leaf extracts reported carbohydrates, alkaloids, tannins and phenolics, flavonoids, glycosides, terpenoids, proteins, fats and steroids, whereas chloroform extracts yielded a narrower profile of carbohydrates, alkaloids, fats, glycosides and steroids; the same study quantified total phenolic content at 248.33 ± 3.33 mg gallic acid equivalents (GAE) per g and total flavonoid content at 108.33 ± 1.67 mg quercetin equivalents (QE) per g, with a DPPH radical-scavenging IC₅₀ of 491.124 ± 1.97 µg/mL (Chavda et al., 2021) [22]. This dataset appears in the literature under more than one citation; in this review it is counted once to avoid double-counting of evidence.

A consistent methodological insight across studies is that extraction solvent strongly determines the chemical profile and the apparent bioactivity. In the most comprehensive study to date, Shukla et al. (2025a) compared aqueous, hydroalcoholic, isopropyl alcohol (IPA) and petroleum ether leaf extracts, finding that the IPA extract carried the highest total phenolic (101 mg GAE/g dry weight), flavonoid (402.2 mg QE/g dry weight), carbohydrate and protein contents, and exhibited the strongest DPPH scavenging (IC₅₀ 33.54 µg/mL, superior to ascorbic acid at 37.20 µg/mL in the same assay) and the highest reducing power (absorbance approximately 1.53 at 1000 µg/mL) [12]. LC-MS-QTOF profiling detected approximately 24 compounds in the IPA extract, including plumieride, coumarin, visnagine and olprinone, alongside about 20, 17 and 15 compounds in the aqueous, hydroalcoholic and petroleum ether extracts respectively. Parallel investigations of stems and roots extended this picture: the hydroalcoholic stem extract showed the highest phenolic (105.4 mg GAE/g), flavonoid (401.2 mg QE/g) and saponin contents and the strongest stem antioxidant activity (70.82% DPPH inhibition; IC₅₀ 33.7 µg/mL) (Shukla et al., 2025b) [13], while the hydroalcoholic root extract reached 67.73% DPPH inhibition (IC₅₀

35.20 µg/mL; reducing power absorbance 1.203) with approximately 91 mg GAE/g phenolics and 386 mg QE/g flavonoids (Shukla et al., 2026) [14].

Complementary targeted analyses identified tannins, steroids and alkaloids in mature leaves (Das et al., 2021) [21], and alkaloids, saponin glycosides, phenolics, terpenoids, sterols, proteins and flavonoids in leaf material used for anti-inflammatory assays (Sharma and Jain, 2022) [23]. GC-MS of an ethyl acetate leaf fraction revealed semi-volatile constituents such as 2,4-di-tert-butylphenyl 5-hydroxypentanoate, oxalic acid allyl nonyl ester, dibutyl phthalate and 2,3,5,8-tetramethyldecane (Das et al., 2021) [21]. Two interpretive cautions are warranted. First, detection of a constituent by chromatography does not establish its contribution to bioactivity; attribution requires bioassay-guided isolation. Second, several identified compounds, including dibutyl phthalate, are more plausibly contaminants or processing artefacts of extraction than plant metabolites, and their presence should be confirmed in authenticated plant material before biological interpretation. The emerging phytochemical evidence is summarized in Table 2.

Table 2: Major Phytochemical Groups and Bioactive Constituents Reported in *Plumeria pudica*

Chemical Class	Plant Part / Extract	Analytical Evidence	Representative Values or Constituents	Reference
Phenolics	Leaf, methanolic	Folin-Ciocalteu assay	248.33 ± 3.33 mg GAE/g; IPA leaf 101 mg GAE/g	[12, 22]
Flavonoids	Leaf, methanolic / IPA	Aluminium chloride assay	108.33 ± 1.67 mg QE/g; IPA leaf 402.2 mg QE/g	[12, 22]
Alkaloids	Leaf, multiple solvents	Qualitative screening	Present in methanolic, chloroform and IPA extracts	[13, 21-23]
Tannins	Leaf	Qualitative screening	Present in polar extracts	[21, 22]
Terpenoids / sterols	Leaf, stem	Qualitative screening	Present across leaf and stem extracts	[13, 22, 23]
Saponins	Leaf, stem	Vanillin-sulphuric acid assay	Hydroalcoholic stem 233.4 mg diosgenin equivalents/g	[13]
Coumarins and iridoids	Leaf, stem, root	LC-MS-QTOF	Plumieride, coumarin, visnagine, olprinone	[12-14]
Semi-volatile esters and hydrocarbons	Leaf, ethyl acetate fraction	GC-MS	2,4-Di-tert-butylphenyl 5-hydroxypentanoate;	[21]

			dibutyl phthalate; tetramethyldecane	
Latex proteins (proteinases, inhibitors, chitinases)	Latex	Biochemical and proteomic characterization	Cysteine, serine and metalloproteinases; papain/trypsin inhibitors; chitinases	[6-9]

4. Bioactive Latex Proteins (LPPp): Composition and Multi-Target Mechanisms

The latex of *P. pudica* is pharmacologically the most distinctive and best-characterized matrix of the species. Laticifers in the Apocynaceae are widely understood as a plant defence system, and laticifer proteins typically combine proteolytic enzymes with proteinase inhibitors and pathogenesis-related proteins such as chitinases. In *P. pudica*, the water-soluble latex protein fraction (LPPp) has been characterized as a mixture containing cysteine, serine and metalloproteinase activities, inhibitory activity against papain and trypsin, and chitinolytic activity (Fernandes et al., 2015; Santana et al., 2018; Oliveira et al., 2019) [6, 8, 9]. The coexistence of proteinases and their inhibitors within one fraction is mechanistically interesting: it suggests that the pharmacological effect may depend on the balance between proteolytic activity and its restraint, rather than on any single enzyme.

Three lines of evidence support a causal role for the protein components. First, the fraction is active across multiple, structurally unrelated models of injury (oedema, secretory diarrhoea, colitis, periodontitis, mucositis, liver injury), which is difficult to explain by a single low-molecular-weight contaminant. Second, heat denaturation markedly reduces or abolishes the anti-inflammatory, myeloperoxidase-inhibitory and antidiarrhoeal activities, demonstrating dependence on intact protein structure (Fernandes et al., 2015; Santana et al., 2018) [6, 8]. Third, mass-spectrometric identification of individual latex proteins combined with molecular docking has generated plausible mechanism-level hypotheses, such as interactions of latex cysteine proteases with acetaminophen and its reactive metabolite N-acetyl-p-benzoquinone imine (NAPQI), and of a proteinase inhibitor with CYP2E1 and inflammatory targets (Souza et al., 2026) [11]. These docking results should be regarded as hypothesis-generating rather than confirmatory, since no receptor-binding or enzyme-kinetic validation has yet been published. A mechanistic model integrating the current evidence is presented in Figure 3.

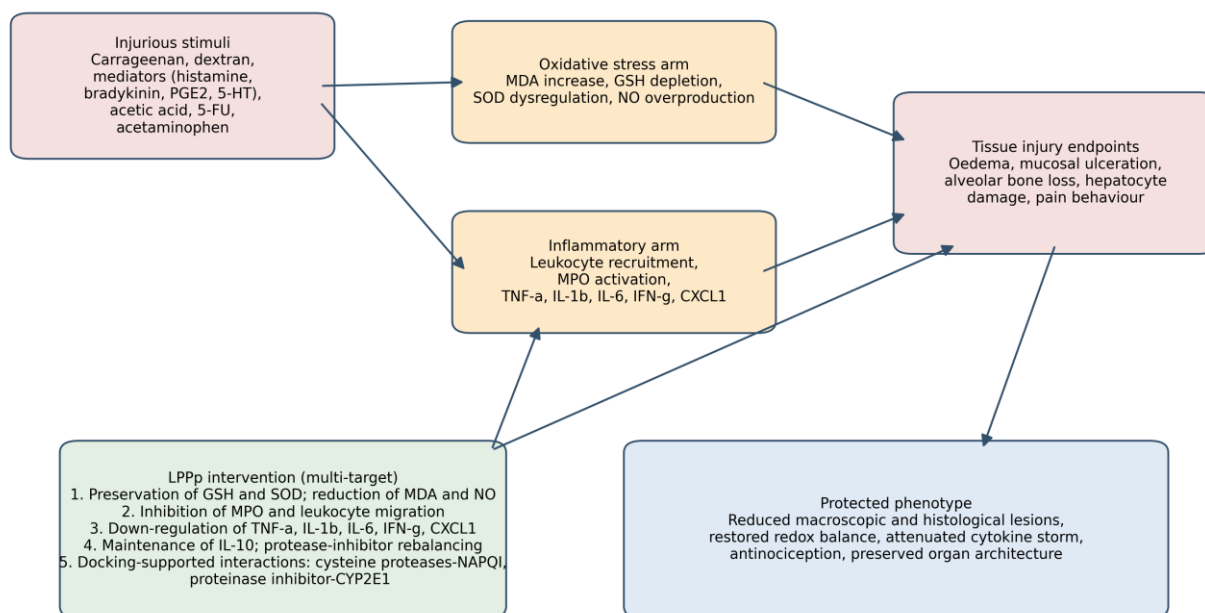


Figure 3: Mechanistic Model of the Multi-Target Protective Action of the Latex Protein Fraction (LPPp) Against Oxidative and Inflammatory Tissue Injury

Two inconsistencies in the primary literature deserve explicit correction. First, the ligature-induced periodontitis study has been cited both as Santos et al. (2021) and as Oliveira et al. (2022); these refer to a single experimental dataset, and the present review cites it once as Oliveira et al. (2022) [7]. Second, the 5-fluorouracil intestinal mucositis work has appeared both as an experimental report (Andrade et al., 2025) [10] and as a review (Andrade et al., 2023) [20] that summarizes the same research programme; the review adds interpretive but no independent experimental value, and the two records should not be counted as replications of one another. Correcting such duplications matters for evidence synthesis because double-counting inflates the apparent robustness of the dataset.

6. Pharmacological Activities: Evidence, Comparisons and Contradictions

6.1 Antioxidant Activity

Antioxidant activity is the most widely, but also the most heterogeneously, measured property of *P. pudica*. Two conceptually distinct mechanisms operate. In chemical assays (DPPH, ABTS, reducing power), leaf, stem and root extracts act directly as radical scavengers and reductants, with activity tracking phenolic and flavonoid content and solvent polarity: the IPA leaf extract (DPPH IC₅₀ 33.54 µg/mL) and hydroalcoholic stem and root extracts (IC₅₀ 33.7 and 35.20 µg/mL respectively) are the strongest performers reported (Shukla et al., 2025a, 2025b, 2026) [12-14]. Earlier methanolic extracts were considerably weaker (IC₅₀ approximately 491 µg/mL), most probably because of lower flavonoid recovery rather than a biological difference between plant populations (Chavda et al., 2021) [22].

In biological systems, by contrast, the latex protein fraction exerts antioxidant effects indirectly by preserving endogenous defences: in acetic-acid colitis, 5-fluorouracil mucositis and acetaminophen liver injury models, LPPp reduced malondialdehyde accumulation and myeloperoxidase activity, preserved

glutathione and superoxide dismutase, and limited nitrate/nitrite production (Oliveira et al., 2019; Andrade et al., 2025; Souza et al., 2026) [9, 10, 11]. This distinction is important for interpretation: crude extract IC₅₀ values in DPPH assays should not be extrapolated to therapeutic antioxidant effects in vivo, and protein-mediated redox modulation should not be conflated with direct scavenging. No study to date has isolated the single compound or protein responsible, so the evidence supports a multi-constituent, synergistic model rather than a single dominant antioxidant.

6.2 Antibacterial Activity

Antibacterial activity has been demonstrated against Gram-positive and Gram-negative organisms, but reported potency rankings differ between studies, and the differences are methodological rather than contradictory. Das et al. (2021) found the ethyl acetate leaf extract most active, with a maximum inhibition zone of 19.50 ± 0.29 mm against *Escherichia coli* and bactericidal MIC/MBC values [21]. Shukla et al. (2025a), testing four solvents against *Kocuria rhizophila*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *E. coli*, found *Klebsiella pneumoniae* most susceptible (largest zone 19.45 mm for the hydroalcoholic extract) and *E. coli* comparatively resistant (zones 7.23-11.61 mm) [12]. These results are reconcilable if solvent polarity, extract composition and strain selection are taken into account: moderately polar and polar fractions are enriched in different active constituents, and *E. coli* tolerance of plant extracts is frequently observed. The reproducible, general conclusion is that *P. pudica* extracts possess genuine antibacterial potential whose magnitude depends on solvent, organism and concentration; claims of species-specific superiority are not yet justified. All evidence remains in vitro, and activity against clinically relevant multidrug-resistant isolates has not been tested.

6.3 Anti-Inflammatory and Antinociceptive Activity

Anti-inflammatory activity is the best-supported pharmacological property of the species and is also where the two bioactive streams converge. Leaf and flower extracts act in vitro and in vivo through mechanisms consistent with interference in early inflammatory events: methanolic leaf extract inhibited albumin denaturation (64.36% at 500 µg/mL) and protease activity (51.37% at 500 µg/mL), and reduced carrageenan-induced oedema by 28.78% and 50.4% at 100 and 200 mg/kg respectively (Sharma and Jain, 2022) [23]. Ethanolic flower extract showed anti-inflammatory and anti-arthritic activity at 150 and 300 mg/kg comparable with diclofenac sodium in carrageenan-oedema and formaldehyde-arthritis models (Ravishankar et al., 2021) [18].

LPPp exhibits a broader and deeper anti-inflammatory profile. It reduced carrageenan- and dextran-induced paw oedema, inhibited oedema induced by histamine, serotonin, bradykinin, prostaglandin E₂ and compound 48/80, suppressed leukocyte migration and myeloperoxidase activity, and lowered TNF- α and IL-1 β ; heat treatment markedly attenuated these effects (Fernandes et al., 2015) [6]. In disease models, LPPp reduced colonic damage and IL-1 β in acetic-acid colitis (Oliveira et al., 2019) [9], improved gingival bleeding, probing depth and alveolar bone loss in ligature-induced periodontitis (Oliveira et al., 2022) [7], attenuated 5-fluorouracil mucositis (Andrade et al., 2025) [10], and in acetaminophen liver injury reduced TNF- α , IL-1 β , IL-6, IFN- γ and CXCL1 while preserving IL-10 (Souza et al., 2026) [11]. The antinociceptive effect demonstrated in writhing and formalin tests (Fernandes et al., 2015) [6] is best interpreted as a consequence of this anti-inflammatory

and mediator-suppressing action rather than as a central analgesic effect, a conclusion consistent with the failure of any study to test centrally acting pathways directly.

6.4 Antidiarrhoeal and Gastrointestinal Protection

The antidiarrhoeal activity of LPPp is among the most mechanistically informative findings in this literature. LPPp reduced castor-oil-induced diarrhoea, intestinal fluid accumulation and intestinal transit, and inhibited fluid secretion induced by prostaglandin E2 and cholera toxin, while preventing castor-oil-induced glutathione depletion and malondialdehyde accumulation; heat denaturation abolished the effect (Santana et al., 2018) [8]. These data position LPPp as an antisecretory and antioxidant agent rather than a simple motility inhibitor. Subsequent studies extended gastrointestinal protection to acetic-acid colitis (Oliveira et al., 2019) [9] and 5-fluorouracil-induced intestinal mucositis (Andrade et al., 2025) [10], with a consistent signature of preserved glutathione, reduced malondialdehyde and myeloperoxidase, and lower pro-inflammatory cytokines. The reproducibility of this signature across four distinct intestinal injury models constitutes the strongest internal validation of the latex-protein pharmacology currently available.

6.5 Hepatoprotective Activity

The most recent extension of LPPp pharmacology is to acetaminophen-induced acute liver injury, in which LPPp reduced alanine aminotransferase and aspartate aminotransferase, malondialdehyde, myeloperoxidase and nitrate/nitrite, preserved glutathione and superoxide dismutase, reduced neutrophil accumulation, and preserved hepatic architecture (Souza et al., 2026) [11]. Because acetaminophen hepatotoxicity is initiated by CYP2E1-generated NAPQI and amplified by oxidative stress and neutrophil-driven inflammation, the observed profile is mechanistically coherent, and the docking analysis linking latex cysteine proteases to NAPQI and a proteinase inhibitor to CYP2E1 offers testable hypotheses. This single study, however, represents the entire hepatoprotective evidence base, and independent replication is required.

6.6 Antidiabetic and Enzyme-Inhibitory Activities

A preliminary report found that *P. pudica* flower extract inhibited alpha-amylase by 76.9% in vitro and exhibited ferric-reducing power slightly above ascorbic acid at the tested concentration (Joseph et al., 2025) [19]. Inhibition of alpha-amylase is a recognized strategy for moderating post-prandial glucose, but a single in vitro assay without kinetic characterization, reference-comparable potency, or any in vivo glycaemic endpoint supports only the conclusion that the flowers contain enzyme-inhibitory constituents. This activity should be treated as a lead for future work, not as evidence of antidiabetic efficacy.

6.7 Critical Appraisal of the Evidence Base

Taken together, the pharmacological literature on *P. pudica* is promising but asymmetrical. Strengths include the use of multiple independent injury models for LPPp, internal consistency of the antioxidant-anti-inflammatory signature across models, and the demonstration that activity is heat-sensitive and therefore protein-dependent. Limitations include the near-absence of bioassay-guided isolation, lack of dose-response and pharmacokinetic characterization, absent selectivity testing (for example, cancer versus normal cells for any cytotoxic claim), no toxicology beyond acute in vivo tolerability implied by

the cited studies, and complete absence of clinical data. Table 3 consolidates the evidence map and grades each activity by model type.

Table 3: Evidence Map of the Pharmacological Activities of *Plumeria pudica*

Activity	Model / Assay	Preparation	Key Outcome	Evidence Level
Anti-inflammatory	Carrageenan/dextran paw oedema; mediator-induced oedema; leukocyte migration	LPPp	Reduced oedema, MPO, IL-1beta, TNF-alpha; heat-sensitive	In vivo, mice [6]
Antinociceptive	Acetic-acid writhing; formalin test	LPPp	Reduced nociceptive behaviour; mediator-linked	In vivo, mice [6]
Antidiarrhoeal / antisecretory	Castor oil; cholera toxin; PGE2	LPPp	Reduced secretion, transit and oxidative markers; denaturation-sensitive	In vivo, mice [8]
Colitis protection	Acetic-acid-induced colitis	LPPp	Reduced lesions, MPO, IL-1beta, MDA; preserved GSH/SOD	In vivo, mice [9]
Periodontal protection	Ligature-induced periodontitis	LPPp	Improved clinical parameters; reduced MPO and bone loss	In vivo, rats [7]
Mucositis protection	5-fluorouracil intestinal mucositis	LPPp	Attenuated oxidative and inflammatory injury	In vivo, mice [10]
Hepatoprotection	Acetaminophen acute liver injury	LPPp	Reduced ALT/AST, MDA, MPO, cytokines; preserved GSH/SOD; docking-supported	In vivo, mice [11]
Anti-inflammatory (extract)	Albumin denaturation; antiprotease; carrageenan oedema	Methanolic leaf extract	64.36% denaturation inhibition; 50.4% oedema reduction at 200 mg/kg	In vitro and in vivo [23]
Anti-arthritic	Carrageenan oedema; formaldehyde arthritis	Ethanollic flower extract	Activity comparable with diclofenac at 150-300 mg/kg	In vitro and in vivo [18]
Antibacterial	Agar diffusion; MIC/MBC	Ethyl acetate, hydroalcoholic, IPA, aqueous	Zones up to 19.5 mm; solvent- and strain-dependent	In vitro [12, 21]

		extracts		
Antioxidant	DPPH; reducing power	Leaf, stem, root extracts	IC50 33.54-35.20 µg/mL for best polar extracts	In vitro chemical [12-14, 22]
Enzyme inhibition	Alpha-amylase; AChE	Flower extract; nanoparticles	76.9% alpha-amylase inhibition (in vitro)	In vitro, preliminary [19]

7. Green Synthesis of Silver Nanoparticles: Opportunities and Interpretive Cautions

An active research front concerns the use of *P. pudica* floral and leaf extracts as reducing and capping agents for silver nanoparticles (AgNPs). This approach belongs to the broader green-synthesis paradigm, in which plant phytochemicals replace chemical reductants and stabilizers, and it is attractive because of its low cost, scalability and reduced environmental burden (Ahmed et al., 2016) [25]. Three studies define the current state of the art. Suriyakala et al. (2021) synthesized predominantly spherical flower-mediated AgNPs of approximately 27.1 nm that showed antibacterial activity (highest zone 16.33 ± 0.14 mm against *E. coli*), radical scavenging in DPPH, hydroxyl, superoxide and ABTS assays (IC50 30.4, 32.5, 30 and 18 µg/mL respectively), larvicidal activity against *Culex quinquefasciatus* (IC50 0.79 µg/mL), acetylcholinesterase inhibition and cytotoxicity against HepG2 cells (IC50 62.07 µg/mL) [15]. Srivastava et al. (2022) confirmed that floral extract reproducibly yields approximately 12 nm spherical nanoparticles [24], and Shrivastava et al. (2023) extended the method to leaf extract, obtaining approximately 19 nm nanoparticles with cytotoxicity against A549 lung cancer cells (IC50 approximately 28 µM) [16].

The single most important interpretive point of this review is that nanoparticle-associated bioactivity must not be attributed to *P. pudica* extracts themselves. Silver nanoparticles exert antibacterial, larvicidal and cytotoxic effects through silver-ion release, reactive oxygen species generation, membrane damage and mitochondrial dysfunction, and the plant-derived capping layer modifies, but does not originate, these properties. Reported particle sizes differ across studies (12, 19 and 27.1 nm), and because size, morphology, crystallinity, surface chemistry and capping composition all influence activity, cross-study comparison of potency is not meaningful. Accordingly, the anticancer potential of *P. pudica* should currently be described as nanoparticle-associated cytotoxicity of a plant-mediated nanomaterial, not as anticancer activity of the plant; direct testing of standardized extracts and purified compounds against cancer cell panels, with normal-cell selectivity controls, has not been performed. Table 4 compares the three synthesis studies.

Table 4: Comparative Overview of Silver Nanoparticles Green-Synthesized Using *Plumeria pudica* Extracts

Study	Plant Part Used	Mean Particle Size	Activities Reported	Interpretation Caution
Suriyakala et al. (2021) [15]	Flowers	27.1 nm, spherical	Antibacterial, antioxidant, larvicidal (IC50 0.79 µg/mL), AChE inhibition,	Effects are properties of the nanomaterial; contribution of free silver ions not

			HepG2 cytotoxicity	separated
Srivastava et al. (2022) [24]	Flowers	12 nm, spherical	Synthesis and physicochemical characterization	No extended biological evaluation; comparability limited by different synthesis conditions
Shrivastava et al. (2023) [16]	Leaves	19 nm	A549 cytotoxicity (IC ₅₀ 28 µM)	Attributed to apoptosis and antiproliferation; not a demonstration of direct extract anticancer activity

7. Future Perspectives

The evidence reviewed here defines a clear research agenda. At the molecular level, the active constituents remain unidentified: bioassay-guided fractionation of LPPp, recombinant production of candidate latex proteins, and purified-compound testing of the major leaf, stem and root metabolites are prerequisite to any structure-activity claim. Mechanistically, the docking hypotheses linking latex cysteine proteases to NAPQI and a proteinase inhibitor to CYP2E1 require experimental validation through enzyme kinetics, target engagement studies and receptor-pathway antagonism. Pharmacokinetically, nothing is known about the absorption, distribution, metabolism or excretion of latex proteins, whose oral bioavailability is questionable and whose in vivo effects may therefore be mediated partly through intestinal mechanisms; this distinction has direct implications for the design of delivery systems. Toxicologically, systematic sub-acute and chronic studies, reproductive safety and immunogenicity assessment of a proteinaceous fraction are absent. Translationally, the antibacterial findings should be extended to multidrug-resistant clinical isolates with in vivo infection models, the larvicidal findings to non-target organism and environmental safety studies, and the cytotoxic findings to standardized extracts tested with normal-cell selectivity controls before any anticancer claim is made. Methodologically, future studies should adopt standardized extraction and reporting, authenticated voucher specimens, and consensus assay panels so that potency rankings become comparable across laboratories.

8. Conclusion

Plumeria pudica Jacq. is a pharmacologically credible but still preclinical multi-target medicinal plant. Its latex protein fraction reproducibly protects against inflammatory and oxidative tissue injury in models spanning oedema, pain, secretory diarrhoea, colitis, periodontitis, intestinal mucositis and acute liver injury, acting through coordinated suppression of myeloperoxidase activity, leukocyte recruitment, pro-inflammatory cytokines and oxidative damage. Its leaf, stem and root extracts carry phenolic- and flavonoid-associated antioxidant and antibacterial activities that vary predictably with solvent polarity, and its floral and leaf extracts serve as effective green reductants for multifunctional silver nanoparticles whose larvicidal, antibacterial and cytotoxic properties belong to the nanomaterials rather than to the plant itself. The species therefore offers two complementary development pathways: a protein-based phytopharmaceutical programme targeting the oxidative-inflammatory axis, and a green-nanomaterials programme for vector control and antimicrobial applications. Realizing either pathway requires the identification of active constituents, mechanistic and pharmacokinetic validation, systematic toxicology,

and ultimately clinical investigation. Until such evidence is generated, claims of therapeutic efficacy for *P. pudica* should be stated with appropriate caution.

References

1. Balunas M.J., Kinghorn A.D., "Drug Discovery from Medicinal Plants", Life Sciences, 2005, 78 (5), 431-441.
2. Bruna da Silva S., Ana Clara Silva S., Lucas Arruda M., Naylla Veras de Moraes O., Francisca Dayane Soares da S., Mayck Silva B., Thalís Ferreira de S., Jefferson Soares de O., "Plumeria Species: A Review of Morphology, Traditional Uses, Phytochemicals, and Pharmacological Activities", Indian Journal of Traditional Knowledge, 2024, 23 (9).
<https://doi.org/10.56042/ijtk.v23i9.13619>
3. Subba Rao C., Ashish S., Prasenjit M., "An Eye-Catching and Comprehensive Review on Plumeria pudica Jacq. (Bridal Bouquet)", Plant Archives, 2020, 20 (2), 2076-2079.
4. Praveen K., Neetu S., Sumeet D., "Ethnomedicinal and Pharmacological Importance of Plumeria pudica Linn.", International Journal of Pharmacy & Life Sciences, 2019, 10 (3), 8-28.
5. Vishal S., Virendra Kumar S., A.K. Singhai, "Phytochemical and Pharmacological Review on Plumeria pudica Jacq.", International Journal of Pharmacy & Life Sciences, 2022, 13 (5), 8-11.
6. Hellen Barbosa F., Dayana L. M., Jorge M. D., Terez V. B., Jalles A. B., Roberto O. S., Ana Cristina T. C. P., Giselle P. F., Mariana V. R., Jand-Venes R. M., Karoline S. A., Ronaldo A. R., Ana Lucia R. B., Jefferson S. de O., "Laticifer Proteins from Plumeria pudica Inhibit the Inflammatory and Nociceptive Responses by Decreasing the Action of Inflammatory Mediators and Pro-inflammatory Cytokines", Revista Brasileira de Farmacognosia, 2015, 25 (3), 269-277.
<https://doi.org/10.1016/j.bjp.2015.05.003>
7. Lidiane E. S. O., Luciana A. M., Bruna S. S., Naylla Veras de Moraes O., Ana Clara S. S., Mayck S. B., Francisca Dayane S. da S., Ana Livia C. F., Vitoria L. R. L., Leucio F. C. F., Erika H. P. A., Cassia D. T. de F., Mariana V. R., Daniele F. P. V., Jefferson S. de O., "Latex Proteins from Plumeria pudica Reduce Ligature-Induced Periodontitis in Rats", Oral Diseases, 2022, 28 (3), 786-795. <https://doi.org/10.1111/odi.13803>
8. Luciane A. B. S., Danielle P. A., Thiago S. L. A., Nataly A. S., Leandro K. M. S., Lidiane E. S. O., Ana Cristina T. C. P., Giselle P. F., Naylla Veras de Moraes O., Bruna S. S., Fabio B. M. S., Mariana V. R., Cassia D. T. de F., Jand-Venes R. M., Jefferson S. de O., "Antidiarrheal Effects of Water-Soluble Proteins from Plumeria pudica Latex in Mice", Biomedicine & Pharmacotherapy, 2018, 97, 1147-1154. <https://doi.org/10.1016/j.biopha.2017.11.019>
9. Naylla Veras de Moraes O., Bruna D. S. S., Luciana A. M., Lidiane E. S. O., Francisco C. B., Danylo A. M., Jalles A. B., Sirleide G. S., Terez V. B., Fabio B. M. S., Erika H. P. A., Daniele F. P. V., Cassia D. T. de F., Mariana V. R., Ana Lucia D. R. B., Jefferson S. de O., "Proteins from Plumeria pudica Latex Exhibit Protective Effect in Acetic Acid Induced Colitis in Mice by Inhibition of Pro-inflammatory Mechanisms and Oxidative Stress", Life Sciences, 2019, 231, 116535.
<https://doi.org/10.1016/j.lfs.2019.06.010>
10. Gabriela L. A., Bruna da Silva S., Ana Carolina S. S., Francisca Dayane S. da S., Thalís F. de S., Alisson P. de O., Jose V. R. M., Luiz P. de S., Andreza F. dos S. B., Amanda J. A., Jose David B. M. Filho, Jose M. T. S., Jefferson S. de O., "Effect of Plumeria pudica Latex Proteins on Intestinal

- Mucositis Caused by 5-Fluorouracil in Mice", Research, Society and Development, 2025, 14 (2), e6914248239.
11. Bruna da Silva S., Ana Clara S. S., Francisca Dayane S. da S., Gabriela L. de A., Thalys F. de S., Alisson P. de O., Anally L. F. L., Gabriela P., Erika H. P. A., Pamela R. C. G., Paulo S. A. S., Silvanio A., Elen B. S. L., Celso M. Q.-Junior, Marcelo M. T., Valeria V. C., Jonathan A. R., Jand-Venes R. M., Cassia D. T. de F., Daniele F. P. V., Jefferson S. de O., "Protective Effect of Latex Proteins from *Plumeria pudica* Against Acetaminophen-Induced Acute Liver Injury", Anais da Academia Brasileira de Ciencias, 2026, 98 (1), e20240815. <https://doi.org/10.1590/0001-3765202620240815>
12. Kajal S., Kishorkumar N. O., Bhanu A. J., "Exploring Phytochemical, Antioxidant, and Antimicrobial Properties of *Plumeria pudica* Jacq. Leaves", Scientific Reports, 2025, 15, 193. <https://doi.org/10.1038/s41598-024-83980-6>
13. Kajal S., Kishorkumar N. O., Bhanu A. J., "Unveiling the Antioxidant and Antimicrobial Properties of *Plumeria pudica* Jacq. Stem Extracts, Backed by Qualitative and Quantitative Phytochemical Analysis", Journal of the Indian Botanical Society, 2025, 105 (4), 324-342. <https://doi.org/10.61289/jibs2025.10.03.0435>
14. Kajal S., Kishorkumar N. O., Bhanu A. J., "Root Extracts of *Plumeria pudica* Jacq. as a Rich Source of Bioactives: Phytochemical, Antioxidant, and Antimicrobial Insights via LC-MS/MS Analysis", New Zealand Journal of Botany, 2026, 64 (1), e70043. <https://doi.org/10.1002/nzb2.70043>
15. Suriyakala G., Sathiyaraj S., Gandhi A. D., Vadakkan K., U. S. M. Rao, Babujanarthanam R., "Plumeria pudica Jacq. Flower Extract-Mediated Silver Nanoparticles: Characterization and Evaluation of Biomedical Applications", Inorganic Chemistry Communications, 2021, 126, 108470. <https://doi.org/10.1016/j.inoche.2021.108470>
16. Shrivastava S. K., Kulshreshtha A., Gangwar R. K., Srivastava S., Tiwari A. P., Singh S., Kumar S., Parveen S., Banerjee M., Chaudhary D. K., "Phyto-Synthesis of Silver Nanoparticles from *Plumeria pudica* Leaf Extract and its Application in Anti-Cancerous Activity", Journal of Experimental Nanoscience, 2023, 18 (1). <https://doi.org/10.1080/17458080.2023.2267183>
17. Matthew J. P., Patrick M. J., Larissa S., Jacqueline B., Isabelle B., Claudio D., Diane C., A. W. S. C., Jodie D., Richard D., Mark D., Jonathan E., Santiago G., Jeremy G., John G., Lars G., Tianjing L., Alicja L., David H., Andrea H., Margaret H., Milos J., Steve J., Deeva K., Andrea K., Iratxe L., Toby L., Nikolas L., Lorna M., Sue M., Giovanni M., Craig O., Craig O., Ioana O., Marie P., James P., France P., Mark S., Jonathan S., Georgia S., James T., Elie T., David T., Virginia T., Lyubov T., Paula W., Penny W., James Y., David M., "The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews", BMJ, 2021, 372, n71.
18. Ravishankar K., Kiranmayi G. V. N., Lalitha Kala M., "Comparative In Vitro, In Vivo Anti-Arthritic and Anti-Inflammatory Activities of *Plumeria pudica* and *Plumeria Rubra* in Albino Rats", Advancement in Medicinal Plant Research, 2021, 9 (2), 40-47.
19. Lincy J., Mathew G., Ajay P., Aleena P., Alen T., Ashin J., Sneha P. K., Vijisha G., "Alpha-Amylase Inhibitory Activity and Ferric Reducing Power of *Plumeria pudica* Flowers", South Asian Research Journal of Pharmaceutical Sciences, 2025, 7 (2), 56-60.
20. Gabriela L. A., Bruna da Silva S., Daniel D. A., Cassia D. T. de F., Jefferson S. de O., "Protective Effect of *Plumeria pudica* Latex Proteins on Intestinal Mucositis Induced by 5-Fluorouracil", Mini-Reviews in Medicinal Chemistry, 2023, 23 (3), 298-306.

21. Das S., Burman S., Chandra G., "In-Vitro Bactericidal Activity of a Novel Plant Source *Plumeria pudica* Against Some Human and Fish Pathogenic Bacteria", *Current Drug Discovery Technologies*, 2021, 18 (4), 503-510.
22. Chavda R., Sharma P., Modi N., "Preliminary Phytochemical Screening, Quantitative Estimation of Total Phenols, Total Flavonoids and Anti-Oxidant Activity of Leaves of *Plumeria pudica* Jacq.", *International Journal of Pharmaceutical Sciences and Research*, 2021.
23. Sharma, Jain, "Evaluation of In Vivo Anti-Inflammatory Action of Leaf Extracts of *Plumeria pudica*", *Current Research in Pharmaceutical Sciences*, 2022.
24. Srivastava S. K., Kulshreshtha A., Srivastava S., Gangwar R. K., "Phytosynthesis of Silver Nanoparticles Using *Plumeria pudica* Floral Extract", *Materials Today: Proceedings*, 2022, 62, 4440-4444. <https://doi.org/10.1016/j.matpr.2022.04.931>
25. Ahmed S., Ahmad M., Swami B. L., Ikram S., "A Review on Plants Extract Mediated Synthesis of Silver Nanoparticles for Antimicrobial Applications: A Green Expertise", *Journal of Advanced Research*, 2016, 7 (1), 17-28.