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Phytochemical and pharmacological potential of medicinal plants used by the Kani tribe of the Southern Western Ghats: An integrative review

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Abstract

The Kani tribe, an indigenous particularly vulnerable tribal group of the Southern Western Ghats of India, possesses a century old ethnomedicinal tradition centered on forest plant resources with significant pharmacological importance. This integrative review examines the phytochemical composition and pharmacological activities of six widely used Kani medicinal species *Triochopus zeylanicus* Gaertn., the primary adaptogenic species, along with *Azadirachta indica* A. Juss., *Ocimum tenuiflorum* L., *Terminalia chebula* Retz., *Centella asiatica* (L.) Urb., and *Syzygium cumini* (L.) Skeels. The major phytochemical groups include alkaloids, flavonoids, phenolic acids, terpenoids, saponins and glycolipids, all of which are associated with key pharmacological properties such as antioxidant, anti-inflammatory, antidiabetic, antimicrobial, hepatoprotective, and adaptogenic effects, supported by both *in vitro* and *in vivo* studies. The glycolipid fractions of *T. zeylanicus* are structurally unique and contribute to adaptogenic activity by modulating the hypothalamic pituitary adrenal axis and enhancing natural killer cell function. Advanced analytical techniques, including gas chromatography-mass spectrometry (GC-MS) and high performance liquid chromatography (HPLC), have enabled the identification of bioactive compounds. However, significant limitations persist, including reliance on crude extracts, lack of phytochemical standardization, insufficient mechanistic validation, and absence of clinical trials. Toxicological data are also limited. Addressing these gaps through bioactivity guided isolation, metabolomics, and clinical validation is essential for translating this traditional knowledge into scientifically validated phytopharmaceutical applications.

1. Introduction

The Western Ghats, extending approximately 1,600 km along the western coastal escarpment of the Indian peninsula, is designated as one of the world's eight biodiversity hotspots, harboring over 5,000 flowering plant species of which nearly one third are endemic (Gaikwad *et al*., 2014; Shigwan *et al*., 2020). Among the tribal communities residing within this biodiversity crucible, the Kani tribe is a particularly vulnerable tribal group inhabiting the Agasthyar Hills of southern Kerala and adjacent Tamil Nadu ranges, stands out for the pharmacological distinctiveness of its medicinal plant knowledge system (Xavier *et al*., 2014). The Kani Pharmacopoeia attained scientific prominence through the landmark identification of *T. zeylanicus*, locally termed Arogyapacha or evergreen health plant as a potent antifatigue and stamina enhancing agent, constituting one of the earliest documented cases of a pharmacologically validated tribal plant preparation in India (Prakash *et al*., 2008). Despite this historical landmark and the pharmacological promise implicit in Kani ethnomedicinal practice, the broader scientific development of this knowledge system has stagnated at the level of ethnobotanical documentation (Xavier *et al*., 2014; Ayyanar and Ignacimuthu, 2011). Systematic phytochemical characterization, compound isolation, mechanistic pharmacology, and most critically clinical validation remain largely absent from the literature. The translation of traditional plant use into evidence-based phytopharmaceuticals require a rigorous, structured research pipeline from phytochemical profiling to clinical trials, a pipeline that has not been adequately applied to Kani medicinal plants (Suntar, 2020; Singh *et al*., 2020). The present integrative review addresses this gap. The objectives are: (i) To systematically correlate identified phytochemical classes with documented pharmacological mechanisms across high use Kani medicinal species, (ii) To critically evaluate the quality and level of pharmacological evidence, differentiating *in vitro*, *in vivo*, and clinical data, (iii) To identify specific translational research gaps, (iv) To articulate a structured research agenda directed toward phytopharmaceutical development. This review is explicitly phytomedicine focused, not ethnobotanical, and is intended to serve as a critical scientific foundation for future drug discovery programs targeting Kani plant resources (Arnason *et al*., 2022).

2. Ethnomedicinal uses

Kani healers use medicinal plants in forms such as aqueous decoctions, fresh juices, pastes, and oil infusions, and these methods of preparation influence the polarity, extraction efficiency, and bioavailability of the active phytochemicals (Sukumaran *et al*., 2021; Priyadharshana *et al*., 2024). Major disease categories addressed include fatigue and physical debility (adaptogenic use), hepatic dysfunction, wound and skin infections, fever, respiratory ailments, and inflammatory conditions. Single plant preparations are preferred for specific therapeutic targets, most notably the use of *T. zeylanicus*

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fruit as a discrete antifatigue agent, whereas polyherbal formulations are used for complex and multisystem disorders. The empirical longevity of these preparations, refined across generations under conditions in which therapeutic failure carried survival consequences, provides strong ecological validity and biological plausibility for systematic pharmacological investigation (Pushpangadan *et al*., 1988).

3. Species selection and justification

Six species were selected based on three clear criteria: (i) High use value reported in multiple ethnobotanical studies of the Kani community, (ii) Availability of phytochemical data with identified compound groups, (iii) Evidence of pharmacological activity in at least one validated experimental system. *T. zeylanicus*, a member of the family Dioscoreaceae and endemic to the Western Ghats, was chosen as the primary species because of its central role in Kani traditional medicine, its unique glycolipid compounds, and its known but not fully understood adaptogenic activity. The other five species were selected based on their wide range of pharmacological effects and the availability of mechanism-based evidence, allowing meaningful comparison of their phytochemical composition and biological activities.

Table 1: Selected Kani medicinal plants: Family, plant part, traditional use, key phytochemicals, and phytochemical class

Scientific name	Family	Part used	Traditional use	Key phytochemicals	Phytochemical class
T. zeylanicus	Dioscoreaceae	Fruit, leaf, seed	Anti-fatigue, hepato-protection, aphrodisiac, stamina	Glycolipids, flavonoids, saponins, sterols	Glycolipids (Primary), Saponins (Secondary)
A. indica	Meliaceae	Leaf, bark, seed	Antimicrobial, anti-inflammatory, antidia-betic, wound healing	Nimbin, azadirachtin, quercetin, nimbidin	Flavonoids (Secondary)
O. tenuiflorum	Lamiaceae	Leaf, seed, whole plant	Fever, antioxidant, respiratory ailments, immunomodulation	Eugenol, rosmarinic acid, ursolic acid, luteolin	Phenolics (Primary), Terpenoids (Secondary)
T. chebula	Combretaceae	Fruit	Liver disorders, digestive complaints, antioxidant, antimicrobial	Gallic acid, chebulinic acid, ellagic acid, tannins	Phenolics (Primary), Tannins (Secondary)
C. asiatica	Apiaceae	Whole plant, leaf	Wound healing, CNS disorders, anti-inflam-matory, adaptogenic	Asiaticoside, madecasso-side, brahmoside, centelloside	Triterpenoids (Primary), Saponins (Secondary)
S. cumini	Myrtaceae	Seed, bark, leaf	Antidiabetic, antioxidant, antimicrobial, gastrointestinal	Myricetin, gallic acid, ellagic acid, anthocyanins	Flavonoids (Primary), Phenolics (Secondary

4. Phytochemical profile

The pharmacological activities of Kani medicinal plants are mainly based on a wide variety of secondary metabolites, whose chemical structures determine how they interact with biological targets such as enzymes, receptors, and cell membranes. These structural differences allow the compounds to produce specific biological effects by binding to active sites or modifying cellular functions. The phytochemical composition of these plants is also influenced by environmental conditions (Mengane and Kamble, 2015). Factors such as altitude, soil type, and the microclimate of the Agasthyar Hills play an important role in shaping the type and concentration of secondary metabolites present in these species (Senguttuvan and Subramaniam, 2016).

4.1 Alkaloids

Alkaloids are nitrogen containing secondary metabolites whose structural variation allows them to interact specifically with biological targets such as enzyme active sites, ion channels, and microbial membranes. In *A. indica*, limonoid type terpenoids (tetranortriter-penoids) such as nimbidin and nimbinine inhibit key enzymes like phospholipase A_2 and cyclooxygenase enzymes (COX), which are involved in the synthesis of proinflammatory prostaglandins from arachidonic acid. This inhibition contributes to the anti-inflammatory activity observed in this species. Alkaloids similar to berberine, reported in several Kani related plants, also show strong inhibitory effects on α-glucosidase at low concentrations, which is important for controlling post meal blood glucose levels (Huang *et al*., 2022). The alkaloid profile of *T. zeylanicus* remains incompletely characterized a significant phytochemical gap for the primary Kani species underscoring the need for comprehensive metabolite profiling of this species using modern analytical platforms (George *et al*., 2016).

4.2 Flavonoids

Flavonoids are polyphenolic compounds with a C6-C3-C6 structural framework, giving them a wide range of biological activities. Compounds such as quercetin, kaempferol, rutin, luteolin, and myricetin have been reported in Kani medicinal plants, with myricetin identified as a major flavonoid in *S. cumini* seeds through chromatographic and spectroscopic analysis (Sultan *et al*., 2023). Their antioxidant activity is mainly due to their ability to neutralize reactive oxygen species through hydrogen atom transfer and metal ion chelation. This activity depends on structural features such as hydroxyl groups and a catechol structure in the B-ring, seen in quercetin and myricetin. Flavonoids also reduce inflammation by regulating signaling pathways and lowering proinflammatory

cytokines such as tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1α), and interleukin-6 (IL-6), along with selective cyclooxygenase-2 (COX-2) inhibition. They also contribute to antidiabetic activity by activating peroxisome proliferator activated receptor gamma (PPAR-γ) receptors and inhibiting α-glucosidase at the intestinal level, helping control postprandial glucose levels. Chromatographic analysis (see section 4.6) has confirmed compounds such as quercetin and kaempferol in standardized extracts of *T. chebula* and *O. tenuiflorum*, supporting their role in dosage standardization (Liu *et al*., 2023; Sultan *et al*., 2023).

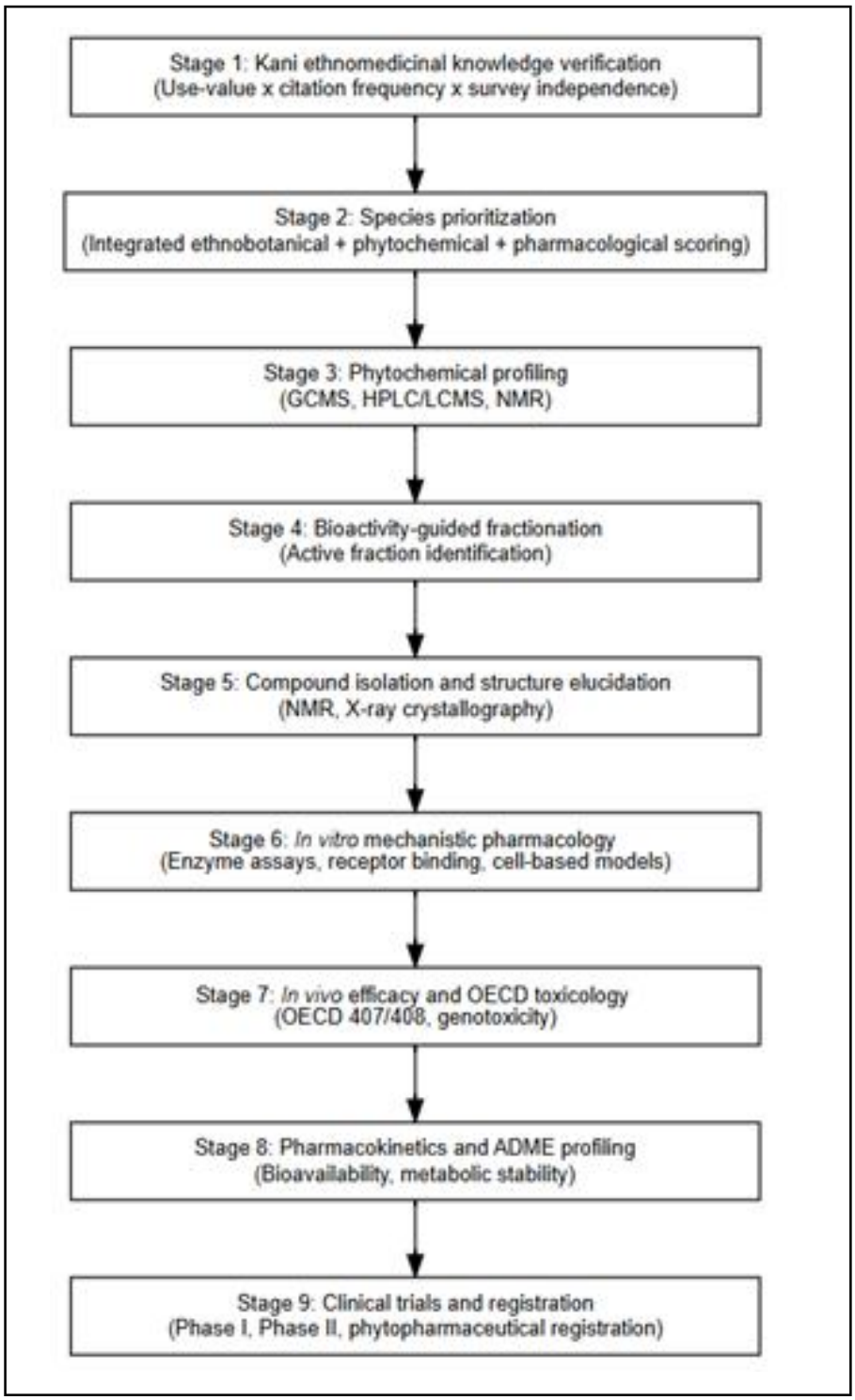

Figure 1: Ethnomedicine to drug discovery research pipeline for Kani medicinal plants.

4.3 Phenolic acids

Phenolic acids are major contributors to the antioxidant activity of several Kani medicinal plants, especially *T. chebula* and *O. tenuiflorum* (Kumar, 2023). In *T. chebula*, compounds such as gallic acid, ellagic acid, and chebulinic acid are present in high amounts and are responsible for strong free radical scavenging activity (Sehgal *et al*., 2024; Dhingra *et al*., 2022). These compounds not only neutralize reactive oxygen species but also enhance cellular antioxidant defense by activating protective pathways. Gallic acid, for example, stimulates the nuclear factor erythroid 2 related factor 2 (Nrf2) pathway, which increases the expression of detoxifying and antioxidant enzymes, providing additional protection to cells. In *O. tenuiflorum*, rosmarinic acid contributes to both antioxidant and anti-inflammatory effects by reducing prostaglandin synthesis and nitric oxide production in immune cells (Beltran-Noboa *et al*., 2022; Bhattarai *et al*., 2024). Although, phenolic compounds are reported in *T. zeylanicus*, their detailed structural characterization remains limited.

4.4 Terpenoids

Terpenoids are a large and diverse group of plant metabolites with important pharmacological roles. They are derived from the mevalonate and methylerythritol phosphate pathways and include monoterpenes, sesquiterpenes, diterpenes, and triterpenes (Huang *et al*., 2022; Dewi and Yuniati, 2025). In *A. indica*, limonoid terpenoids such as nimbin, nimbidin, and azadirachtin show strong anti-inflammatory and antimicrobial activity by inhibiting key inflammatory pathways and affecting microbial cell membranes. In *C. asiatica,* triterpenoid compounds like asiaticoside and madecassoside promote wound healing by stimulating collagen synthesis in skin cells through growth factor mediated signaling (Bandopadhyay *et al*., 2023; Handayani *et al*., 2025). Ursolic acid, present in *O. tenuiflorum* and *T. chebula*, contributes to liver protection by stabilizing cellular membranes and reducing fibrotic changes in liver tissue.

Table 2: Phytochemical classes, key compounds, mechanisms of action, and corresponding pharmacological activity

Phytochemical class	Key compounds	Mechanism of action	Pharmacological activity	References
Alkaloids	Nimbidin, berberine, nimbinine	Inhibition of α-glucosidase and acetylcholinesterase (AChE), disruption of microbial membranes	Antidiabetic, antimicrobial, central nervous system modulation.	Bhat *et al*., 2011
Flavonoids	Quercetin, kaempferol, myricetin, rutin, luteolin	Reactive oxygen species (ROS) scavenging *via* hydrogen atom transfer (HAT) /single electron transfer (SET), nuclear factor kappa B (NF-κB) pathway suppression, COX-2 inhibition, PPAR-γ activation	Antioxidant, anti-inflammatory, antidiabetic	Sharma and Yadav, 2022
Phenolic acids	Gallic acid, rosmarinic acid, ellagic acid, chebulinic acid	Activation of nuclear factor erythroid 2 related factor 2 (Nrf2)/heme oxygenase-1 pathway, protein binding, inhibition of Fenton reaction	Antioxidant, hepatoprotective, antimicrobial	Chen *et al*., 2025
Terpenoids	Nimbin, azadirachtin, ursolic acid, asiaticoside madecassoside	Cyclooxygenase (COX) and lipoxygenase (LOX) inhibition, NF-κB pathway inhibition, stimulation of collagen synthesis *via* TGF-α1	Anti-inflammatory, wound healing, antimicrobial, hepato protective	Bandopadhyay *et al*., 2023
Saponins/glycolipids	Asiaticoside, madecassoside, brahmoside	Regulation of the hypothalamic pituitary adrenal (HPA) axis, activation of NK cells, stabilization of hepatocyte membranes	Adaptogenic, immunomodulatory, hepatoprotective	Singh *et al*., 2005
Tannins	Chebulagic acid, punicalagin, ellagitannins, gallotannins	Protein precipitation; inhibition of biofilm formation, free radical scavenging DPPH (2,2-diphenyl-1-picrylhydrazyl)	Antimicrobial, antioxidant, antidiarrheal	Cheng *et al*., 2003

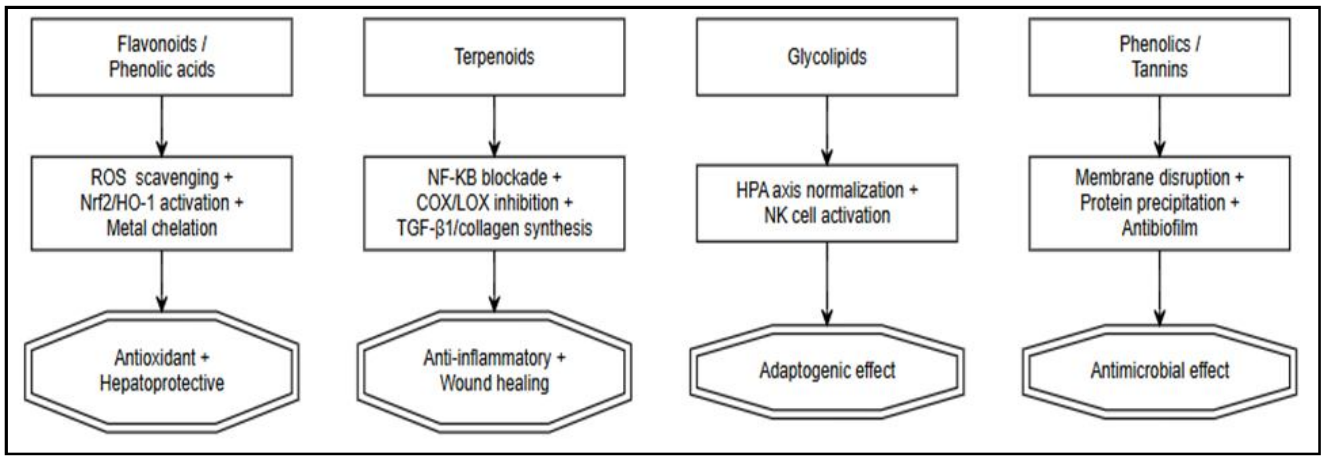

Figure 2: Molecular mechanism pathways of key phytochemical classes in Kani medicinal plants.

5. Pharmacological activities

5.1 Saponins and glycolipids

Saponins and glycolipids form an important class of bioactive compounds in Kani medicinal plants, with the glycolipid fraction of *T. zeylanicus* being particularly significant. These compounds are amphiphilic in nature, allowing them to interact with both aqueous and lipid environments, which influences their biological activity. Glycolipids isolated from the ripe fruits of *T. zeylanicus* have been shown to enhance physical endurance, regulate stress related hormonal responses, and improve immune function. These effects are associated with modulation of the hypothalamic pituitary adrenal axis and increased activity of natural killer cells, supporting their adaptogenic role. The structural features of these glycolipids differ from commonly known plant saponins, indicating a distinct class of bioactive molecules. In *C. asiatica*, triterpenoid saponins such as asiaticoside and madecassoside contribute to immunomodulatory and wound healing activities by influencing inflammatory pathways and promoting tissue repair processes (Bandopadhyay *et al*., 2023).

i. *In vitro* evidence

All six reviewed species show antioxidant activity in standard *in vitro* assays, although the strength and underlying mechanisms vary between species and extract fractions. *T. chebula* shows the highest DPPH radical scavenging activity, mainly due to its high content of hydrolysable tannins such as gallic acid, ellagic acid, and chebulinic acid, which act as effective hydrogen donors in free radical neutralization (Cheng *et al*., 2003). Extracts of *S. cumini* seeds also demonstrate strong antioxidant potential in 2,2 azinobis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS) assays, with myricetin rich flavonoid fractions contributing through both hydrogen atom transfer and single electron transfer mechanisms (Syama *et al*., 2018). This is further supported by high ferric reducing antioxidant power (FRAP) values. Flavonoids such as quercetin and myricetin also contribute through metal ion chelation, reducing Fe^{2+} mediated fenton reactions and thereby limiting hydroxyl radical formation. In *O. tenuiflorum*, eugenol shows strong DPPH scavenging activity at low micromolar concentrations, while rosmarinic acid enhances antioxidant effects through activation of the Nrf2/HO-1 pathway (Wei *et al*., 2018).

ii. *In vivo* evidence

In vivo studies further support the antioxidant potential of these plants. Administration of *O. tenuiflorum* leaf extract increases antioxidant enzyme levels such as superoxide dismutase (SOD) and catalase, while reducing malondialdehyde (MDA), a key marker of lipid peroxidation, in chronically stressed rodents (Jiang *et al*., 2021). Similarly, *T. chebula* extract restores hepatic reduced glutathione levels in paracetamol induced hepatotoxic rats, consistent with activation of Nrf2 mediated antioxidant pathways. These findings confirm that antioxidant activity observed in *in vitro* assays is also reflected at the tissue level under physiological conditions.

iii. Clinical evidence

Clinical evidence supporting antioxidant activity in Kani specific plant preparations is currently lacking. Available clinical studies on *C. asiatica* focus mainly on disease related outcomes rather than systemic antioxidant biomarkers and do not involve preparations directly linked to Kani practice. This highlights the need for well-designed clinical studies to validate these findings in human populations.

5.2 Anti-inflammatory activity

i. *In vitro* evidence

The anti-inflammatory activity of Kani medicinal plants mainly involves regulation of key pathways such as nuclear factor kappa B (NF-κB) signaling and COX/LOX enzyme activity. In *A. indica*, limonoid compounds, especially nimbidin, inhibit NF-κB activation in LPS stimulated RAW 264.7 macrophages, leading to reduced production of proinflammatory cytokines such as TNF-α, IL-1α, and IL-6, along with decreased nitric oxide formation through inducible nitric oxide synthase (iNOS) inhibition (Ugwu and Suru, 2021). Eugenol from *O. tenuiflorum* shows selective inhibition of COX-2 in enzyme-based assays, with IC_{50} values below 10 µM, indicating strong anti-inflammatory potential through interaction with the arachidonic acid pathway. Flavonoids such as myricetin and quercetin from *S. cumini* also inhibit 5-lipoxygenase (5-LOX), resulting in reduced synthesis of both prostaglandins and leukotrienes (Syama *et al*., 2018). This combined COX/LOX inhibition provides broader anti-inflammatory effects compared to single-pathway inhibition. In *C. asiatica*, asiaticoside suppresses NF-κB and mitogen activated protein kinase (MAPK) signaling pathways and reduces prostaglandin E2 production in cell-based models.

ii. *In vivo* evidence

In vivo anti-inflammatory activity has been widely evaluated using the carrageenan induced paw edema model in Wistar rats. Ethanolic extracts of *A. indica* leaves at a dose of 400 mg/kg significantly reduce edema volume by 500-60%, showing effects comparable to standard drugs such as indomethacin. Triterpene rich fractions from *C. asiatica* reduce inflammatory markers including IL-6, TNF-α, and C-reactive protein (CRP), along with suppression of NF-κB and MAPK signaling in tissue samples (Jiang *et al*., 2021). These findings indicate that the molecular effects observed *in vitro* are also reflected in whole-animal models.

iii. Clinical evidence

No randomized controlled trials examining the anti-inflammatory efficacy of Kani specific plant formulations in defined clinical inflammatory conditions have been published. Observational studies of topical *A. indica* preparations in dermatological inflammation exist but lack randomization, standardization, and validated inflammatory biomarker endpoints.

5.3 Antimicrobial activity

i. *In vitro* evidence

S. cumini has been the most extensively studied species for antidiabetic activity among the reviewed plants. Standardized hydroalcoholic seed extracts show strong inhibition of carbohydrate digesting enzymes such as α-amylase and α-glucosidase, with IC_{50} values for α-glucosidase inhibition ranging from 0.8-1.4 mg/ml, which falls within the pharmacologically relevant range for controlling postprandial blood glucose levels (Shinde *et al*., 2008). Myricetin has been identified as the main active compound, acting through competitive inhibition at the enzyme active site, supported by enzyme kinetics and molecular docking studies. In *T. chebula*, tannin components such as gallic acid and chebulinic acid also inhibit α-glucosidase, though through non competitive mechanisms, with activity observed at physiologically relevant concentrations (Feng *et al*., 2021). In *O. tenuiflorum*, eugenol shows partial inhibition of α-amylase and protein tyrosine phosphatase, which plays a role in insulin signaling, providing a dual mechanism for glucose regulation (Varadharajan *et al*., 2025). The antidiabetic activity of *T. zeylanicus* has not been studied, indicating an important research gap.

ii. *In vivo* evidence

In vivo antidiabetic studies have mainly used streptozotocin (STZ) induced and alloxan induced diabetic rat models. Extracts of *S. cumini* bark and seeds significantly reduce fasting blood glucose levels by 30-45% and improve serum insulin levels in STZ induced diabetic rats (Kumar *et al*., 2008; Prabakaran and Shanmugavel, 2017). Histological studies also show improvement in pancreatic β-cell structure, suggesting partial insulinotropic effects in addition to enzyme inhibition. *T. chebula* fruit extract reduces blood glucose levels and also improves lipid profiles, including reductions in triglycerides and low density lipoprotein cholesterol, which is relevant for managing metabolic complications of diabetes. Extracts of *O. tenuiflorum* also lower blood glucose levels by increasing peripheral glucose utilization and partially inhibiting á-glucosidase in alloxan-induced diabetic models.

iii. Clinical evidence

Non randomized clinical studies have reported modest fasting blood glucose reduction with *S. cumini* seed preparations in type 2 diabetic patients (Bhat *et al*., 2011). These studies are invariably limited by small sample sizes (n<30), absence of active drug comparators, non-standardized phytochemical preparations, and lack of glycated hemoglobin (HbA1c) follow up precluding definitive clinical interpretation. No clinical antidiabetic trial using Kani-attributed preparations has been reported.

5.4 Antimicrobial activity

i. *In vitro* evidence

A. indica leaf, bark, and seed extracts show broad spectrum antimicrobial activity against organisms such as *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella typhi*, and *Candida albicans* in disc diffusion and broth microdilution assays. Reported minimum inhibitory concentration (MIC) values range from 0.5-4.0 mg/ml for bacteria and 1.0-8.0 mg/ml for fungi. Limonoid terpenoids such as nimbidin and azadirachtin act mainly by disrupting microbial cell membranes and interfering with electron transport processes. Flavonoid and phenolic compounds contribute through protein binding and inhibition of cell wall synthesis. Tannin rich fractions from *T. chebula* also show strong antibiofilm activity against methicillin resistant *Staphylococcus aureus* by inhibiting biofilm matrix formation, which is important in chronic infections. In *O. tenuiflorum*, essential oil shows antimicrobial activity against *S. aureus*, with MIC values ranging from 0.5 to 2.0 mg/ml across studies, though results vary due to differences in experimental conditions.

ii. *In vivo* and clinical evidence

In vivo antimicrobial studies are mainly limited to wound infection models, where topical application of *A. indica* extracts improves bacterial clearance and accelerates wound healing in rodent models. Clinical evidence is limited to observational reports of topical formulations for minor skin infections. Systematic clinical trials evaluating systemic antimicrobial effects have not been reported, indicating an important gap in translational research.

5.5 Hepatoprotective activity

i. *In vitro* and *in vivo* evidence

Glycolipid fractions from *T. zeylanicus* represent one of the most significant hepatoprotective components among the reviewed species. In carbon tetrachloride induced hepatotoxicity models in Wistar rats, which simulate oxidative liver damage, treatment with these glycolipids leads to a marked reduction in serum alanine aminotransferase (ALT) aspartate aminotransferase (AST) levels by 45-60% compared to untreated controls, along with decreased lipid peroxidation, restoration of hepatic glutathione (GSH), and improvement in liver histology, including reduced hepatocyte damage and necrosis. These effects are linked to stabilization of mitochondrial function and activation of Nrf2 mediated antioxidant pathways (Chen *et al*., 2025). *T. chebula* also shows hepatoprotective effects, mainly due to gallic acid, which activates Nrf2/HO-1 signaling and suppresses NF-κB, leading to reduced oxidative stress and inflammation in paracetamol induced liver injury models. Ursolic acid from *O. tenuiflorum* further contributes by inhibiting transforming growth

factor (TGF)-β1 signaling in hepatic stellate cells, thereby reducing fibrosis and collagen deposition, which is important in chronic liver disease (Wang *et al*., 2019; Zheng *et al*., 2024).

ii. Clinical evidence

Clinical evidence for hepatoprotective activity of Kani specific plant preparations is not available. Some studies on polyherbal formulations containing *T. chebula*, such as Triphala, report improvements in liver function, but these are limited to small observational studies. Well-designed clinical trials with standardized preparations and validated endpoints are still lacking.

5.6 Adaptogenic activity

i. *In vitro* and *in vivo* evidence

Adaptogenic activity, defined as the ability to enhance resistance to physical, chemical, and biological stress, represents one of the most distinctive pharmacological properties of Kani medicinal plants, with *T. zeylanicus* showing the strongest evidence among the reviewed species. Glycolipid fractions isolated from the ripe fruits of this plant exhibit significant adaptogenic effects, as reflected by increased physical endurance, reduced stress induced organ changes, and lowered stress hormone levels in experimental models. These effects are also associated with reduced oxidative stress, indicated by decreased lipid peroxidation. At the cellular level, these glycolipid fractions enhance immune response by increasing natural killer cell activity, which is important in conditions of stress induced immunosuppression. The underlying mechanism involves regulation of HPA axis, maintaining hormonal balance, along with induction of heat shock proteins such as HSP70, which protect cells under stress conditions. Although, similar functional effects are observed in established adaptogens such as *Panax ginseng* and *Withania somnifera*, the glycolipid compounds of *T. zeylanicus* are structurally distinct, suggesting the presence of a unique adaptogenic class. *O. tenuiflorum* also shows moderate adaptogenic activity. Its leaf extracts help regulate stress hormone levels, reduce stress related gastric damage, and improve immune function. These effects are linked to eugenol mediated anti-inflammatory action, heat shock protein induction, and partial regulation of the HPA axis, complementing the stronger activity observed in *T. zeylanicus*.

ii. Clinical evidence

Clinical evidence supporting adaptogenic activity of *T. zeylanicus* is currently not available. Data on pharmacokinetics, including absorption, distribution, metabolism, and elimination of glycolipid compounds, have not been reported. This represents an important gap in translating strong preclinical findings into clinical application.

Table 3: Summary of pharmacological evidence by study type, species, activity, and evidence level

Study type	Species	Activity	Key finding	Model used	Evidence level
In vitro	*T. zeylanicus*	Adaptogenic/ Hepatoprotective	Glycolipid fractions enhance NK cell activity and show hepatocyte protection	Cell-free/cell-based assays	High mechanism clearly defined
In vivo	*T. zeylanicus*	Adaptogenic	Increased endurance, reduced adrenal enlargement, and lower corticosterone levels under stress	Forced swim/rodent stress models	Moderate pharmacok-inetic data lacking
In vitro	*A. indica*	Anti-inflammatory/ Antimicrobial	Suppression of NF-κB in macrophages; antimicrobial activity against *S. aureus* and *E. coli*	RAW 264.7 cells/ MIC assays	High mechanism defined
In vivo	*A. indica*	Anti-inflammatory	Reduction of paw edema by limonoid fractions	Carrageenan induced rat model	Moderate crude extract used
In vitro	*O. tenuiflorum*	Antioxidant/ COX inhibition	Strong DPPH and ABTS sca-venging; eugenol shows COX-2 inhibition (IC_{50} < μM)	DPPH/ABTS/enzyme assays	High active compound identified
In vivo	*O. tenuiflorum*	Antioxidant/ Immunomodulatory	Increased SOD and catalase, reduced MDA, enhanced immune response under stress	Chronic stress rodent model	Moderate extract standardization limited
In vitro	*T. chebula*	Antioxidant/ Antimicrobial	High DPPH activity, tannins inhibit MRSA biofilm formation	DPPH/biofilm inhibi tion assays	High compounds identified
In vivo	*T. chebula*	Hepatoprotective	Reduction in liver injury markers (ALT, AST) and restoration of GSH levels	Rat hepatotoxicity models	Moderate active compound inferred
In vitro	*C. asiatica*	Wound healing/ Neuroprotective	Stimulates collagen synthesis, shows AChE inhibition	Fibroblast culture/ enzyme assays	High asiaticoside characterized
***In vivo* + clinical**	*C. asiatica*	Wound healing/Venous insufficiency	Improved wound healing, supported by Phase II clinical study	Diabetic rat model/ clinical trial	Highest among reviewed species
In vitro	*S. cumini*	Antidiabetic/Anti-oxidant	Inhibition of α-amylase and α-glucosidase, antioxidant activity linked to myricetin	Enzyme assays/DPPH	High active compound identified
In vivo	*S. cumini*	Antidiabetic	Reduced blood glucose and improved β-cell structure	STZ induced diabetic rat model	Moderate crude extract used

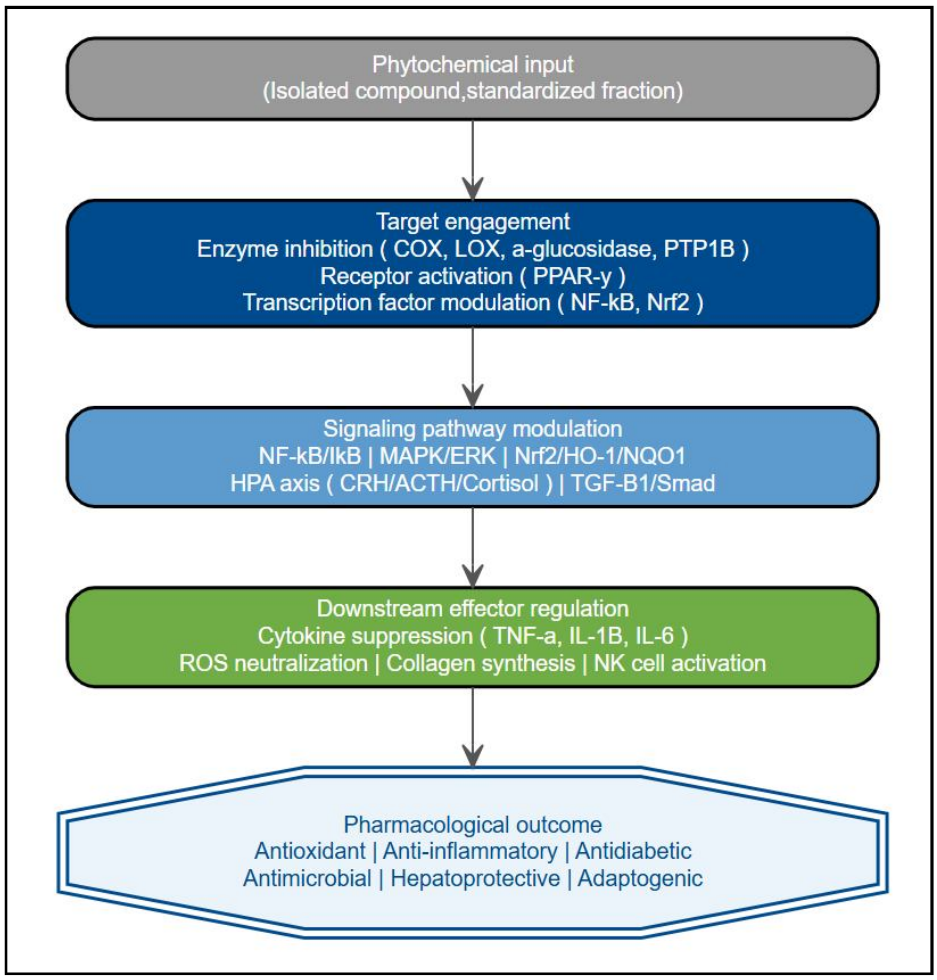

Figure 3: Pharmacological pathway flowchart: Phytochemicals to biological outcomes.

6. Toxicological consideration and safety profile

A major but often overlooked limitation in the current Kani phytomedicine literature is the lack of comprehensive toxicological evaluation, meaning that the safety of these medicinal plants has not been adequately established (Maru and Belemkar, 2025). Most of the available studies are limited to acute oral toxicity assessments, which involve administering a single high dose to animal models and observing short term effects. In the case of *T. zeylanicus*, acute toxicity studies have reported no mortality or observable behavioural changes in experimental animals, with the median lethal dose (LD_{50}) exceeding 3000 mg/kg body weight, indicating a wide margin of short term safety (George *et al*., 2016). However, essential long term evaluations such as subchronic (28 day) and chronic (90 day) toxicity studies, as outlined in Organisation for Economic Co-operation and Development (OECD) guidelines 407 and 408, have not been conducted for any of the reviewed species, particularly in the context of Kani specific formulations (Deshpande *et al*., 2017; Lim *et al*., 2021). Similarly, there is a complete absence of genotoxicity studies, including standard tests like the Ames bacterial reverse mutation test, micronucleus assay, and chromosomal aberration test, which are necessary to determine potential DNA damage (Chen *et al*., 2022). Reproductive and developmental toxicity studies, which assess effects on fertility, pregnancy, and offspring development, are also lacking. This gap creates both a regulatory barrier, as such data are required for clinical trials and drug approval, and a scientific barrier, as it prevents accurate determination of safe and effective dosage ranges. The use of polyherbal formulations in Kani practice further complicates the issue, as interactions between phytochemicals from different plant species may lead to unexpected or emergent toxicity that cannot be predicted from studies on individual plants alone. In addition, the presence of structurally unique glycolipids in *T. zeylanicus* raises specific concerns, as their amphiphilic nature suggests that they may behave like surfactants and potentially disrupt cell membranes at higher concentrations, effects that are unlikely to be detected through standard acute toxicity testing. Therefore, detailed studies on absorption, distribution, metabolism, and excretion, along with toxicokinetic evaluation, are necessary to fully understand their behaviour in the body. Overall, systematic toxicological assessment following international regulatory standards is essential and cannot be overlooked if these ethnomedicinal resources are to be developed into safe and effective therapeutic agents (Lim *et al*., 2021).

7. Critical appraisal: Research limitations

A rigorous critical assessment of the evidence base for Kani medicinal plants reveals five interconnected methodological limitations that

fundamentally constrain translational progress (Kaggwa *et al*., 2023). First, the near complete reliance on crude, unfractionated plant extracts represent the most pervasive limitation. Crude extract pharmacology precludes mechanistic attribution of biological activity to specific chemical entities, renders inter laboratory comparison methodologically invalid due to compositional variability, and produces pharmacologically uninterpretable potency values (IC_{50}, MIC) that cannot be translated into compound specific dose response relationships (Panchal *et al*., 2022). Active constituents, inactive compounds, and potential antagonists co-exist in crude extracts without differentiation, systematically confounding pharmacological interpretation (Shruti *et al*., 2025).

Second, phytochemical standardization is conspicuously absent from the literature. The absence of validated analytical methods for marker compound specification and batch quality control means that 'extract' designations across studies cannot be reliably compared-a preparation of *T. chebula* fruit in one study may differ compositionally from another by an order of magnitude depending on harvest location, season, drying method, and extraction protocol. The pharmacological consequences of this compositional variability are entirely uncharacterized. Third, compound-level mechanistic pharmacology molecular target identification, receptor binding affinity characterization, kinetic enzyme inhibition parameters, downstream signaling cascade delineation, and pharmacophore mapping-is largely absent for all reviewed Kani species, most critically for *T. zeylanicus* glycolipids.

Fourth, the absence of OECD compliant *in vivo* toxicological datasets for all reviewed species in their Kani preparation forms constitutes actual regulatory regulatory and ethical barrier to clinical investigation. This cannot be overcome by extrapolation from acute toxicity data alone. Fifth and most critically from translational perspective clinical trial evidence is non existent for all Kani specific plant preparations. The entire evidence base is preclinical, leaving an unbridged gap between animal pharmacology and human therapeutic application that no amount of additional *in vitro or in vivo* data can substitute for. These five limitations are not independent, crude extract dependency precludes standardization, which precludes compound level mechanistic studies, which in turn undermines the scientific rationale and dosage rationalization required for clinical trial design (Shruti *et al*., 2025).

Table 4: Major research gaps, scientific impact, and recommended future directions for Kani medicinal plant research

Research gap	Scientific impact	Future direction
Use of crude extracts	Biological activity cannot be clearly linked to specific compounds; results may lack reproducibility	Bioactivity guided fractionation and isolation of active compounds for each species
Lack of phytochemical standardization	Difficult to compare results across studies, dosage optimization becomes unclear	HPLC fingerprinting and validation of marker compounds for standardization
Absence of compound level mechanistic studies	Target interactions and downstream signaling pathways remain unclear	Molecular docking, target identification, and in vitro pathway analysis
Limited toxicological data	Safety at therapeutic doses not well established, limits clinical translation	Sub chronic and chronic toxicity studies following OECD guidelines (407/408); genotoxicity tests such as Ames and micronucleus assays
No clinical trials	Gap between preclinical findings and human outcomes	Phase I safety studies followed by Phase II randomized controlled trials
Lack of metabolomics studies	Interactions within complex plant mixtures remain unclear	Untargeted LCMS metabolomics and chemometric analysis
Incomplete characterization of Trichopus glycolipids	Structural details, pharmacokinetics, and biological behaviour not fully understood	Detailed structural analysis and pharmacokinetic studies including bioavailability

8. Future perspectives

A structured, multi-stage research program is required to convert the pharmacological promise of Kani medicinal plants into evidence-based phytopharmaceuticals. The immediate priority is bioactivity guided fractionation of *T. zeylanicus* fruit, leading to isolation of individual glycolipid components, their complete stereochemical characterization by high field nuclear magnetic resonance spectroscopy and, where crystallizable, single crystal X-ray diffraction, and their individual pharmacological profiling in validated adaptogenic, hepatoprotective, and immunomodulatory assay systems (Singh *et al*., 2005). This must be followed by pharmacokinetic characterization oral bioavailability via *in situ* intestinal perfusion or Caco-2 monolayer permeability, plasma protein binding, metabolic stability in human liver microsome incubations, and tissue distribution data entirely absent from the current literature.

Untargeted metabolomics using high resolution LCMS, combined with multivariate chemometric analysis (principal component analysis, orthogonal partial least squares), should be applied to comprehensively profile the secondary metabolite space of all reviewed species under ecologically representative growing conditions from Kani habitats. This approach will identify previously unreported bioactive constituents, model the phytochemical basis of synergistic interactions in polyherbal Kani formulations, and enable batch to batch quality control fingerprinting. In silico network pharmacology reverse docking and target fishing of identified metabolites against disease relevant protein interactomes will efficiently prioritize compound target interactions for experimental validation, substantially reducing early discovery resource requirements (Sharma and Yadav, 2022). Mechanism based *in vivo* pharmacology using genetically defined disease models (STZ/ high fat diet combined type 2 diabetes model, CCl_4, chronic fibrosis model, HPA axis hyperactivation chronic stress model) with isolated,

analytically characterized compounds will establish rigorous causal pharmacology. Standardized, multi site reproducible *in vivo* datasets will then provide the scientific and regulatory foundation for OECD compliant sub chronic and chronic toxicology, followed by Phase I dose escalation safety trials and Phase II randomized efficacy trials in defined clinical indications.

9. Conclusion

The medicinal plants of the Kani tribe represent a pharmacologically coherent ethnomedicinal system whose preclinical evidence base is sufficiently robust to justify a structured drug discovery program, but insufficiently developed to support clinical recommendations. The phytochemical richness of the reviewed species encompassing structurally diverse alkaloids, flavonoids, phenolic acids, terpenoids, tannins, and the pharmacologically unique glycolipids of *T. zeylanicus* provides mechanistically plausible chemical explanations for the antioxidant, anti-inflammatory, antidiabetic, antimicrobial, hepatoprotective, and adaptogenic activities documented in cell-based and animal experimental systems. Pharmacological evidence is strongest for anti-inflammatory (NF-κB/COX mechanisms), antioxidant (Nrf2/ROS mechanisms), and hepatoprotective activities across multiple species, and for adaptogenic activity specific to *T. zeylanicus* glycolipids. The antidiabetic pharmacology of *S. cumini* and *T. chebula* is well supported mechanistically, with enzyme inhibition kinetics established for key phytoconstituents. *T. zeylanicus* warrants unambiguous designation as the highest priority target for advanced phytopharmaceutical development within the Kani medicinal plant repertoire and its glycolipid fractions constitute a structurally novel, mechanistically distinctive adaptogenic pharmacophore class without equivalent in mainstream botanical medicine. If fully isolated, structurally characterized, and clinically validated, these glycolipids could represent a genuinely new class of adaptogenic phytopharmaceuticals with applications in stress related disorders, exercise physiology, and stress induced immuno-suppression. The path to achieving this therapeutic potential is clear but demanding: bioactivity guided compound isolation, complete stereochemical structure elucidation, mechanism based pharmacology, absorption, distribution, metabolism, and excretion (ADME) and pharmacokinetic characterization, comprehensive OECD compliant toxicological profiling, and randomized clinical trials with analytically standardized preparations are the sequential, non-negotiable research imperatives. Safety characterization currently absent for all species across chronic exposure regimes-must be prioritized as an ethical and regulatory prerequisite to clinical investigation. The biodiversity of the Western Ghats and the pharmacological knowledge encoded by the Kani community represent an irreplaceable resource for drug discovery. Rigorous, ethically conducted scientific investigation of this heritage is both a therapeutic opportunity and a conservation responsibility.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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