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(REVIEW ARTICLE)

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Botanical description, phytochemistry, traditional uses, and pharmacology of *Anthocephalus cadamba*: An updated review

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Abstract

Background: *Anthocephalus cadamba* (Roxb.) Miq. is an important medicinal plant of the Rubiaceae family. It is widespread in the tropical and subtropical regions of India and the world. It became popular for the use of folklore in a variety of illnesses, including diabetes Mellitus, diarrhea, fever, inflammation, hemophilia, cough, vomiting, wounds, ulcer, and debility, and also useful for snake bites.

Results: The current review focuses on plant descriptions and ethnographic and traditional uses of *Anthocephalus cadamba* (Roxb.) Miq. along with the reported pharmacological activity. The main chemical composition and pharmacological aspects of *Anthocephalus cadamba* (Roxb.) Miq. has been thoroughly studied to reveal the unexplored ethnomedicinal uses of this plant, and researchers working on this plant may be able to gain new facts to continue further research on plants. Pharmacological aspects like Analgesic, antipyretic and anti-inflammatory, Antidiabetic, Antidiarrhoeal, Diuretic and laxative, Anti-hepatotoxic, Hypolipidemic, Antioxidant, Antimicrobial and wound healing, Anthelmintic potentials are evaluated by different in vitro/in vivo methods on this plant have been reported.

Conclusion: Various conventional uses have been reported that require profound scientific investigation. several pharmacological activities have been reported for the *Anthocephalus cadamba* . The present review intends to deliver a concise account of its ethnobotanical uses, and phytochemistry with an in-depth study of its phytoconstituents, facts, and prospects of the potential pharmacological activities of this golden plant. An extensive literature survey was undertaken through different online platforms viz. Google Scholar and online databases namely PubMed, Science Direct, and Springer. All papers based on traditional medicinal uses and pharmacological properties were included.

Keywords: *Anthocephalus cadamba*; Phytoconstituents; Ethnographic; Pharmacology; Antioxidant.

1. Introduction

Plant materials are used worldwide as raw materials for home remedies, dietary supplements, over-the-counter drugs, and food and pharmaceutical industries in both developed and developing countries, and have a large share of the global pharmaceutical market (1). Natural products played an important role in ancient traditional medical systems such as China, Ayurveda, and Egypt, which are still widely used today. According to the World Health Organization (WHO), 75% of people around the world still rely on traditional herbs for primary health care (2). The Cadamba is commonly known

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"burflower-tree" as "Kadamba" in Sanskrit and as "Kodom" in Bengali. It is an evergreen tropical tree found in different parts of India, Bangladesh, Nepal, Myanmar, Sri Lanka, Cambodia, Laos, Philippines, Malaysia, Indonesia, Papua New Guinea, and Australia (3). *Anthocephalus cadamba* (Roxb.) Miq. is one such ayurvedic remedy that is used and mentioned in many Indian kinds of literature for its pharmacological activity like anti-diarrheal and detoxifier, analgesic, and seminal fluids. In the traditional system, aqueous extract of the *Anthocephalus cadamba* (Roxb.) Miq. leaf has been used to alleviate pain swelling, and wounds as well as treatment of menorrhagia (4). In Siddha medicinal system plant is known as Kadambu and its various parts Leaf, fruits, Seeds, and Bark are used for fever, eye disease, toxic bite, anasarca, indigestion, periodic fever, and arthritis (5).

2. Geographical description

The tree is a medium to large-sized deciduous tree attaining a height of 20-40 m. It is frequently found all over India on the slopes of evergreen forests up to 500 m. It is found in the sub-Himalayan tract from Nepal eastwards on the lower hills of Darjeeling terai in West Bengal where it is common; in Chota Nagpur (Bihar), Orissa, and Andhra Pradesh, in the Andamans, it is very common in damp places along large streams, and Karnataka and Kerala on the west coast, and western ghats at a low level in wet places. It is also distributed in Thailand and Indo-china and eastward in the Malaysian archipelago to Papua New Guinea (6). The flowering period commonly lasts 2–5 months. In India, flowering starts in May–June, and fruiting in January–February. It is a favored plantation species inside and outside its native range. It has been planted as an ornamental and plantation tree and has been successfully introduced into Costa Rica, Puerto Rico, South Africa, Surinam, Taiwan, Venezuela, and other tropical and subtropical countries (7).

3. Botanical description

Anthocephalus cadamba (Roxb.) Miq. Miq. (Family: Rubiaceae, subfamily; Cinchonoideae) having synonyms *Anthocephalus Chinensis, Anthocephalus macrophyllus., Nauclea cadamba Neolamarckia cadamba, Sarcocephalus cadamba., Anthocephalus indicus* A. Rich., *Anthocephalus morindaefolius* Korth. is commonly known as the Marathi [Kadamba], Hindi [Kadamb], Sanskrit [Kadamba], Telugu [Kadambamu], Bengali [Kadam] Tamil [Kapam, Vellai], Malayalam [Attutek] Kannada [Kadawala], English [Wild cinchona, Cadam, Kadam], Assam[Roghu, Kadam] in different regions of India (8).

3.1. Taxonomy

The taxonomical data of this plant is detailed below (9).

- Kingdom : Plantae
- Subkingdom : Tracheobionta
- Division : Magnoliophyta
- Superdivision : Spermatophyta
- Class : Magnoliopsida
- Subclass : Asteridae
- Order : Gentianales
- Family : Rubiaceae
- Genus : *Anthocephalus*
- Species : *Anthocephalus indicus Miq.*

3.2. Macroscopic characteristics

Anthocephalus cadamba (Roxb.) Miq. is a large tree with a broad umbrella-shaped crown and a straight cylindrical bole. The branches are characteristically arranged in tree. The tree may reach a height of 45 m with a stem diameter of 100–160 cm and sometimes it has a small buttress up to 2 m high (7). Bark grey, fissured; leaves coriaceous, broadly ovate,elliptic-oblong,7.5-18cm and 4.5-16 cm; flower heads globose, yellow, solitary, terminal,3.7 cm in diam. Consisting of small, yellow, or orange-colored, scented flower; fruit a fleshy, orange, globose pseudocarp of the compressed angular capsule with the persistent calyx; seeds small, muriculate (9-10).

3.3. Histological characteristics

The microscopic study of leaf powder. The reported stomatal number for the upper epidermis and lower epidermis, the stomatal index for the upper epidermis is 27.2% and lower epidermis is 26.9%, whereas the vein islet number and vein

termination number are 11 and 21. Presence of unicellular, lignified trichomes, paracytic stomata, simple starch grains, and sandy balls of calcium oxalate crystals (8). The bark is grayish-yellow on the outside, with small irregular wood scales with shallow cracks and flakes. Inside, the bark is light red to reddish-brown and easily peels off from the inner bark with tangential stripes. The bark has a bitter taste. The outermost zone of the bark shows a rhytidoma with 4-6 layers of cork. It consists of thin-walled rectangular cells. Phloem fiber is same structure found on the inner bark. The middle bark consists of rectangular or tangentially elongated cells with no intercellular space. Some of these cells are included chlorophyll. Most cells are thick-walled, but some thin-walled cells contain prismatic crystals of calcium oxalate (2).

3.4. Traditional/ethno medicinal uses

Shushrutasamhita describes the leaves for their analgesic effect and helps with diseases and glandular inflammation. Charaka Samhita describes fruits as helping to reduce high fever and thirst. Ayurveda prescribes fruit for cooling It has an analgesic effect and its decoction is used for mouth ulcers. According to Shukla Yajurveda, pollen strengthens the body and mind (2).

In the Dooars region of West Bengal, the Leaves, Bark, and Fruits of the plant are used for the Decoction of leaves for ulcers and wounds, bark as an expectorant, and fruits for gastric irritability and fever (12). Indian tribes used leaf paste to treat dyspepsia and applied it topically to oral ulcers in children. Lodhas boils crushed leaves to remove subcutaneous inflammatory deposits (8). the stem bark decoction is used for a fair complexion of the skin. A powder of the dried stem bark is mixed with honey or lime juice and taken orally as a mucolytic (13). The potent wound-healing capacity of *Anthocephalus cadamba* (Roxb.) Miq. as shown by the wound contraction and increased tensile strength has thus validated the ethno-therapeutic claim (14). Various parts of the plant and tree are also mentioned in the figure no.1. Some of the traditional uses of *Anthocephalus cadamba* (Roxb.) Miq. have been mentioned in Table 1.

Table 1 Traditional uses of *Anthocephalus cadamba*

S.No.	Part used/Method	Folk area	Disease
1	PNS (Parts not specified)	Namakkal District (Tamilnadu)	Anti-diabetic, diarrhea, fever, anti-inflammatory, cough, vomiting. (19)
2	Leaves, bark, Fruits	Dooars region of West Bengal	Decoction of leaves for ulcers and wounds, bark as an expectorant, and fruits for gastric irritability and fever (12)
3	Leaf	District Sonbhadra, (Uttar Pradesh)	Leaf juice is used for stomach pain, wounds, fever (20)
4	Bark;	Begnas-Rupa lake (Nepal)	Bitter and cooling properties and used as febrifuge, astringent, and tonic. It is taken to cure cough, fever, inflammation of the eye, and snakebite. (21)
5	Bark	Siddis of Uttar Kannada district, (Karnataka)	Skin disease and to give a fair colour to skin, Mucolytic agent (13)
6	Fruits	Tribes of Sahebganj District, Jharkhand	As vegetable (22)
7	Stem bark, fruit juice	Chitrakoot District (U.P.)	Stem bark paste (3 gm.) with common salt (1 gm.) is used as a cure for eye inflammation. The fruit juice quenched excessive thirst in fevers. (23)
8	Bark	Bajali Subdivision, Barpeta District, Assam	Dysentery, fever, and cholera. (24)
9	Leaves, bark	Srinagar valley and its adjacent villages of Garhwal Himalayan (Uttarakhand),	Cancer (25)

		Fatehpur district(Uttar Pradesh)	
10	Flowers	----------	induces lactation (Ayurveda) Used in arthritis (Siddha) (26)
11	Bark powder + bark of Mangifera indica + Shorea robusta + shell lime powder	Taungya villages located in Gorakhpur and Maharajganj districts (Uttar Pradesh)	Sunstroke, cholera(27)
12	Bark, flowers, fruits, leaves	Assam	Antioxidant (28)

Figure 1 Various parts of the plant *Anthocephalus cadamba* (Roxb.) Miq. (Roxb.) Miq. (74)

3.5. Phytochemistry

Phytochemical evaluation of *Anthocephalus cadamba* (Roxb.) Miq. (Roxb.) Miq. Showed the presence of Tannins, Phenols, Alkaloids, Saponins, Iridoids, Quercetin, Kaempferol, Catechin, Coumarin, 6,7-Dimethoxy coumarin, 5-Methoxy genistein, Anthocyanin, Proanthocyanin, Carbohydrates, Flavonoids, Glycosides, and Proteins (15-16). The stem bark contains showed the presence of flavonoids, alkaloids, carbohydrates, proteins, and glycoside compounds. (17) The leaves of *Anthocephalus cadamba* (Roxb.) Miq. were reported to contain saponin glycoside (18). Preliminary phytochemical screening of methanol and aqueous extracts of *Anthocephalus cadamba* (Roxb.) Miq. roots showed the presence of alkaloids, saponins, flavonoids, tannins, and sugars (16, 18). The preliminary phytochemical screening of the\ extracts of *Anthocephalus cadamba* (Roxb.) Miq. leaves revealed the presence of saponins, alkaloids, glycosides and tannins, phenolic compounds, flavonoids, and steroid (2).

3.5.1. Cadambines

Indole alkaloids amino-cadambines were isolated from the leaves of N. cadamba. possess an unprecedented polycyclic system featuring a tetrahydrofuran unit and a 1,2,3,4-tetrahydropyridine ring (29). Vincosamide-N-oxide and isodihydroamino cadambine along with seven known alkaloids and triterpenoids vincosamide, vallesiachotamine, iso-vallesiachotamine, dihydrocadambine, cadambine, ursolic acid and oleanolic acid having anti-arrhythmic, anticancer and anti-malarial properties are, found in the Apocynaceae, Loganiaceae, Rubiaceae and Nyssaceae Families (30).

3.5.2. β-sitosterol

Beta-sitosterol is a type of chemical called plant sterol. It's similar to cholesterol and is found in fruits, vegetables, nuts, and seeds. β-sitosterol is a well-known natural sterol in the composition of known herbal drugs for the treatment of benign prostatic hyperplasia and prostate cancer. Besides, the compound elevated enzymatic and non-enzymatic antioxidants in cells making it effective in anti-diabetic, neuroprotective and chemoprotective action (31).

3.5.3. Quinovic acid

Quinovic acid is a triterpene glycoside obtained from the bark of the plant. the two main types of triterpene glycosides are 3-O-[a-L-rhamnopyranosyl]-quinovic acid-28-O-[b-D-glucopyranosyl] ester and 3-O-[b-D-glucopyranosyl]-quinovic acid-28-O-[b-D-glucopyranosyl] ester respectively (32). It is responsible for Antifungal, Immunomodulatory, Molluscicidal Activity, Spermicidal, Hypoglycemic, Antitumor, Hypocholesterolemic, Antiaging, Cardiovascular, Antiviral, Antisweet, Analgesic Activity (33).

3.5.4. Ursolic acid

Ursolic acids are ubiquitous triterpenoids in the plant kingdom, and medicinal herbs, and are an integral part of the human diet. A variety of novel pharmacological effects produced by these triterpenoids have been reported, including their beneficial effects on cardiovascular systems interaction with cytochrome P450s protection against kainate-induced excitotoxicity in rat hippocampal neurons and immunomodulatory effects, as well as its effects on intracellular redox balance and osteoclast formation (34).

3.5.5. Amygdalin

Amygdalin is commonly distributed in plants of the Rosaceae, such as peach, plum, loquat, apple, and bayberry. It is a naturally aromatic cyanogenic compound, it has long been used in Asia, Europe, and other regions for the treatment of various diseases including cough, asthma, nausea, leprosy, and leukoderma (35).

3.5.6. Quercetin

Quercetin is one of a group of over 4000 naturally available plant phenolic compounds. Flavonoids are classified among phenolic constituents found in food plants. These include the phenolic acids (cinnamic and benzoic acid derivatives), the flavonoids, such as the flavan-3-ols (i.e. catechins), and the flavan-3,4-diols (i.e. quercetin, myricetin, and kaempferol), and condensed tannins. Quercetin has antiviral and antitumour action (36).

3.5.7. 2´-hydroxy 2, 4, 4´, 6'-tetra methoxy chalcone

Chalcones, or 1,3-diphenyl-2-propen-1-ones, are one of the most important classes of flavonoids across the whole plant kingdom. Chalcones are open-chain precursors for biosynthesis of flavonoids and isoflavonoids and occur mainly as polyphenolic compounds (37). Promising biological activities to be generated e.g., anti-inflammatory (38), anti-gout (39) anti-histaminic (40) anti-oxidant (41) anti-obesity (42) anti-protozoal, (43) hypnotic (44) anti-spasmodic (45).

3.5.8. Dihydrowogonin

Wogonin chemically known as 5, 7-dihydroxy-8-methoxy flavone is obtained from Scutellaria baicalensis Georgi and is a herb traditionally used in Chinese folk medicine (46). It has anti-inflammatory, antioxidant, antiangiogenic, and antitumor properties (47).

3.5.9. Naringenin

Naringenin is a naturally-occurring flavonoid, predominantly found in some edible fruits, like Citrus species and tomatoes. Chemically named as 2,3-dihydro-5,7-dihydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one (48). Naringenin is endowed with broad biological effects on human health which includes a decrease in lipid peroxidation biomarkers and protein carbonylation, promotes carbohydrate metabolism, increases antioxidant defenses, scavenging

reactive oxygen species, modulates immune system activity, and also exerts anti-atherogenic and anti-inflammatory (49) and antiallergic effects (40).

3.5.10. Chrysin

Chrysin, which has the ubiquitous 15-carbon flavone backbone, is one of the most important bioactive constituents of different fruits, vegetables, and even mushrooms. Chrysin has a common chemical structure, consisting of two fused rings, A and C, and a phenyl ring, B, attached to the second position of the C ring. It shares the common flavone structure, with an additional hydroxyl group at the 5th and 7th positions of the A ring (50). Chrysin has been recently shown to be a potent inhibitor of activation of the human immunodeficiency virus (HIV) in models of latent infection (51). Chrysin shows anti-inflammatory (52), and antioxidant action (53).

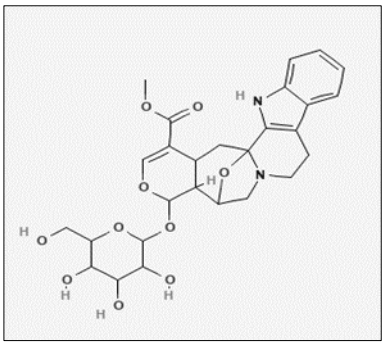
3.5.11. Apigenin

It can be classified as polyphenols. It has one or more hydroxyl substituents in its structure. It is composed of a flavone nucleus of 15 carbon atoms (C6-C3-C6) and is diphenyl-propanoids. The C6 and C3 moieties are arranged to form two fused rings in which the first is an oxygen-containing heterocycle and the second one is a benzene ring constituting a phenyl chromane nucleus (2, 3-dihydro-2-phenyl chroman-4-one) (54). It exhibits various pharmacological properties such as anti-mutagenic (55), free-radical scavengers, antioxidants, anti-inflammatory, and antiviral effects (54).

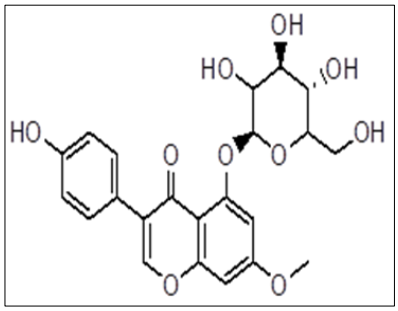
Sakuranetin, chemically named 4′, 5-dihydroxy-7- methoxy flavanone has consisted of two fused rings, A and C, and a phenyl ring B, which is attached to the C ring at the C-2 position. This flavanone is characterized by the absence of a double bond between C2-C3 in the C ring, and also by the presence of a 5-hydroxy-7-methoxy substitution pattern in the A ring and a single 4′-hydroxyl group in ring B. Sakuranetin is the O-methylated derivative of the best-known citrus flavanone naringenin (56). it exhibits biological properties namely Anticancer Effects (57), and Antimicrobial Activity (56).

3.5.12. Afzelin

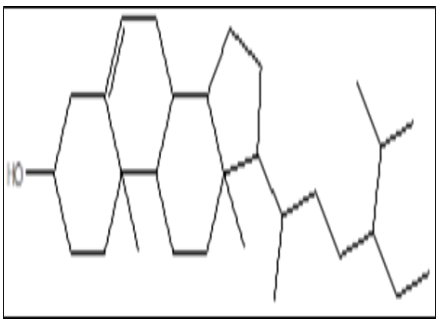
Afzelin (kaempferol 3-O-rhamnoside) is a flavonol glycoside found in Houttuynia cordata and it is widely used to prepare antibacterial and antipyretic agents, detoxicates, and for the treatment of inflammation (58).



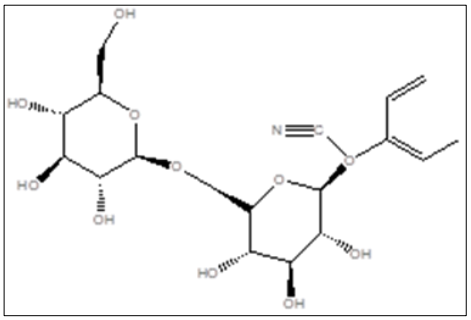
Cadambine



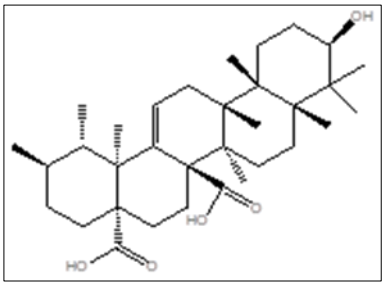
Prunetinoside



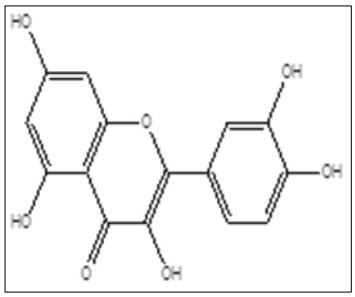
β-sitosterol



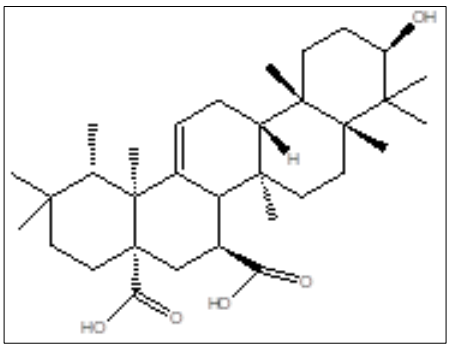
Amygdalin



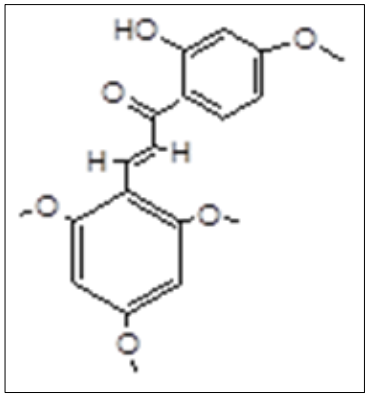
Quinovic



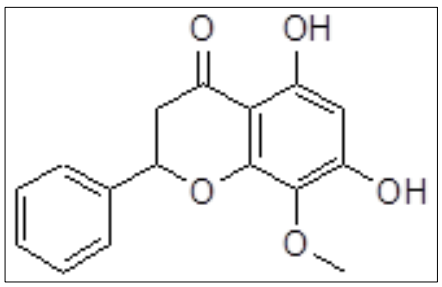
Quercetin



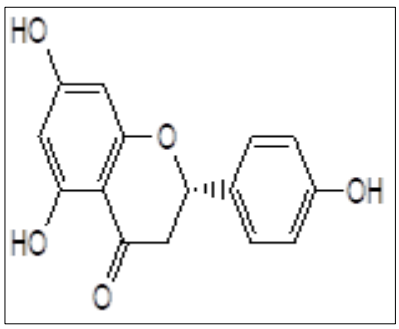
Cadambagenic acid



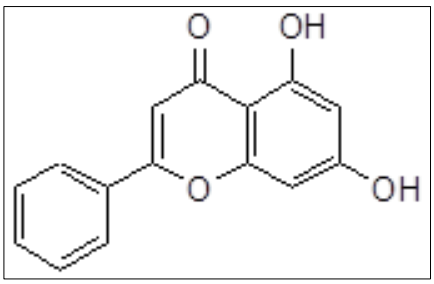
2´hydroxy 2, 4, 4´, 6'-tetramethoxychalcone



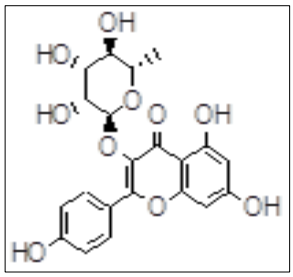
Dihydrowogonin



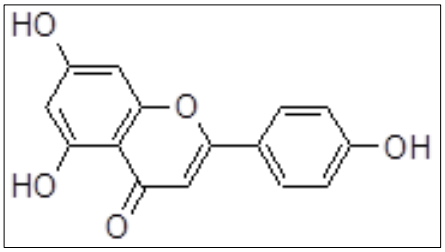
Naringenin



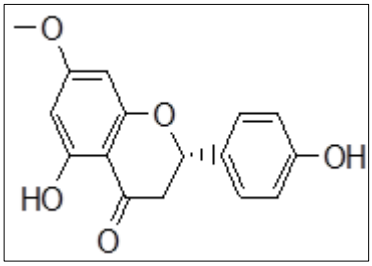
Chrysin



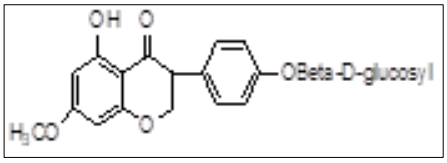
Afzelin



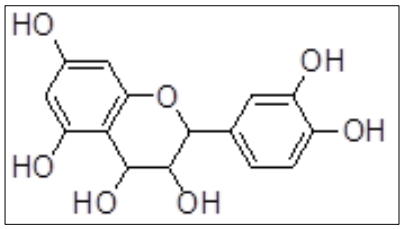
Apigenin



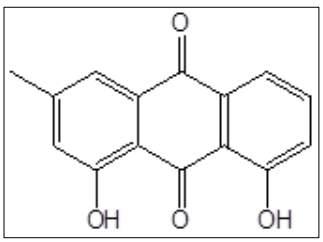
Sakuranetin



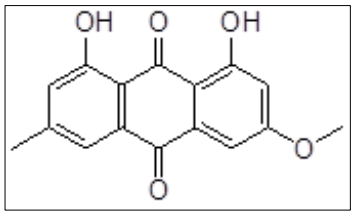
Padmakastein



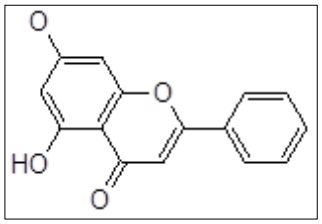
Leucocyanidin



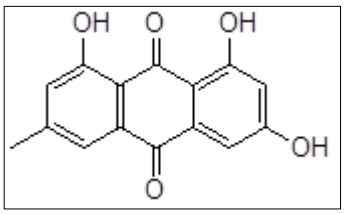
Chrysophenol



Physcion



Tectochrysin



Emodin

Figure 2 Various Phytochemical Const. present in *Anthocephalus cadamba* (Roxb.) Miq.

Physcion is (1,8-Dihydroxy-3-methoxy-6-methyl-anthraquinone), also known as parietin (PubChem CID: 10639), is an anthraquinone derivative widely isolated and characterized from both terrestrial and marine sources. Physcion 8-O-β-glucopyranoside is the major natural bioactive glucopyranoside of physcion. (59). it exhibits various pharmacological actions like a laxative, anti-tumor, anti-inflammatory, antibacterial, antioxidant, anti-injury, acetylcholinesterase inhibitory, and other activities (60).

4. Pharmacological activities

Owing to its widespread traditional and medicinal uses, *Anthocephalus cadamba* (Roxb.) Miq. has been exploited for various pharmacological activities as mentioned below-

4.1. Abortifacient activity

Methanolic extract of stem bark of *Anthocephalus cadamba* (Roxb.) Miq. (MEAC) exhibits abortifacient potential. The activity was more marked in 1000 and 1500 mg/kg b.w. of the extract and was comparable to that of mifepristone. The mechanism of abortion possibly will be in the course of changes in the uterine mileu, altered hormone levels, luteolysis, and partly, estrogenicity. This study hence justifies the ethnobotanical allege of MEAC as an abortifacient. (61).

4.2. Anti-microbial activity

antimicrobial efficiency of Hexane, Ethyl acetate, Ethanolic extracts of *Anthocephalus cadamba* , leaves against human pathogens like Staphylococcus aureus (MTCC-3160), Escherichia coli (MTCC-1652) and fungi Aspergillus niger (MTCC-282) studied by using agar well diffusion method. The antibacterial assay was carried out by microdilution method To investigate the antifungal activity of the extracts, a modified microdilution technique was used For all the tested microorganisms Hexane and Ethyl acetate showed maximum antibacterial activity In Hexane extract, maximum inhibition zone diameter was obtained in S. aureus and in E. coli with the diameter (2.36 ± 0.585mm, 2.26 ± 0.493mm, respectively. Similarly, Ethyl acetate extract showed a maximum inhibition zone with a diameter of 1.2 ± 0.1mm in E. coli and 1.63 ± 0.351 mm in S. aureus. For the antifungal activity, A. niger (0.93 ± 0.251 mm) showed efficient antifungal activity for hexane plant extract compared to the ethyl acetate and ethanolic extracts. Ethyl acetate extract showed a maximum inhibition zone with a diameter of (0.83 ± 0.416 mm) and ethanolic extract showed the lowest inhibition zone (0.36 ± 0.057 mm) against all pathogenic fungal strains, respectively the MIC value of the active plant extracts obtained in this study was lower than the MBC values suggesting that the plant extracts were bacteriostatic at lower concentration but bactericidal at higher concentration (62).

Antimicrobial activity of chopped unripened fruit extracts of plant was evaluated for antimicrobial activity using the disk diffusion method on three reference microorganisms (Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus. Acetone & 80% of Methanol extract of *Anthocephalus cadamba* (Roxb.) Miq. showed maximum sensitivity and zone of inhibition of 13.5 mm & 12 mm respectively against S. aureus (63).

Hot aqueous extract (HAE) of leaves of *Anthocephalus cadamba* (Roxb.) Miq. (Roxb.) Miq, Rubiaceae has been screened for antimicrobial activity. The agar disc diffusion method was used to investigate antimicrobial activity against B. cereus, S. aureus, E. coli and P. auregenosa Extract exhibit significant ($p<0.01$) antibacterial and antifungal activity against (B. cereus, S. aureus, E. coli, P. aureginosa, A. niger. and S. aureus was found to be the most sensitive followed by E. coli and P. aeruginosa (64).

Ethanol extract of *Anthocephalus cadamba* (Roxb.) Miq. stem bark was evaluated for antimicrobial potentialities by disc diffusion method .four Grampositive, six Gram-negative bacteria, and six species of fungi at a concentration of 500 µg/disc. Kanamycin 30 µg/disc was used as the standard drug. Extracts confirm the activity of A. Cadamba as a broad-spectrum antimicrobial agent since inhibited the growth of Gram-positive and Gram-negative bacteria as well as Some fungal species (65).

The alcoholic and aqueous extract of the whole plant showed significant antibacterial and antifungal activity against almost all the organisms: Micrococcus luteus, Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, and four fungi Candida albicans, Trichophyton rubrum—dermatophyte fungi, Aspergillus niger, Aspergillus flavus, and Aspergillus nidulans—systemic fungi, with especially good activity against the dermatophyte (Trichophyton rubrum) and some infectious bacteria (Escherichia coli, Proteus mirabilis, and Staphylococcus aureus) with a MIC of 2.5 µg/disc. The disc diffusion method was used to determine the inhibition zones of A. cadamba extracts (organic and aqueous). The plant showed significant antibacterial and antifungal activity against almost all the organisms and especially good activity were found against the dermatophytes Significant antimicrobial activity was observed in ethanolic and aqueous extracts. Amongst the test organisms used, a dermatophyte Trichophyton rubrum was found to be the most sensitive (66).

Methanol and Ethyl acetate extract from Ripened *Anthocephalus cadamba* (Roxb.) Miq. fruits and Ethanol and Methanol extract from *Anthocephalus cadamba* (Roxb.) Miq. fruits were used for the evaluation of antimicrobial activity against 2-gram positive bacteria Staphylococcus aureus (S. aureus) and Bacillus cereus (B. cereus) and 3-gram negative bacteria Escherichia coli (E. coli), Salmonella abony (S. abony) and Shigella boydii (S. boydii) by using determined using agar well diffusion method and microdilution method. ripened *Anthocephalus cadamba* (Roxb.) Miq. showed greater antimicrobial activity as compared to unripened *Anthocephalus cadamba* . The activity of potent extracts against all the pathogens (except E. coli) was found to be comparable with that of positive control (67).

Petroleum ether, chloroform, and acetone extracts. of the leaves of *Anthocephalus cadamba* (Roxb.) Miq. were used for the evaluation of The antimicrobial activity by using agar cup plate diffusion method using Gentamycin (10 µg/ml) and Ketoconazole as standard. Chloroform and acetone extracts exhibited strong activity against bacteria and fungi and the zone of inhibition was comparable with the standard drug (68).

4.3. Anti-diabetic activity

Anthocephalus cadamba (Roxb.) Miq. methanol and aqueous extracts of the roots significantly decreased blood glucose in alloxan-induced rats diabetic rats. the test extracts exhibited a significant reduction in blood glucose concentration in a dose-dependent manner as compared to the control (69).

Methanolic extract of *Anthocephalus cadamba* (Roxb.) Miq. bark was used for the evaluation of hypoglycemic action of *Anthocephalus cadamba* (Roxb.) Miq. The Methanolic extract of the drug showed marked effects for decreasing the blood glucose level and rectifying the problem like fatigue and irritation associated with the disease the methanolic extract 400mg/kg showed significant effect on the blood glucose level but extract of 200 mg/kg did not show the significant decrease in blood glucose level. The value of p is less than 0.001 except in 200 mg/kg in glucose tolerance test (11).

The hydroethanolic extract of the flowering tops of *Anthocephalus cadamba* (Roxb.) Miq. was used for its potential hypoglycemic effect in alloxan-induced diabetic rats. The extract significantly decreased the blood glucose level ($p<0.05$.) prevented the weight loss in alloxaninduced diabetic rats (70).

4.4. Anti-cancer activity

In an *in-vitro* study, Hydro-methanolic (HM) bark extract of Neolamarckia cadamba was studied on hepatoma cancerous cell line using sulforhodamine (SRB) assay Evaluation of the anticancer activity of different concentrations (10, 20, 40, and 80 µg/ml) of HM extract was done against N1S1 rat . Percentage of control cell growth was -37.66 and -34.13 at 40 µg/ml and 80 µg/ml respectively. Dose-dependent decrease in the percentage of control cell growth was observed. LC50, TGI and GI50 of HM extract was found to be 75.92, 46.73 and 17.46 µg/ml respectively (64). Evaluation of the antiproliferative and apoptogenic action of methanol extract of *Anthocephalus cadamba* (Roxb.) Miq. (MEAC) on Dalton's lymphoma ascites (DLA) cells treated mice exhibited a significant ($p<0.01$) decrease in the tumor volume, viable cell count, and tumor weight and elevated the life span of DLA tumor-bearing mice. MEAC possesses potent antitumor activity via induction of cancer cell apoptosis mechanism. Qualitative screening of MEAC revealed the presence of steroids, glycosides, saponins, alkaloids, phenolics, and flavonoids. The MEAC was able to reduce the viability of the DLA cells in a dose-dependent manner, and the IC_{50} value was found to be 90.45±3.94 µg/mL. (71).

4.5. Analgesic and Anti-inflammatory activities-

Flavonoids in Cadamba like quercetin, silymarin apigenin, daidzein, and genistein are known to have analgesic and anti-inflammatory activities. Research is being done to identify more and more active constituents in Cadamba having anti-inflammatory activity. The anti-inflammatory activities of Cadamba are studied using active enzyme expressions of cyclooxygenase and lipoxygenase. Further, an intact lysosomal membrane is important as the release of lysosomal constituents of activated neutrophils such as bacterial enzymes and proteases occurs during tissue inflammation. It has been reported that ethanolic extract of Cadamba leaves exhibited significant membrane stability as found from the heat-induced hemolytic effect on the erythrocyte membrane (3).

4.6. Antidiarrheal activity

The dry hydroethanolic extract of the flowering tops of the Cadamba has exhibited a dose-dependent decrease in the frequency of fecal droppings in castor oil-induced diarrhea in mice. The extract also produced a dose-dependent reduction in intestinal fluid accumulation (72).

4.7. Hypolipidemic activity

It has been found from experimental studies that alloxan has the capacity of reducing lipid levels by 30% as observed in diabetic mice. In comparison to this drug, the oral administration of root extract of the Cadamba for 30 days in dyslipidemic animals resulted in a significant decrease of 80% in total cholesterol, phospholipids, triglycerides, and lipid peroxides, with a reduction in lipid levels in diabetic mice (3).

4.8. Antihepatotoxic effects

The Cadamba has been reported to be used for its hepatoprotective activity. The hepatoprotective activity is due to the presence of chlorogenic acid (CGA) isolated from the Cadamba plant. It was also found that the intraperitoneal administration of CGA to mice at a dose of 100 mg/kg for 8 days exhibited better (73).

5. Conclusion

The Cadamba is a significant plant with outstanding therapeutic qualities. Various biological and pharmacological functions of the cadamba have been highlighted in this review. The bark and leaves in particular are quite important. Most unexpectedly, very few investigations have been conducted despite the Cadamba being a remarkable plant. There aren't many known derivatives of the cadamba that have been commercialised or suggested for use by individuals in their daily lives. In-depth research on this plant is urgently needed in order to use it to treat a variety of fatal diseases that are widespread throughout the world.

Compliance with ethical standard

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Disclosure of conflict of interest

All authors have none to declare.

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