WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 14, 515-539. Review Article ISSN 2277–7105

A COMPREHENSIVE REVIEW ON PHYTOCHEMICAL, PHARMACOLOGICAL, AND ETHNOBOTANICAL FACETS OF *CLAUSENA* GENUS IN INDIA

Fidha Sumayya[1]* and Dr. Beesha S. Kamal[2]

[1]M. Pharm Student, College of Pharmaceutical Sciences, Govt. Medical College, Thiruvananthapuram, Kerala, India, 695011.

[2]Assistant Professor, College of Pharmaceutical Sciences, Govt. Medical College, Thiruvananthapuram, Kerala, India, 695011.

Article Received on
26 May 2024,

Revised on 16 June 2024,
Accepted on 06 July 2024

DOI: 10.20959/wjpr202414-33231

***Corresponding Author**
Fidha Sumayya
M. Pharm Student, College of Pharmaceutical Sciences, Govt. Medical College, Thiruvananthapuram, Kerala, India, 695011.

ABSTRACT

Natural ecosystems are the store houses of biodiversity and they are being regulated by the variety of species present there. India is well known for its abundant biodiversity; it ranks ninth in terms of plant species richness. The Rutaceae family boasts numerous advantages and a rich array of phytonutrients. Among the genera that belong to this family, *Clausena* stands out as a crucial component in traditional medicines. Among the Indian Species, the well-documented species in the genus are *Clausena anisata*, *Clausena excavata*, and *Clausena indica*. These species have a wide range of traditional therapeutic benefits in both folklore and Ayurvedic medicine. This genus is characterized by three types of secondary metabolites: flavonoids, terpenoids, and alkaloids. However, the most prominent phytochemicals found in *Clausena* plants are coumarins and carbazole alkaloids. *Clausena* genus is rich in volatile oil, which makes them aromatic. These compounds possess potent medicinal properties, including anti-parasitic, anti-bacterial, anti-cancer, and anti-diabetic effects. It is worth noting that only seven out of the twenty known species of *Clausena* exist globally are found in India. Despite reports of extensive ethno medicinal applications for plants in the genus, *Clausena austroindica*, *Clausena agasthyamalayana*, *Clausena pentaphylla*, and *Clausena heptaphylla*, very little is known about the chemical composition and biological activity of these species. This article

provides a comprehensive summary of the botanical description, ethno medicinal values, phytochemical composition, and therapeutic potential of the seven Indian species.

KEYWORDS: *Clausena agasthyamalayana, Clausena anisata, Clausena austroindica, Clausena excavata, Clausena heptaphylla, Clausena indica, Clausena pentaphylla,* Rutaceae.

Abbreviations: HIV- Human Immunodeficiency virus, mapK- Mitogen activated protein kinase, nf-kb- nuclear factor kappa B, A549- Adeno carcinomic human alveolar basal epithelial cells, MCF7- Michigan cancer foundation, KB- Keratin forming tumor cell line, KB-IN- Subline of KB, CEM-SS-Cellosaurus cell line, MDR- Multi drug resistance, HSP70- Heat shock protein, IC_{50}- Half maximal inhibitory concentration, UV- Ultraviolet, ROS- Reactive oxygen species, GCMS- Gas chromatography mass spectroscopy, L929 – NCTC 929 clone of strain L(A Mouse fibroblast cell line).

INTRODUCTION

The Rutaceae family is renowned for its abundant medicinal plants and repository of phytonutrients. This family is composed of approximately 150 genera and over 1500 species,[1,4] which are widely distributed across tropical and temperate regions. India has reported about 25 genera and 80 species of this family to date. Rutaceae is globally recognized family of plants that is particularly known for its juicy fruits such as oranges, lemons, grapefruits, etc., which are rich in vitamin C and several alkaloids and the family also contains a number of economically important ornamental species.[1] Rutaceae plants are characterized by their unique features, including trees, shrubs, or herbs with simple to compound leaves and usually bisexual, actinomorphic, hypogynous, 4-5 numerous flowers typically with an annular, nectariferous disk, fruit a schizocarp, berry, hesperidium or drupe. Secretory glands containing ethereal oils are found in many tissues, appearing as pellucid-punctate glands in the leaves and pericarp.[2] Some of the important genera of this family that have been cited in these historical texts include *Aegle, Citrus, Murraya, Clausena*, among others. Members of this family often feature aromatic leaves with oil glands on the surfaces.

The secondary metabolites from the roots, stems, rhizomes, twigs, seeds, fruits, and flowers of several *Clausena* species have been widely examined and were found to be more effective. This genus is well known to include shrubs and trees. They are characterized by having berry-like fruits with pinnate leaves. Secondary metabolites such as alkaloids, flavonoids, and terpenoids are reported to be abundant in *Clausena* plants but the principal components in

Clausena plants are the carbazole alkaloids and coumarins with the alkaloids being known to exhibit high anti-bacterial, anti-cancer, anti-diabetic, anti-parasitic activities.[3]

There are 20 accepted species globally, but only 7 species are found in India. They include *Clausena agasthyamalayana, Clausena anisata, Clausena austroindica, Clausena excavata, Clausena heptaphylla, Clausena indica, Clausena pentaphylla.* This review provides an overview of the above said 7 Indian species their botanical description, phytoconstituents and pharmacological properties respectively. The objective of this article is to assist researchers in their future bioprospecting of these potentially therapeutic plants by offering a thorough and succinct analysis of these species.

CLAUSENA ANISATA (WILLD) HOOK, F., DE WILD. & STANER

Clausena anisata, also referred to as Horsewood, is a member of the Rutaceae family and is primarily found in Africa, India, and China's seasonally dry tropical biome. This is the most explored plant species among *Clausena* genus. This particular species is associated with botanical synonyms and holds significant importance.[5] The plant possesses synonyms which includes *Clausena sumatrana* Wight & Arn, *Clausena inaequalis* (DC) Benth, *Elaphrium inaequale* DC.[27] This is a tropical shrub or tree that usually grows up to 10 meters in height, typically found in evergreen forests. The local name for this plant is "Mbiet Ekpene," commonly recognized by the Ibibio's residing in the Niger delta region of Nigeria.[6] This evergreen shrub is widely dispersed throughout the African continent and is known as Samandua in the Akan language of Ghana. Its botanical characteristics make it a unique and valuable plant that has been used for various purposes.[7] The plant is cultivated in Malaysia, Indonesia, Vietnam, Thailand, and the Philippines for its oil with medicinal flavor, which is used in the local brandy anisdos in the Philippines. In Kenya, the plants are commonly placed under the bed for sleeping or carried by the Maasai during wars because of their aromatic properties.[5] In India it is mainly located in the state of Kerala in the districts of Kollam, Thrissur, Palakkad, Idukki, Wayanad, Thiruvananthapuram. Indian synonyms in Malayalam is Kattukariveppila, Kariveppila, Suganthaveppu, Potti & in Tamil Kattu-veppilai, Kattukarveppilai, Pothi etc.[27]

Botanical description: The foliage of this botanical specimen exhibits a compound and paripinnate structure, characterized by several leaflets arranged on either side of a central stem. The leaves are heavily punctuated by glands and exude a potent anise-like aroma upon being crushed. Typically, they are clustered towards the extremities of twigs. The flowers are

minute and white, with orange-yellow stamens, and form a branched axillary spray. The fruit of this plant manifests as a berry, measuring approximately 1.3 centimeters in width, and the seeds possess an oblong shape.[7] During the spring season, this particular plant yields yellow blooms that draw insects. These insects, in turn, become food for birds that feed on insects. As the plant's fruit ripens and changes color from red to black, it becomes a preferred food source for small animals and birds, which help to spread the plant's seeds. Furthermore, this plant also serves as a habitat for various butterfly species.

Clausena anisata thrives in full sun to semi-shade and requires ample water. It grows quickly and can tolerate frost and drought. The tree can be propagated using stem cuttings or sowing seeds.[8]

Ethnobotany

C. anisata is a plant used in African folk medicine for various ailments. Different parts of the plant are used to prepare various remedies. For respiratory ailments, decoctions of *C. anisata* leaves mixed with *Lippia javanica* and *Eucalyptus grandis* leaves are used. For skin irritation, the leaves of *C. anisata*, *Solanecio gigas*, and *Justicia schimperiana* are pounded together and applied dermally. The leaves and stem bark are the most used parts for preparing herbal remedies.[5] The efficacy of the extracts obtained from both the fruits and leaves of *C. anisata* in killing mosquito larvae provides scientific validation for the traditional use of this plant species for controlling mosquito populations.[26] It is a traditional remedy used to cure various ailments, including malaria, inflammation, and pain. The Ibibio's in Nigeria use it for febrile illnesses, malaria, and hemorrhoids. The analgesic and anti plasmodial potentials of the plant's leaves are being evaluated.[6] In India, decoctions made from the leaves or roots are used to treat intestinal problems, fever, pneumonia, headaches, hypotension, sinusitis, sore throats, venereal diseases, aphrodisiacs, anthelmintic, pregnant women's tonics, and infants' tonics to prevent rickets and control convulsions. Additionally, root decoctions and infusions are used to treat skin conditions such as epilepsy, syphilis, malaria, irregular menses, threatening abortions, whooping cough, and kidney ailments. They are also given to women before and after parturition to facilitate delivery, help expel blood from the uterus, and later increase milk production. In addition to being administered topically to burns, hemorrhoids, rheumatism, mouth infections, otitis, and abscesses, crushed leaves are also used as an antibacterial and analgesic for general body ailments.[27]

Phytochemistry

C. anisata extracts contain therapeutic secondary metabolites such as flavonoids, saponins, coumarins, phenols, alkaloids, phytosterols, tannins, triterpenes, steroids, cardiac glycosides, proanthocyanidins, terpenoids, and saponosides, indicating their potential use for natural remedies.[5] The gas chromatogram of the essential oil displays significant chemical compounds, including α-pinene, myrcene, d-limonene, 1,8-cineole, (e)-β-ocimene, umbelliferone, linalool, pulegone, estragole, anethole, α-caryophyllene, α-humulene, germacrene-d, β-elemene, germacrene-a, caryophyllene oxide, β-pinene, 1,8-cineole, and sabinene.[9] Carbazole alkaloids are the primary components found in this particular plant. Clausenol and clausenine are two alkaloids that were isolated from the alcoholic extract of the stem bark of *C. anisata*. Additionally, from the combined stem bark and root extracts of *C. anisata*, four known alkaloids (heptaphylline, girinimbine, ekeberginine, and 3-methyl carbazole) were isolated along with two new alkaloids 1-methyl-3,4-dimethoxy-2-quinolone and 3-formyl-1-hydroxy carbazole.[10,11,12] A study on *C. anisata* discovered imperatonin, xanthotoxol, lansamide-1, and three furanocoumarin lactone derivatives. Two geranyl coumarins were also isolated from the leaves and named anisocoumarins i and j. The essential oil extracted from the leaves was characterized by phenyl propanoids, with anethole as the most abundant compound.[11] Six tetranor triterpenoids were isolated from *C. anisata* stem bark and roots: limonene, zapoterin, clausenolide, clausenolide-l-ethyl ether, clausenarin (11β-hydroxy diacetyl nomilin), and 1-O-methylclausenolide.[5] Three carbazole alkaloids [girinimbine, murrayamine-a, and ekeberginine], two peptide derivatives [aurantiamide acetate and n-benzoyl-l-phenylalaninyl-n-benzoyl-l-phenylalanine] and also a mixture of sitosterol and stigmasterol were isolated from the stem bark and roots.[13] Spectroscopic techniques were utilized to analyze and detect quercetin 3,4’-dimethyl ether, clausine b, and clauseno-coumarin.[14] So many chemical compounds have been isolated from the various parts of the plant, including terpenoid hydrocarbons, sesquiterpenoids and fatty acids(methyl chavicol, myrcene, umbelliferone, scopoletin, xanthotoxin, pimpenellin, xanthotoxol, bergapten), alkaloids(clausanitine and mupamine), more than 20 coumarins (chalepin, osthole, coumarrayin, xanthoxyletin, heliettin, imperatorin) limonoids, volatile oil containing phenylpropanoids, and furanocoumarin lactones,(indicolactonediol, anisolactone and 2′,3′-epoxyanisolactone).[15]

Pharmacology

Antimicrobial: *Clausena anisata* is a plant that has strong antimicrobial properties. Its leaves have been used by traditional healers to treat various microbial infections. The ethanol leaf extract and its fractions have shown varying degrees of antimicrobial activity against different organisms. The plant's antibacterial and antifungal properties may be attributed to the phytochemical constituents present in it.[16] The major chemical compounds in the essential oil of *C. anisata* could be responsible for its significant antimicrobial activity. α-pinene and 1,8-cineole are well-known chemicals with strong antimicrobial properties. They have been found to exhibit antimicrobial activity against *E. coli, P. aeruginosa, Salmonella typhimurium,* and *Staphyllococcus aureus,* Salmonella *typhimurium* is the gram-negative bacteria that the essential oil of *C. anisata* shows the highest level of antibacterial activity against, followed by *Pseudomonas aeruginosa*.[9]

Anti-inflammatory: The crude ethanol extract and chemical constituents of *Clausena anisata* roots were found to have considerable anti-inflammatory effects in the carrageenan-induced edema model. The evaluation of these extracts revealed their efficacy in reducing inflammation.[17] The effect of the extract in suppressing dinitrophenol, amphetamine, and yeast-induced pyrexia was observed with great care. The plant's traditional use in treating febrile illnesses and inflammatory conditions is supported by research.[18] The *Clausena anisata* leaves extract has the capability to relieve pain by interacting with opioidergic, noradrenergic, serotonergic, and l-arginine-nitric oxide pathways. Additionally, the extract has anti-inflammatory properties that may be useful in treating arthritis. This could be due to its ability to prevent the release of inflammatory mediators and reduce oxidative and nitrosative stress.[19]

Anti-oxidant & anti-cancer: *Clausena anisata* relieves osteoarthritis pain and has strong antioxidant properties (acetone extract). Extracts from this plant have bioactivity against cancer cells.[20] Compounds from *Clausena anisata* leaves/bark are cytotoxic to HeLa cancer cells with no toxicity to normal Vero cells. They may be useful topically against cancer.[21] Studies into the medicinal properties of *clausena* plants have uncovered that carbazole alkaloids and coumarins extracted from these plants have the potential to fight cancer.[22] The plasmicidal activity of the extract could have been affected by certain metabolites such as alkaloids, flavonoids, and triterpenoids, specifically limonoids and quassinoids, which are found in the extract.[6]

Antimalarial: Heptaphylline and Imperatorin have shown promising results in killing the *Plasmodium falciparum* parasite in vitro, which makes them potential anti-malarial agents. These compounds are highly selective and have low toxicity towards human red blood cells.[23] Tests were conducted to evaluate the effectiveness of malaria prevention and treatment. Results showed potential in reducing malaria prevalence through suppression and prophylactic treatments.[24]

Epilepsy: Study suggests that the ethanolic root bark extract of *Clausena anisata* contains bioactive constituents that may be beneficial in petitmal epilepsy and lend pharmacological credence to the ethnomedicinal claim for the use of the plant in the management of epilepsy.[25]

***CLAUSENA EXCAVATA* BURM. F.**

This species is originally from tropical and subtropical Asia and usually grows as a shrub or tree. Its natural habitat is found in the seasonally dry tropical biome. Globally the plant is distributed in Bangladesh, Bhutan, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Nepal, Philippines, Thailand, Vietnam. The synonyms of the plant are reported to be *Amyris punctata* Roxb., *Clausena forbesii* Engl., *Clausena javensis* J.F. Gmel, *Clausena sumatrana* Wight & Arn. respectively.[27] *C. excavata* is a plant native to the Himalayas that has an overpowering and unpleasant odor. It is referred to locally as "Cherek Hitam," "Chemama," and "Kemantu hitam" in Malaysia and as "San Soak" in Thailand.[28] In India mainly located on Barak Valley, Nagaon, Sivasagar. It is called "Dieng-tyner" in Kannada and "Bengjari" in Assamese, "Narasingha," and "Theng-sah-saharong".[27]

Botanical description: Trees up to 6 m in height have cylindrical branchlets, 4-5 mm in diameter, that are pubescent for a short time before becoming glandular-pubescent or grey-tomentose. Petiole has gently tomentose or glabrescent, complex, alternating leaves. Terminating panicles of flowers. Oblong, glandular-punctate berries are greenish-white when immature and pink when fully grown. One or two big, oval seeds. Blooming from March to May, Fruitful: August to October.[29] After being crushed, the leaflets smell strongly like curry. It features gynophores that are remarkably hourglass-shaped and entirely glabrous.[28] Much of the plant's area is highly valued for its edible fruit, which is frequently collected for local use from the wild. Typically grown as a decorative tree, it also provides edible leaves.[30]

Ethnobotany

One of the plant species with strong antioxidant qualities is *Clausena excavata* Burm. F. Folk medicine uses its leaves and stem to treat a variety of illnesses, including colic, fever, wounds, rhinitis, cough, and detoxification.[39] Numerous species of this genus have been employed as medicinal remedies in conventional medicine. To treat colds, gastrointestinal issues, and snakebites, for instance, *Clausena excavata* was utilized.[4] For gastrointestinal problems, especially colic, leaf decoction is used postpartum. Colic and decaying teeth are treated with rootstock. The juice of this plant is used as a vermifuge and cough cure in Java, and axe handles are made of wood.[28] Fumigation-related burns Smashing and putting on the skin, Keeps lice and insects away from beneath the bed. Used in the chicken rings to ward off chicken mites and protect the fourth-instar *Aedes aegypti* and *Aedes albopictus* larvae using its essential oils.[42]

Phytochemistry

Over the span of the previous 20 years, numerous secondary metabolites, including alkaloids, coumarins, and a small number of limonoids, have been isolated from various plant sections using various extraction and purification processes. Several spectroscopic techniques have also been used to clarify the structures of these substances.[28] Tetranor triterpenoids, coumarins, and carbazole alkaloids were among the chemical components of this plant that were discovered in earlier research.[31] The Malaysian *C. excavata* stem bark was subjected to an ethyl acetate extract investigation, which produced two recognized carbazole alkaloids, clausine-H and clausine-B, as well as a new carbazole alkaloid, 3-carbomethoxy-2-hydroxy-7-methoxycarbazole, or clausine-TY. The novel carbazole alkaloid sansoakamine was also isolated by an extraction procedure on the stems of *C. excavata*.[28] Studies also elucidate different constituents like binorpocitrin, xanthoxyletyin, nordentalin, scopoletin, clausine, murrayafoline-A, clauszoline-I, clausine-H, heptaphylline, etc.[32] In a study, two previously unidentified chemicals were identified: "lichexanthone (xanthone)" and "atranorin (depside)".[33] Positive findings for flavonoids, glycosides, and phenols are obtained from the phytochemical study.[34] The bioactive properties of the coumarins extracted from this plant have drawn attention. For example, the pyranocoumarin clausenidin isolated from roots demonstrated anti-HIV-1 activity, while the furanone-coumarins named clauslactones A–J isolated from leaves showed tumor promotion inhibitory effects.[35] The leaves of *C. excavata* were used to isolate ten furanone-coumarins, including clauslactones A, B, C, D, E, F, G, H, I, and J. Furthermore, isolated were clausenidin, 3-formyl-2,7-dimethoxycarbazole, o-

methylmukonal, and clausezoline-J. These structural characteristics are unique to this instance in the realm of nature. In comparison to alkaloids and coumarins, limonoids from the *C. excavata* plant have been identified less frequently. Crude ethanol extract contained a novel limonoid called clausenolide-1-ethylether. They have also isolated limonoids and coumarins, specifically excavatins A-M.[28]

Pharmacology

Numerous secondary metabolites with a range of biological activity, such as anticancer, insecticidal, antifungal, antiplatelet, anti plasmodial, anti-nociceptive, immunomodulatory, anti-mycobacterial, and anti-HIV-1 qualities, have been found through *C. excavata's* phytochemical research.[28]

Antioxidant & anti-inflammatory: Research reveals noteworthy antioxidant activity in the methanolic extract of *C. excavata* leaves.[34] Rich in polyphenols like flavonoids and furocoumarins that control inflammation by blocking the mapk/nf-κb pathways, the methanolic extract of *C. excavata* bears this out.[35] Through the inhibition of inflammatory mediators and apoptosis in the methanolic extract of *C. excavata*, furocoumarins and flavonoids demonstrate immune-modulating and antioxidant qualities that expedite wound healing.[37] With its anti-inflammatory and antioxidant qualities, possibly because of its high polyphenolic content, the studies demonstrated the usefulness of *Clausena excavata* methanolic extract in wound healing by improving contraction, re-epithelialization, and collagen deposition.[39]

Anticancer: Four naturally occurring pyranocoumarins, namely clausenidin, nordentatin, clausarin, and xanthoxyletin, have been identified in the Malaysian medicinal plant *C. excavata*. These pyranocoumarins have demonstrated cytotoxic activity against human cancer cell lines (A549, MCF7, KB, and KB-IN). One potential source of treatment for breast cancer is the fruit oil of *C. excavata*. This plant's O-methylmukonal has anti-HIV-1 properties. The stem bark extract was found to contain Clausine-TY, a new carbazole alkaloid that exhibited considerable cytotoxicity against the CEM-SS cell line. Superior cytotoxic activity against MCF-7 cells was demonstrated by the fruit oil of *C. excavata*, indicating potential as a breast cancer treatment.[28] Studies on adenocarcinomic human alveolar basal epithelial cells and cervical cancer have documented the anticancer properties of excavatine A, a carbazole alkaloid.[36]

Antidiabetic & Antimicrobial: Promising natural antidiabetic compounds were discovered in the form of dentatin and heptaphylline, which are bio actives derived from the root of the medicinal plant, *C. excavata*.[38] *C. excavata* leaves may be used to treat gastrointestinal illnesses; however, more research is required to ascertain the antibacterial qualities of these leaves against MDR *Enterococcus faecalis.* The ethyl acetate fraction is a possible herbicide since studies indicate it has anti-*E. faecalis* activity and anti-colorectal characteristics.[36] Three antifungal compounds derived from the Malaysian *C. excavata* plant include muronal, 3-formylcarbazole, and 3-methoxycarbonylcarbazole.[28]

Antimalarial: The hot acetone and aqueous extracts, as well as the folklore preparation, contained the most active components. Clausine-D from *C. excavata* showed mild anti-malarial efficacy against *Plasmodium falciparum*, antiplatelet action, and reduced the formation of thromboxine A2.[28] Against mosquito larvae, the essential oils of *C. excavata* leaves and twigs are used which contain terpene hydrocarbon compounds such as limonene, γ-terpinene, terpinolene, β-myrcene, 3-carene, and P-cymene that show notable efficacy.[41]

The anti-secretory, mucus-producing, antioxidant, and HSP70 actions of dentatin, which was isolated from *Clausena excavata*, can be responsible for its gastro-protective properties.[40]

***CLAUSENA INDICA* (DALZ.) OLIVER**

Citrus shrubs like *Clausena indica* are grown throughout Southeast Asia and South China. Its essential oil contains antibacterial qualities, and its leaves and roots are utilized in traditional medicine for a variety of health conditions. The fruits scent is enhanced when cooked with them as natural spices. The therapeutic qualities of the plant play a major role in its application.[43] The synonyms of the plant are reported to be *Piptotylis indica* Dalz & *Bergera nitida* Thw respectively. Globally distributed in Peninsular India and Sri Lanka and in India mainly located on Maharashtra: Kolhapur, Sindhudurg, Karnataka: Belgaum, N. Kanara, Shimoga, Kerala: Idukki, Kannur, Malappuram, Palakkad, Thrissur, Tamil Nadu: Coimbatore, Kanniyakumari, Nilgiri, Theni.[27] In Tamil, it's called Kattaveppilai; in Tamil, in Malayalam, Kattukariveppu; and in Kannada, gorakotta.[29]

Botanical description: Smaller in size, this plant is a shrub or tree with glabrous glands, zigzag petiole and rachis, and obtuse to bluntly acuminate leaves. Peduncle, heavily puberulous branches, and inflorescence terminal, Bulbous flowers within buds both the berries and the ovary are sub globose, 1-seeded, and globose when ripe. In evergreen to semi-

evergreen forests, it grows between 600 and 1300 meters above sea level. In the wild, it is also harvested for local use. It produces stunning blossoms in February and fruits in June.[3]

Ethnobotany

Ayurvedic medicine makes extensive use of the popular herb *C. Indica* to treat and prevent a wide range of ailments. Rheumatism, colic, headaches, joint dislocation, colds, flu, and fractures are all treated by its leaves and roots. Because of their scent, the fruits are employed in South Indian and Vietnamese cuisine. Its chemical components and potential therapeutic use are, however, rarely known.[50] *Clausena indica* fruit is widely used in tropical countries for food ingredients and traditional medicines, with its plant parts serving multiple purposes.[43] Additionally, the plant is used to cure malaria in traditional medicine.[52] Due to its ability to enhance the aesthetics of fields and surroundings, the plant is valued for its decorative qualities. When its medical qualities are used, especially in traditional Asian medicine, it also has financial significance in certain areas.[53]

Phytochemistry

The *Clausena* genus contains phytochemical components like coumarins, carbazole alkaloids, and sesquiterpenes that may have anticancer properties. Roots of *C. indica* were used to purify three pure compounds. Six primary molecules are identified, categorized into coumarin and fatty acids, and five chemicals are divided into benzodioxoles, fatty acids, phenols, alcohols, and sesquiterpenes.[43] There were thirty-four components found to make up 99.0% of the leaf oil. Key components included γ-terpinene, sabinene, terpinen-4-ol, and β-phellandrene.[44] Particularly for the deep-eutectic solvent-derived extracts, arbutin, (-)-epigallocatechin, procyanidin B1, (+)-catechin, and (-)-epicatechin were the predominant ingredients in the fruit extracts.[45] Furanocoumarins imperatorin, phellopterin, chalepensin, and the dihydro furanocoumarin, chalepin have all been identified from the roots of *Clausena indica* Oliv. It's been demonstrated that chalepensin and xylotenin are indistinguishable.[46] Essential oils are primarily composed of phenylpropanoids, with trace amounts of oxygenated terpenoids and terpenic derivatives. The oil also contains three non-terpenic aldehydes: aromatic benzaldehyde and aliphatic open-chain compounds (E)-2-hexenal and pentadecanal.[47] Four new tryptamine-derived amides were identified with distinct acid moieties, in addition to the previously identified phenethyl cinnamide. These amides are called balasubramide and prebalamide in cinnamic acid, and madugin and methylmadugin in isovaleric acid.[48]

PHARMACOLOGY

Antimicrobial: The *C. indica* essential oil showed antimicrobial activity against representative Gram-negative (*Escherichia coli, Pseudomonas aeruginosa*) and Gram-positive (*Bacillus subtilis, Staphylococcus aureus*) bacteria, moulds (*Aspergillus niger, Fusarium oxysporum*), and yeasts (*Saccharomyces cerevisae, Candida albicans*).[47] The roots of *C. indica* were used to isolate nordentatin and clausine K, which exhibited encouraging antioxidant, anti-α-amylase, and tyrosinase inhibitory properties.[49] Flavonoids in *C. indica* fruits show antimicrobial effects against Gram-positive bacteria, with methanol extract showing the highest total phenolic content and remarkable antioxidant activity with the lowest IC50 values, excluding fungi and yeast species.[50]

Antidiabetic: Utilizing bioguided isolation of ethyl acetate extract, research projects explore the production of antidiabetic compounds from *C. indica* roots. Hypoglycemic action is suggested by anti-α-amylase activity shown by dentatin, clausine K, and nordentatin. Major chemicals that have anti-α-amylase action are called coumarins. Cell signaling pathways reflect extensively on *C. indica.* Though more research is required to find new, affordable, and effective drugs, *C. indica*, which is abundant in phytochemical components such as sesquiterpenes, coumarins, and carbazole alkaloids, may have anticancer potential.[50]

Antiageing: Elastase and tyrosinase, two significant enzymes linked to skin ageing that contribute to the deterioration of skin elasticity and the production of freckles as a result of UV exposure and ROS accumulation, are inhibited by *C. indica* extracts and compounds, according to in vitro enzymatic studies.[49]

Research indicates that the essential oils derived from *C. indica* fruits have the ability to inhibit xanthine oxidase, which could lead to advancements in dietetics and the emergence of antioxidants and anti-gout medications.[51]

CLAUSENA HEPTAPHYLLA (ROXB.) WIGHT & ARN

Known for its traditional uses and therapeutic qualities, *Clausena heptaphylla* is a shrub or small tree that is native to India, Bangladesh, and other places. When extracted, the volatile chemicals that make up its essential oils have a light yellow color.[54] The synonyms of the plant are reported to be *Amyris heptaphylla* Roxb., *Cookia macrophylla* Lindl respectively Globally distributed on India: Assam, Tamil Nadu; Nepal, Myanmar and in India it is mainly on the Barak valley areas.[27]

Botanical description: The compound leaves of this plant are elliptic-oblong, ovate to oblong-lanceolate, cuneate at base, and asymmetrical. Its terminal paniculate cymes have inflorescences and uniseriate glands throughout. The berries are 10–15 mm long, and the blossoms are 5 mm long. The seeds have a narcotic effect and are highly fragrant. In Bengali, it is frequently referred to as Pan-kafur or Karan phal. It blooms on: March–April, Fruiting: May to August.[29] *C. heptaphylla* is a self-supporting species of tree in the Rutaceae family. The plant is largely collected in the wild for its essential oil, which is used locally to flavor alcoholic beverages in a manner similar to that of *C. anisum-olens*.[3] Research suggests that direct organogenesis can be induced from nodal explants and shoot apex to enable large-scale micro propagation and conservation of *Clausena heptaphylla*, a valuable medicinal and aromatic plant. This method encourages micro propagation on a large scale, allowing regenerates to be used for extracting essential oils in various industries.[55]

Ethnobotany

Shaty-kiyi, also known as *Clausena heptaphylla*, is used ethno botanically to treat fever, cure nicotine addiction, and get rid of bad breath when eaten with betel leaf. After being chewed, fresh leaves are either thrown away or consumed. The antimicrobial properties of *Clausena heptaphylla*, a fever treatment used by the Tripuras, have been demonstrated.[63] *Clausena heptaphylla* is useful in treating paralysis, ulcerated noses, headaches, and muscle aches, according to an ethnobotanical investigation. In addition, they may be used as an astringent, diuretic, insecticide, tonic, vermifuge, and antiseptic. Cattle sprains and wounds are treated using the bark of the shrub. For ophthalmic and skin inflammation, plant essential oils and flower extracts are utilized. According to a recent study, *C. heptaphylla* leaf aqueous extracts were used to reduce cravings for cigarettes and prevent obesity.[60] This plant is also used to treat impotence, according to ethnobotanical investigations. The folks suggested a dosage of one glass of water extract of leaves, one spoon of ghee, and one spoon of honey to be taken in the morning for the desired treatment.[64] Also, they are used to treat rheumatism, body discomfort, and fever (one spoonful of leaf and root juice taken two to three times a day for three days; the root juice is applied topically to the affected area and one teaspoon is taken with honey).[65] Crushed fruit extracts are also applied to the forehead to treat headaches.[66] When treated externally to wounds caused by magical-religious beliefs, root paste, *Mimosa pudica* roots, and *Crateva adansonii* bark are utilized.[67]

Phytochemistry

Previous phytochemical studies have identified the presence of rutin, clausine-L, safrole, glutinol, steroidal glycosides, clausenlactum, and clausine alkaloids in the plant's stem and roots, as well as coumarins, clausines, and clausenin in the leaves.[55] Although *Clausena heptaphylla*'s ethanolic stem bark extract lacks tannins, anthraquinones, and resins, it does contain flavonoids, alkaloids, saponins, and steroids.[56] Physical, chemical, and synthetic investigations led to the isolation of a novel carbazole alkaloid from *Clausena heptaphylla* leaves, named clausenal, and its structure turned out to be 1,8-dimethoxy-3-formylcarbazole.[57] Furthermore, from the stem bark of *Clausena heptaphylla*, a novel carbazole alkaloid known as clausenalene was isolated, and its structure was determined to be 3-methyl-6,7-methylenedioxy carbazole.[58] Additionally, two pyranocoumarins have been identified from the roots.[59] It has been discovered that essential oils, especially those derived from *Clausena heptaphylla*, provide beneficial effects for an array of illnesses. One of the key ingredients, anethole, is a flavoring agent used in food, cosmetics, perfumes, and medicines. Its immunomodulatory, anti-carcinogenic, and antithrombotic properties are among its health advantages.[60] Also, heptazolicine, a novel carbazole alkaloid, has been detected and derived from *Clausena heptaphylla* roots. [2,2-dimethyl-3,4-dihydropyrano-(5, 6-a)] 3 hydroxy-8-formyl carbazole has been identified based on spectroscopic and molecular data.[61] Anethole, anisaldehyde, estragole, anisyl ketone, and α-elemene have been found to be the primary constituents of the essential oil extracted from the leaves of *C. heptaphylla*.[62]

Pharmacology

As evidence of its capacity to scavenge free radicals, the study discovered that *C. heptaphylla* possesses a high concentration of scavenging agents. The extract exhibited pesticidal, antibacterial, and dose-dependent mortality properties. It was also able to lyse clots more effectively than streptokinase, exhibiting notable in vitro thrombolytic activity. Additionally, demonstrating cytotoxic and antibacterial properties in the crude ethanol extract of *C. heptaphylla*.[56] Rich in anethole and other chemicals, the plant's essential oil holds possibilities for drug formulation due to its potential to prevent inflammation and have anti-diabetic properties. Because of its high concentration of anethole, the plant extract of *C. heptaphylla* offers better skin-whitening capability than regular kojic acid. Smaller chemicals may augment the neuroprotective impact of the plant's essential oil. The leaf alcoholic extract exhibited the strongest inhibition against *Staphylococcus aureus, Bacillus Cereus, and Bacillus Subtilis*.[54]

CLAUSENA AUSTROINDICA B.C. STONE & K.K. NAIR

Botanical description: Found in evergreen woods, or "sholas," in the southern Western Ghats of peninsular India, *Clausena austroindica* B.C. Stone & K.K.N. Nair is an indigenous shrub or small tree that can grow to a height of 10 meters. Usually, it flowers from February to April, and in July or August, fruits begin to ripen.[68] In India it is mainly seen on the state of Kerala where it is distributed on districts of Palakkad, Kollam, Idukki, Pathanamthita, Malappuram, Kannur, Thiruvananthapuram, Thrissur, Wayanad respectively.[27] Substrate in evergreen, semi-evergreen, dry-evergreen, and wet deciduous forests; leaves are lanceolate to obovate, alternate, puberulent, or glabrous. terminal inflorescence, Subglobose flowers with cordate, oblong, or rhomboid anthers Seated atop a small yet distinctive gynophore, ovary berries are glandular, globose, oblate, and greenish. Native to the South Sahyadri region of the southern Western Ghats.[29]

Ethnobotany

Ear infection treated with root bark extract.[69] Primarily in the Coorg district of Karnataka, in the southern western Ghats,[71] Karianshola, Coimbatore district of Tamilnadu.[70] Its fruit is similarly beneficial, and the book "medicinal plants known from Wayanad" lists it.[72]

Phytochemistry

Very little research has been done on the plant species *Clausena austroindica*. A GC-MS investigation is used to examine only essential oils. The compounds that make them constitute were cis- and trans-ocimene, Z-nonanone, methyl chavicol, anisaldehyde, trans-anethole, δ-Elemene, anisyl methyl ketone, cis-cadina-1(6),4-diene, γ-Murolene, trans-methyl isoeugenol, bicyclogermacrene, and so on. Trans-anethole was determined to be the primary constituent in *C. austroindica* leaf oil using column chromatography.[68]

Pharmacology

Trans-anethole, the main component of *C. austroindica* leaf oil, and its insecticidal potential were determined by toxicity bioassays, namely contact and fumigant toxicity. Trans-anethole and *C. austroindica* leaf oil have not shown any harm to mammalian cells (L929 cell line). A new natural source of trans-anethole, *C. austroindica* leaf oil, shown insecticidal effectiveness against pests of stored products.[68]

CLAUSENA PENTAPHYLLA LAM. EX. DC

Botanical description: *Clausena pentaphylla* DC., also known as Ratanjote, is a tiny, fragrant, deciduous perennial shrub that can grow up to two meters in height. It is found in some of the Gorakhpur Division's forests in Uttar Pradesh, India.[73] The Himalayas and Assam comprise the natural range of this species. Growing mostly in subtropical regions.[27] *Gallesioa pentaphylla* Wight & Arn. Ex M. Roem, *Polycyema pentaphyllum* voigt are the synonyms reported for the plant.[29] Often referred to as Teyrar, Rowana, Surjmukha, and Ratanjote in India.[74]

Ethnobotany

Folk medicine employs a number of species from the genus *Clausena*, including *C. anisata*, *C. heptaphylla*, and *C. pentaphylla*, to treat human illnesses. Ethnobotanical data indicated that *C. pentaphylla* bark powder is applied topically to newly opened wounds to promote rapid healing. For diarrhoea, the leaf is decocted and combined with barley seeds (*Hordeum vulgare*) and black pepper (*Piper nigrum*) twice a day. An isolated substance from *C. pentaphylla* leaves called clausmarin has blood pressure-lowering and spasmolytic properties.[2] Animal sprains and wounds are treated with a blend of sweet oil and root powder.[81]

Phytochemistry

17 molecules, comprising 11 monoterpene hydrocarbons, 5 oxygenated monoterpenes, and 1 sesquiterpene hydrocarbon, were identified using GC and GC/MS analysis of the *C. pentaphylla* oil, accounting for approximately 97.5% of the oil. Sabinene, terpinolene, limonene, methyl eugenol, and safrole were the main volatile components.[73] The roots of *Clausena pentaphylla* have yielded the new coumarin clausarin as well as methyl linolenate, dentatin, clausenidin, β-sitosterol, and heptaphylline.[75] From *Clausena pentaphylla's* roots and stem bark, three coumarins were identified. Their structures as 3, 10-bis (1, 1-dimethyl prop-2-en-1-yl) were validated by spectral data analysis. Bergapten, xanthotoxin, pyranochromen-2-one, -5, 6, 7-trihydroxy-8, 8-dimethyl-7, and 8-dihydro.[74] From the aerial fragments of *Clausena pentaphylla*, a novel C33 terpenoid called O-Methylclausenol (1) has been identified. Its structure is 3-3-methoxy-23,24,24-trimethyl[anosta9(ll)-25-diene], according to spectroscopic techniques.[76] Additionally, *Clausena pentaphylla* has yielded the new terpenoid coumarin clausmarin-C.[77] A flavanone glycoside, 5,7-dihydroxy3',4'-

dimethoxyflavanone 6-C- [α-rhamnopyranosyl-(1 - 6)] -β-glucopyranoside, was extracted using ethyl acetate from the roots of *Clausena pentaphylla*.[78]

Pharmacology

The isolated guinea-pig ileum preparation was subjected to different levels of spasmolytic action by ethanolic extracts of five different *Clausena* species. *Clausena pentaphylla* was more active in its aerial portions. Its unique coumarin terpenoid active principle, clausmarin-A, was also assessed.[79] Oil from *Clausena pentaphylla* was found to be more successful in preventing the mycelial growth of all test fungus, and it may be sold as an alternative to pharmaceutical fumigants for grain storage management.[80]

***CLAUSENA AGASTHYAMALAYANA SP.* NOV.**

Botanical description: Up to 1.5 meters tall shrubs with greenish-black bark and cylindrical, minutely puberulent, lenticellate branchlets terminal inflorescence, buds of subglobose flowers, Petals five, obtuse at the tip, imbricate, elliptic, three-nerved, with barely noticeable glands Subglobose ovary, Fruits: ellipsoid berries, smooth, glabrous seeds. *Clausena agasthyamalayana* was mostly observed in the open alpine woodlands nestled amid the boulders. The type locality, Agasthyamala Biosphere Reserve, is referred to by the specific epithet. Its dwarf habit, greenish-black bark, smaller and fewer leaflets, obovate and coriaceous leaves with obtuse or emarginated apex, elliptic and obtuse petals, oblong-cordate anthers, consistently 4-locular ovary with two ovules in each chamber, and ellipsoid fruit set it apart from *C. indica*.[82]

CONCLUSION

Extensive research has demonstrated the beneficial role of *Clausena* genus in medicine. The genus is distributed globally, with Indo-China being a significant region. Despite extensive testing, no medication has yet been created from this genus. To promote the therapeutic potential of these plants, a comprehensive and methodical investigation is required. This article highlights seven Indian plants that contain different bioactive components for treating various ailments, including anti-cancer, anti-oxidant, anti-microbial, and anti-plasmodial properties. Regardless of their ethnobotanical significance, plants like *Clausena agasthyamalayana, Clausena anisata, Clausena austroindica, Clausena excavata, Clausena heptaphylla, Clausena indica,* and *Clausena pentaphylla* are not as widely used for the extraction and isolation of different phytoconstituents and require a variety of phytopharmacological studies to support their claimed biological activities, according to the

review. It is anticipated that this publication will lead to more studies on these possible therapeutic plants in the future.

Funding

Nil.

Conflict of interest

No conflict of interest.

REFERENCES

1. Panda M, Kumar S, Mahalik G. An overview of medicinal plants of the family Rutaceae as a source of complementary therapeutics. Journal of Biodiversity and Conservation, 2020; 3(4): 13-4.
2. Simpson MG. Diversity and classification of flowering plants: eudicots. Plant systematics, 2010; 2010: 275-448.
3. Musa A, Aminah NS, Davies-Bolorunduro OF, Kristanti AN, Suhaili, Islami AI, Wai TS, Naing TT. Antimicrobial activities of the extracts and secondary metabolites from *Clausena* genus–A review. Open Chemistry, Jul. 13, 2022; 20(1): 627-50.
4. Truong DH, Ngo NH, Van HT. Chemical constituents and biological effects of essential oils of genus (): A review. Herba Polonica, 2022; 68(3): 17-26.
5. Omara T, Kiprop AK, Kosgei VJ, Kagoya S. *Clausena anisata* (Willd.) Hook. f. ex Benth. (Rutaceae): ethnomedicinal uses, phytochemistry, pharmacological activities, toxicity, and clinical application.
6. Okokon JE, Etebong EO, Udobang JA, Essien GE. Antiplasmodial and analgesic activities of *Clausena anisata*. Asian Pacific Journal of Tropical Medicine, Mar. 1, 2012; 5(3): 214-9.
7. Thomford KP, Yorke J, Thomford AK, Amponsah IK. A formulation of *Clausena anisata* (Willd.) Hook. f. Ex Benth and *Cassia sieberiana* DC. alleviates the symptoms associated with osteoarthritis: a single-blind, randomised controlled trial of a traditional Ghanaian remedy. Clinical Phytoscience, Dec. 2021; 7: 1-2.
8. Boon R, Pooley E. Pooley's trees of eastern South Africa. Flora and Fauna Publications Trust, 2010.
9. Senthilkumar A, Venkatesalu V. Phytochemical analysis and antibacterial activity of the essential oil of *Clausena anisata* (Willd.) Hook. f. ex Benth. Int J Integr Biol., May. 20, 2009; 5(2): 116-20.

10. Ito C, Itoigawa M, Aizawa K, Yoshida K, Ruangrungsi N, Furukawa H. Gamma-lactone carbazoles from *Clausena anisata.* J Nat Prod., Jun. 2009; 72(6): 1202-4. doi: 10.1021/np800735m. PMID: 19459693.
11. Arbab IA, Abdul AB, Aspollah M, Abdullah R, Abdelwahab SI, Ibrahim MY, Ali LZ. A review of traditional uses, phytochemical and pharmacological aspects of selected members of *Clausena* genus (Rutaceae). Journal of Medicinal Plants Research, Oct. 3, 2012; 6(38): 5107-18.
12. Chakraborty A, Chowdhury BK, Bhattacharyya P. Clausenol and clausenine—two carbazole alkaloids from *Clausena anisata*. Phytochemistry, Sep. 1, 1995; 40(1): 295-8.
13. Songue JL, Kouam, Dongo E, Mpondo TN, White RL. Chemical constituents from stem bark and roots of *Clausena anisata*. Molecules, Nov. 20, 2012; 17(11): 13673-86.
14. Lawal IO, Galadima M, Ogunbamowo PO. Isolation of bioactive compounds of *Clausena anisata* (Willd.) Hook. growing in South Africa by liquid chromatography–mass spectroscopy profiling, and their antibacterial activities. Journal of Medicinal Plants for Economic Development, Apr. 25, 2018; 2(1): 1-0.
15. Ojewole JA. Hypoglycaemic effect of *Clausena anisata* (Willd) Hook methanolic root extract in rats. Journal of Ethnopharmacology, Jul. 1, 2002; 81(2): 231-7.
16. Agyepong N, Agyare C, Adarkwa-Yiadom M, Gbedema SY. Phytochemical investigation and anti-microbial activity of *Clausena anisata* (Willd), Hook. African Journal of Traditional, Complementary and Alternative Medicines, Jul. 10, 2014; 11(3): 200-9.
17. Kumatia EK, Annan K, Dickson RA, Mensah AY, Amponsah IK, Appiah AA, Tung NH, Edoh DA, Habtemariam S. Anti-inflammatory and analgesic effects in rodent models of ethanol extract of *Clausena anisata* roots and their chemical constituents. Natural Product Communications, Jan. 2017; 12(1): 1934578X1701200119.
18. Okokon JE, Udoh AE, Andrew UE, Amazu LU. Antiinflammatory and antipyretic activities of *Clausena anisata*. Molecular and Clinical Pharmacology, 2012; 3(1): 47-54.
19. Ishola IO, Olayemi SO, Oreagba IA, Ifeanyi CI, Popoola TD. Antinociceptive and anti-arthritic properties of hydroethanolic leaf extract of *Clausena anisata* (Willd.) Hook. f. ex Benth (Rutaceae) in Rodents: possible mechanism of actions. Nigerian Journal of Physiological Sciences, 2015; 30(1-2): 39-49.
20. Omara T, Kiprop AK, Kosgei VJ, Kagoya S. *Clausena anisata* (Willd.) Hook. f. ex Benth. (Rutaceae): ethnomedicinal uses, phytochemistry, pharmacological activities, toxicity, and clinical application.

21. Tatsimo SJ, Tamokou JD, Lamshöft M, Mouafo FT, Lannang AM, Sarkar P, Bag PK, Spiteller M. LC-MS guided isolation of antibacterial and cytotoxic constituents from *Clausena anisata.* Medicinal Chemistry Research, Apr. 2015; 24: 1468-79.
22. Huang L, Zhe-Ling FE, Yi-Tao WA, Li-Gen LI. Anticancer carbazole alkaloids and coumarins from *Clausena* plants: A review. Chinese Journal of Natural Medicines, Dec. 1, 2017; 15(12): 881-8.
23. Kumatia EK, Zoiku FK, Asase A, Tung NH. Anti-malarial activity of the alkaloid, heptaphylline, and the furanocoumarin, imperatorin, from *Clausena anisata* against human Plasmodium falciparum malaria parasites: ex vivo trophozoitocidal, schizonticidal and gametocytocidal approach. Malaria Journal, Sep. 9, 2023; 22(1): 264.
24. Irungu BN, Mbabu MJ, Kiboi DM, Moindi E, Kinyua J, Mwirichia RK. In vivo antimalarial and acute toxicity properties of hexane and chloroform extracts from *Clausena anisata* (Willd.) Benth.
25. Kenechukwu FC, Mbah CJ, Momoh MA, Chime SA, Umeyor CE, Ogbonna JD. Pharmacological justification for the ethnomedical use of *Clausena anisata* root-bark extract in the management of epilepsy. Journal of Applied Pharmaceutical Science, Sep. 28, 2012; 2(9): 036-40.
26. Makirita W MW, Chacha M. Larvicidal activity of *Clausena anisata* fruits and leaves extracts against Anopheles gambiae Giles ss, Culex quinquefasciatus Say and Aedes egyptiae.
27. Nayar TS, Sibi M, Rasiya Beegam A, Mohanan N, Rajkumar G. Flowering plants of Kerala: status and statistics. Rheedea, 2008; 18(2): 96.
28. Arbab IA, Abdul AB, Aspollah M, Abdullah R, Abdelwahab SI, Mohan S, Abdelmageed AH. *Clausena excavata* Burm. f.(Rutaceae): A review of its traditional uses, pharmacological and phytochemical properties. Journal of Medicinal Plants Research, Dec. 31, 2011; 5(33): 7177-84.
29. Hajra PK, Nair VJ, Daniel P. Flora of India, (Malpighiaceae–Dichapetalaceae). Botanical Survey of India, Calcutta, 1997; 4.
30. Singh KP, Singh DK, Roy Choudhury P. Flora of Mizoram Volume-I. Botanical survey of India (Ministry of Environment and forest), 2002; 845.
31. Xin ZQ, Lu JJ, Ke CQ, Hu CX, Lin LP, Ye Y. Constituents from *Clausena excavata*. Chemical and Pharmaceutical Bulletin, Jun. 1, 2008; 56(6): 827-30.

32. Sripisut T, Cheenpracha S, Ritthiwigrom T, Prawat U, Laphookhieo S. Chemical constituents from the roots of *Clausena excavata* and their cytotoxicity. Rec Nat Prod., Oct. 1, 2012; 6(4): 386-9.
33. Lim PC, Ramli H, Kassim NK, Ali Z, Khan IA, Shaari K, Ismail A. Chemical constituents from the stem bark of *Clausena excavata* Burm. f. Biochemical Systematics and Ecology, Feb. 1, 2019; 82: 52-5.
34. Guntupalli C, Kumar GS, Kumar AS, Tubati T. Evaluation of antioxidant activity of the methanolic leaf extract of *Clausena excavata* Burm. f.(Rutaceae) using the lipid peroxidation model. Pharmacognosy Journal, Dec. 1, 2012; 4(34): 22-5.
35. Kumar R, Saha A, Saha D. A new antifungal coumarin from Clausena excavata. Fitoterapia, Jan. 1, 2012; 83(1): 230-3.
36. Albaayit SF, Maharjan R, Abdullah R, Noor MH. Anti-Enterococcus faecalis, cytotoxicity, phytotoxicity, and anticancer studies on *Clausena excavata* Burum. f.(Rutaceae) Leaves. BioMed Research International, Feb. 23, 2021; 2021: 1-9.
37. Albaayit SF, Rasedee A, Abdullah N, Abba Y. Methanolic extract of *Clausena excavata* promotes wound healing via anti-inflammatory and anti-apoptotic activities. Asian Pacific Journal of Tropical Biomedicine, May. 1, 2020; 10(5): 232-8.
38. Thant TM, Aminah NS, Kristanti AN, Ramadhan R, Aung HT, Takaya Y. Antidiabetes and antioxidant agents from *Clausena excavata* root as medicinal plant of Myanmar. Open Chemistry, Dec. 31, 2019; 17(1): 1339-44.
39. Albaayit SF, Abba Y, Rasedee A, Abdullah N. Effect of *Clausena excavata* Burm. f.(Rutaceae) leaf extract on wound healing and antioxidant activity in rats. Drug design, Development and Therapy, Jul. 13, 2015: 3507-18.
40. Sidahmed HM, Vadivelu J, Loke MF, Arbab IA, Abdul B, Sukari MA, Abdelwahab SI. Anti-ulcerogenic activity of dentatin from *Clausena excavata* Burm. f. against ethanol-induced gastric ulcer in rats: Possible role of mucus and anti-oxidant effect. Phytomedicine, Mar. 1, 2019; 55: 31-9.
41. Cheng SS, Chang HT, Lin CY, Chen PS, Huang CG, Chen WJ, Chang ST. Insecticidal activities of leaf and twig essential oils from *Clausena excavata* against Aedes aegypti and Aedes albopictus larvae. Pest Management Science: formerly Pesticide Science, Mar. 2009; 65(3): 339-43.
42. Gou Y, Li Z, Fan R, Qiu Z, Wang L, Wang C, Wang Y. Ethnobotanical survey of plants traditionally used against hematophagous invertebrates by ethnic groups in the

mountainous area of Xishuangbanna, Southwest China. Plant diversity, Dec. 1, 2020; 42(6): 415-26.

43. Hoang Anh L, Xuan TD, Dieu Thuy NT, Quan NV, Trang LT. Antioxidant and α-amylase inhibitory activities and phytocompounds of *Clausena indica* fruits. Medicines, Feb. 28, 2020; 7(3): 10.
44. John JA, Kurup SR, Pradeep NS, Sabulal B. Chemical composition and antibacterial activity of the leaf oil of *Clausena indica* from South India. Journal of Essential Oil Bearing Plants, Jan. 1, 2011; 14(6): 776-81.
45. Wang R, He R, Li Z, Wang L. LC-Q-Orbitrap-MS/MS characterization, antioxidant activity, and α-glucosidase-inhibiting activity within silico analysis of extract from *Clausena indica* (Datz.) Oliv fruit pericarps. Frontiers in Nutrition, Sep. 1, 2021; 8: 727087.
46. Joshi BS, Gawad DH. Isolation of some furanocoumarins from *Clausena indica* and identity of chalepensin with xylotenin. Phytochemistry, Feb. 1, 1971; 10(2): 480-1.
47. Diep PT, Pawlowska AM, Cioni PL, Van Minh C, Huong LM, Braca A. Chemical composition and antimicrobial activity of *Clausena indica* (Dalz) Oliv. (Rutaceae) essential oil from Vietnam. Natural Product Communications, Jun. 2009; 4(6): 1934578X0900400627.
48. Riemer B, Hofer O, Greger H. Tryptamine derived amides from *Clausena indica*. Phytochemistry, May. 1, 1997; 45(2): 337-41.
49. Quan NV, Xuan TD, Anh LH, Tran HD. Bio-guided isolation of prospective bioactive constituents from roots of *Clausena indica* (Dalzell) Oliv. Molecules, Dec. 4, 2019; 24(24): 4442.
50. Abeysinghe DT, Alwis DD, Kumara KA, Chandrika UG. Nutritive importance and therapeutics uses of three different varieties *(Murraya koenigii, Micromelum minutum, and Clausena indica)* of curry leaves: An updated review. Evidence-Based Complementary and Alternative Medicine, Oct. 31, 2021; 2021.
51. Quan NV, Anh LH, Lam VQ, Takami A, Teschke R, Khanh TD, Xuan TD. Anti-diabetes, anti-gout, and anti-leukemia properties of essential oils from natural spices *Clausena indica, Zanthoxylum rhetsa, and Michelia tonkinensis.* Molecules, Jan. 25, 2022; 27(3): 774.
52. Krishnakumar NM, Ceasar SA. A mini review on ethnomedicinal uses, phytochemistry and pharmacological properties of Indian wampi plant: *Clausena indica* (Dalzell) Oliv. Current Traditional Medicine, 2023; 10.

53. Mao AA, Dash SS. Flowering plants of India an annotated checklist: dicotyledons, 2020.
54. Lal M, Begum T, Gogoi R, Sarma N, Munda S, Pandey SK, Baruah J, Tamang R, Saikia S. Anethole rich *Clausena heptaphylla* (Roxb.) Wight & Arn., essential oil pharmacology and genotoxic efficiencies. Scientific Reports, Jun. 15, 2022; 12(1): 9978.
55. Majumder S, Rahman MM. Effect of different plant growth regulators on in vitro propagation of *Clausena heptaphylla* (Roxb.)-An aromatic and medicinal shrub. Journal of Pharmacognosy and Phytochemistry, 2016; 5(4): 58-63.
56. Fakruddin M, Mannan KS, Mazumdar RM, Afroz H. Antibacterial, antifungal and antioxidant activities of the ethanol extract of the stem bark of *Clausena heptaphylla.* BMC Complementary and Alternative Medicine, Dec. 2012; 12: 1-9.
57. Chakraborty A, Saha C, Podder G, Chowdhury BK, Bhattacharyya P. Carbazole alkaloid with antimicrobial activity from *Clausena heptaphylla.* Phytochemistry, Feb. 1, 1995; 38(3): 787-9.
58. Bhattacharyya P, Biswas GK, Barua AK, Saha C, Roy IB, Chowdhury BK. Clausenalene, a carbazole alkaloid from *Clausena heptaphylla*. Phytochemistry, Apr. 29, 1993; 33(1): 248-50.
59. Joshi BS, Kamat VN, Saksena AK. Structures of clausenin and clausenidin two new pyranocoumarins from the roots of *Clausena heptaphylla* Wt. & Arn. Tetrahedron, Jan. 1, 1967; 23(12): 4785-9.
60. Lal M, Munda S, Gogoi A, Begum T, Baruah J. Use of stability statistics in the selection of *Clausena heptaphylla* (Roxb.) Wight & Arn for novel anethole rich strain (Jor Lab CH-2). Frontiers in Plant Science, Dec. 14, 2022; 13: 1060492.
61. Bhattacharyya P, Chakraborty A, Chowdhury BK. Heptazolicine, a carbazole alkaloid from *Clausena heptaphylla*. Phytochemistry, Jan. 1, 1984; 23(10): 2409-10.
62. Lockwood GB. The essential oil from leaves of *Clausena heptaphylla.*
63. Hossan MS, Hanif A, Khan M, Bari S, Jahan R, Rahmatullah M. Ethnobotanical survey of the Tripura tribe of Bangladesh. American Eurasian Journal of Sustainable Agriculture, May. 1, 2009; 3(2): 253-61.
64. Sajeeb BK, Uddin MZ, Bachar R, Bachar SC. Ethnobotanical study on medicinal plants used by the ethnic people of Khagrachhari district, Bangladesh. Dhaka Univ. J. Pharm. Sci., 2022; 21: 217-30.
65. Kadir MF, Sayeed MS, Setu NI, Mostafa A, Mia MM. Ethno pharmacological survey of medicinal plants used by traditional health practitioners in Thanchi, Bandarban Hill Tracts, Bangladesh. Journal of Ethno Pharmacology, Aug. 8, 2014; 155(1): 495-508.

66. Rahman MA, Uddin SB, Wilcock CC. Medicinal plants used by Chakma tribe in Hill Tracts districts of Bangladesh.
67. Balasubramanian P, Narendra Prasad S. Medicinal plants among the Irulars of Attappady and Boluvampatti forests in the Nilgiri Biosphere Reserve. J. Econ. Taxonomic Bot., 1996; 12: 253-9.
68. Johnson AJ, Venukumar V, Varghese TS, Viswanathan G, Leeladevi PS, Remadevi RK, Baby S. Insecticidal properties of *Clausena austroindica* leaf essential oil and its major constituent, trans-anethole, against *Sitophilus oryzae* and *Tribolium castaneum.* Industrial Crops and Products, Aug. 1, 2022; 182: 114854.
69. Muralidhara Rao D, Pullaiah T. Ethnobotanical studies on some rare and endemic floristic elements of Eastern Ghats-Hill Ranges of South East Asia, India. Ethnobotanical leaflets, 2007; 2007(1): 10.
70. Ramachandran VS, Selvalakshmi S, Betty T. Floral diversity of Karianshola MPCA, Coimbatore district, Tamilnadu, with special emphasis on the conservation of ret and endemic plants of Anamalai hills. Elixir Appl. Botany, Jan. 3, 2014; 66: 20653-5.
71. Udayan PS, Ravikumar K. Additions to the flora of Coorg district, Karnataka State, 2002; 38(3): 225-232.
72. Kumar NA, Salim PM, Balakrishnan V, Sivan VV. Medicinal plants known from Wayanad. MS Swaminathan Research Foundation Community Agrobiodiversity Centre Puthoorvayal, Nov. 23, 2001; 6-7.
73. Pandey AK, Singh P, Mohan M, Tripathi NN. New report on the chemical composition of the essential oil from leaves of *Clausena pentaphylla* from India. Chemistry of Natural Compounds, Nov. 48, 2012: 896-7.
74. Intekhab J, Aslam M. Coumarins from the roots of *Clausena pentaphylla.* FABAD J. Pharm. Sci., 2008; 33: 67-70.
75. Anwer F, Shoeb A, Kapil RS, Popli SP. Clausarin—a novel coumarin from *Clausena pentaphylla* (Roxb.) DC. Experientia, Apr. 1977; 33(4): 412-3.
76. Manandhar MD, Shoeb A, Kapil RS, Popli SP. O-methylclausenol—AC 33 terpenoid from *Clausena pentaphylla*. Experientia, Feb. 1977; 33: 153-.
77. Raj K, Sharma M, Misra N. Clausmarin-C: a novel terpenoid coumarin from *Clausena pentaphylla*. Natural Product Research, Dec. 15, 2009; 23(18): 1671-6.
78. Intekhab J, Aslam M, Bhadauria V, Singh P. A new flavanone glycoside from *Clausena pentaphylla*. Chemistry of Natural Compounds, Sep. 2012; 48: 568-9.

79. Patnaik GK, Dhawan BN. Evaluation of spasmolytic activity of clausmarin-A. A novel coumarin from *Clausena pentaphylla* (Roxb.) DC. Journal of Ethnopharmacology, Sep. 1, 1982; 6(2): 127-37.
80. Pandey AK, Palni UT, Tripathi NN. Evaluation of *Clausena pentaphylla* (Roxb.) DC oil as a fungitoxicant against storage mycoflora of pigeon pea seeds. Journal of the Science of Food and Agriculture, May. 2013; 93(7): 1680-6.
81. Maheshwari JK. Ethnobotany in South Asia. Scientific Publishers, 1996.
82. Kumar ES, Shareef SM, Roy PE, Veldkamp JF. *Clausena agasthyamalayana* sp. Nov.(Rutaceae) from Kerala, India. Nordic journal of botany, Apr. 2015; 33(2): 151-4.