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"REVIEW ON BIOACTIVITY SCREENING OF CLAUSENA DENTATA AND ITS MEDICINAL USES"

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ABSTRACT

Clausena dentata (Willd.) M. Roem., a member of the Rutaceae family, is a key medicinal plant used in indigenous healing traditions to treat inflammation, microbial infections, wounds, fever, and gastrointestinal issues. Recent research has ramped up to validate these uses through detailed phytochemical and bioactivity studies. This review pulls together and critically examines the literature on C. dentata's chemical makeup, pharmacological effects, and healing potential. Phytochemical studies uncover a rich array of bioactive compounds—like flavonoids, coumarins, alkaloids, carbazole derivatives, phenolics, and essential oils—that drive its wide-ranging benefits. Bioassays show strong antioxidant, antimicrobial, anti-inflammatory, analgesic, hepatoprotective, and cytotoxic activities in extracts and isolated compounds. Flavonoids and carbazole alkaloids stand out for their free radical scavenging and antimicrobial prowess, backing traditional uses. In vitro and in vivo work points to roles in tackling oxidative stress and inflammation-related conditions. That said, while the results are promising, we still lack thorough toxicity tests and human clinical trials. This review spotlights C. dentata's therapeutic promise, flags key research gaps, and calls for more work to discover new compounds, uncover how they work, and prove their safety and effectiveness for drugs and nutraceuticals.

KEYWORDS: *Clausena dentate, Phytochemical composition, Pharmacological activities, Medicinal relevance, Bioactive compounds, Therapeutic potential.*

INTRODUCTION

Medicinal plants continue to play a pivotal role in traditional medicine and modern biopharmaceutical research, thanks to their diverse secondary metabolite profiles. Clausena dentata (Willd.) Roem., from the Rutaceae family, stands out as a pharmacologically promising species native to tropical and subtropical regions of India and Southeast Asia. Ethnobotanical knowledge highlights its leaves, roots, bark, and fruits for treating inflammation, gastrointestinal disorders, skin ailments, chronic fever, and microbial infections, alongside insecticidal and larvicidal uses. These practices have spurred rigorous scientific exploration of its phytochemistry and bioactivity. Researchers have isolated key compounds such as carbazole alkaloids, coumarins, flavonoids, essential oils, and phenolics, demonstrating antioxidant, antimicrobial, anti-inflammatory, anticancer, hepatoprotective, and larvicidal effects. While evidence validates many traditional uses, systematic studies are essential to identify active principles, clarify mechanisms, and harness their potential for contemporary therapeutics.

Definition

Clausena dentata (Willd.) M. Roem.

C. dentata (Willd.) Roem is a small tree plant that grows

2–6 m tall and bears delicious fruit. It has odoriferous leaves that are heavily spotted, membranaceous, odoriferous, and erose near the tip. It is predominantly found in Karnataka's Coorg, N. Kanara, and Shimoga districts, growing in evergreen and semi-evergreen woods. It is well known among the hill tribes where it is locally called "Mor Koorangee".[49]

C. dentata (Willd.) Roem is a small tree well-known for its usage in traditional Chinese medicine. It is primarilyfound in India, Sri Lanka, and China. It produces tasty fruit blooms in April and ripens in late June. "MorKoorangee" is the local name given to the tree by the hill tribes.

PHYTOCHEMICAL PROFILE OF CLAUSENA DENTATA

Family: Rutaceae

Clausena dentata is chemically rich and known for producing diverse secondary metabolites, particularly coumarins and carbazole alkaloids, which are characteristic of the genus Clausena.

Major Phytochemical Classes and Constituents

1. Coumarins (Major Bioactive Group)

Coumarins are the most prominent compounds contributing to the plant's pharmacological activity.

- Dentatin
- Clausenidin
- Nordentatin
- Xanthoxyletin
- Umbelliferone

Biological significance

- Anti-inflammatory, anticancer, antioxidant, antimicrobial.

2. Carbazole Alkaloids

- These nitrogen-containing compounds show strong biological activities.
- Clausine
- Clauszoline
- Girinimbine
- Mahanine

Biological significance

- Anticancer, neuroprotective, antimicrobial.

3. Flavonoids

- Quercetin
- Kaempferol
- Rutin

Biological significance

- Antioxidant, anti-inflammatory, hepatoprotective.

4. Terpenoids and Essential Oils

- Identified mainly by GC–MS analysis.
- Limonene
- β-Caryophyllene
- α-Pinene
- Sabinene
- Biological significance:
- Antimicrobial, anti-inflammatory, insecticidal.

5. Phenolic Compounds

- Gallic acid
- Ferulic acid
- Caffeic acid
- Biological significance
- Free-radical scavenging, protective against oxidative stress.

Pharmacological Activities of *Clausena dentate*

1. **Anti-inflammatory activity**

- Extracts show inhibition of inflammatory mediators.
- Supports its traditional use in **rheumatism and swelling**.

2. **Analgesic (pain-relieving) activity**

- Leaf and root extracts demonstrate **reduction in pain responses** in experimental models.

3. **Antimicrobial activity**

- Exhibits **antibacterial and antifungal effects** against several pathogens.
- Attributed mainly to carbazole alkaloids and essential oils.

4. Antioxidant activity

- Flavonoids and phenolic compounds help **neutralize free radicals**.
- Suggests protective effects against **oxidative stress**.

5. Antipyretic activity

- Some studies report **fever-reducing effects**, supporting traditional use.

6. Insecticidal / larvicidal activity

- Essential oils show activity against **mosquito larvae**, of pharmacological and public-health interest.

7. Cytotoxic / anticancer potential (experimental)

- Certain isolated carbazole alkaloids show **cytotoxic effects in vitro**.
- This is **preliminary research**, not a clinical use.

Limitations

- Most studies are **in vitro or animal-based**.
- **No established clinical dosage** or standardized formulation.
- Requires further **toxicological and clinical evaluation**.

Traditional Medicinal Uses

Different parts of the plant (leaves, roots, bark) are used.

1. Digestive health

❖ Leaves are traditionally used to help with **indigestion, stomach pain, and loss of appetite**.

❖ Sometimes used as a **carminative** (to reduce gas).

2. Anti-inflammatory & pain relief

❖ Leaf and root preparations are used for **joint pain, swelling, and rheumatism**.

❖ Applied externally for **muscle aches**.

3. Antimicrobial uses

❖ Traditionally used to help treat **skin infections, wounds, and ulcers**.

❖ Studies suggest it contains compounds with **antibacterial and antifungal** activity.

4. Fever and infections

- Used in folk medicine to help reduce **fever** and support recovery from **minor infections**.

5. Insect-repellent properties

- Leaves are sometimes used to **repel insects** due to their strong aroma and essential oils.

6. Antioxidant properties

- The plant contains **carbazole alkaloids and flavonoids**, which are known for **antioxidant activity**.

Flavonoids in Clausena dentata

Flavonoids are indeed present in Clausena dentata extracts, particularly ethanolic bark extracts, alongside other phytochemicals like coumarins. Studies, such as those in Pakistan Journal of Pharmaceutical Sciences, confirm their detection and link them to hepatoprotective effects in rat models of acetaminophen-induced liver damage. These compounds drive antioxidant activity by scavenging free radicals and reducing oxidative stress, a pattern seen across the Clausena genus.

Pharmacological Activities Supported by EvidenceYour summary aligns well with available research. Here's a refined overview of flavonoid-linked activities in C. dentata, drawing from cited sources and genus-wide data.

Antioxidant

Flavonoids neutralize reactive oxygen species (ROS) and boost endogenous defenses like superoxide dismutase. While direct assays on C. dentata are limited, related species like C. excavata show strong DPPH radical scavenging.

Anti-inflammatory and Analgesic

Ethanolic extracts reduce paw edema and writhing in mice, inhibiting prostaglandin pathways and COX enzymes—classic flavonoid mechanisms.

Hepatoprotective

Extracts lower ALT/AST levels and histopathological damage in toxin-exposed rats, with flavonoids credited for anti-inflammatory and antioxidant **synergy** Carbazole alkaloids.

Medicinal Uses (Traditional & Potential)

- Historically and in modern research, carbazole alkaloids have been linked to:
- Treatment of **infections** (bacterial and fungal)
- **Inflammatory conditions**
- **Cancer therapy** (as anticancer leads)
- **Neurological disorders**
- **Cardiovascular protection**
- **Metabolic disorders** such as diabetes
- Many of these uses come from traditional medicine and are now being investigated scientifically.

Pharmacological Activities

Anticancer / Antitumor Activity

- Carbazole alkaloids can
- Inhibit cancer cell proliferation
- Induce apoptosis (programmed cell death)
- Interfere with DNA replication and cell cycle
- Examples
- **Mahanine**
- **Girinimbine**
- Studied against breast, lung, colon, and leukemia cancer cell lines.

Antimicrobial Activity

- Effective against
- Gram-positive and Gram-negative bacteria
- Fungi
- Mechanism includes disruption of microbial cell membranes and enzyme inhibition
- Useful in combating drug-resistant strains.

Antioxidant Activity

- Scavenge free radicals
- Reduce oxidative stress
- Protect cells from damage linked to aging and chronic diseases.

Anti-inflammatory Activity

- Inhibit inflammatory mediators such as:
- Prostaglandins
- Nitric oxide
- Cytokines
- Potential use in arthritis and other inflammatory disorders..

Neuroprotective Activity

- Some carbazole derivatives protect neurons by:
- Reducing oxidative damage
- Modulating neurotransmitter systems
- Investigated for **Alzheimer's and Parkinson's disease.**

Antidiabetic Activity

- Improve glucose metabolism
- Enhance insulin sensitivity
- Inhibit carbohydrate-digesting enzymes.

Cardioprotective Activity

- Protect heart tissue from oxidative and ischemic damage
- Improve lipid profiles in some experimental models.

Antiviral Activity

- Certain carbazole alkaloids show activity against:
- HIV
- Hepatitis viruses
- Act by inhibiting viral enzymes or replication.

Examples of Important Carbazole Alkaloids

Alkaloid	Plant Source	Key Activities
Mahanine	*Murraya koenigii*	Anticancer, anti-inflammatory
Girinimbine	*Murraya koenigii*	Anticancer, antioxidant
Clausine	*Clausena* spp.	Antimicrobial

Importance in Drug Development

- Serve as **lead compounds** for synthetic drug design
- Carbazole nucleus is used in developing

- Anticancer drugs
- CNS-active agents
- Antimicrobial drugs.

1. Chemical Composition

- The essential oil from *Clausena dentata* leaves typically contains a mix of **monoterpenes and sesquiterpenes**, such as

- **Sabinene**
- **β-Caryophyllene oxide**
- **Borneol**
- **Biofloratriene**
- **β-Bisabolol**,

2. ANTI CANCER

- In vitro studies show that *C. dentata* leaf essential oil exhibits **concentration-dependent cytotoxicity** against

- **HeLa cervical cancer cells**
- **NIH-3T3 normal fibroblasts**

Pharmacological Effects

Though not specific to *C. dentata*, essential oils from other *Clausena* plants have demonstrated

- **Antioxidant** and **anti-inflammatory effects** (e.g., inhibition of free radicals and inflammatory enzymes)
- **Anti-diabetic actions** (like α-glucosidase inhibition) in related species

These activities are often linked to shared terpenoids or phenolic compounds present in essential oils of this genus.

Pharmacological Activities

Activity	Evidence Source
Cytotoxic / Potential anticancer	*In vitro* assays with HeLa and NIH-3T3 cells
Larvicidal (mosquito control)	Bioassays against *Aedes aegypti* larva
Mosquito repellent	Human repellent tests (traditional use)
Possible antimicrobial	Inferred from genus-wide data (*Clausena* species)
Antioxidant / anti-inflammatory (genus)	Activities seen in essential oils of other *Clausena* spp

Clausena dentata contains various secondary metabolites, with carbazole alkaloids being principal components of the genus. Specific examples isolated from different parts of the plant and closely related species include:

- **Clausenine**
- **Mukonal**
- **Clausenol**
- **Clausine B**
- **Mupamine** (a pyranocarbazole alkaloid)
- These alkaloids and other compounds contribute to a wide range of traditional and pharmacologically validated uses of *C. dentata* as a medicinal plant.

The percentage of biological activities of the material of clausena genus.

Biological activity	Plant species					
	C.excavate (%)	C.anisata (%)	C.lanisum (%)	C.harmandian (%)	C.dendata (%)	C.indica (%)
Anti-cancer	69	32	26	29	19	13
Anti-microbial	56	25	12	22	05	00
Anti-oxidant	66	19	21	22	12	12
Anti-fungal	18	12	00	09	03	00
Anti-viral	22	11	00	08	11	02
Anti-diabetic	34	00	02	05	00	08
Anti-diarrhoeal	33	03	11	00	23	07
Anti-malerial	45	22	33	00	11	10
Immunomodulatory	51	13	21	14	09	11
Larvicidal	44	06	00	17	08	04
Antiplasmodial	27	04	09	02	02	00
Anti-inflammatory	48	15	00	16	00	03

Anti inflammatory medicinal use and biological activity of clausena dentate

Clausena dentata exhibits significant anti-inflammatory and analgesic (pain-relieving) biological activity, which provides scientific support for its traditional medicinal uses. The anti-inflammatory effects have been observed in scientific studies, and the activity is linked to the presence of specific phytochemicals.

Traditional Medicinal Uses

Various parts of the C. dentata plant have been used in traditional medicine for treating conditions associated with pain and inflammation.

Wounds and Sprains

The stem bark is traditionally used in veterinary medicine as a treatment for wounds and sprains.

Sores and Ulceration

The pounded root and leaves are used as a poultice for sores, including ulcerations of the nose.

Bowel Complaints/Colic

A decoction of the roots or boiled flowers and leaves is drunk for bowel complaints and colic.

Other Uses

The leaves are also traditionally used to cure cold, abdominal pain, malaria, and dysentery, while the expressed juice is used for coughs and as a vermifuge in some regions.

The Healing Power of Clausena dentata

A Simplified Overview The Clausena plant family—specifically Clausena dentata—is a natural pharmacy. Packed with powerful compounds like coumarins, alkaloids, and essential oils, these plants are being studied for their impressive ability to fight disease and manage pain.

Here is a breakdown of what the science says this plant can do.

✓ **Fighting Cancer (Cytotoxicity)]**

○ Research suggests that the essential oils found in Clausena dentata may have anti-cancer properties.

❖ ● Lab Results: In laboratory settings (in vitro), the oil has shown the ability to kill or inhibit specific cancer cells, such as cervical cancer cells (HeLa).

❖ ● The Cause: This activity is likely due to terpenoids and coumarins, compounds known to disrupt cancer cell growth and trigger cell death.

○ Battling Bacteria and Bugs (Antimicrobial)

❖ This plant has a strong defense system against pathogens.

❖ ● Antibacterial: Extracts from the bark (using solvents like methanol or hexane) have proven effective against dangerous bacteria, including Vibrio cholerae (cholera) and Pseudomonas aeruginosa.

❖ ● Insect Control: It's not just for humans; nanoparticles made from the leaves are effective against disease-carrying pests, such as mosquito larvae.

- Relieving Pain and Swelling (Analgesic & Anti-inflammatory)

❖ Before modern pills, nature provided pain relief. Clausena dentata appears to act similarly to anti-inflammatory drugs.

❖ ● Evidence: Animal studies have shown that bark extracts can significantly reduce pain responses and decrease swelling (edema).

❖ ● How it works: The plant's alkaloids and coumarins likely block the chemical pathways in the body that cause inflammation and pain signals.

- The Chemical "Secret Sauce"

❖ Why is this plant so effective? It comes down to its rich chemical profile. While related species show immune-boosting and anti-malaria potential, Clausena dentata relies on three main groups

❖ ● Coumarins (e.g., dentatin): The heavy hitters for fighting cancer and microbes.

❖ ● Carbazole Alkaloids: Known for a wide range of biological activities

❖ ● Terpenoids: Found in the essential oils, these provide pain relief and antiseptic properties.

CONCLUSION

Clausena dentata emerges as a pharmacologically significant medicinal plant, bridging the gap between ethnomedicinal tradition and modern scientific validation. Its therapeutic efficacy is underpinned by a diverse phytochemical profile, most notably coumarins and carbazole alkaloids, complemented by flavonoids, phenolics, and terpenoid-rich essential oils. Empirical studies have corroborated a broad spectrum of bioactivities—including antioxidant, antimicrobial, antifungal, antiviral, anti-inflammatory, analgesic, cytotoxic, and larvicidal effects—thereby providing a rigorous scientific rationale for its traditional utilization in managing pain, inflammation, infections, and gastrointestinal disorders. Comparative analyses within the Clausena genus highlight distinct bioactivity profiles: while C. excavata is renowned for potent anticancer and antioxidant properties, C. dentata exhibits particularly significant anti-inflammatory and analgesic activities. This specific efficacy supports its historical application in treating rheumatism, sprains, and colic. However, despite promising preclinical data, the translation of these findings remains constrained by a lack of mechanistic depth, standardization protocols, and comprehensive toxicity profiling. The

current absence of clinical trials and validated safety data presents a critical barrier to commercial and clinical adoption. Consequently, future research trajectories must prioritize the isolation of novel bioactive compounds, the elucidation of molecular mechanisms, long-term toxicological assessments, and controlled clinical trials. Such rigorous scientific advancement is essential to transform Clausena dentata from a traditional remedy into a standardized, safe, and effective phytopharmaceutical or nutraceutical candidate. Ultimately, while the plant represents a promising therapeutic reservoir, its integration into modern healthcare frameworks relies on systematic and robust validation.

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