

PHARMACOLOGICAL AND TOXICOLOGICAL PROFILES ON NEOLAMARCKIA CADAMBA: A REVIEW

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ABSTRACT

Neolamarckia cadamba (Roxb.) Bosser, Often known as Kadamba, is a member of the Rubiaceae family and has a long history of use in Ayurvedic, Vedic, and ethnomedical literature. This study provides a concise summary of N. cadamba's botanical description, traditional usage, phytochemical components, pharmacological actions, and toxicological profile. Historically, a variety of plant parts, such as the bark, leaves, flowers, fruits, seeds, and roots, have been used to treat diabetes, fever, inflammation, diarrhea, wounds, liver ailments, infections, cancer, and neurological disorders. Phytochemical investigations reveal alkaloids including cadambine, dihydrocadambine, and neolamarckines, as well as flavonoids, tannins, saponins, terpenoids, triterpene glycosides, phenolic acids, steroids, polysaccharides, and essential Oils rich in linalool and geraniol. Pharmacological study has demonstrated

antioxidant, antidiabetic, hepatoprotective, anti-inflammatory, analgesic, antipyretic, antimicrobial, antifungal, anthelmintic, anticancer, wound-healing, gastroprotective, diuretic, sedative, antiepileptic, and urolithiatic activities. Toxicological evaluations in experimental animal models demonstrate no discernible acute or subacute toxicity, indicating safety at therapeutic levels. All things considered, Neolamarckia cadamba is a promising source of bioactive compounds with substantial therapeutic potential, underscoring the need for further systematic research, clinical validation, and standardization to support its development as powerful phytopharmaceutical agents. Future research should focus on molecular mechanisms, dosage optimization, formulation development, and human therapeutic trials.

KEYWORDS: Neolamarckia cadamba; Rubiaceae; Tropical medicinal tree; Herbal origin; Plant-based medicine.

INTRODUCTION

Neolamarckia cadamba, commonly known as kadam or cadamba, belongs to the Rubiaceae family and is also known as Leichhardt pine, bur-flower tree, and laran. In India, kadam trees are frequently found on the 500-meter-high slopes of evergreen forests. The tree can reach a height of 45 meters.^[1] Complete growth takes six to eight years. Smooth bark and a grayish-green stem characterize younger trees. As they age, the bark gets tougher, grayer, and develops big fissures. After the tree has developed for four to five years, the blooming season starts-Neolamarckia cadamba's fleshy yellow-orange fruit contains over 8000 seeds that are closely packed together and resemble small, velvety pouches.^[2] The phytomedicines that can prevent and treat chronic and lifestyle diseases in humans include alkaloids, flavones, anthocyanins, terpenoids, flavonol, proanthocyanins, phenolic acids, tannins, and other chemical compounds found in Neolamarckia Cadamba. Diabetes, fever, anemia, blood disorders, stomatitis, uterine issues, leprosy, skin difficulties, various malignancies, eye irritation, tumors, diarrhea, and infections are just a few of the conditions that are commonly treated with the plant.^[3] The plant has been proven to offer many biological and medical advantages, such as antidiabetic, antibacterial, anti-inflammatory, wound healing, antioxidant, anti-parasitic, anti-cancer, and heart-protective properties.^[4] The bark of the plant is used to cure eye discomfort and fever. The flowers are used to make vegetables. The leaf decoction is beneficial for ulcers and sores-The blooms are used to make vegetables. The leaf infusion is beneficial for ulcers and sores.^[5] Light construction, veneer, pulp, fiberboard, and blockboard are just a few of the goods that may be made from wood.^[2]

PLANT DESCRIPTION

TAXONOMICAL CLASSIFICATION

Kingdom: Plantae

Class: Magnoliopsida

Order: Gentianales

Family: Rubiaceae

Genus: Neolamarckia

Species: Neolamarckia cadamba

Botanical Name: Neolamarckia cadamba (Roxb.) Bosser

Synonym: *Neolamarckiacadamba* (Roxb.) Bosser.

PYTOCHEMICAL REVIEW

❖ FRUIT

Steroids are not present in *N. cadamba* fruit aqueous extract, but it does include tannins, cardiac glycosides, saponins, terpenoids, and flavonoids. Ripe fruits have the highest total phenolic content (TPC) when compared to mature and immature phases-Fruit TPC is significantly lower than that of extracts from leaves and bark, and there is little information on fruit phenolics.^[6]

❖ LEAF

The leaf extracts of *N. cadamba* included a wide range of secondary metabolites, including glycosides, alkaloids, tannins, polyphenols, steroids, and flavonoids.^[7]

❖ BARK

Cadambine and its derivatives, saponins, glycosides, triterpenoids, cadambagic acid, quinovic acid, and β -sitosterol are among the alkaloids found in *Neolamarckia cadamba* bark. In a variety of seizure models, these alkaloids, steroids, and flavonoids exhibit strong antiepileptic properties.^[8]

❖ FLOWER

Linalool, geraniol, geranylacetate, linalyl acetate, α -selinene, 2-nonanol, phellandrene, α -bergamottin, p-cymol, curcumenol, terpinolene, camphene, and myrcene were the primary components of the essential Oils that were extracted from *N. cadamba* flowers.^[4]

❖ SEEDS

The seeds of *N. cadamba* contain the water-soluble polysaccharides D-xylose, D-mannose, and D-glucose.^[4]

PYTOCHEMICAL CONSTITUENTS

Tannins, steroids, alkaloids, saponins, cadamba genic acid, quinovic acid, and β -sitosterol are all found in the Stem bark of *N. cadamba*.^[8] According to mass spectrum research, the bark of *Neolamarckia cadamba* is rich in triterpene glycosides, specifically triterpene glycoside A (C₄₂H₆₆O₄) and triterpene glycoside B (C₄₂H₆₆O₅). Important bioactive substances including quinovic acid, sitosterol, and cadambagenic acid are also found in the stem bark, and its steroidal and alkaloidal components have been extensively researched for possible

medicinal uses. Triterpene glycoside B is a 3-O-[β -D-glucopyranosyl] ester of quinovic acid, whereas triterpene glycoside A is a 3-O-[α -L-rhamnopyranosyl]-quinovic acid-28-O-[β -D-glucopyranosyl] ester.^[8] The leaves of *N. cadamba* include glycosides, steroids, flavonoids, and alkaloids. Indole alkaloids, including cadambine, vincosamide, anthocephaline, and strictosamide. Additionally, the leaves contain cadambine and isocadambine, glycoalkaloids, and non-glycosidic isomeric indole alkaloids. From the 80% ethanol extract of NC leaf.^[8] Eight potential bioactive chemicals were identified, including two indole alkaloids, Neolamarckine A and Neolamarckine B. Levoglucosan, phenol, 2, 4-Bis (1,1-dimethylethyl), myoinositol, Oleic acid, hexadecanoic acid, octadecanoic acid, and β -D-(+)-talopyranose.^[9] Linalool, geraniol, geranyl acetate, linalyl acetate, α -selinene, 2-nonanol, and pphellandrene are essential Oils found in flowers. The main constituents Of the essential Oil extracted from *Neolamarckia cadamba* flowers include linalool, geraniol, geranyl acetate, linalyl acetate, α -selinene, 2nonanol, β -phellandrene, A-bergamottin, p-cymol, curcumene, terpinolene, camphene, and myrcene.^[4] Phytochemical screening revealed the presence of tannins, cardiac glycosides, saponins, terpenoids, and flavonoids in the aqueous extracts of *N. cadamba* fruits; steroids were absent at every developmental stage.^[6]

PHARMACOLOGICAL PROFILE

Neolamarckia cadamba, commonly known as Cadamb, is one of the most significant medicinal herbs. It belongs to the Rubiaceae family. Records or prior literature indicate that practically every aspect of the *Neolamarckia cadamba* plant has been treated for generations to treat a range of diseases. The leaf infusion is sometimes used as a gargle to heal wounds, aphthae, stomatitis, and ulcers. Fever, vomiting, inflammation, diarrhea, cough, diabetes, burning sensations, diuresis, sores, ulcers, and snake bites are all treated with the plant's bark.^[3] The fruit juice of this plant has been used as a lactodepurant to boost nursing women's milk production. The leaves and bark of *Neolamarckia cadamba* have antiinflammatory, antipyretic, and analgesic qualities-The leaf infusion is frequently used as a gargle to treat wounds, ulcers, aphthae, and stomatitis. The bark of the plant is used to treat a wide range of ailments, such as fever, vomiting, diarrhea, cough, diabetes, burning sensations, diuresis, sores, ulcers, and snake bites.^[5] The fruit juice from this plant has been used as a lactodepurant to help nursing mothers produce more milk. *Neolamarckia cadamba*'s leaves and bark have anti-inflammatory, analgesic, and antipyretic qualities.

ANTIOXIDANT ACTIVITY

Rich in phenolic compounds with antioxidant qualities, *Neolamarckia cadamba* extracts lower oxidative stress by quenching singlet/triplet oxygen, redox action, peroxide breakdown, and free-radical scavenging. In DPPH assays, methanolic bark, fruit, and leaf extracts demonstrated significant dose-dependent in vitro antioxidant activity, with the leaf extract exhibiting the greatest level. Plasmid DNA (pBR322) was shielded from Fenton reaction hydroxyl radical damage and antioxidant activity was enhanced by ethanolic leaf extract fractionation into ethyl acetate, butanol, and aqueous fractions. In both enzymatic and nonenzymatic in vitro systems, root extract (50—500 mM) inhibited deoxyribose breakdown, lowered hydroxyl radicals in the hypoxanthine—xanthine oxidase system, and reduced the formation of superoxide anion and hydroxyl radicals. Fruit hydroethanolic extract (200 & 400 mg/kg) enhanced catalase and peroxidase activity and reduced lipid peroxidation in alloxan-induced diabetic mice. Antioxidant activity prevents degenerative illnesses by reducing oxidative modification of proteins and lipids; bark paste demonstrates antioxidant and genoprotective characteristics commonly used with ginger and Turmeric.^[8]

ANTI DIABETIC ACTIVITY

The antidiabetic effects Of methanolic extracts from *N. cadamba* leaves and bark are comparable. Methanol and aqueous root extracts significantly lowered blood glucose in both normoglycemic and alloxan-induced diabetic Wistar albino rats in a dose-dependent manner; methanol extract had a greater effect, comparable to glibenclamide. An aqueous extract of *A. indicus* fruit (400 mg/kg bw) reduced blood glucose in adult male Sprague Dawley rats, just like glibenclamide (10 mg/kg bw). The liver and pancreatic cells of treated diabetic rats resembled those of normal rats, according to histological findings. A methanol extract of *N. cadamba* roots increased hepatic glycogen and stimulated up-glycogenesis in the livers of diabetic rats. Root extracts likely have an antidiabetic effect via boosting the release of insulin from healthy β -cells since they raise liver glycogen. Blood sugar can be lowered by either better insulin release from the pancreas or increased absorption of glucose. *N. cadamba* leaves can be used for up to ten months; cadambine reduces insulin receptor insensitivity and dihydrocinchonine controls endogenous insulin production. Hypolipidemic (root), antidiarrheal (flowering top), analgesic (leaf, stem bark), and antidiabetic (stem bark) properties are among the biological traits that have been reported.^[8]

ANTI CANCER ACTIVITY

The earliest plant-based anticancer drugs investigated in the early 1950s included vinblastine, vincristine, vinca alkaloids, and podophyllotoxins. *Neolamarckia cadamba* leaves have not yet shown promise as a breast cancer treatment. The NC leaf ethanol extract was tested in vitro using the MCF-7 breast cancer cell line. 0.2 mg/mL was the IC₅₀ value against MCF-7 cells. The extract suppressed cancer cells in a time-dependent and dose-dependent manner. The extract halted the MCF-7 cell cycle at the G₀/G₁ stage. After 72 hours, apoptosis was discovered using the Annexin-V test. Cell cycle arrest was associated with down-regulation of CDK2 and up-regulation of p21 and cyclin-E. The extract induced apoptosis through the mitochondrial pathway. It was discovered that D-pinitol and myoinositol are significant bioactive compounds. In human breast cancer cells, NC extract showed antitumor activity through cell cycle arrest and cell death.^[10]

DIURETICS AND LAXATIVES

Wistar albino rats were used to test the laxative and diuretic effects of *Neolamarckia cadamba* bark extracts. Agar-agar and furosemide used as reference standards. At tested doses, methanol extract considerably raised urine output and urine electrolyte content, which was comparable to the reference standard. The laxative action of chloroform extract was evident. The presence of different phytoconstituents in *N. cadamba* preparations may be the cause of different actions.^[11]

WOUND HEALING ACTIVITY

Extracts from the bark, leaves, flowers, and fruits of the entire *N. cadamba* plant exhibit potent wound-healing properties. Increased tensile strength and improved wound contraction are two benefits of wound healing. By preventing lipid peroxidation and raising SOD and catalase levels, extracts demonstrated strong antioxidant activity. The methanolic leaf extract's ethyl acetate fraction demonstrated strong wound-healing properties. Additionally, in excision and incision wounds, the leaf extract fraction showed strong antioxidant and free radical scavenging activity.^[12]

UROLITHIATIC ACTIVITY

In Wistar albino rats with calcium oxalate-induced nephrolithiasis, methanol fruit extract from *N. cadamba* demonstrated efficacy. At 200 and 400 mg/kg (p.o.), extract was successful in both the preventative and curative therapy groups. Picrotoxin staining and histological analyses revealed a reduction in calcium oxalate crystals following extract treatment.^[12]

GASTROPROTECTIVE ACTIVITY

Aqueous and methanol extracts Of *N. cadamba* leaves and bark were tested for their antiulcer properties-Models Of aspirin-induced ulcers and pylorus ligation were employed-At doses of 200 and 400 mg/kg (p.o.), both extracts considerably decreased stomach lesions.Gastric volume, pH, free acidity, total acidity, ulcer index, and ulcer inhibition percentage were all reduced by extracts.^[12]

HEPATOPROTECTIVE ACTIVITY

After gathering, shade-drying, granulating, and extracting the bark from *N. cadamba* stems using a two-fold cold maceration process, the bark was evaluated for phytochemicals and medicines-The study's objective was to evaluate the hepatoprotective qualities of the hydroalcoholic stem bark extract (NCHAE) of *N. cadamba*. Swiss albino mice's livers were damaged using iron overdose models and chloroform-Chloroform and maize Oil (0.75 mg/kg body weight, p.o.) were administered for seven days to induce liver damage. A seven-day intraperitoneal iron excess (100 mg/kg) caused hepatic damage.B100d biochemical indicators and liver histology were evaluated. Silymarin (50 mg/kg body weight) was the standard hepatoprotective drug. Iron overload and chloroform increased liver marker enzymes and hepatocyte damage. NCHAE repaired biochemical alterations in both hepatotoxicity models. Significant hepatoprotective activity ($p < 0.01$) was found by NCHAE against both inducing agents.^[10]

ANTI DIARRHOEAL ACTIVITY

Mice's diarrhea caused by castor Oil was lessened in a dose-dependent manner by a dry hydroethanolic extract of *N. cadamba* flowering tops (200—500 mg/kg). Fecal droppingfrequency dropped dose-dependently-There was a dose-dependent inhibition of intestinal fluid buildup. In test animals, the hydroethanolic extract of *Anthocephalus cadamba* flowering tips was tested for its antidiarrheal properties. Mice's total fecal output was dosedependently decreased by dry hydroethanolic extract (250—500 mg/kg, p.o.). At 250 and 500 mg/kg, intestinal fluid buildup and intestinal transit were considerably and dose-dependently decreased-The control group's reduction rate was 37.83%, whereas the conventional drug group's was 73.97%.

ANTI FUNGAL ACTIVITY

Cadamba leaf and bark extracts displayed antifungal effectiveness against *Candida albicans* and *Aspergillus fumigatus*. Compared to bark extract, leaf extract revealed stronger

antifungal efficacy. Cadamba possesses strong antifungal qualities-Alcoholic and aqueous fruit extracts showed strong antifungal activity against *Trichophyton rubrum*, *Candida albicans*, *Microsporum*, and *Aspergillus niger*. The greatest zone of inhibition against *Trichophyton rubrum* was 15.0 mm for the ethanolic extract and 12.0 mm for the hot water extract. The minimum inhibitory concentrations (MIC) of ethanolic ripe fruit extract against *Aspergillus niger* and *Trichophyton rubrum* were 2.5 and 2.10 mg/ml, respectively.^[11]

ANTI ARTHRITIS ACTIVITY

Autoantigen production and denaturation of proteins are associated to inflammatory and arthritic diseases-Albumin and protein denaturation procedures were used to evaluate the in vitro antiarthritic efficacy. Ethanol and watery bark extracts from *Anthocephalus cadamba* Roxb. (Ma-u) were investigated-The typical anti-arthritis medicine was diclofenac sodium-The absorbance at 660 nm was measured at 500, 250, and 125 gg/mL. Anti-arthritic activity was assessed using denaturation of the bovine serum albumin protein-Protein denaturation was greatly reduced by ethanol and watery extracts-The most effective antiarthritis doses were 500 gg/mL and 125 gg/mL. The protection against arthritis in the bovine serum albumin method was 45.58% for ethanol extract, 31.62% for watery extract, and 97.79% for diclofenac sodium at 500gg/mL. At 500 gg/mL, the denaturation Of egg albumin was 62.5% for ethanol extract, 30.55% for watery extract, and 97.22% for diclofenac sodium-At 500 pg/mL, ethanol extract was much more effective than diclofenac sodium in both methods. In treating arthritis, the bark ethanol extract worked better than the watery extract.^[14]

ANTI HELMENTIC ACTIVITY

Neolamarckia cadamba bark extracts have anthelmintic action against *Pheritima posthuma* in a dose-dependent manner; piperazine citrate showed similar anthelmintic effects; extracts of ether and chloroform showed potential action. In the Konkan, newborns are fed fresh bark juice when the fontanelle descends. The Sahara tribes of Orissa treat children with helminthiasis by making a decoction from fresh bark. The study reports on cadamba roots. Powdered root was extracted using petroleum ether, chloroform, methanol, and water in a Soxhlet extractor. Anthelmintic activity was measured using an adult Indian earthworm called *Pheritima posthuma*. Six groups of earthworms were treated with piperazine, extracts (10, 15, and 20 mg/ml), and citrate.^[10]

HYPOLIPIDERMIC ACTIVITY

Rats with 150 mg/kg body weight of alloxan experienced altered lipid levels and hyperglycemia. Over the course of 30 days, oral *A. cadamba* root extract (500 mg/kg body weight) reduced total cholesterol, phospholipids, triglycerides, and lipid peroxides in rats with dyslipidemia. Root extract enhanced postheparin lipolytic activity and reduced plasma lipids in hyperlipidemic mice-Bark and leaf extracts corrected abnormal lipid profiles in Medoroga and hyperlipidemia. When it came to curing Medoroga, leaves were a little better than bark.^[12]

ANALGESIC, ANTIPYRETIC & ANTI INFLAMMATORY

Neolamarckia cadamba methanol bark extract exhibits antipyretic, analgesic, and antiinflammatory properties. In mice, acute oral toxicity exceeded 300 mg/kg. Mice's writhing caused by acetic acid was considerably lessened by extract at 400 and 600 mg/kg. At 200, 400, and 600 mg/kg (p.o.), heat-induced discomfort was considerably lessened. The suppression of oedema caused by carrageenan was dose-dependent. Rats' fever caused by yeast was much decreased at 400 and 600 mg/kg, while it had no effect at 200 mg/kg. Traditional applications are supported by the results, however more research is needed to assess safety and mechanisms of action.^[10]

SEDATIVE & ANTI EPILEPTIC ACTIVITY

In experimental animal models, the ethanolic bark extract of *N. cadamba* exhibits sedative and antiepileptic properties. The length of ketamine-induced sleep was considerably extended by the extract at 100, 200, and 400 mg/kg p.o. In seizure models caused by maximum electroshock, isoniazid, and pentylenetetrazol, the extract increased tonic extension, delay to chronic convulsion, and time of death at all tested doses.^[12]

TOXICOLOGICAL PROFILE

Neolamarckia cadamba fruits and roots at 500 mg/kg body weight have not been the subject of any published toxicological investigations-Animal models were used to assess the toxicity of methanolic bark extract-At doses higher than 3000 mg/kg, acute toxicity was noted; at 3000 mg/kg, there was no death-At a dose of 600 mg/kg, subacute toxicity was evaluated-According to the results, 600 mg/kg body weight of *Neolamarckia cadamba* might not be dangerous.^[15]

ACUTE TOXICITY

CPCSEA, India evaluated the acute oral toxicity of *Neolamarckia cadamba* ethanolic extract in accordance with OECD draft guidelines 423 (2001). Young female albino mice were given extract orally at doses of 100, 500, 1000, 1500, and 2000 mg/kg. Six groups of mice weighing 25–30 g were utilized; the control group was given 10 mL/kg of distilled water. For the first four hours, the animals were observed constantly; for the next twentyfour hours, they were observed intermittently; after seventy-two hours, the animals' mortality was evaluated. Locomotor activity, tremors, convulsions, tonic extension, Straub tail, muscle spasm, loss of righting reflex, ataxia, drowsiness, hypnosis, lacrimation, diarrhea, salivation, writhing, and alterations in skin, fur, eyes, and mucous membranes were all noted. For additional pharmacological research, a tenth, half, and double of the maximum safe dose were used.^[7]

SUBACUTE TOXICITY

A 14-day sub-acute toxicity study of *N. cadamba* methanol extract was carried out at 600 mg/kg p.o. once daily. On day fifteen, the animals were slaughtered, and biochemical parameters were assessed. There were no discernible variations in body weight between the extract-treated and control groups. Heart, liver, and kidney weights did not differ from the control. There were no notable changes in the biochemical and haematological markers (hepatic and renal function tests). The findings show that 600 mg/kg p.o. of *N. cadamba* methanol extract is safe.

CONCLUSION

Neolamarckia cadamba (Roxb.) Bosser is an adaptable medicinal herb with solid traditional and medical support. Alkaloids, flavonoids, tannins, saponins, phenolic acids, polysaccharides, terpenoids, triterpene glycosides, and essential Oils are examples of phytochemicals. Bark, leaves, fruits, flowers, seeds, and roots have been shown to have hepatoprotective, antiinflammatory, analgesic, antipyretic, antimicrobial, antifungal, anthelmintic, anticancer, antiarthritic, woundhealing, gastroprotective, diuretic, laxative, sedative, antiepileptic, and urolithiatic properties. Numerous beneficial properties are based on antioxidant activity, which is mostly derived from phenolics and flavonoids and lowers oxidative stress. Traditional use for metabolic and liver problems is supported by antidiabetic and hepatoprotective benefits in animal models. Extracts are generally safe at therapeutic dosages; no notable acute or subacute toxicity has been recorded.

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