CHAPTER 05

Toxic gooseberry (*Cleistanthus collinus*): traditional uses and toxicological aspects

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ABSTRACT

Toxic Gooseberry (*Cleistanthus collinus* Roxb.), a member of the family Euphorbiaceae, is a lesser-known but culturally significant tree of peninsular India. Traditionally, various parts of the plant, particularly leaves and roots, have been used in indigenous medicine, despite their toxic nature. Folk practices among tribal and rural communities attribute the use of plants in treating skin ailments, intestinal disorders, cough, scabies, and as a purgative or abortifacient. Decoctions prepared from diluted forms of the plant are believed to have detoxifying and antimicrobial properties. Phytochemical studies reveal the presence of lignans, diphyllin derivatives, cleistanthin A and B, collinusin, and other arylnaphthalide lignans responsible for both its medicinal and toxic activities. This chapter highlights the traditional ethnomedicinal uses of *C. collinus*, supported by scientific findings on its pharmacology, phytochemistry, and toxicological implications.

KEYWORDS: Toxic gooseberry, poisonous plant, phytochemicals, biopesticide, ethnobotany, toxicity, traditional use

INTRODUCTION

Ethnobotany bridges the knowledge of traditional plant use with modern pharmacology, uncovering both healing and toxic properties of natural resources. *Cleistanthus collinus* (Roxb.), commonly known as "Toxic Gooseberry" in English, "Karada" in Odia, "Garari" in Hindi, "Oduvanthalai" in Tamil, "Vadisaaku" in Telugu, and "Kodithoova" in Malayalam, represents a unique example of a plant revered and feared simultaneously (Kazi and Gude 2022). Belonging to the Euphorbiaceae family, it is a small tree native to dry deciduous forests of southern India and parts of Sri Lanka, thriving in arid scrublands and rocky terrains. The genus *Cleistanthus* comprises more than 160 species, widely distributed in tropical Asia and Africa (Priyadharsini et al. 2024). Among them, *C. collinus* stands out due to its distinctive ethnomedical relevance and potent chemical profile. Local healers and tribal practitioners have long utilized the plant in controlled doses for ailments such as skin infections, intestinal worms, chronic cough, and as an abortifacient agent (Mohan and Harikrishna 2019). Traditionally, *C. collinus* has been employed by rural and tribal communities for various practical and medicinal purposes. The leaves, twigs, and roots have been used as fish poison, rodenticide, insect repellent, and acaricide in agriculture to protect crops such as rice from pests (Sankar and Thirunavukkarasu 2022; Kazi and Gude 2022). It also serves as a green manure for soil enrichment and has been studied for biopesticidal activity comparable to synthetic acaricides, demonstrating eco-friendly pest control potential. This traditional knowledge highlights an indigenous understanding of plant toxicity and detoxification, a theme still underexplored in modern pharmacological studies (Chichaghare et al. 2019; Sankar and Thirunavukkarasu 2022). Phytochemical investigations have identified arylnaphthalide lignans such as cleistanthin A, cleistanthin B, diphyllin, and collinusin, which exhibit cytotoxic, antimicrobial, and enzyme-inhibiting activities (Priyadharsini et al. 2024). These same compounds are also responsible for oxidative stress, nephrotoxicity, and cardiotoxicity upon ingestion (Mohan and Harikrishna 2019). The ethnomedicinal and toxicological duality of *C. collinus* presents a compelling narrative, a medicinal plant deeply rooted in traditional practices but demanding scientific caution.

MORPHOLOGY

C. collinus is a small deciduous tree, typically reaching 3- 15 m in height, with pale grey bark and slender branches (Kumar et al. 2022; Priyadharsini et al. 2024; Figure 1).

Stem and bark: The bark is thin, smooth, and greyish-brown, often exfoliating in irregular patches.

Leaves: The leaves are simple, alternate, and appear in two ranks, with lamina being elliptic, sub-orbicular, or obovate, measuring about 3–11.5 cm long and 1.5–8 cm wide; leathery, glossy, and glabrous above, and glaucous below with prominent lateral veins, and are supported by slender petioles, 3–10 mm long. The foliage appears pale green, turning yellowish before shedding in dry seasons.

Inflorescence: The inflorescences are axillary clusters or short panicles bearing small greenish-yellow flowers.

Flowers: Flowers are unisexual; male and female flowers are borne on separate inflorescences of the same tree. Flowers are yellowish-green, clustered in glomerules on leafy and lateral branchlets. Male flowers typically have 5–6 triangular-oblong or lanceolate sepals with linear petals and oblong anthers, while female flowers have 4–5 triangular-lanceolate sepals and subulate petals, featuring a superior, sub-globose ovary with bifid, recurved styles.

Fruits: The fruit is a sub-globose or oblong capsule, 18–22 mm in diameter, glossy and black or dark brown when mature, truncate at the top, and shallowly three-lobed, 1–1.5 cm long.

Seeds: Each capsule contains 2–3 smooth, shiny seeds.

TRADITIONAL MEDICINAL USES

Despite its toxicity, *C. collinus* holds a prominent place in indigenous medicinal systems across southern India. Its careful use by tribal healers shows the potency of the plant within local ethnomedicine. In Tamil Nadu, traditional healers among the Irula and Malayali tribes use leaf decoctions for treating scabies, eczema, and intestinal worms (Lourthuraj et al. 2016; Chichaghare et al. 2019). Dried leaves are sometimes boiled in water and externally applied for skin rashes and chronic itching. In Andhra Pradesh, the Chenchu tribe prepares an aqueous extract of leaves as a purgative and abortifacient (Priyadharsini et al. 2024). The plant's bitter taste and irritant property are considered cleansing agents for impure blood, reflecting humoral beliefs in indigenous medicine (Mohan et al. 2016). In Kerala, powdered roots mixed with tamarind or curd are used in small doses to relieve chronic cough, colds, and sore throats (Lourthuraj et al. 2016; Kumar

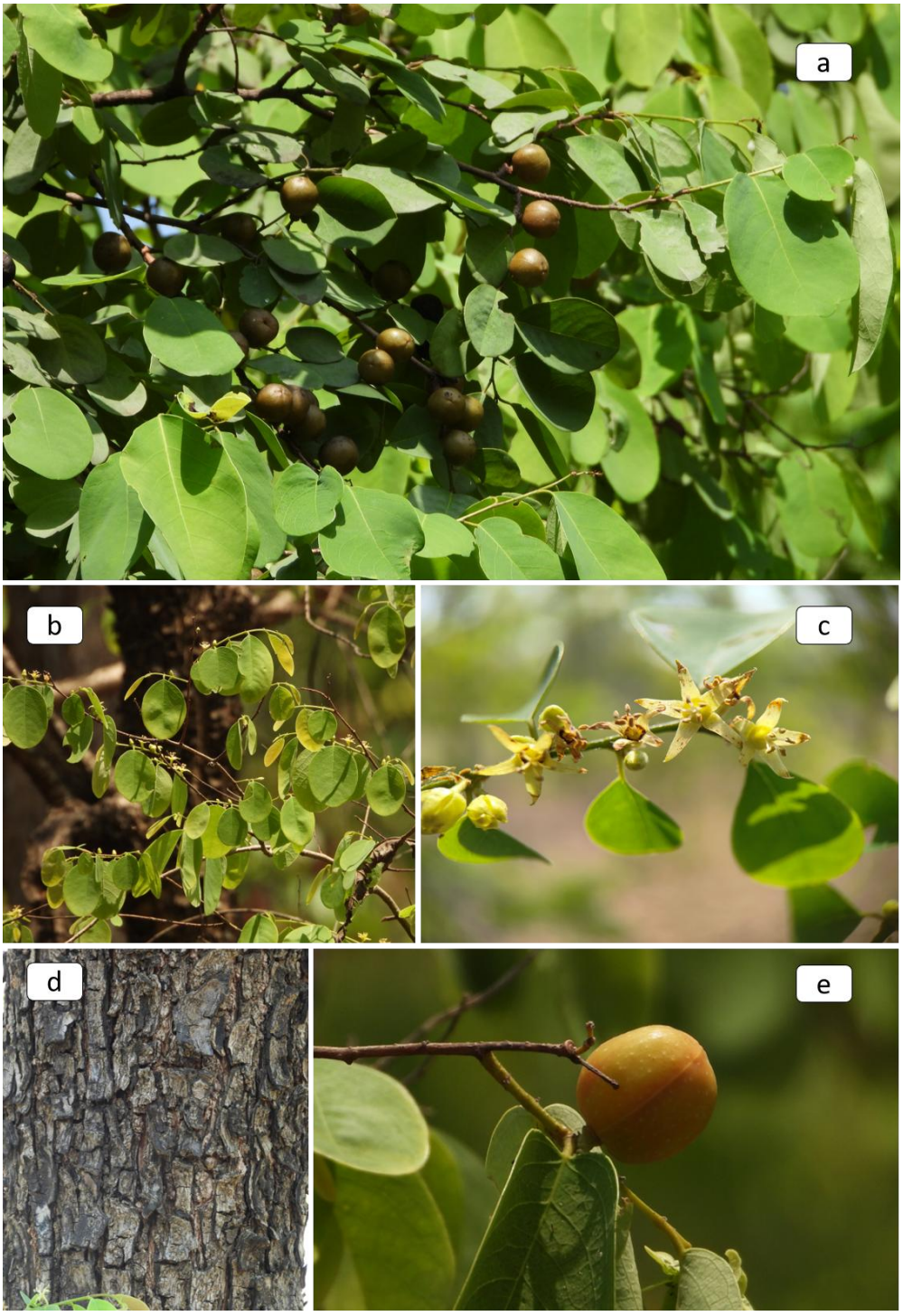


Figure 1: Vegetative parts of *C. collinus*; a) Canopy; b) Leaves, c) Flowers, d) Bark, e) Fruit

et al. 2022). The latex, when diluted, is applied to parasitic infections and wounds. In Odisha and Jharkhand, certain tribal groups utilize *C. collinus* in ritualistic healing, burning leaves as fumigants to drive away insects and evil spirits, highlighting its symbolic as well as medicinal role (Kumar et al. 2022). In the Siddha system, small quantities of leaf powder mixed with honey have been prescribed for intestinal disturbances and as an antidote to certain poisons. However, such use requires precise dosing, as an excess may lead to severe poisoning. To reduce toxicity, practitioners employ several traditional methods: Boiling leaves in cow milk or lime water before medicinal use. Sun-drying and burning leaves to ash, then mixing with castor oil for external applications. Combining *C. collinus* extracts with herbs like *Andrographis paniculata* or *Phyllanthus niruri* to balance toxicity (Mohan et al. 2016; Lourthuraj et al. 2016; Figure 2).

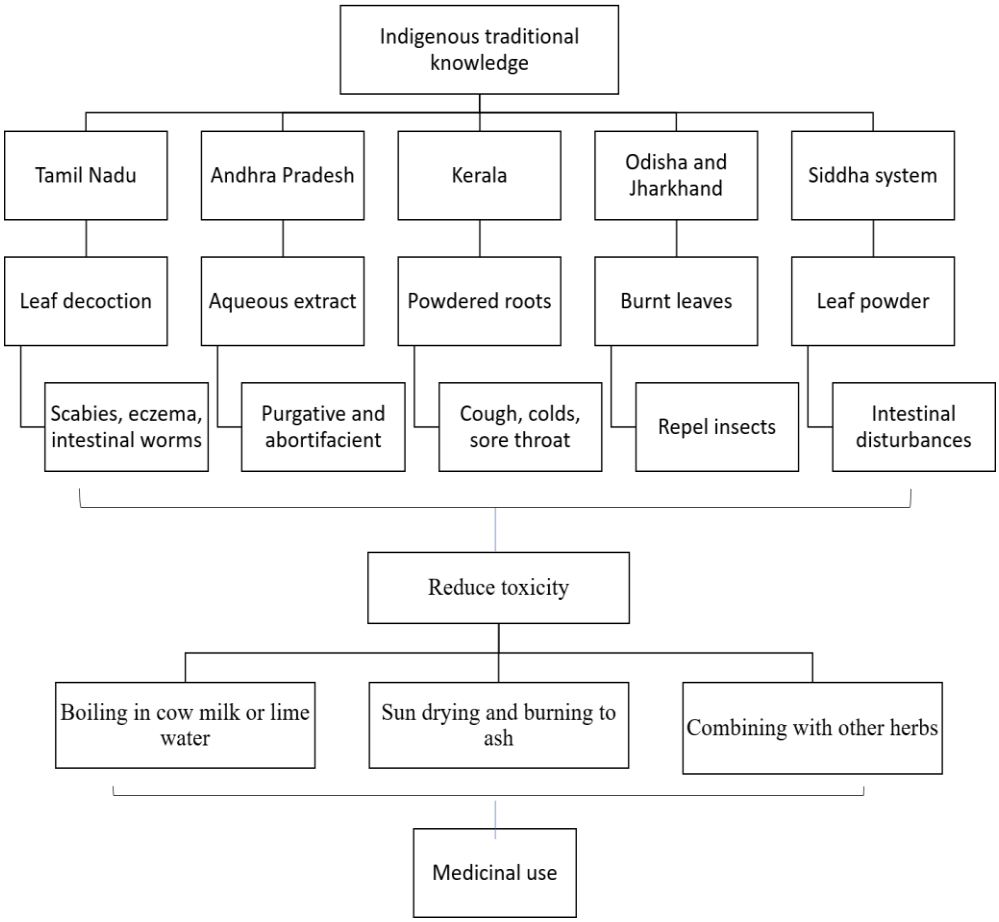


Figure 2: Traditional medicinal uses of *C. collinus*

BIOACTIVE COMPOUNDS

C. collinus contains a variety of bioactive compounds that account for both its medicinal and poisonous properties. Phytochemical investigations have revealed the presence of arylnaphthalide lignans, primarily cleistanthin A, cleistanthin B, diphyllin, and collinusin, which are concentrated in the leaves and bark (Priyadharsini et al. 2024). These lignans exhibit potent cytotoxic and enzyme-inhibitory activities, particularly against Na^+/K^+-ATPase and mitochondrial respiratory enzymes. In addition to lignans, the plant contains flavonoids, tannins, saponins, terpenoids, phenolic compounds, and trace alkaloids, contributing to its antimicrobial and antioxidant potential (Govindachari et al. 1967; Kazi and Gude 2022). The cleistanthins are responsible for the toxicity, causing oxidative stress, cardiac arrhythmia, and respiratory depression when ingested in high doses. At lower and controlled concentrations, extracts have shown antimicrobial, anti-inflammatory, and anticancer properties, suggesting potential pharmacological value (Suman et al. 2013). The phenolic and flavonoid components act as antioxidants, scavenging free radicals and protecting cells from oxidative damage. Analytical studies using HPLC, GC-MS, and NMR have confirmed these compounds (Fan et al. 2020; Table 1).

PHARMACOLOGICAL USES

Antimicrobial activity: Ethanolic and methanolic extracts of *C. collinus* leaves have demonstrated broad-spectrum antibacterial effects, particularly against *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. The flavonoids, lignans, and tannins in the extracts are believed to damage microbial cell membranes and inhibit enzyme synthesis (Jain et al. 2010; Kazi and Gude 2022).

Antioxidant potential: Methanolic leaf extracts possess significant DPPH free radical scavenging activity, attributed to the presence of phenolic and flavonoid compounds. The antioxidant activity helps in neutralizing oxidative stress and lipid peroxidation, suggesting a protective role against cellular damage (Satapathy et al. 2025).

Anti-inflammatory and analgesic effects: In vitro assays indicate that lignans from *C. collinus* can suppress nitric oxide (NO) and prostaglandin E2 (PGE2) production in activated macrophages. The anti-inflammatory action may result from the inhibition of COX and iNOS enzymes, a mechanism similar to that seen in nonsteroidal anti-inflammatory drugs (NSAIDs).

Ethanol extracts have also shown mild analgesic activity in animal pain models (Satapathy et al. 2025).

Cytotoxic and anticancer properties: Cleistanthin A and B exhibit potent cytotoxic effects on various human cancer cell lines (HeLa, MCF-7, and HepG2). They induce apoptosis through mitochondrial membrane potential disruption and DNA fragmentation (Rajendran et al., 2016). Structural analogues of these lignans are being explored as lead molecules for anticancer drug design (Thamburaj et al. 2014).

Hepatoprotective activity: In certain detoxified preparations, leaf extracts are used to support liver cleansing and treat bile disorders. Antioxidant-rich fractions could reduce hepatic oxidative stress (Priyadharsini et al. 2024).

Table 1: Major bioactive compounds of *C. collinus* and their reported biological activities

Compound	Chemical class	Plant parts	Reported activity
Cleistanthin A	Arylnaphthalide lignan	Leaves, stem bark	Potent cytotoxic agent; inhibits Na^+/K^+-ATPase; causes oxidative stress and mitochondrial dysfunction.
Cleistanthin B	Arylnaphthalide lignan	Leaves	Induces apoptosis; causes hypokalemia and cardiotoxicity; exhibits moderate antibacterial effect.
Diphyllin	Lignan lactone	Leaves, twigs	Anticancer, antiviral, and antimicrobial activities; disrupts mitochondrial respiration.
Collinusin	Lignan	Leaves	Exhibits cytotoxic and enzyme inhibitory activity; structurally similar to cleistanthins.
Cleistanone	Phenolic ketone	Roots	Mild antimicrobial and antioxidant potential.

Tannins and Phenolics	Polyphenols	Bark, leaves	Exhibit antioxidant, wound healing, and antimicrobial effects.
Flavonoids (e.g., quercetin derivatives)	Flavonols	Leaf extracts	Free radical scavenging; anti-inflammatory effects.
Saponins and Terpenoids	Triterpenoids and glycosides	Leaves and bark	Contribute to surface activity and may assist detoxification mechanisms.
Alkaloids (trace)	Nitrogenous bases	Roots	Weak neuroactive potential; present in minute quantities.

TOXICOLOGICAL ASPECTS

The toxicological aspects of *C. collinus* are primarily attributed to its lignan compounds, chiefly cleistanthin A, cleistanthin B, and cleistanthoside A, which exert potent cytotoxic and systemic effects. These compounds interfere with essential cellular functions by inhibiting nucleic acid synthesis, particularly by blocking thymidine and uridine incorporation into DNA and RNA, thereby inducing cell cycle arrest at the G1–S phase and triggering apoptosis through DNA strand breaks (Kazi and Gude 2022). The plant's aqueous extracts also lead to significant oxidative stress due to depletion of thiol-containing enzymes and suppression of the glutathione system, which impairs antioxidant defenses in hepatic, renal, and neuronal tissues. A major toxicological mechanism involves inhibition of vacuolar-type H^+-ATPase (V-ATPase) in renal distal tubular cells, resulting in distal renal tubular acidosis (dRTA), hypokalemia, and metabolic acidosis, characteristic clinical features observed in human and animal poisoning. Cardiotoxic effects are manifested as arrhythmias, QT prolongation, hypotension, and in severe cases, cardiac arrest, primarily due to myocardial oxidative damage and electrolyte imbalance (Kettimuthu et al. 2011). Neuromuscular weakness resembling myasthenia gravis has also been reported, attributed to postsynaptic acetylcholine receptor blockade. No specific antidote exists, but thiol donors such as N-acetylcysteine have shown some protective effects by restoring thiol enzyme activity and mitigating oxidative injury. *C. collinus* exerts multi-organ toxicity involving hepatic, renal, cardiac, and neurological systems, driven by oxidative stress, enzyme inhibition, and mitochondrial dysfunction (Kazi and Gude 2022; Mishra et al. 2023).

CONCLUSION

C. collinus is a toxic yet pharmacologically significant plant widely distributed in tropical India. Despite being a poisonous species, recent studies have highlighted its diverse biological properties, including antioxidant, anti-inflammatory, and insecticidal activities. The plant contains a variety of phytochemicals such as lignans, alkaloids, and phenolic compounds that contribute to its therapeutic and pesticidal potential. Traditional communities in rural and tribal regions of India have long utilized *C. collinus* as a biopesticide and medicinal resource. Due to its inherent toxicity, careful extraction, dosage regulation, and toxicological evaluation are crucial for its safe pharmacological or agricultural application. Further research focusing on bioactive compound isolation, mechanism of action, and controlled utilization could transform this poisonous plant into a valuable source of natural products for medicine and sustainable pest management.

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