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Neolamarckia cadamba: A Comprehensive review on its Physiological, Ecological, Phytochemical and Pharmacological Perspectives

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ABSTRACT

Research on *Neolamarckia cadamba*, or "kadam", has been in trend till now; considering its various immunomodulatory, anti-microbial, anti-diabetic, anti-oxidant, and other medicinal properties. It can be useful in developing various preventative therapies and disease-curing strategies around the world. Even though profound research investigations have been conducted on *Neolamarckia cadamba*, or "kadam", for its use in ailment treatments, a wise understanding of the physiological, ecological, phytochemical, and pharmacological behaviour of "kadam" has to be addressed. This paper presents a comprehensive survey of various studies that have been reported on physiological, ecological, phytochemical, and pharmacological behaviour with the same objective. This review will provide researchers with a clear onset of the importance of medical values discovered in the cadamba plant.

Key words: *Immuno-modulatory, Anti-microbial, Anti-diabetic, Anti-oxidant and kadam*

Introduction

The tropical tree *Neolamarckia cadamba Miq* popularly known as kadam, is endemic to the South and Southeast asia, particularly Indonesia. Although Kadamba has a bitter, pungent, and astringent flavour called rasa, along with a pungent post-digestive impact known as vipaka, it balances all of the doshas, especially kapha and pitta. As reported by Slik (2006), the production of cadamba in Indonesia has been very widespread for many years ago, around the 1930s. The plant has been grown in Java, west and east of Kalimantan, Sulawesi, Sumbawa, and Irian Jaya worldwide (Martawijaya *et al*., 1989). In India, kadamba is a plant that grows all over the country. Predominantly, it is found in India's sub-Himalayan region, stretching from one side to Nepal, another side to West Bengal and Assam. It can also be seen in some northern and south-eastern regions of India like Bihar, Chhattisgarh, Madhya Pradesh (MP), and Andhra Pradesh (AP). In other Indian states like Karnataka and Kerala, it is a part of evergreen forests (Selvan and Parthiban, 2018). *Neolamarckia cadamba* is found in Uttarakhand's Haldwani Division, where it grows on the damp and swampy ground (Osmaston, 1927), in southern tropical semi-evergreen forests, in northern tropical wet deciduous forests, and in tropical freshwater swamp forests in the tropics (Champion and Seth, 1968). Which numerous species of this tree are widely planted in India, especially in agroforestry by farm-forestry method. For wood-based industries,

this species is becoming increasingly essential.

Research Methodology

The research methodology for the present comprehensive literature survey is described in this section. The present review methodology consists of three different phases, which include planning, executing, and documentation. The planning further consists of three different steps. The first step in planning is determining the need for the review; the second is formulating research questions; and the third is analyzing the physiological, ecological, phytochemical and pharmacological actions of the "cadamba plant". The various research articles based on macro and microscopic studies have been investigated as part of methodologies analysis. In the executing phase, the author searched for articles relevant to the area, screened articles based on the year of publication, and performed a quality assessment based on the articles' findings. The datasets or research articles that have been selected for this review are from Scopus, PubMed, and Web of Science journals, published in the last few years.

Physiology

While exploring its physical aspects, *Neolamarckia cadamba* is overall a big tree with a wide crown in the shape of umbrella and a cylindrical bole. The arms or branches of the tree are organised in tiers. It usually grows to moderate size of 15-20cm and has a rounded crown. But kadambas may have a maximum height of 45 metres, with 100 to 160 cm stem's diameter and a little buttress up to 2 metres high. The branches are horizontally extended, arranged in tiers and simply terminate at the tip. Its bark is deep grey with longitudinal fissures and thin scales that exfoliate. The leaves are oval in shape with pronounced veins measuring around 30*30 cm in length and width similar to those of madhuka. The flowers are small, orange, and globose in shape. The fruit is usually seen as fleshy, small capsulated structure which form yellowish-orange infructescence which contain nearly 7000 seeds. Further, the mature fruit is spherical, firm and yellow in colour with a sweet and tart flavour. Seed are trigonal or irregular in shape. If primarily discussing its wood characteristics, it has lightweight wood and is hard in strength. This heartwood is white with a yellow hue that darkens to creamy yellow when exposed, and it isn't easy to distinguish it from sapwood (Martawijaya *et al*., 1989). Other characteristics of this wood include having a fine or moderate texture, a straight grain, and a low gloss, with no distinct odour or flavour. Also, the wood of the "cadamba tree" is very useful for various mild construction materials such as floors, shafts and rafters, boxes and crates, tea-chests, etc. The most crucial factor in cadamba's survival is light. The highest temperature in its natural habitat ranges from 32 °C to 42 °C, while the lowest temperature varies between 3 °C to 15.5 °C. Frost is a problem for *Neolamarckia cadamba*. For its growth, there is a need for the average yearly rainfall to vary from 1500 to 5000 mm. Few cadamba trees may flourish locally in considerably drier locations with annual rainfall as low as 200 mm in various central regions of South Sulawesi. The ideal growing altitude for this tree is between 300 and 800 metres above sea level.

Ecology

While discussing the ecological behaviour of "*Neolamarckia cadamba*" distinctively, it is observed that it is a peculiar species that prefer deep and w*et al*luvial soils and is frequently seen in secondary woods along banks of rivers and the transitional zone between marshy, constantly flooded. Soil condition plays a crucial role in its yield as it grows on a vast range of soils, but it thrives mainly on well-accelerated fertile soils, which are more plentiful and dominant. Even though the physical conditions are ideal, sometimes it does not thrive in leachable or inadequately aerated soils, as mentioned by Jansen *et al*. (1993).

Furthermore, seeds are sown in the month of February after mixing them with sterilized sand. Sowing in the winter season has been found to be least successful. And after the sowing process, watering is done which is followed by germination in about 2-3 weeks. Generally, sowing in *A. cadamba* occurs at the age of 5 in planting circumstances. Somewhere around the age of four, the tree begins to bloom. Flowering lasts about 2–5 months on average and months of flowering varies from region to region depending on their climatic condition. Flowering occurs in Indonesia from April to August, while the fruits mature between sixth (June) to eighth (August) month of the year (Martawijaya *et al*., 1989). Onset time for flowering and fruiting of the tree differ for different nations. Here in this sec-

tion, Table 1 presents the flowering period of cadamba for various countries throughout the year.

Biological and medicinal significance of *Neolamarckia cadamba*

The Cadamba, highly known for its medicinal properties, is an important member of family Rubiaceae. The plant is rich in secondary metabolites and several phytochemicals such as cadambagenic acid, â-sitosterol, cadamine, cadambine, quinovic acid, etc. Which have significant role to play in nature due to its biological and pharmacological characteristics. Also, it can be put to use as a substitute to different synthetic compounds for the prevention and cure of several diseases. More than 10 decades took to discover different phytochemicals and their implications. Furthermore, the Cadamba has its unique ornamental value together with religious significance. The use of *Neolamarckia cadamba* is not limited to its biology only; it has a variety of other applications in ayurvedic treatment that have been listed in several Indian medical literary and mythological books. The phytochemistrical study of "cadamba plant" provides us with various curing techniques for numerous diseases such as diarrhoea, temperature, inflammation, haemoptysis, coughing, vomit, sores, ulcers, debility, antimicrobials, etc. The "cadamba plant" contains triterpenes, triterpenoid glycosides, flavanoids, saponins, indole alkaloids; cadambine, cadamine, isocadambine, isodihydrocadambineas as its major constituents (Table 3). Through investigation of the pharmacological activities of "cadamba plant," it is determined that it has various immunomodulatory, anti-microbial, anti-diabetic, anti-oxidant, and other medicinal properties, which can help develop various preventative therapies and disease-curing strategies. With the same objective, the author has provided a comprehensive survey of various investigation works reported on chemical constituents and pharmacological actions of the "cadamba plant" in the current work. So that the medical professionals working in this area can refer to the present study for an apparent onset of the importance of medical values discovered in the cadamba plant before starting their investigation or experimentation.

Phytochemical Study of *Neolamarckia cadamba*

The phytochemicals that are found frequently within distinct types of *Neolamarckia indicus* are called Indole alkaloids, saponins, terpenes, terpenoids, lipids, steroids, reducing sugars, etc. In addition, tannins and an astringent essence are also present in the bark of cadama, which is attributable to the existence of an acid comparable to cincho-tannic acid. Cadambagenic acid can be extracted from stem bark of *Neolamarckia cadamba*, together with quinovic acid and sitosterol. The steroidal and alkaloidal elements of *Neolamarckia indicus* dry stem bark have been investigated by various researchers for their medicinal potential.

Furthermore, *Neolamarckia indicus* has also been the subject of some chemical research. This tree's heartwood and leaves contain cadambine and isomers of dihydrocadambine and isodihydrocadambine. Cadambogic acid, sitosterol, and quinovic acid are all found in stem bark. The mentioned chemicals are responsible for the benefits of the tree's arial portions. Besides, extract from the roots of *Neolamarckia cadamba* is also beneficial in curing various urological diseases such as dysurea calculi and glycosuria. Table 3 presented below shows a different Phytochemicals found in various sections of *N. cadamba* with method of indentifying the same reported in latest articles. The Phytochemical studies presented in Table 3, reveal a lot of information regarding the existence of phenolic components in various sections of the cadamba plant,

Table 1. Flowering and Fruiting period of "*Neolamarckia cadamba*" in different countries of the world annually

Flowering	Fruiting	Country Name
5th May to 6th June month of same year	1st (Jan) to 2nd (Feb) month of same year	India
4th April to 8th August month of same year	6th (June) to 8th (August)	Indonesia
—	month of same year	Laos
4th April to 5th May month of year	10th (October) to 12th (December) month of same year	Philippines
6th June to 9th September month of same year	9th (September) to 2nd (February) month of next year	Malaysia
9th September month of same year	–	Sri Lanka

Table 2. Description of Physical parts of *Neolamarckia cadamba* and their uses (Dubey *et al.*,2011)

Physical part	Description	Use	Name of State
Bark	Dark gray or brown, roughish bark peels off in tiny scales along longitudinal fissures.	✓ Mixture of water with honey and cumin works as a remedy for throat hoarseness. ✓ Decoction can also be used to treat stomatitis and gum problems. ✓ Treating eye infection with aqueous paste and lemon juice. When the eyes are inflamed, the bark juice is mixed equally to amount of lime juice, opium juice, and alum juice and rubbed around the orbit. ✓ Skin problems are treated with dried paste. To use it as an antiseptic, soak it in shower water. ✓ When the fontanel descends, juice is administered to infant's head. They are given a modest amount of juice with cumin and sugar dissolved in it. ✓ Fever is treated with paste. Cholera is treated with juice derived by grinding the barks of the cadamba tree, with another trees bark known as *Mangifera indica*, and *Shorea robusta*. Dyspepsia is treated using a decoction.	Chhattisgarh, India (1-3), Western Ghats, India (4), Konkancoast, India(5), Jharkhand, India(6)
Leaf	Coriaceous leaf, elliptic-oblong or ovate, whole edge, pulvinus base, acute shortly acuminate, length of around 0.18-0.30 m and 0.1-0.16 m wide hairy underside	✓ Inflammation, urine retention, temperature, cough, diarrhoea, menorrhagia, burning feeling, sores, and ulcers are all symptoms of urinary retention. ✓ It is being used to cover wounds and sores. Stomach ache can be relieved by drinking juice. ✓ Stomach ache can be relieved by combining leaf juice with ordinary salt. ✓ Elephantiasis curing	Madhya Pradesh (1), Jharkhand, India (2), Odisha, India(3), Bangladesh (4)
Flower	Tiny yellow or orange flowers bloom in globose heads that measure 3-5 cm in diameter.	✓ For preparation of perfumes	Uttar Pradesh (1)
Fruit	Ripe fruits are juicy, orange, globose pseudocarp with a diameter of 5-7 cm and a golden colour.	✓ Skin infection or diseases, tumour, anaemia, diarrhoea and eye inflammation etc.	India (1)
Seed	Seeds are tiny and murky.	–	–

Table 3. Phytochemicals across different sections of A. Cadamba

Section of A. Cadamba	Type of Phytochemicals	Extraction	Technique	Finding	Reference
Leaf	Alkaloids, Flavanoids, Terpenoids, Saponin, Glycosides	–	Radical scavengenging and Invitro cytotoxicity	Total alkaloid content higher in stems	(Sharma and Mathur, 2021)
	Ascorbic acid, Total phenol	–	Proximate and Phytochemical analysis	Ca and Fe both are predominant minerals in the range of 186, 6.30 and 398, 13.80 mg/100g respectably in fresh and dried cadambaleaf powder	(Batta, 2021)
Stem	Alkaloid, Anthraquinone, Flavonoid, Steroid, Terpenoid, Volatile Oil, Tannins and Phenol	–	Dragendroff's Test, Wagner Test, Borntrager's test, -Shinoda test, -NaOH test, Buchardst test, Salkowski test, Libermann test and Phenol test	–	(Khareta *et al*., 2021)
	Chlorogenic acid, dihydrocadambine, Kaemferol 3-O-Glucoside, β-sitosterol, Catechin/ EpicatechinFeruloyquinic acid, Dihydrocadambine, Cadambine	Hexane, petroleum, ethyl acetate, chloroform and methanol	Gas chromatography and mass spectrometry	44.88% n-hexadecanoic acid, 17.96% hexadecanoic acid ethyl ester and 11.71% octadecanoic acid	(Zayed *et al*., 2014)
	Chlorogenic, Epicatechin, Catechin, Rutin, and Feruloyquinic acid	Ethanol,Ethyl acetate n-butanol and Water	DPPH assay, ABTS assay, colorimetric	EAAC fraction proven to have a higher antio-xidant in comparison to NBAC fraction and WAC fraction	(Chandel *et al*., 2012)
Bark	Alkaloids, Flavanoids, Terpenoids, Saponin, Glycosides	–	Column chromatography, and spectral techniques	AC-4 compound had better oral bioavailability	(Ansari *et al*., 2022)
		hydro alcoholic	Column chromatography.	Neolamarckia cadamba stem bark has proven excellent cytotoxic activity	Pola *et al*., 2021
		Water, ethanol (EtOH), ethyl	EDXRF technique	Ca (5.422 %), K (3.691 %), S (0.412%)	Moe *et al*., 2020

Table 3. *Continued ...*

Section of A. Cadamba	Type of Phytochemicals	Extraction	Technique	Finding	Reference
		acetate (EtOAc) and petroleum ether (PE)		and C (90.289 %) are dominant constituents in samples collected form Ayeyarwady Region	
		———	DPPH assay, ABTS assay,	Alkaloids are rich in bark	Chandel *et al.*, 2014)
Flower	Linalool, Geraniol, á Selinene, 2-Nonanol, Geranylacetate,	———	———	———	(Dubey *et al.*,2011)
Fruit	Indole alkaloids, saponins, triterpenes and secoiridoids	Methanol	NBT assay, 2-diphenyl-1-picrylhydrazyl (DPPH),	Scavenging of extract of fruit is higher than extract of leaf	(Ganjewala *et al.*, 2014)

which are linked to a variety of health points. These phenolic compounds with antioxidant properties have a minimum of one benzene ring connected to one or more hydroxyl groups and range in complexity from general molecules to highly polymerized greater molecular weight polymers. These phenolic chemicals and flavonoids help plants protect themselves and stimulate their growth under adverse situations, and they impact the configuration, substitution, functional group organisation, and quantity of hydroxyl groups in plants.

Pharmacology Study of *Neolamarckia cadamba*

According to records or previous literature, practically all parts of the *Neolamarckia cadamba* plant have been employed in the treatment of numerous ailments over centuries. For example, the leaf decoction is often used as a gargle to cure aphthae or stomatitis, ulcers, wounds, and metorrhea. Fever, vomit, inflammation, diarrhoea, cough, diabetes, burning feelings, diuresis, wounds, ulcers, and snake bites are examples of all conditions treated using the plant's bark. Indicus is an Ayurvedic treatment that has been described as an antidiarrheal, detoxifier, analgesic, and purifier of seminal fluids in numerous Indian medical texts. A hot aqueous extract from leaves of *Neolamarckia indicus* has been employed in traditional medicine to relieve pain and swelling;it also promotes wound healing and treats menorrhagia. This plant's bark skin decoction can help with diarrhoea, dysentery, and colitis. The plant's fruit juice has been used to increase the amount of mother's milk produced by breastfeeding moms and also acts as a lactodepurant.

Various parts of *Neolamarckia cadamba* have been proven to have antidiabetic, analgesic, antipyretic, anti-inflammatory, antidiarrheal, diuretic, laxative, and antihepatotoxic properties that could be used to treat a variety of diseases. For example, in an experiment of alloxan of around 120-150 mg/kg induced in diabetic rats, an alcoholic extract of the stem bark of *Neolamarckia cadamba* has been found to have an antidiabetic capability. In addition to that, the existence of avonoids, which activate insulin secretion or have an insulin-like effect, is assumed to be responsible for the effectiveness of around 400 to 500 mg/kg extract of medicine in the curing of diabetes, as per experimental investigations by Bussa and Jyothi (2010).

In an investigation by Acharyya *et al*. (2010), the extracts like alcoholic and aqueous *Neolamarckia cadamba* roots were evaluated for normoglycemic and alloxan-induced hyperglycaemic rats and shown to have antidiabetic action in doses of 400 mg/kg body weight. The extracts from the bark and leaf of *Neolamarckia cadamba*

Table 4. Reviewed article's distribution according to their research on pharmacological properties of cadamba plant

Pharmacological Properties	Part	Extract	Active concentration	Active compound	References
Antidiabetic	Leaves	Ascorbic acid, Phenolics	FNL= 567.29±2.60, DNLP 422.71±9.28, FNL= 9.60±1.50, DNLP 22.10±1.10	Phenolics	Batta & Rajput, 2021
	Leaves, Stem Bark	–	–	–	Nepal and Chakraborty, 2021
	Leaf, stem bark and root	Phenolics and flavonoids	NCFE at 500mg, NCFE (250mg) and metformin (425mg)	Phenolic	Munira *et al.*, 2020
	Stems	Phenolic	α-Amylase, for Test 1=1 mg/ml and for Test 3 =5 mg/ml	Phenolic	(Chauhan *et al.*, 2020)
	Bark	Methanolic	200 mg/kg and 400 mg/kg	Phenolic	(Gurjar *et al.*, 2010)
	Root	Methanol and		Root	Methanol and
Analgesic, Antipyretic and Anti-inflammatory	leaves and barks	Strictosidine, epoxystrictosidine, 3α-dihydrocadambine and cadambine	2n = 44 chromosomes	tryptamine	(Zhao *et al.*, 2022)
	Leave, stem bark	Methanolic, ethyl acetate and aqueous (AQS) fraction	ME fraction, EA fraction, and AQS fraction of 200 and 400 mg/kg and two important constituents at 50 and 100 mg/kg via	EA fraction	(Yuan *et al.*, 2020)
	Leave	Ethanolic	Dose 400mg/kg	Ethanolic	(Verma *et al.*, 2020)
	Bark	Methanolic	61 constituents in the methanolic	Methanolic	(Kareti and Subash, 2020)
	Bark	Methanolic	79.63% of inhibition =286 mg/kg and 74.97% of inhibition =667 mg/kg and 32.69% of inhibition =600 mg/kg	Neolamarkines, alkaloids, steroid	(Nagar *et al.*, 2012)
Antidiarrhoeal	Leave	miRNA	Nano Drop=1000 spectrophotometer at 260/280nm at ratio=2.0	miR-858b	(He *et al.*, 2020)
	Stem Bark	NCHAE, chloroform	NanoDrop=1000 spectrophotometer at 260/280 nm at ratio=2.0	NCHAE	(Das *et al.*, 2022)
	Leaves	Ursolic acid	Dose of 0.75 mg/kg	Ursolic acid	(George *et al.*, 2021)
	Plant	Phenolics and flavanoids	—	Phenolics and flavanoids	(Sharma *et al.*, 2021)
	Leave	Ethanol	IC50 against MCF-7 at 0.2 mg/mL	Ethanol	(Razali *et al.*, 2021)
	Fruits	Methanolic	–	Methanolic	(Chatterjee *et al.*, 2021)
	Stem bark	Methanolic	ENC & AQNC 5, 50, 300, 1000 mg/kg	Methanolic	(Kaur *et al.*, 2021)
	Leaf	Aqueous	Dose of 60 mg/kg	VEGF	(Ali *et al.*, 2021)
	Leaves, stem, and root	Glycosides, Aqueous	Aqueous-1.5 ml	Aqueous stem	(Kumar *et al.*, 2020)
	Fruit	Methanol	IC50 =1.53 mg/ml for DPPH	Phenolic	(Islam *et al.*, 2015)
	Leaves	Ethanolic	IC50 values in µg/ml DPPH assay 63.94 for Ethanolic	Flavonoid	(Chandel *et al.*, 2012)
	Root	Ethyl alcohol	Superoxide radical, 500 µM, Hydroxyl ion radical, 500 µM	Phenolic	(Kumar *et al.*, 2010)

have all analgesic, antipyretic, and antiinammatory properties. At distinct concentrations of around 50 mg/kg, 100 mg/kg, 300 mg/kg, and 500 mg/kg, a defatted aqueous extract of *N. cadamba* leaves showed significant analgesic and anti-inflammatory effects, as proved by Bachhav *et al*. (2009) and Ambujakshi *et al*. (2009).

The dry hydroethanolic extract of around 200 mg/kg to 500 mg/kg of A. cadamba'sowering tops reduced the rate of faecal drop in castor oil-induced diarrhea in mice in a dose-based manner. According to Alam *et al*. (2008), this extract can also reduce the accumulation of intestinal uids in a dose-dependent manner. According to Mandal *et al*. (2009), different diuretic and laxative behaviours of different extracts of the tree's bark were investigated, and it was discovered that the bark's methanol extract of around 300 mg/kg significantly increased urinary output (diuresis) when compared to aqueous, chloroform, and other extracts, and the chloroform extract of around 300 mg/kg can be a significant laxative agent. Furthermore, by suppressing lipid oxidation and increasing superoxide dismutase and catalase activity, the extract of *Neolamarckia cadamba Syn. A. indicus* has significant antioxidant action, as proved by Kumar *et al*. (2010). Here, in the present section, the author has investigated various pharmacological properties of the cadamba plant through investigating the various latest studies that have been reported in terms of research articles and book chapters. Table 4 presents the various experiments that have been performed previously by various researchers in order to find and report the pharmacological properties of the cadamba plant. It describes the pharmacological properties of the cadamba plant against the part from which the extract was taken for the experiment and the active concentration and active compound of the same.

Conclusion

Neolamarckia cadamba tree has long been used as an ayurvedic cure in several Indian traditional remedies and various medical formulations, including antibacterial ointments and herbal syrups. Even though profound research investigations have been conducted on *Neolamarckia cadamba*, or "kadam", for its use in disease treatments, a wise understanding of the physiological, ecological, phytochemical, and pharmacological behaviour of "kadam" has to be addressed**.** With this objective, current review paper presents a comprehensive survey of various studies has been reported on physiological, ecological, phytochemical and pharmacological behaviour.It further highlights the limits in information regarding cadamba's pharmacological properties, together with safety, and accuracy. The active ingredients aren't adequately defined, and there's little information on toxicity or negative health impacts. In-depth research is needed on the toxicological analyses and its properties of pharmacological as well on biologically active extracts. Furthermore, there is insufficient data available on the production of food products from cadamba through report work.In addition to this, the extraction and evaluation of the active constituents of the cadamba plant appear to be valuable in determining the chemical structure and technique of action of the bio-active substances at the cellular scale, as well as assessing their usefulness in foods and medications for medical benefits. Although some of the pharmacological activities of cadamba have indeed been studied in animal studies, more in-depth research and understanding of their modes of action is required. It is also advised that attempts be made to extract, isolate, and collect the reported as well as undiscovered chemicals from *N. cadamba*, in order to improve its pharmacologic characteristics and establish it as a contender for potential drug development.

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