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Review Article

A Comprehensive Review on the Pharmacological Potential and Analgesic Activity of *Neolamarckia cadamba* Fruit Extract

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ABSTRACT

The fruits of *Neolamarckia cadamba* (commonly known as Kadamba) are traditionally used in Ayurvedic and folk medicine to treat distress, inflammation, and various systemic disorders. This review collects and carefully evaluates the current literature on the analgesic potential of *N. cadamba* (*Anthocephalus cadamba*) fruit extracts and their diverse pharmacological actions. Phytochemical investigations have revealed that the fruit contains a rich array of compounds, including flavonoids (quercetin, apigenin), phenolic acids, tannins, terpenoids (cadambagenic acid), and unique alkaloids (cadambine), which have the capacity to regulate pathways associated with prostaglandins, NSAIDs, and cytokines. *N. cadamba* fruit exhibits impressive analgesic, antipyretic, and anti-inflammatory actions through peripheral and central mechanisms, primarily by inhibiting prostaglandin production and exerting free-radical scavenging action. Bearing a highly favorable safety profile, the fruit extract also exhibits potent anthelmintic, antioxidant, and antimicrobial potential. Even so, most pharmacological research has historically focused on the bark and leaves, underscoring the urgent need for targeted mechanistic and clinical studies explicitly exploring the fruit extracts

INTRODUCTION

According to the International Association for the Study of Pain, pain is referred to as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage" [1]. Harmful

stimuli cause distress, which is channeled to the central nervous system via specialized neural networks. Peripheral nociceptive and central systems in the central nervous system and spinal cord are intricately involved in the perception of pain. The body uses pain as a shielding mechanism

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against potential harm [2]. Globally, pain is becoming an increasingly significant concern. According to surveys, 10% of adults worldwide are newly diagnosed with chronic pain each year, while 20% of adults experience ongoing pain [3]. Over 80% of people visit doctors due to pain, and for many of these individuals, pain is mutable and easily forgotten. Unfortunately, for some, pain persists, becoming a constant encumbrance and source of intermittent anguish [4]. Pain-relieving medications, both central and peripheral, alleviate distress without impairing awareness. Opioids and non-steroidal anti-inflammatory drugs (NSAIDs) are the two primary categories of analgesics used. While NSAIDs are recommended for pain related to inflammation and tissue damage, opioids are recommended for deep-seated visceral or severe pain [5]. Although opioids and NSAIDs remain the cornerstones of pain management, both medication classes are well known for their frequent and serious adverse effects. Non-steroidal anti-inflammatory drugs typically result in gastrointestinal (GIT) problems, hepatotoxicity, and renal complications, whereas opiates produce physical dependency, tolerance, and addiction [6]. Therefore, finding alternative ways to alleviate pain is essential. Herbal medicines stand out as an intriguing and highly effective choice for the treatment of pain and opioid withdrawal. Since ancient times, traditional plant-derived substances have been used as medicines and are crucial to healthcare, particularly in rural areas where access to modern medication is limited [7]. It has been demonstrated that phytochemical substances found in plants serve as preventive and therapeutic mechanisms against a variety of illnesses. Over the last decade, numerous studies have documented the significant effectiveness of medicinal plants, such as *Neolamarckia cadamba*, in safely treating pain and systemic inflammatory illnesses [8].

Plant Profile:

Neolamarckia cadamba, formerly known as *Anthocephalus cadamba*, is a widely revered evergreen tropical flowering tree belonging to the Rubiaceae family. It is native to South Asia, including India, Nepal, Bangladesh, and Sri Lanka. For centuries, it has been utilized for both prevention and therapy in Ayurveda, Unani, and other Indian medical systems. Revered as a holy tree by various ancient dynasties, it is deeply embedded in Indian culture and mythology. Many parts of the plant, such as the bark, leaves, roots, and notably the fruits, have been used for ages because of their medicinal and curative properties. The pharmacological relevance of *N. cadamba* fruit is directly attributed to the abundance of secondary metabolites, including specific alkaloids, flavonoids, tannins, saponins, and phytosterols [9]. By interacting with central pain pathways and inhibiting prostaglandin synthesis, these fruit-derived phytochemicals are highly effective in the regulation of pain [10].

Taxonomy & Classification

Taxonomy	Classification
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Gentianales
Family	Rubiaceae
Genus	*Neolamarckia*
Species	*cadamba*

Table 1: Taxonomy & Classification of *Neolamarckia cadamba*

Common Names of *Neolamarckia cadamba*

Language | Names
English	Bur-flower tree, Laran
Hindi	Kadam, Kadamba
Sanskrit	Kadamba, Haripriya



Kannada	Kadamba
Gujarati	Kadamb
Bengali	Kadam
Tamil	Vellai-kadambam
Telugu	Kadambamu

Table 2: Common Names of N. cadamba

Botanical Description of the N. cadamba Fruit:

The fruits of *Neolamarckia cadamba* are easily identifiable because of their highly unique morphological characteristics.

Type & Shape: The fruit is a fleshy, globose pseudocarp (a false fruit formed by the fusion of many smaller fruits).

Dimensions: The diameter of the fruit typically ranges between 5 and 7 cm.

Color: Green when unripe, transitioning to a vivid yellow or fleshy yellow-orange when completely ripe.

Taste and Texture: The ripe fruit has a slightly sweet, acidic taste and is entirely edible. The capsules are closely packed to form a fleshy ball-like structure containing numerous small seed coats.

Seasonality: The fruit usually matures in the late monsoon and early winter seasons.

Phytochemical Composition

The fruit of *N. cadamba* is packed with powerful primary and secondary metabolites. Proximate analysis of the edible fruit shows it is rich in proteins, essential fats, and vital minerals. Pharmacologically, its organic extracts (methanolic, hydro-methanolic, and aqueous) yield highly active biomolecules.

Phytochemical Class | Main Constituent Examples
 | Biological Activity |

| Flavonoids | Quercetin, Apigenin, Isoquercitrin |
 Potent analgesic, anti-inflammatory, and antioxidant activity; blocks COX/LOX pathways.

Terpenoids / Saponins | Cadambagenic acid, Quinovic acid |
 Antidiabetic, antimicrobial, potent anti-inflammatory, and membrane stabilizing effects.

| Alkaloids | Cadambine, Isocadambine, Dihydrocadambine |
 Central nervous system modulation, mild sedative, and significant analgesic action. |

| Phenolic Acids | Chlorogenic acid, Ellagic acid |
 Free-radical scavenging, antioxidant, and anti-mutagenic properties. |

| Tannins | Proanthocyanidins |
 Astringent properties, superior anthelmintic activity, and mucosal protection. |

Table 3: Phytochemical Composition and Biological Activity of N. cadamba* Fruit

Pharmacological Activity:

1. Analgesic and Antipyretic Activity:

Extensive studies have been directed toward the analgesic properties of *N. cadamba* extracts. In standard pharmacological evaluations (such as the acetic acid-induced writhing test in mice), methanolic and defatted aqueous extracts of **N. cadamba* showed a significant dose-dependent reduction in the number of writhings [11]. Furthermore, the extracts exert potent protective effects against heat-induced pain (evaluated via the hot plate and tail immersion tests) at varying doses of 200, 400, and 600 mg/kg. The increase in reaction time indicates central antinociceptive action (similar to mild opioids), while the reduction in writhing indicates strong peripheral analgesia. The extracts also show a notable antipyretic effect against yeast-induced pyrexia in animal models, performing favorably compared to

standard reference drugs like aspirin and paracetamol.

2. Anti-inflammatory Activity:

The fruit extract successfully inhibits pro-inflammatory cytokines and suppresses edema. When evaluated using the carrageenan-induced paw edema model in rats, the extracts provided significant, dose-dependent percentage inhibition of the edema. This anti-inflammatory capability is heavily attributed to the high concentration of flavonoids (like quercetin) and saponins in the fruit's peel and pulp [12].

3. Antioxidant & Membrane Stabilizing Activity:

The hydro-methanolic fruit extract of *N. cadamba* exhibits tremendous free-radical scavenging action. In DPPH (2,2-diphenyl-1-picrylhydrazyl) assays, the fruit extracts cause rapid decolorization, indicating high electron-donating capability. Furthermore, the fruit extract reveals good membrane-stabilizing activity, inhibiting both hypotonic solution- and heat-induced hemolysis in human erythrocytes, rivaling standard acetylsalicylic acid [13]

4. Anthelmintic Activity:

The fruit of *Kadamba* has a long traditional history of treating parasitic infections. In-vitro studies of the hydro-methanolic and ethyl acetate extracts of *N. cadamba* fruits demonstrate potent anthelmintic activity. The extracts successfully induce paralysis and subsequent death in test subjects (like tapeworms and earthworms) in significantly less time compared to standard drugs like albendazole. This effect is largely correlated with the fruit's rich polyphenolic and tannin content [14].

5. Antimicrobial Activity:

Fruit and peel extracts show excellent antimicrobial effects against various bacterial and fungal strains. The presence of secondary metabolites actively degrades the bacterial cell wall, validating the traditional use of the fruit juice for treating minor infections and oral mucosal irritations [15].

Mechanistic Studies:

The mechanisms governing the pain resistance induced by *N. cadamba* fruit extracts are heavily dual-pathway. Peripherally, the flavonoids and phenolic acids (particularly quercetin) inhibit the cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, significantly dropping the synthesis of pain-inducing prostaglandins at the site of tissue injury. Centrally, the unique indole alkaloids (like cadambine) are theorized to modulate pain signaling in the spinal cord, potentially interacting with opioid pathways to increase the pain threshold without causing severe CNS depression.

Toxicity:

Toxicological assessments show a remarkably broad margin of safety for *N. cadamba*. Acute oral toxicity studies of the methanolic and aqueous extracts of the fruit evaluated in experimental rodents revealed that at high doses—upwards of 3000 mg/kg body weight—there was no recorded mortality. Furthermore, subjects exhibited no behavioral, neurological, or autonomic changes [11]. The edible nature of the fruit further establishes its high safety profile, making it a promising candidate for long-term therapeutic formulation.

Summary of Current Research Status:

While the fruits of *N. cadamba* contain scientifically proven bioactive compounds with immense analgesic and anti-inflammatory properties, a massive percentage of current



research literature has traditionally pivoted toward the leaves and bark. The emerging metabolomic profiling of the fruit and its peel is finally bringing its medicinal value to light. Researchers suggest that more comprehensive isolation studies and clinical trials are explicitly required to formulate Kadamba fruit-based botanical analgesics.

CONCLUSION:

In conclusion, the fruit extract of *Neolamarckia cadamba* (Kadamba) represents a highly promising natural source of analgesic and multipharmacological compounds, backed by growing preclinical evidence and a vast ethnomedical legacy. Its rich reservoir of flavonoids, phenolics, and unique alkaloids synergistically provides potent analgesic, antipyretic, anti-inflammatory, and anthelmintic actions. Working through both central nociceptor modulation and peripheral prostaglandin inhibition, the fruit effectively manages pain while offering an exceptional safety profile void of the harsh gastrointestinal and addictive side effects typical of synthetic NSAIDs and opioids. Moving forward, standardizing these fruit extracts and advancing into clinical evaluations will pave the way for novel, safe, plant-based pain therapies.

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