Comparative Analysis of the Medicinal Properties of *Combretum indicum* and *Thevetia peruviana*: Phytochemistry, Pharmacology, and Potential Applications

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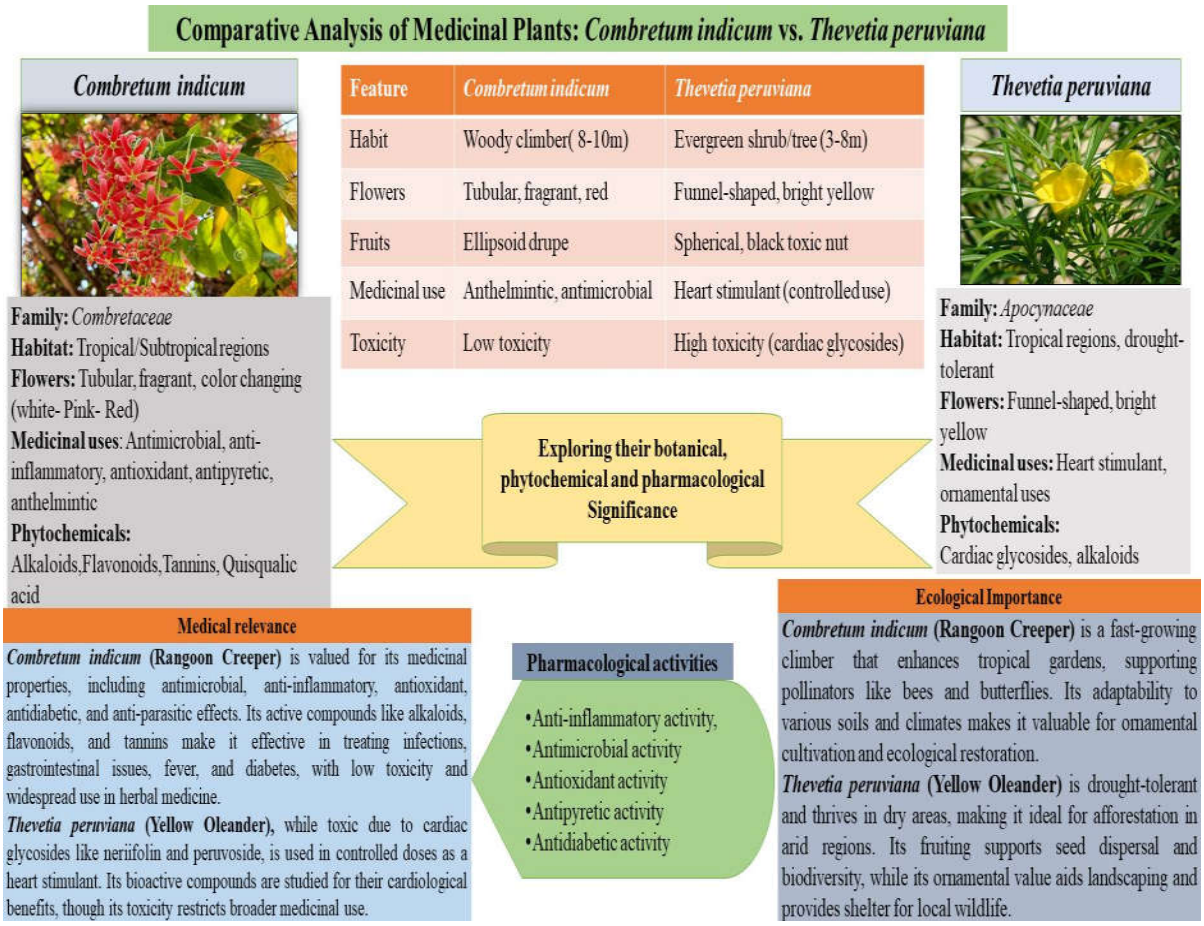
ABSTRACT

Medicinal plants serve as essential therapeutic agents in traditional and modern medicine, offering a wide spectrum of pharmacological applications. This review focuses on the comparative phytochemical and pharmacological profiles of *Combretum indicum* (Rangoon creeper) and *Thevetia peruviana* (Yellow oleander), two extensively used species in ethnomedicine. *C. indicum*, a tropical liana from the Combretaceae family, is rich in flavonoids, tannins, and triterpenoids, exhibiting diverse biological activities including antimicrobial, antioxidant, anti-inflammatory, antidiabetic, and anthelmintic properties. Its methanolic extracts have demonstrated significant free radical scavenging and anti-tumor potential. In contrast, *T. peruviana*, belonging to the Apocynaceae family, is known for its toxic cardiac glycosides such as thevetin A, peruvoside, and neriifolin. Despite its toxicity, the plant demonstrates notable antidiarrheal, larvicidal, cytotoxic, and gastroprotective effects when used in controlled dosages. Both species contain bioactive secondary metabolites responsible for their therapeutic efficacy. Comparative evaluation reveals that while *C. indicum* is relatively safer and broader in application, *T. peruviana* holds potential for targeted treatments. The findings support their inclusion in pharmaceutical research, emphasizing their value in developing novel plant-based drugs for diverse health conditions.

Keywords: Medicinal Plants, Phytochemical Constituents, Pharmacological Activity, *C. indicum* (Rangoon Creeper), *Thevetia peruviana* (Yellow Oleander), Traditional Medicine

GRAPHICAL ABSTRACT



INTRODUCTION

Medicinal plants are botanical species characterized by their therapeutic properties or the ability to elicit pharmacologically advantageous effects on human and animal physiology. These plants constitute essential constituents in the development of numerous pharmaceutical formulations. As reported by the World Health Organization (WHO), an estimated 80% of the global population depends on medicinal plants for managing a wide range of health disorders.[1, 2] Herbal medicine has been integral to healthcare systems worldwide, with various cultures utilizing plant-based remedies for therapeutic purposes. Notably, *Combretum indicum* (commonly known as Rangoon creeper) and *Thevetia peruviana* (yellow oleander) have been extensively employed in traditional medicine due to their pharmacological properties. This review provides a comparative analysis of their medicinal relevance and investigates their potential applications in pharmaceutical development.

Combretum indicum (Linn.), commonly known as Rangoon Creeper, belongs to the family Combretaceae, which encompasses over 600 species across 20 genera. This liana thrives in tropical and subtropical climates, with a primary distribution in Southeast Asia and the Philippines.[3] The species requires regular water supply and abundant sunlight, utilizing an adaptive climbing mechanism enabled by hook-shaped petioles formed from abscised leaves. A notable phenological characteristic of *C. indicum* is its perpetual flowering cycle, with blossoms exhibiting a diurnal color transition opening nocturnally and intensifying to a deep red hue during daylight. This transformation is accompanied by a distinct pungent fragrance, serving as a crucial diagnostic feature. Furthermore, the leaves display a coriaceous texture and emit a characteristic odor, contributing to species identification.[4, 5] Microscopic analysis of the leaf midrib demonstrates a single-layered endodermis surrounding the vascular bundle, which exhibits a high concentration of starch granules, thereby playing a crucial role in its unique physiological characteristics.[5] The phyllotactic pattern and morphological adaptations of *C. indicum* contribute to its accelerated growth and widespread propagation, establishing it as a readily available species with considerable ecological and pharmacological significance.[3, 5]

Thevetia peruviana (Pers.) K. Schum, belonging to the Apocynaceae family, is native to North America and Mexico but has been extensively propagated throughout South-East Asia. This species is well-documented in various traditional medicinal practices and is referred to by several vernacular names, including Ashvaghna (अश्वाघना), Divyapusha (दिव्यपूषा), and Haripriya (हरिप्रिया). The genus *Thevetia* encompasses eight species, with *T. peruviana* being the most extensively cultivated within the South-East Asian region.[6] A key feature of *Thevetia peruviana* is its production of a milky latex rich in bioactive cardiac glycosides, which confer both pharmacological relevance and inherent toxicity.[7] This species exhibits a high fruiting capacity, producing approximately 400–800 fruits per year, depending on environmental factors such as precipitation levels and the plant's developmental stage. The fruits are initially green and spherical, gradually darkening to black as they reach maturity. Anatomically, each fruit encloses a variable number of seeds (ranging from one to four) within its pericarp, which can be discerned through both transverse and oblique sectioning. Notably, all vegetative and reproductive structures of this species contain a latex-like exudate rich in bioactive cardiac glycosides, including neriifolin and peruvoside, which have been extensively studied for their pharmacological properties.[8]

BOTANICAL DESCRIPTION [9-18]

Combretum indicum (family: Combretaceae), commonly referred to as Rangoon Creeper, Chinese honeysuckle, or Burma Creeper, is a rapidly growing, extensively spreading liana or vine. Native to tropical regions of Asia and Africa, this species is extensively cultivated for its ornamental appeal and pharmacological significance.

Thevetia peruviana (family: Apocynaceae) is a toxic, evergreen shrub indigenous to South America, capable of reaching a height of approximately 6 meters. It is characterized by its light-grey bark, the presence of milky latex, and spirally arranged linear leaves. The plant produces trumpet-shaped yellow flowers, while its dark red or black fruit encloses a highly toxic nut. Widely cultivated for ornamental purposes, *T. peruviana* contains cardiac glycosides, which have notable medicinal applications.

Table 1: *Combretum indicum* & *Thevetia peruviana* Plants description

Feature	*Combretum indicum*	*Thevetia peruviana*
Habit	A woody, scrambling climber that reaches heights of 8–10 meters, utilizing twining growth for structural support.	A small, evergreen tree or shrub, typically growing between 3–8 meters with a densely branched crown.
Stem and Bark	Young stems are smooth and green, maturing into a woody texture with fissured bark. The plant lacks tendrils and climbs via twining.	Initially green stems that transition to a silvery-grey hue with age. The bark is light-grey and exudes milky latex upon incision.
Leaves	Opposite or sub-opposite, simple, ovate to elliptic, measuring 7–15 cm in length and 3–7 cm in width. Prominent venation, bright green, glabrous texture.	Simple, alternate leaves with reticulate venation, arranged spirally. Dark green, glossy, measuring 13–15 cm in length.
Flowers	Tubular, fragrant, changing from white to pink and then deep red. Found in axillary or terminal racemes, with a corolla tube length of 5–7 cm.	Bright yellow, funnel-shaped flowers, spirally twisted, occurring in terminal cymes. Each flower is 5–6 cm long.
Fruit and Seeds	Ellipsoid or oblong drupe with five longitudinal ridges, measuring 2–3 cm in length. Initially green, turning brown upon maturation, containing a single hard seed.	Slightly fleshy, spherical fruit measuring 4–5 cm in diameter, turning black upon maturation. Each fruit contains a nut, divided longitudinally and transversely, with 1–4 seeds.
Root System	Fibrous root system with occasional taproot formation, allowing deep soil penetration.	Adapted to drought-prone areas, capable of thriving in dry conditions.
Ecology and Habitat	Thrives in tropical and subtropical regions with well-drained loamy to clayey soils, preferring full sun to partial shade.	Native to South and Central America but widely cultivated in tropical and subtropical regions. Found in dry regions, pastures, roadsides, and open woodlands.
Toxicity & Chemical Compounds	Contains quisqualic acid, contributing to its medicinal anthelmintic properties.	All plant parts secrete a toxic milky latex containing cardiac glycosides such as neriifolin and peruvoside, making it highly toxic.
Economic & Medicinal Importance	Extensively used in traditional medicine for treating gastrointestinal issues, fever, and infections. Also cultivated for ornamental purposes.	Cultivated for ornamental purposes due to its showy flowers. Despite its toxicity, it is used in controlled medical applications as a heart stimulant.
Cultivation	Requires moderate watering and thrives in well-drained soil with ample sunlight.	Tolerates drought and various soil types. Often grown as an ornamental tree or potted plant, with occasional pruning for maintenance.

TAXONOMY[11, 19]

Table 2: Taxonomy of *Combretum indicum* & *Thevetia peruviana*

Taxonomic Rank	*Combretum indicum*	*Thevetia peruviana*
Kingdom	Plantae	Plantae
Phylum	Spermatophyta	Tracheophyta
Class	Dicotyledonae	Magnoliopsida
Order	Myrtales	Gentianales
Family	Combretaceae	Apocynaceae
Genus	*Combretum*	*Cascabela* Raf.
Species	*Combretum indicum*	*Thevetia peruviana* (Pers.) K. Schum.

VERNACULAR NAME [20-22]

Table 3: Vernacular name of *Combretum indicum* & *Thevetia peruviana*

Language	*Combretum indicum* (Rangoon Creeper)	*Thevetia peruviana* (Yellow Oleander)
English	Rangoon creeper, Chinese honeysuckle, Burma creeper	Yellow Oleander, Be-still Tree, Lucky Nut, Cook Tree, Mexican Oleander
Hindi	Madhu Malati	Peeli Kaner, Kulkephul
Telugu	Rodha Manoharam	Pachaganeru
Tamil	Irangunmalle	Thiruvachipoo, Ponnarali
Malayalam	Pullanni	Manja Areli, Pachcha Areli
Marathi	Vilayati Chambeli	Bitti
Manipuri	Parijat	Utonglei
Others	Konyar Phul, Kadukasi, Kanogalu, Udani	Manjaaralie, Shatakunda, Pachaganeru, Ponnarali, Ashvaghna, Ashvamaraka

PHYTOCHEMICAL CONSTITUENTS

Combretum indicum

Combretum indicum exhibits a remarkable spectrum of bioactive compounds that contribute to its extensive pharmacological properties. Phytochemical analysis has confirmed the presence of various secondary metabolites, including alkaloids, flavonoids, tannins, glycosides, saponins, steroids, and phenolic compounds throughout the plant.[23] A detailed examination of *C. indicum* leaves has identified rutin[24], trigonelline[25], L-proline[26], L-asparagine, and quisqualic acid as principal constituents[27]. The petroleum ether extract of the leaves predominantly contains palmitic acid (27.73%) in the saponifiable fraction, while α-amyrin is isolated from the unsaponifiable portion[28]. Additionally, *C. indicum* is abundant in various phytochemicals such as rutin, pelargonidin-3-glucoside, quisqualic acid, trigonelline, pelargonidin, and mannitol, along with amino acids including arginine, aspartic acid, glutamic acid, serine, glycine, proline, leucine, valine, alanine, threonine, asparagine, histidine, and lysine[23]. Furthermore, the methanolic extract of *C. indicum* leaves has been found to contain eight major compounds: asiatic acid, arjunolic acid, oleanolic acid, benzyl-β-D-xylopyranosyl-(1″ →6′)-β-D-glucopyranoside, nudifloric acid, vanillin, gallic acid, and β-sitosterol[29].

Thevetia peruviana [30, 31]

The plant *Thevetia peruviana* has been identified as a rich source of diverse secondary metabolites, including alkaloids, flavonoids, steroids, terpenoids, tannins, saponins, and cardiac glycosides. The kernels of *Thevetia* *peruviana* predominantly contain cardioactive glycosides such as Thevetin A, Thevetin B (cerebroside), Peruvosides, Nerrifolin, Thevenenin, and peruvosidic acid. Additionally, notable bioactive compounds present include Thevetin A, Thevetin B, Peruvoside, and Digitoxigenin.

PHARMACOLOGICAL ACTIVITY (*Combretum indicum)*

Medicinal plants serve as a fundamental source of therapeutics in traditional medical systems. Among these, *Combretum indicum* is predominantly utilized as an herbal remedy, although it possesses various other medicinal applications. The pharmacological potential of *C. indicum* is attributed to the presence of multiple bioactive constituents distributed throughout the plant. This species exhibits a broad spectrum of pharmacological properties, including anti-inflammatory, antimicrobial, antioxidant, antipyretic, anthelmintic, immunomodulatory, anti-staphylococcal, anti-rheumatic, antiviral, antifungal, antiseptic, anti-diabetic, antihyperlipidemic, anti-cancer, acetylcholinesterase inhibitory, diabetes wound-healing, antidyslipidemic, larvicidal, and central nervous system-modulating activities, along with its ability to reduce blood lipid levels. The diverse pharmacological effects of this plant are attributed to specific phytochemical compounds with medicinal activity.[32]

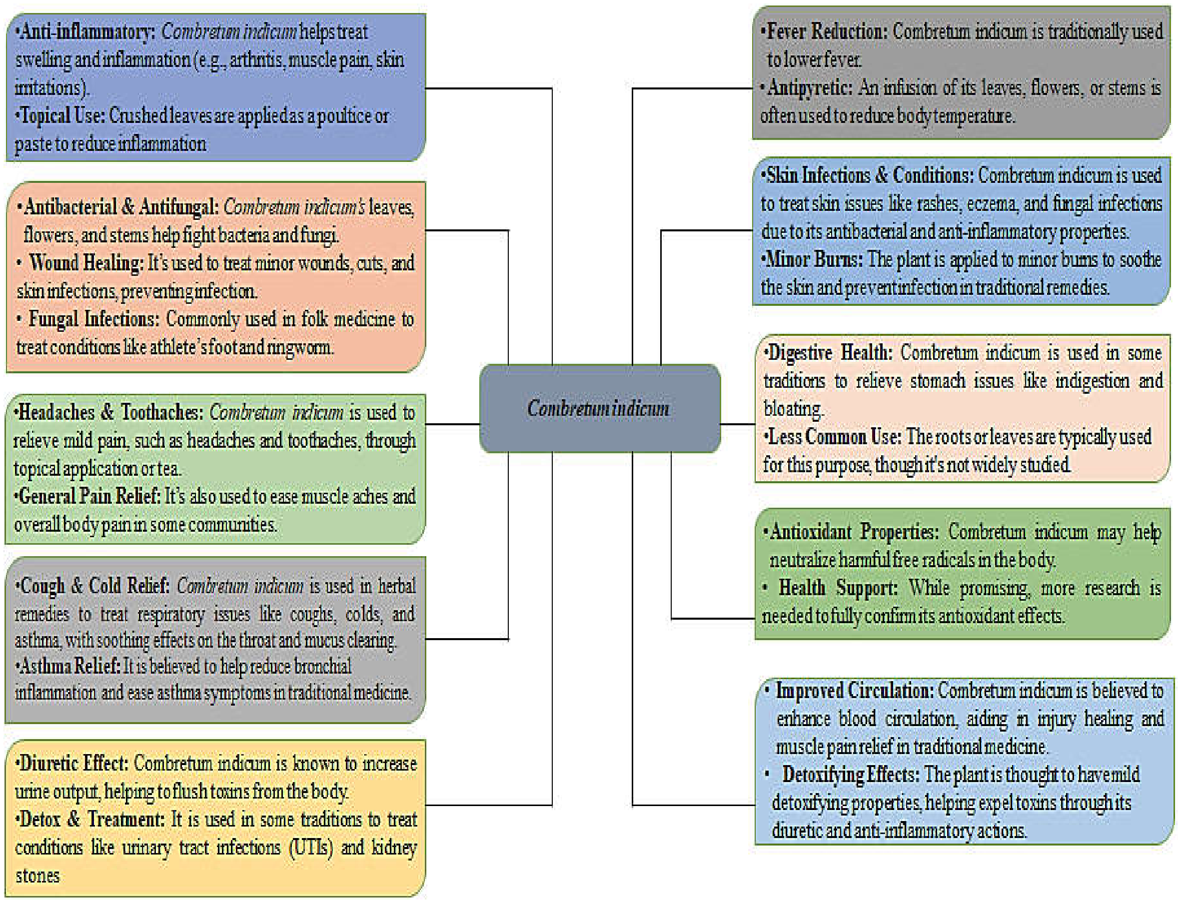


Figure 1: Pharmacalogical uses of *Combretum indicum* Plant

Anthelminthic activity

A *C. indicum* Patra Kashaya was administered to earthworms, with albendazole used as the standard reference. The presence of tannins was responsible for the observed anthelmintic activity. The leaf extract of *Combretum indicum* (L.) contains tannins, which exhibit larvicidal properties, thereby impacting the viability of helminth larvae. This plant demonstrates potential for the eradication of helminthiasis.[33]

Antimicrobial activity

To evaluate the antimicrobial properties of various extracts from *Combretum indicum*, ethanol, methanol, acetone, hexane, and aqueous extracts demonstrated activity against bacterial and fungal strains. The hot aqueous leaf extract and ethanolic extract exhibited inhibitory effects against all bacterial isolates, with the most pronounced activity observed against *Bacillus licheniformis* (MTCC 530). Among the tested extracts, the ethanolic leaf extract exhibited the highest susceptibility, with an inhibition zone measuring 27.67 ± 0.33 mm, followed by *Pseudomonas aeruginosa* (MTCC 2453) at 27.33 ± 0.33 mm, *Bacillus subtilis* (MTCC 441) at 27.00 ± 0.00 mm, *Pseudomonas fluorescens* (MTCC 103) at 26.67 ± 0.33 mm, *Bacillus mycoides* (MTCC 7343) at 24.67 ± 0.33 mm, *Escherichia coli* (MTCC 739) at 23.67 ± 0.33 mm, and *Pseudomonas putida* (MTCC 1654) at 21.33 ± 0.33 mm in diameter, respectively.[34] The ethanolic extract fraction exhibited antifungal activity, with an inhibition rate of 97.72% against *Alternaria alternata*, 92.30% against *Fusarium oxysporum*, 85.71% against *Aspergillus flavus*, and 66.66% against *Pithomyces pallidum*.[35] Additionally, the methanolic extract derived from the leaves and stem bark of *C. indicum* demonstrated antibacterial efficacy against *Staphylococcus* infections.[36] The antibacterial activity was determined by assessing the MIC_{50} (Minimal Inhibitory Concentration 50) through in vitro assays, while toxicity was evaluated via LD_{50} (Lethal Dose, 50%) in in vivo studies.[37,38] Furthermore, the leaf and bark extracts of *Combretum* species exhibited notable antibacterial activity against *Bacillus subtilis*, with inhibition zones measuring 22.4 mm and 18.6 mm, respectively.[39]

Anti-inflammatory activity

Inflammation plays a pivotal role in the pathogenesis of numerous diseases, including rheumatoid arthritis, atherosclerosis, and asthma, all of which exhibit a high global prevalence. The inflammatory response is characterized by the release of pro-inflammatory cytokines such as interleukin (IL)-1, tumor necrosis factor (TNF), interferon-gamma (IFN-γ), IL-6, IL-12, IL-18, and granulocyte-macrophage colony-stimulating factor. Conversely, this response is modulated by anti-inflammatory cytokines, including IL-4, IL-10, IL-13, interferon-alpha (IFN-α), and transforming growth factor, which function to counterbalance inflammation.[40] The anti-inflammatory mechanism involves the inhibition of prostaglandin (PG) synthesis, particularly through the suppression of cyclooxygenase (COX) activity at the site of injury. This results in a reduction of prostaglandin E2 and prostacyclin levels, subsequently leading to decreased vasodilation and, indirectly, diminished oedema. However, reducing the accumulation of inflammatory cells does not necessarily attenuate the production of other mediators, such as leukotrienes, platelet-activating factor (PAF), and cytokines, emphasizing the necessity for multifaceted anti-inflammatory strategies.[41,42]

The hydroalcoholic extract of *Combretum indicum* exhibits significant anti-inflammatory activity in experimental models, including the cotton pellet-induced granuloma model and acetic acid-induced vascular permeability. Phytochemical analysis of the extract has confirmed the presence of flavonoids and polyphenols, which are known for their potent anti-inflammatory effects. The polyphenols exert these effects by inhibiting prostaglandin biosynthesis, thereby reducing the inflammatory response. Consequently, the anti-inflammatory properties of the hydroalcoholic extract of *Quisqualis indica* Linn can be attributed to the suppression of prostaglandin synthesis and bradykinin production mediated by polyphenols.[43, 44]

Antioxidants activity

An antioxidant functions by inhibiting the oxidation of other molecules. Oxidation is a chemical process in which a substance undergoes electron or hydrogen loss to an oxidizing agent. This reaction can generate free radicals, which in turn may trigger chain reactions. These chain reactions within cells have the potential to damage or degrade nucleic acids, proteins, lipids, and DNA, ultimately contributing to the onset of degenerative diseases. Antioxidants mitigate these chain reactions by neutralizing free radical intermediates and preventing further oxidative processes. Typically, antioxidants act as reducing agents, such as thiols, ascorbic acid, or polyphenols, undergoing oxidation themselves in the process.[45, 46]

The methanolic extract of *C. indicum* Linn demonstrates 95% antioxidant activity, attributed to its redox potential. It functions as a reducing agent, effectively scavenging reactive oxygen species such as peroxides, hydroperoxides, and lipid peroxyl radicals. This activity inhibits oxidative pathways implicated in the progression of degenerative diseases. Additionally, studies indicate that the methanolic extract of *Q. indica* (stem bark), particularly its chloroform-soluble fraction, exhibits significant antioxidant properties.[47, 48]

Antipyretic activity

The antipyretic potential of the methanolic leaf extract of *Quisqualis indica* Linn. was systematically evaluated in rats subjected to a Brewer's yeast-induced pyrexia model. The extract demonstrated significant efficacy at dose levels of 100 mg/kg and 200 mg/kg, exhibiting potent and comparable effects. These findings support the therapeutic potential of *Quisqualis indica* Linn. as a promising antipyretic plant species.[49]

Anti-diabetic activity

An experimental rat model was employed to assess the antidiabetic potential of *Combretum indicum* L. leaf extract. The methanolic extract, containing steroidal compounds, was administered at varying dosages to both Streptozotocin-induced diabetic and non-diabetic rats. Following a 7-day treatment period, the animals were sacrificed for further analysis. The administration of *C. indicum* leaf methanolic extract resulted in a significant reduction in elevated blood glucose levels, total cholesterol, triglycerides, and low-density lipoprotein cholesterol in diabetic rats. These findings suggest the therapeutic potential of *C. indicum* leaf extract in alleviating diabetic symptoms.[50]

Anti-tumour activity

A comprehensive investigation has been conducted to evaluate the antitumor potential of the methanolic extract derived from the leaves and stems of *Combretum indicum* Linn. This study specifically examined the impact of *C. indicum* extract on the proliferative response of various tumor cell lines.[51-53] The methanolic stem bark extract was tested on HEK293 cells, and recent findings indicate that this extract, exhibiting IC_{50} values below 20 µg/mL, holds significant promise for further pharmaceutical development. It is recognized as a conventional anticancer agent.[54]

Anti -asthmatic Activity

The leaf extracts of *Combretum indicum* demonstrated anti-allergic properties by inhibiting mast cell degranulation and reducing eosinophil and white blood cell counts. At a dosage of 400 mg/kg, both LPE and LME extracts provided mast cell protection in tissue, with LME exhibiting the most potent effect, comp arable to the standard drug.[55]

PHARMACOLOGICAL ACTIVITIES (*Thevetia peruviana)*

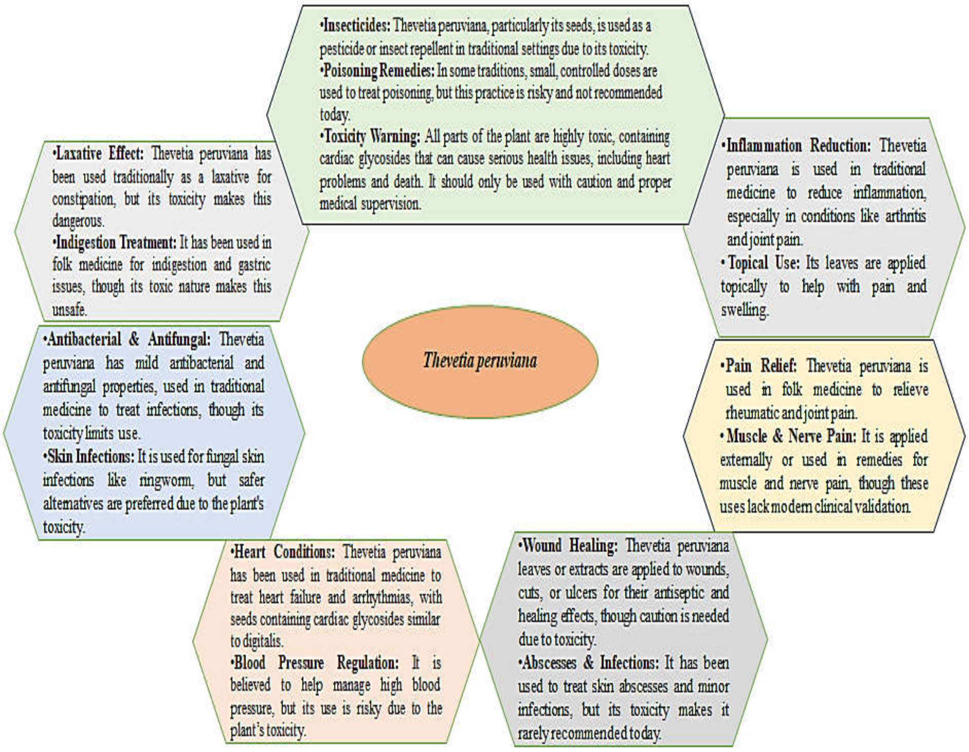


Figure 2: Pharmacalogical uses of *Thevetia peruviana* Plant

Anti-diarrhoeal activity and Antimicrobial activity

The present study investigated the antidiarrheal, antibacterial, and cytotoxic properties of yellow oleander (*Thevetia peruviana*) leaves. The antidiarrheal efficacy of the extract was assessed using an albino rat model subjected to castor oil-induced diarrhea, where it demonstrated significant inhibitory activity ($P < 0.01$). The antibacterial potential of the extract was evaluated in vitro using the disc diffusion method, revealing a lack of efficacy against both Gram-positive and Gram-negative bacteria, particularly Bacillus species. However, an ethanol-based decoction of yellow oleander leaves exhibited inhibitory effects against bacterial strains including *Shigella flexneri*, *Shigella sonnei*, *Klebsiella* spp., *Staphylococcus aureus*, and *Salmonella typhi*. Additionally, the cytotoxic effects of the plant extract were analyzed using *Artemia salina* (brine shrimp nauplii) bioassay, where the LC_{50} value was determined to be 627.21µg/mL. The broad range of the LC_{50} value suggests a relatively safe toxicity profile of the extract.[56]

Larvicidal activity

The efficacy of *Thevetia peruviana* leaf extracts was evaluated against the larvae of *Aedes aegypti*, *Anopheles stephensi*, and dengue vectors, which are responsible for malaria transmission. Following a 24-hour exposure period, the mean LC_{50} values for *T. peruviana* leaf extracts in acetone (C_3H_6O), petroleum ether, chloroform ($CHCl_3$), and methanol were determined to be 0.045, >0.05, 0.026, 0.041, and 0.038, >0.05, 0.021, and 0.036%, respectively. Furthermore, the prolonged effect observed with the chloroform extract after three days suggests that larvicidal activity is likely mediated through the inhibition of insect growth.[57]

Gastro-protective activity

Pragati and colleagues investigated the gastro-therapeutic potential of *Thevetia peruviana* and demonstrated its efficacy in mitigating gastric lesions induced by indomethacin and ethanol as experimental models.[58]

Locomotor activity

Pragati and her research team conducted an investigation into the locomotor behavior of *T. peruviana*. In comparison to the control group, locomotor activity was assessed in mice following either oral administration of the treatment oil at a dosage of 100 mg/kg or exposure to the substance through inhalation for a duration of 60 minutes.[58]

Cytotoxic activity

Hassan et al. conducted an experimental study utilizing the brine shrimp lethality assay to evaluate the cytotoxic activity of *Thevetia nerifolia* leaf extract. The investigation demonstrated a dose-dependent mortality rate in *Artemia salina* following exposure to six different concentrations of *T. peruviana* leaf extracts. Specifically, at concentrations of 62.5, 125, 250, 500, 1000, and 2000 µg/mL, the observed mortality rates were 0%, 5%, 10%, 35%, 65%, and 100%, respectively.[59]

CONCLUSION

Medicinal plants, such as *Combretum indicum* and *Thevetia peruviana*, have long played a vital role in traditional medicine due to their diverse pharmacological properties. *Combretum indicum*, known for its antimicrobial, anti-inflammatory, antioxidant, and anthelmintic activities, contains bioactive compounds like flavonoids, tannins, and glycosides, making it a valuable resource for pharmaceutical applications. Similarly, *Thevetia peruviana*, despite its toxicity, exhibits significant pharmacological potential, particularly in antidiarrheal, cytotoxic, and cardiotonic activities due to its rich cardiac glycoside content.

The comparative analysis of these plants highlights their unique medicinal benefits and potential risks. While *C. indicum* demonstrates broad-spectrum therapeutic properties with minimal toxicity, *T. peruviana* requires careful dosage management due to its toxic compounds. Further research is essential to explore their full pharmaceutical potential, optimize their medicinal applications, and ensure safe usage. By integrating these traditional remedies into modern healthcare, they can contribute significantly to the development of natural, plant-based therapeutics.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this review paper. The research was conducted independently, and no financial, commercial, or institutional relationships influenced the content or conclusions of this work.

DATA AVAILABILITY STATEMENT

No new data were generated or analyzed in this study. All information presented in this review is derived from previously published literature, which has been appropriately cited in the manuscript. Therefore, data availability is not applicable.

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