



Neolamarckia cadamba in Obesity Management: A Comprehensive Review of Phytochemistry, Mechanisms, and Safety

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ABSTRACT

Background: Obesity, a global epidemic affecting over 650 million adults, is linked to insulin resistance, dyslipidemia, non-alcoholic fatty liver disease, and cardiovascular risks. Current pharmacotherapies offer limited efficacy and pose safety concerns, prompting exploration of multi-target phytotherapeutics. *Neolamarckia cadamba* (Roxb.) Bosser (kadamba), a Rubiaceae tree native to South and Southeast Asia, has been traditionally used for liver disorders, inflammation, and metabolic issues, with preclinical evidence of antioxidant, hepatoprotective, and hypolipidemic properties.

Objective: This review synthesizes evidence on the botany, ethnomedicine, phytochemistry, and pharmacological effects of *N. cadamba* in obesity management, proposing mechanisms involving lipid modulation, serotonergic signaling, oxidative stress reduction, and the gut–liver–brain axis.

Methods: A comprehensive literature search was conducted using databases such as PubMed, Scopus, and Google Scholar, focusing on studies from 1965–2025. Inclusion criteria encompassed ethnomedicinal reports, phytochemical analyses, and *in vivo/in vitro* studies on metabolic effects. Data were synthesized narratively, with emphasis on high-fat-diet rodent models and bioactive constituents.

Results: *N. cadamba* bark and fruit extracts (100–400 mg/kg) attenuate high-fat-diet-induced weight gain, adiposity, dyslipidemia, and hepatic steatosis in rodents, enhancing glucose tolerance and antioxidant defenses (↑GSH, ↓MDA). Key phytoconstituents include indole alkaloids (cadambine), flavonoids (quercetin), triterpenoids (ursolic acid), and phenolics, mediating multi-target actions. Short-term studies indicate good tolerability, with hepatoprotective trends. Serotonergic modulation via indole structures is hypothesized but unconfirmed.

Conclusion: *N. cadamba* emerges as a promising phytomedicine for obesity, supported by preclinical data. However, standardized extracts, mechanistic validation, toxicology, and clinical trials are essential for therapeutic translation.

Keywords: *Neolamarckia cadamba*; Diet-induced obesity; Serotonin; Phytomedicine; Dyslipidemia; Oxidative stress

INTRODUCTION

The prevalence of overweight and obesity has increased dramatically over the last four decades, and obesity is now recognized as a major global health threat.^{1–3} According to World Health Organization estimates, more than 1.9 billion adults are overweight and over 650 million are obese, with the burden growing among children and adolescents. Obesity is closely associated with type 2 diabetes, hypertension, dyslipidemia, non-alcoholic fatty liver disease (NAFLD), cardiovascular disease, and several cancers, leading to substantial morbidity, mortality, and economic cost.^{2,3}

Lifestyle modification—primarily dietary change and increased physical activity—remains the basis of obesity therapy. However, sustained weight loss is difficult for many patients. Pharmacological agents such as orlistat, GLP-1 receptor agonists, and centrally acting drugs (liraglutide, semaglutide, combination therapies) can facilitate additional weight loss, but their use is limited by cost, gastrointestinal adverse effects, and in some cases long-term safety concerns.^{4–6} The withdrawal of centrally acting appetite suppressants such as rimonabant, sibutramine, and later lorcaserin illustrates these challenges.^{5,6}

This situation has stimulated interest in medicinal plants

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with metabolic, antioxidant, and organ-protective actions. *Neolamarckia cadamba*, a medicinal tree widely used in Indian and Southeast Asian traditional medicine, has attracted attention due to hepatoprotective, antioxidant, and hypolipidemic effects, and more recently its reported anti-obesity activity in high-fat-diet models.⁷⁻¹² This review synthesizes the current evidence on *N. cadamba* in the context of obesity and proposes mechanistic links—including serotonergic pathways and oxidative stress—supported by preclinical data.

BOTANICAL DESCRIPTION, DISTRIBUTION, AND TRADITIONAL USES

The scientific name of *Neolamarckia cadamba* has been debated extensively for almost a century, largely due to confusion regarding the identity and origin of historical type specimens. The issue began in 1785, when Jean-Baptiste Lamarck described a specimen as *Cephalanthus chinensis*, reporting its origin as Madagascar.¹³ Many decades later, Achille Richard introduced the name *Anthocephalus indicus* in 1830, claiming that his description was based on the same specimen Lamarck had examined, though he referred to the plant as an Asian species.¹⁴

Under modern nomenclatural rules, Richard should have retained Lamarck's specific epithet—producing the name *Anthocephalus chinensis*—but he changed it, creating further inconsistencies.¹⁵ For much of the 19th and 20th centuries, botanists widely adopted *Anthocephalus chinensis* for the kadam tree, even though later taxonomic reviews showed that Richard's *Anthocephalus* corresponds to Lamarck's Madagascan species rather than the Asian one.^{15,16} Subsequent revisions determined that *Cephalanthus chinensis* is actually a Madagascan taxon belonging to the genus *Breonia*, now

recognized as *Breonia chinensis* (Lam.) Capuron. Thus, the traditional use of the name *Anthocephalus chinensis* for the kadam tree is considered a misapplication, often indicated as "*A. chinensis* auct".

Once Richard's name was rejected for the Asian species, the earliest valid name became *Nauclea cadamba*, formally published by William Roxburgh in 1824.¹⁷ To resolve the generic confusion, Jean-Marie Bosser established the new genus *Neolamarckia* in 1984, which accommodates Asian species matching Richard's descriptions, and transferred Roxburgh's species as *Neolamarckia cadamba* (Roxb.) Bosser.¹⁸ This treatment is now accepted by most contemporary taxonomic databases and floristic sources.¹⁹ One reason for the prolonged debate is the uncertainty surrounding whether Richard truly examined the same specimen described by Lamarck. Their descriptions differ significantly—Lamarck noted axillary inflorescences, whereas Richard described terminal inflorescences—and their reported geographical origins conflict.^{13,14}

Neolamarckia cadamba (Roxb.) Bosser (syn. *Anthocephalus cadamba* Miq.) is a member of the Rubiaceae family. It is native to South and Southeast Asia and widely distributed in India, Bangladesh, Sri Lanka, Nepal, Myanmar, and neighboring countries. The tree is fast-growing, often 20–30 m tall, with a straight trunk, broad spreading crown, and distinctive spherical, orange-yellow flower heads. Leaves are opposite, broad, ovate to elliptic with a prominent midrib and entire margin. The inflorescences are globose, highly fragrant flower clusters that give rise to a multiple fruit—a fleshy, ball-like syncarp composed of numerous small fruits.^{7,20} These ethnomedicinal indications (Table 1), especially for liver and inflammatory conditions, are consistent with the hepatoprotective and antioxidant effects observed in modern pharmacological studies.^{8-12,21}

Table 1: Plant parts and their traditional uses.

Plant Part	Traditional System/Region	Traditional Uses
Bark	Ayurveda, Siddha, Unani, Tribal medicine	Treats liver ailments (jaundice, hepatomegaly); used for fever and malarial fever; anti-inflammatory and analgesic agent; decoction for digestive disorders, anorexia, indigestion; astringent for diarrhea and dysentery; helps in urinary disorders; used in postpartum recovery and gynecological strengthening[21]
Leaves	Folk and Tribal medicine	Applied as poultice on ulcers, boils, fungal infections; used for wound healing and burns; relieves headaches when applied topically; mild antiseptic and anti-inflammatory action[21]
Fruits	Ayurvedic and Southeast Asian medicine	Used in diarrhea and stomach upset; cooling, mildly astringent tonic; given in fever and excessive thirst; digestive support in children and elderly[21]
Flowers	Traditional and ritual medicine	Aromatic and cooling effect; mild astringent properties; used in ritual preparations and calming remedies[21]
Roots (less commonly used)	Tribal medicine	Occasionally used for fever and inflammatory swelling[21]
Whole plant/general uses	Across multiple traditions	Blood purification; detoxifying agent; used for respiratory complaints like cough and mild asthma; supportive remedy for metabolic imbalance[21]

Phytochemical Profile of *Neolamarckia cadamba*

Neolamarckia cadamba, commonly known as Kadamba, is a medicinally important tree belonging to the family Rubiaceae. Its phytochemical composition has been extensively studied due to its long-standing ethnomedicinal use in liver disorders, inflammation, fever, infections, wounds, and metabolic disturbances. Modern phytochemical research has identified diverse classes of bioactive compounds—including alkaloids, flavonoids, triterpenoids, phenolics, tannins, saponins, and phytosterols—which collectively account for the plant's multi-target therapeutic properties. The following subsections detail each phytochemical class, its distribution within the plant, and its pharmacological significance, particularly in relation to metabolic diseases such as obesity.

Alkaloids

Alkaloids are among the most characteristic and extensively studied constituents of *N. cadamba*, predominantly present in the bark and leaves. Reported alkaloids include cadambine, isocadambine, dihydrocadambine, cadamine, and 3 α -dihydrocadambine. These compounds belong to the indole and oxindole structural group, making them chemically related to tryptamine derivatives. Because of structural similarities to serotonin precursors, these alkaloids have generated scientific interest in their potential modulation of central nervous system pathways, including serotonergic receptors. Although direct receptor-binding data are limited, preliminary evidence suggests possible influence on neural signaling, appetite regulation, and mood-related pathways, supporting the emerging metabolic benefits observed *in vivo*. In addition, indole alkaloids exhibit antimicrobial and hepatoprotective effects, aligning with the plant's historical use for fevers, liver ailments, and infections.^{7,22}

Flavonoids

Flavonoids are widely distributed throughout the leaves, flowers, and fruits of the plant. The primary flavonoids reported include quercetin, kaempferol, rutin, and their glycosides.²³⁻²⁵ These compounds are potent antioxidants, capable of neutralizing reactive oxygen species (ROS) and preventing oxidative damage to lipids, proteins, and DNA. Flavonoids contribute significantly to the anti-obesity potential of *N. cadamba* because oxidative stress plays a key role in the pathogenesis of insulin resistance, lipid accumulation, and hepatic steatosis. By suppressing oxidative stress and modulating metabolic enzymes such as HMG-CoA reductase and lipoprotein lipase, flavonoids improve lipid profiles and reduce adipocyte hypertrophy.²⁶ Their ability to enhance endothelial function and insulin sensitivity further strengthens the metabolic relevance of this phytochemical class.

Triterpenoids

Triterpenoids form another prominent group of phytochemicals in *N. cadamba*, with compounds such as ursolic acid and oleanolic acid reported in various plant parts.^{7,27} These pentacyclic triterpenes possess multiple pharmacological actions, including anti-inflammatory, hepatoprotective, antioxidant, and hypolipidemic effects. Ursolic acid, in particular, is known to influence adipogenesis, lipid metabolism, and energy expenditure. Studies in other botanical models have shown that it enhances brown adipose tissue thermogenesis, reduces lipid synthesis, and improves mitochondrial respiration—mechanisms relevant to obesity control.²⁸ Triterpenoids also protect hepatocytes from lipid peroxidation, making them vital for the plant's reported hepatoprotective activity.

Phenolic Acids and Other Phenolics

Phenolic compounds represent a major secondary metabolite category in *N. cadamba*. Identified phenolic acids include gallic acid, caffeic acid, chlorogenic acid, and ferulic acid.^{23,25,29} These molecules exhibit strong antioxidant and anti-inflammatory properties. Phenolic acids contribute to metabolic benefits by mitigating obesity-associated oxidative stress, improving glucose homeostasis, and inhibiting carbohydrate-hydrolyzing enzymes such as α -amylase and α -glucosidase, thus reducing postprandial glucose spikes.³⁰ Their antioxidant actions complement flavonoids in protecting against hepatocellular damage and systemic inflammation typically associated with high-fat-diet models.

Saponins

Triterpenoid saponins are key contributors to the plant's cholesterol-lowering activity. Saponins form complexes with bile acids, promoting their excretion and, in turn, reducing serum cholesterol levels due to increased conversion of hepatic cholesterol into new bile acids.^[31] Additionally, saponins exhibit immunomodulatory and anti-inflammatory actions, supporting their traditional use in detoxification and fever conditions. Their amphiphilic nature influences gastrointestinal fat emulsification and absorption, indirectly affecting lipid metabolism and adiposity.

Glycosides

Neolamarckia cadamba contains multiple glycosides, including iridoid glycosides and phenolic glycosides, which enhance solubility and transport of active compounds *in vivo*. These glycosides possess antioxidant and organ-protective properties and have been reported to support liver and kidney health in experimental models. Their role in maintaining hepatocellular integrity and regulating inflammation complements the actions of phenolics and triterpenoids, collectively contributing to the plant's multi-system metabolic effects.^{24,32}

Phytosterols

Phytosterols such as β -sitosterol, campesterol, and stigmasterol have been identified in *N. cadamba*.^{23,33} Structurally similar to cholesterol, these molecules inhibit intestinal cholesterol absorption by competing for micelle incorporation. β -Sitosterol is known to reduce adipogenesis, improve serum lipid profiles, and suppress inflammatory mediators involved in obesity-associated metabolic dysfunction.³⁴ Its presence supports the lipid-lowering effects observed in studies using bark or fruit extracts of the plant.

Carbohydrates and Polysaccharides

Simple sugars, polysaccharides (Table 2), and glycoproteins contribute to the nutritive and immunomodulatory value of *N. cadamba*. Polysaccharides can act as prebiotics, influencing gut microbiota composition, which is increasingly recognized as a key regulator of metabolic health and body weight.³⁵

Volatile Constituents

Although present in small quantities, volatile oils from the flowers and leaves impart fragrance and possess mild antimicrobial activities. These volatile compounds play a supportive role in the plant's overall therapeutic profile and contribute to its use in traditional aromatic preparations.³⁶

Table 2: Phytochemical class and their role in obesity.

Class	Examples / Comments	Potential Role in Obesity
Alkaloids	Cadambine, oxindole alkaloids[7,22]	Possible interaction with CNS receptors, including serotonergic targets
Triterpenoids	Ursolic-acid-type compounds	Anti-inflammatory, lipid-lowering, hepatoprotective
Flavonoids	Quercetin, kaempferol derivatives	Antioxidant, insulin-sensitizing, vascular benefits
Phenolic acids	Gallic/caffeic-acid-like phenolics	ROS scavenging, anti-glycation, gut effects
Saponins	Various	Hypolipidemic, modulation of bile acids and gut barrier
Tannins	Condensed and hydrolysable tannins	Antioxidant, anti-inflammatory, astringent

OBESITY, SEROTONIN, AND EXPERIMENTAL MODELS

Diet-Induced Obesity in Rodents

Diet-induced obesity (DIO) models in mice and rats are widely used to study the pathophysiology of obesity and to evaluate anti-obesity interventions. High-fat diets, typically providing ≥ 45 % of energy from fat, lead to increased body weight, visceral adiposity, insulin resistance, hyperlipidemia,

and hepatic steatosis, closely resembling human metabolic syndrome.^{37,38} These models are frequently used to test plant extracts that may act on multiple metabolic targets.

Serotonin and Metabolic Regulation

Serotonin (5-HT) plays a central role in appetite and energy homeostasis. In the hypothalamus, stimulation of 5-HT_{2C} receptors on pro-opiomelanocortin (POMC) neurons enhances melanocortin signaling, reducing food intake and body weight.^{39,40} Mice lacking 5-HT_{2C} receptors exhibit hyperphagia, obesity, and seizures, underscoring the importance of this pathway.⁴⁰

In peripheral tissues, serotonin synthesized primarily by intestinal enterochromaffin cells influences gut motility, hepatic metabolism, pancreatic function, and thermogenesis in adipose tissue.⁴¹⁻⁴³ Inhibition of peripheral 5-HT synthesis has been shown to enhance brown adipose tissue thermogenesis and protect against diet-induced obesity.^{41,44} Nutrient-induced changes in intestinal serotonin may modulate the gut-brain axis and inflammatory responses.^{42,43}

These insights informed the development of centrally acting 5-HT_{2C} agonists such as lorcaserin, which produced clinically meaningful but modest weight loss in randomized trials.⁴⁵ Concerns about long-term safety, including a possible increase in cancer risk, led to lorcaserin's withdrawal.⁴⁶ This has prompted exploration of plant-derived agents capable of modulating serotonergic pathways more gently and, potentially, more safely than synthetic drugs.

EXPERIMENTAL EVIDENCE FOR ANTI-OBESITY EFFECTS OF NEOLAMARCKIA CADAMBA

Antioxidant and Hepatoprotective Actions

Multiple studies have evaluated *N. cadamba* in models of liver injury and oxidative stress. Ahmed and Urooj showed that bark extract significantly reduced serum ALT and AST and improved histological features in rats exposed to hepatotoxic insults, indicating hepatoprotective activity.⁹ Ahmed and colleagues also documented strong antioxidant properties of *N. cadamba* extracts *in vitro* and *in vivo*, attributing these to phenolic and flavonoid constituents.⁴⁷

Hypolipidemic and Anti-Obesity Effects

In HFD-induced hyperlipidemic rats, researchers reported that bark extract of *N. cadamba* lowered total cholesterol, triglycerides, and LDL-cholesterol while raising HDL-cholesterol and enhancing antioxidant status.¹⁰ Explorers had evaluated fruit extract in HFD-fed rats and found reductions in body-weight gain, adiposity index, and serum lipid levels, along with decreases in malondialdehyde (MDA) and increases in glutathione (GSH).¹¹ Collectively, these studies suggest that both bark and fruit extracts of *N. cadamba* have beneficial effects on lipid metabolism and oxidative stress in diet-induced metabolic disorders.

Summary of *In vivo* Findings

Study	Model	Extract (Part / Type)	Dose (mg/kg)	Duration	Main Outcomes
Ahmed & Urooj[8]	Liver injury models	Bark, hydroalcoholic	200–400	1–2 weeks	Hepatoprotection, improved enzymes
Rajasekaran et al.[10]	HFD-induced hyper-lipidemia	Bark extract	200–400	4–6 weeks	↓TC, ↓TG, ↓LDL, ↑HDL, ↑antioxidants
Ahmed et al.[11]	<i>In vitro/in vivo</i> oxidative stress	Various parts	–	–	Strong antioxidant capacity
Kausar et al.[9]	HFD-fed obese rats	Fruit extract	200–400	8 weeks	↓BW gain, ↓adiposity, ↓lipids, ↓MDA, ↑GSH

(↓ indicates reduction; ↑ indicates increase.)

PROPOSED MECHANISMS OF ANTI-OBESITY ACTION

Modulation of Lipid Metabolism

The consistent improvements in serum lipid profile—reduced total cholesterol, triglycerides, and LDL-cholesterol, and higher HDL-cholesterol—imply that *N. cadamba* modulates lipid synthesis, catabolism, and transport. Triterpenoids, saponins, and flavonoids present in the plant are known in other contexts to affect enzymes such as HMG-CoA reductase, to alter bile acid excretion, and to influence lipoprotein lipase and hormone-sensitive lipase, which may explain these effects.^{10,11}

Serotonin-Linked Pathways

Because *N. cadamba* contains indole and oxindole alkaloids, and serotonin is central to the regulation of appetite and adipose tissue metabolism, it is plausible that *N. cadamba* could modulate serotonergic signaling. Central 5-HT_{2C} receptors mediate anorectic effects, while peripheral serotonin affects thermogenesis and lipid handling.^{39–42,44} If *N. cadamba* alters brain or gut serotonin levels or receptor activity, this may partially account for reductions in body-weight gain and improvements in glucose tolerance observed in HFD models. However, this mechanistic link remains hypothetical and requires targeted receptor-binding, signaling, and gene-expression studies.^{7,22}

Antioxidant and Anti-Inflammatory Effects

Obesity is accompanied by elevated oxidative stress and low-grade inflammation, especially in liver and adipose tissue.^{2,37} *N. cadamba* extracts reduce MDA and increase endogenous antioxidant defenses (GSH, superoxide dismutase, catalase) in several models, consistent with strong antioxidant capacity.^{11,47} This may protect hepatocytes from lipid peroxidation and help preserve insulin signaling and metabolic flexibility. Histological improvements in hepatic steatosis and inflammation observed in diet-induced models support this organ-protective role.^{8–11}

Potential Involvement of the Gut–Liver–Brain Axis

Polyphenols and saponins from various plants can modulate gut microbiota and intestinal barrier integrity, which in turn influence systemic inflammation and metabolic homeostasis. Given that gut-derived serotonin also participates in metabolic regulation, it is conceivable that *N. cadamba* may affect the gut–liver–brain axis through combined actions on microbiota, intestinal serotonin, and barrier function. This area remains unexplored for *N. cadamba* and represents an important direction for future research.^{42,43}

SAFETY AND TOXICOLOGICAL CONSIDERATIONS

Rodent studies using *N. cadamba* extracts at doses around 100–400 mg/kg typically report no mortality, no gross behavioral abnormalities, and no clear evidence of organ toxicity. In many models, liver and kidney function markers actually improve, consistent with hepatoprotective and possible nephroprotective effects. Histopathology often shows attenuation of hepatic steatosis and inflammatory changes in HFD-fed animals rather than any treatment-induced damage.^{8–10}

CONCLUSION

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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