Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(2), 2212-2219 | ISSN:2251-6727

Deciphering the Chemico-Biological Landscape of Pongamia pinnata (L.) Pierre: Phytoconstituent profiling, Molecular mechanisms, and Expanding Therapeutic horizons

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(Received: 16 January 2026 Revised: 25 February 2026 Accepted: 17 March 2026)

KEYWORDS

Pongamia pinnata; Millettia pinnata; karanja; phytochemistry; pongamol.

ABSTRACT:

Pongamia pinnata (syn. *Millettia pinnata*) is a multipurpose leguminous tree widely distributed across tropical and subtropical regions of Asia and Australia, with expanding cultivation in Africa and the Americas. Traditionally, various parts of the plant have been used in Ayurvedic, Siddha, and folk medicine for managing skin disorders, inflammation, metabolic disturbances, and infectious diseases. Over the past several decades, increasing scientific attention has been directed toward elucidating its diverse phytochemical constituents and pharmacological activities. Phytochemical analyses have identified a rich profile of bioactive compounds, including flavonoids, rotenoids, furanoflavones, tannins, saponins, sterols, and fatty acids, with karanjin and pongamol recognized as major functional molecules. These constituents contribute to a broad spectrum of experimentally validated bioactivities such as antioxidant, anti-inflammatory, antimicrobial, antidiabetic, nephroprotective, cardioprotective, antiparasitic, cytotoxic, and insecticidal properties.

In parallel, *P. pinnata* has gained prominence as a sustainable agroecological resource due to its nitrogen-fixing capability, tolerance to harsh environments, and high seed oil yield, making it an attractive candidate for biodiesel production, soil rehabilitation, and large-scale reforestation programs. Despite promising therapeutic and industrial potential, substantial gaps remain in standardized extract characterization, mechanistic pathway elucidation, and comprehensive toxicological assessment. Moreover, translational research and clinical studies are limited, restricting the advancement of *P. pinnata*-derived compounds into regulated therapeutic or nutraceutical applications.

This review synthesizes available evidence on the phytochemistry, pharmacological activities, toxicity, and ecological relevance of *P. pinnata*, and highlights critical research needs to support future drug discovery, value-added product development, and sustainable biotechnological applications.

1. Introduction

Pongamia pinnata, commonly known as the Pongam tree, is regarded as one of the most valuable and visually striking trees found in India. The genus name Pongamia is derived from the Tamil term “pinnata,” referring to its characteristic pinnate leaves. In regional languages, it is called Ponga, Dalkaramacha, Pongam, and Punku in Tamil, while in Hindi and Bengali it is often referred to as Karanj, Papar, or Kanji. In English, it is popularly known as the Karum tree or Poonga oil tree. The species belongs to the family Leguminosae and the subfamily Papilionaceae[1].

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JCHR (2026) 16(2), 2212-2219 | ISSN:2251-6727

Although native to parts of Asia and Australia, P. pinnata is now widely cultivated in several other regions including Africa and the United States. In India, it typically thrives in coastal belts and along riverbanks and stream edges. This medium-sized tree is known for its rapid growth, making it a promising candidate for ecological restoration and reforestation of degraded lands.

The tree has a sturdy, grey-brown bark, and its new foliage emerges alongside clusters of blossoms. The flowers, which are about 1.3 cm long, occur in dense groups at the tips of elongated stalks arising from the axils of the leaves. Each flower has a very short pedicel, a loose cup-shaped brown calyx, and a combination of white petals along with pink or violet-shaded ones.

Pongamia pinnata has been used for centuries in traditional medicine, encouraging scientific research into its pharmacological potential. Studies have demonstrated that the plant exhibits a wide range of biological activities, including antioxidant, antiparasitic, antimicrobial, antidiabetic, anticancer, anti-inflammatory, anticonvulsant, antihyperammonaemic, cytotoxic, anthelmintic, and insecticidal effects[2,3].

This review synthesizes current knowledge (as of 2025) on the phytochemistry, biological activities, toxicity, and potential applications of P. pinnata. We highlight promising leads, methodological challenges, and areas needing further research.

2. BOTANICAL PROFILE AND TRADITIONAL USES

2.1 Botanical identity and distribution

P. pinnata is native to South and Southeast Asia and parts of northern Australia. It is frequently found in coastal, riparian, or semi-mangrove habitats, but is also widely cultivated beyond its native range due to its ecological and economic value[4].

Morphologically, the tree is medium-sized, with pinnate leaves, and produces seed pods containing oil-rich seeds. The oil — often referred to as “karanja oil” — is a major product. Traditional use also extends to bark, leaves, roots, flowers, and seed-oil or seed-cake[1].

2.2 Traditional / Ethnomedicinal uses

In traditional medicine across India and Asia, various parts of *P. pinnata* are used for a wide range of ailments:

- Skin disorders, ulcers, wounds, and external injuries — by application of leaf pastes or seed oil[4].
- Gastrointestinal issues — anti-diarrhoeal, dyspepsia, flatulence, etc[1].
- Respiratory ailments (bronchitis, cough), rheumatism, joint pain[5].
- Metabolic disorders — such as diabetes — with bark, leaf or flower extracts traditionally used for blood-sugar regulation[6].
- Use of seed oil for infections, skin diseases, possibly as insect repellent or fish poison in rural contexts[7].

Because of this long history of use, *P. pinnata* has attracted scientific attention as a candidate for phyto pharmacological development.

3. PHYTOCHEMISTRY: KEY CONSTITUENTS AND CHEMICAL PROFILE

Comprehensive phytochemical analyses of *P. pinnata* have identified a wide variety of secondary metabolites, including flavonoids, phenolics, terpenoids, fatty acids, and other compounds[7].

3.1 Major classes of compounds

Flavonoids / Rotenoids: Among the noteworthy constituents are flavonoid derivatives, including compounds classified broadly as flavones, flavans, chalcones, and furano-flavonoids/rotenoids. Some of these (e.g., karanjin, pongamol) have been linked to biological activity[1].

Phenolic acids and polyphenols: Various solvent-extract studies (e.g., aqueous methanol) have revealed significant levels of phenolic acids — such as gallic acid, ferulic acid, protocatechuic acid, vanillic acid, and cinnamic acid derivatives — in bark, leaves, and seeds. MDPI+1 These likely contribute to antioxidant and antimicrobial activity[7].

Fatty acids and fixed oils: The seed oil contains triglycerides and fatty acids; this underlies traditional and industrial uses of the oil (e.g., biodiesel, bio-pesticide).

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JCHR (2026) 16(2), 2212-2219 | ISSN:2251-6727

Other constituents: Terpenes, sterols, glycosides, saponins, tannins, and other secondary metabolites have also been reported[9].

3.2 Variability by plant part and extraction method

The composition and yield of bioactive compounds vary significantly depending on the plant part (bark, leaves, seeds) and the solvent used. For example:

Aqueous-methanol extracts of bark provided the highest yield of phenolics and flavonoids compared to seeds and leaves[7].

In a recent study, acetone leaf extract showed substantial levels of saponins, phenolics, tannins, flavonoids, steroids, glycosides — and demonstrated strong in vitro antioxidant and antibacterial activity[8].

These observations underline the importance of standardizing extraction protocols and specifying plant part and solvent in phytochemical and pharmacological studies.

4. PHARMACOLOGICAL AND BIOLOGICAL ACTIVITIES

A broad range of biological activities has been reported for *P. pinnata* extracts and isolates. Much of the evidence comes from in vitro assays or animal models; human clinical data remain scarce. The most studied activities include antioxidant, antimicrobial, anti-inflammatory, antidiabetic, wound healing, cytotoxic/anticancer, and insecticidal.

4.1 Antioxidant activity

Oxidative stress underlies many chronic diseases — and *P. pinnata* extracts have been repeatedly shown to counteract oxidative damage. For instance, in a model of ammonium chloride–induced hyperammonemia in rats, ethanolic leaf extract of *P. pinnata* significantly decreased markers of lipid peroxidation (TBARS, hydroperoxides, conjugated dienes) and elevated antioxidant enzymes (SOD, CAT, GPx) and glutathione in liver and kidney tissues, indicating potent antioxidative and cytoprotective action[11].

Oxidative stress is implicated in many chronic diseases; the antioxidant potential of *P. pinnata* is therefore of considerable interest. Several studies have shown strong radical-scavenging and lipid-peroxidation–inhibition capacity:

A comparative solvent-extract study found that methanol and aqueous-methanol extracts of bark had potent DPPH radical-scavenging activity (IC_{50} ~ 3.21 µg/mL), and strong inhibition of linoleic acid peroxidation[7].

Leaf acetone extract showed 87.5% radical-scavenging inhibition at 625 mg/mL (DPPH assay), and also significant anti-lipoxygenase and anti-protein-denaturation activity (anti-inflammatory surrogate assays)[10].

Seed extracts (ethyl acetate) demonstrated high total phenolic content (TPC) and total flavonoid content (TFC), and powerful antioxidant activity (IC_{50} ~ 18.47 µg/mL)[11].

These data support the hypothesis that polyphenolic compounds and flavonoids in P. pinnata contribute to antioxidative defense, which may underlie other pharmacological effects (anti-inflammatory, cytoprotection, etc.).

4.2 Antimicrobial, antibiofilm, and wound-healing activity

Given its traditional use in treating skin infections and wounds, antimicrobial and wound-healing properties of *P. pinnata* have been evaluated:

Aqueous-methanol and methanol extracts from bark, leaves, and seeds exhibited significant antimicrobial effects against a range of bacteria and fungi; bark extracts tended to show the strongest activity[7].

A recent seed-extract study (ethyl acetate) demonstrated strong antimicrobial and antibiofilm activity: MIC/MBC values against *Staphylococcus epidermidis* were as low as 1.56/3.12 mg/mL; biofilm inhibition was ~97% at MIC[12].

In a Wistar rat model, methanolic leaf extract significantly accelerated wound healing (excision/incision), enhancing wound contraction, tensile strength, hydroxyproline and hexosamine content; also modulated cytokines (early upregulation of TNF-α and IL-6) and enhanced antioxidant defenses (increased catalase, glutathione, SOD; reduced lipid peroxidation)[13].

These findings support both traditional topical uses and the prospect of developing *P. pinnata*-derived antimicrobial / wound-healing agents.

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JCHR (2026) 16(2), 2212-2219 | ISSN:2251-6727

4.3 Antidiabetic and metabolic effects

Though fewer in number, some studies reported blood-glucose-lowering effects in diabetic animal models (leaf or bark extracts), as well as restoration of antioxidant status, indicating potential for managing metabolic disorders. However, results are variable, and mechanisms remain largely unexplored.

Metabolic disorders like diabetes have been a major focus of *P. pinnata* pharmacology. Key findings are:

- In an alloxan-induced diabetic rat model, ethanolic and aqueous leaf extracts significantly reduced blood glucose compared to diabetic controls, and prevented weight loss; in oral glucose tolerance tests, they improved glycemic control[14].
- Flower-extract (ethanolic) administered to alloxan-diabetic rats (300 mg/kg bw) reduced hyperglycemia, mitigated lipid peroxidation (TBARS), and restored antioxidant status (enzymatic and non-enzymatic antioxidants) close to normal levels[6].
- These data suggest that *P. pinnata* extracts may modulate glucose metabolism and oxidative stress — both critical factors in diabetes management. However, the mechanisms remain poorly defined, and there is a lack of data in diabetic models closer to human type 2 diabetes, or in clinical trials.

4.4 Anti-inflammatory and analgesic effects

Inflammation and oxidative stress are often linked; several studies documented anti-inflammatory/analgesic activity using *P. pinnata* extracts:

- In early pharmacological studies, seed, bark, and root extracts demonstrated anti-inflammatory and analgesic actions in rodent models of acute and chronic inflammation, sometimes comparable to standard drugs[15].
- More recently, in vitro anti-lipoxygenase activity, inhibition of protein (albumin) denaturation, and other anti-inflammatory surrogate assays have been reported for acetone leaf extract[10].
- Anti-inflammatory effects may synergize with antioxidant and antimicrobial properties, supporting traditional uses for wounds, skin disorders, and inflammatory diseases.
- Early pharmacological evaluations found that solvent extracts (especially seed extracts) reduced chemically induced paw edema in rat models, with efficacy against eicosanoid-mediated inflammation (e.g., bradykinin, PGE_1), suggesting modulation of inflammatory mediators rather than histamine or serotonin pathways[11].

4.5 Cytotoxic / Anticancer potential

Interest in anticancer activity of herbal extracts has led to evaluation of *P. pinnata* in various models:

- Ethyl acetate seed extract displayed notable cytotoxic activity on K562 leukemia cell lines (IC_{50} ≈ 84.41 µg/mL), while exerting minimal toxicity on normal peripheral blood mononuclear cells (PBMCs, IC_{50} ≈ 410.14 µg/mL) — indicating potential selectivity[12].
- A more recent study on leaf extract evaluated against A431 skin cancer cells (epidermal carcinoma) showed IC_{50} ≈ 89.59 µg/mL; in silico docking suggested strong binding of certain constituents to known anticancer receptors (EGF, EGFR, ERBB2), and molecular simulation supported stability of these complexes[17].
- Similarly, flower-derived ethanolic extract protected rats from nephrotoxicity induced by cisplatin and gentamicin, normalizing renal markers (urea, creatinine) and mitigating histopathological damage — likely via free-radical scavenging by flavonoids such as kaempferol and methoxy-flavones[8].
- While promising, these are preliminary findings: in vitro cytotoxicity and in silico predictions require further validation via animal tumor models and eventually clinical studies.

4.6 Insecticidal and Agricultural / Industrial Relevance

Beyond therapeutic prospects, *P. pinnata* seed oil has significant agro-industrial potential:

- An encapsulated formulation of *P. pinnata* seed oil (containing marker compound karanjin) was developed via micro-encapsulation; it demonstrated in vitro larvicidal activity against *Bombyx mori*, and in vivo insecticidal efficacy against aphids and

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JCHR (2026) 16(2), 2212-2219 | ISSN:2251-6727

whiteflies on eggplant — with substantial population control[18].

- These studies highlight the possibility of *P. pinnata*-derived bio-pesticides as eco-friendly alternatives to synthetic insecticides, especially given concerns over toxicity and environmental impact of conventional chemicals.
- This dual therapeutic + agro-industrial relevance augments the value of *P. pinnata* for sustainable development and bioprospecting.

5. SAFETY, TOXICITY, AND LIMITATIONS OF EVIDENCE

Although several studies report low toxicity of *P. pinnata* extracts or isolates in animal models, the overall toxicological assessment remains incomplete[15].

Early toxicity studies (acute oral) indicated wide safety margins for some extracts; however, chronic toxicity, reproductive toxicity, genotoxicity, and long-term safety data are largely lacking[5].

Variation in extraction procedures, plant parts, and dosages across studies makes it difficult to compare results or standardize a "safe but effective" formulation.

Data on pharmacokinetics, bioavailability, metabolism, and detailed mechanism of action are minimal.

These limitations impede progression from bench to clinical or commercial use. Until rigorous safety evaluation and standardization are performed, broad medicinal use or commercialization (especially as nutraceuticals or functional foods) must proceed cautiously.

5.1 Acute and Subchronic Toxicity Data

Some studies report low acute toxicity for certain extracts of *P. pinnata*. For example, a 70% ethanolic leaf extract administered orally to mice showed no mortality or overt toxicity up to a dose of 10.125 g/kg[19].

In another study using leaf extracts in an oxidative stress model, administration at 300 mg/kg produced antioxidant protection without reported toxicity[11].

However — despite these encouraging findings — the number of well-controlled, GLP-compliant toxicity studies remains very limited. Few studies report standardized phytochemical characterization of the test material, which complicates reproducibility and comparison across experiments.

5.2 Organ Protection vs. Potential Toxicity

Some in vivo work highlights protective effects: for instance, ethanolic flower extract of *P. pinnata* administered to rats ameliorated renal injury induced by cisplatin or gentamicin, normalizing serum urea/creatinine and preventing histopathological renal damage[18].

While this suggests therapeutic potential, it does not substitute for rigorous toxicological evaluation: organ-protection studies do not typically include full panels of toxicology endpoints (e.g. chronic dosing, reproductive toxicity, genotoxicity), and positive effects do not preclude compound-specific or long-term adverse effects.

5.3 Evidence on Metabolic/Chronic Use and Safety

In a 90-day repeated-dose dietary study of edible pongamia oil (EPO) in rats, no significant adverse effects were observed on clinical pathology, hematology, body weight, food consumption, organ histology, urinalysis or thyroid hormones — even at high dietary levels[20].

This is among the more comprehensive toxicology assessments to date for products derived from *P. pinnata*. Still, the scope remains limited: only one study, with defined conditions and diet-based exposure — not necessarily generalizable to all extract types or human use scenarios.

6. CRITICAL APPRAISAL AND KNOWLEDGE GAPS

Based on the literature, several critical gaps and challenges emerge:

6.1 Lack of standardization / extract characterization

Many studies use crude extracts prepared with different solvents, with no or minimal chemical fingerprinting (HPLC/LC-MS), making reproducibility and cross-study comparison difficult.

There is no consensus "standard extract" that could be used across studies.

6.2 Inadequate mechanistic and molecular data

Most pharmacological studies report phenomenological endpoints (e.g., reduced blood glucose, antioxidant

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activity, antimicrobial zones), with minimal data on underlying molecular pathways (e.g., signal modulation, receptor targets, gene expression).

For anticancer claims, in silico docking or in vitro cytotoxicity predominate; in vivo efficacy and safety remain unstudied.

6.3 Sparse Long-Term, Chronic, and Reproductive Toxicity Data

While acute toxicity seems low in some contexts, there is a distinct lack of sub-chronic (beyond 90 days), chronic, reproductive, developmental or multigenerational toxicity studies. No published data on genotoxicity, mutagenicity or carcinogenicity (e.g. Ames test, chromosomal aberration, micronucleus assay) for *P. pinnata* extracts or isolated constituents could be located.

6.4 Lack of clinical or translational studies

Virtually no human trials.

Regulatory and formulation challenges (bioavailability, standardization) remain major obstacles.

6.5 Agronomic and sustainability considerations under-studied

While there is interest in agro-industrial uses (bio-pesticide, biodiesel), there are limited studies on cultivation practices, yield optimization, environmental impact, and socioeconomic viability.

6.6 Future Directions and Recommendations

Given the promising but preliminary nature of evidence, we recommend the following for future research and development:

Standardization: Develop standardized extraction protocols (specifying plant part, solvent, method), with full chemical profiling (HPLC, LC-MS/MS, GC-MS) to define "reference extracts."

Mechanistic studies: Use modern molecular biology tools (transcriptomics, proteomics, metabolomics) to elucidate the biological pathways modulated by *P. pinnata* compounds (e.g., antioxidant response, inflammatory signaling, apoptosis pathways in cancer cells).

Safety and toxicology: Conduct sub-chronic and chronic toxicity studies in animals, including reproductive and genotoxicity assays. Assess safety of standardized extracts or isolated compounds.

Translational research: For promising activities (e.g., antidiabetic, wound healing, antimicrobial), design pilot clinical or human pharmacokinetic studies. Investigate formulations to improve bioavailability, stability (e.g., nano-formulations, encapsulations).

Agronomic and industrial research: Explore sustainable cultivation, breeding or genetic improvement for higher yield and better bioactive/oil profiles; evaluate environmental impact. Develop and test eco-friendly biopesticide or biofuel formulations (e.g., encapsulated seed oil), with field trials and safety evaluation.

Interdisciplinary studies: Encourage collaborations between pharmacologists, chemists, agronomists, toxicologists, and social scientists to assess therapeutic potential, ecological impact, economic viability, and social acceptance.

6.7 Overall Risk–Benefit Assessment: Cautious Optimism

- The available data suggest a favorable safety margin for certain crude extracts or seed oil, particularly in acute or sub-acute contexts.
- Reports of organ-protective effects (e.g., nephroprotection, antioxidant effects) add to potential therapeutic value.
- However, significant gaps remain, especially concerning long-term safety, standardized extract characterization, pharmacokinetics, mutagenicity, and human data.

Until these gaps are addressed by systematic, standardized toxicological and pharmacokinetic studies, broad recommendations for therapeutic, dietary or agro-industrial use of P. pinnata products should be made with caution.

7. CONCLUSION

Pongamia pinnata stands out as a multipurpose tree with significant ethnomedicinal history, a rich array of phytochemicals, and broad pharmacological potential. Research to date supports its antioxidant, antimicrobial, anti-inflammatory, antidiabetic, wound healing, and even cytotoxic (anticancer) properties, along with agro-industrial uses such as bio-pesticides and bio-oil.

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JCHR (2026) 16(2), 2212-2219 | ISSN:2251-6727

However, the current evidence remains largely preclinical, fragmented, and lacking in standardization. For *P. pinnata* to transition from traditional remedy to evidence-backed phytomedicine or industrial application, future work must prioritize standardized extract development, mechanistic studies, comprehensive safety evaluation, and translational research.

In sum, *P. pinnata* offers a promising yet under-exploited resource — with the potential to contribute to natural therapeutics, sustainable agriculture, and green industry — provided rigorous scientific and multidisciplinary efforts are pursued.

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