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Pharmacology and Phytochemistry of *Caryota mitis*: A Brief Review

Sandesh Kumar Pattanaik[1], Sudipta Jena[2], Diptirani Rath[1]*

[1]Department of Pharmacology, School of Pharmaceutical Sciences, Siksha 'O' Anusandhan Deemed to be University, Bhubaneswar, Odisha, India,[2]Centre of Biotechnology, Siksha 'O' Anusandhan Deemed to be University, Bhubaneswar, Odisha India. *Corresponding Author's Email: diptiranirath@soa.ac.in

Abstract

Arecaceae have more than 2500 species and are widely distributed in tropical, subtropical areas. *Caryota mitis* (*C. mitis*), popularly known as Fishtail plants, has been documented in ethno pharmacology in various countries and regions. In ancient times, people used these plants to treat diseases such as headaches, gastrointestinal-associated diseases, snake bite poisoning, wounds, hair loss, diarrhoea, inflammation, tooth ailments, lesions, bronchitis, emetic, etc. Due to its pharmacological properties, *C. mitis* has recently garnered considerable global interest as a significant medicinal plant. Thus, this study systematically summarized ethnopharmacology, phytochemistry, pharmacology activity and potential uses of this plant. The different databases are searched till August 2024, including Scopus, Web of Science, PubMed, Science Direct, Research Gate, and Google Scholar using "*Caryota mitis* L." OR "Fishtail Plant" with "Pharmacology," "Phytochemistry," "Toxicology," and "Ethnopharmacology" and collects relevant information on *C. mitis*. The current phytochemical investigation suggests that *C. mitis* is rich in alkaloids, flavonoids, terpenoids, phenolic, and fatty acids. The purslane extracts, or compounds, exhibited various pharmacological activities such as anti-inflammatory, anti-bacterial, anti-fungal, antitumor, antiplatelet, anti-asthmatic, and antioxidant properties. Based on the review, *C. mitis* exhibit a variety of phytochemicals that may be offered and continue to be the focus of future research in treating different diseases. Some preliminary *in-vitro* and *in-vivo* pharmacological studies of *C. mitis* have been demonstrated, while other traditional uses still need to be confirmed by research.

Keywords: Antioxidant, Arecaceae, *Caryota mitis*, Ethnopharmacology, Fishtail Palm, Flavonoids, Pharmacological Potential.

Introduction

Profound history, human civilization has employed plant components in the form of oils and extracts to treat various ailments and diseases. Collecting plant components and utilizing them directly for medicinal purposes are common in traditional practice. These practices are well documented in Ayurveda, Traditional Chinese medicine, and Thai traditional medicine (1-3). As per the World Health Organization (WHO), traditionally used herbal medicinal practices are gaining popularity as a primary therapeutic approach worldwide (4). The growing popularity of ethnomedicine can be attributed to its low cost, minimal risk, and convenient accessibility. Over the past few years, numerous successful medication review programs have been launched, yet 50 % of ethnomedicine examined globally to date (5). Despite the ongoing research, continuous study is needed to find ways to isolate active compounds, explore mechanisms, and develop herbal therapies for various disease elements. These are considered valuable resource alternatives for synthetic pharmaceutical drugs (6, 7). More than 2500 species and 200 genera are in the varied Arecaceae family, widely distributed in tropical and subtropical climates. The Arecaceae (Palms) trees are evergreen plants in South-east and South Asia, including China, Thailand, Myanmar, Philippines, India, and Bangladesh (8). Palm species and their heartwoods, spadix, sap, coat, seed, fiber, endocarp, fruits, branches, roots, barks, and leaves are well known for their therapeutic and nutritional values. For their sugary taste, they are also used to prepare wine. The trunk is a rich starch source, traditionally used in flour in India, China, Thieben, and Bangladesh. It is used in many therapeutic applications such as parasite infection, kidney injuries, diabetes, arthritis, etc. (8). *Caryota mitis* L. (*C. mitis*) is popularly known

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as the fishtail plant found in public parks and gardens. This plant is native to Southeast Asia and North America. Leaves are distinctive fishtail-like shapes with asymmetrical edges. This is clumping palm, new shoots emerging from the base. Traditionally, the plant's leaves, stem, fruits, and roots are used to treat asthma, headache, snake bite poising, diarrhoea, diabetes, and emetic and tooth elements (8). Phytochemical studies revealed that *C. mitis* contains major compounds like alkaloids, flavonoids, terpenoids, phenolic, and fatty acids. Despite the ethnopharmacological knowledge and known benefits of phytochemicals, few *in-vitro* and *in-vivo* pharmacological activities have been investigated, providing evidence for their therapeutic potential. However, many traditional uses of *C. mitis* remain unexplored and require further scientific research to confirm their efficacy, safety and mechanism of action. Thus, this study comprehensively reviews the content of different studies on *C. mitis*, starting from botanical aspects and then ethnopharmacological relevance. It also summarises the phytochemicals of *C. mitis* and discusses its pharmacological effects. Lastly, we also discussed the future research direction of this plant. Hence, this study will help to understand the current research progress of *C. mitis* and bridge the gap between traditional knowledge and modern pharmacological validation, ensuring their safe and practical application in healthcare.

Botanical Aspects

C. mitis is a member of the Arecaceae family and is well-known as an ornamental/decorative plant found in parks and private gardens worldwide.

Distribution

The plant instigated across Southeast Asia, including Vietnam, Thailand, Sumatera, Sulawesi, Myanmar, Southeast China, Cambodia, Bangladesh, and India (9).

Taxonomy Classification

Taxonomical classification is presented in Table 1.

Table 1: Taxonomical Classification of *C. mitis* Plant

Binominal name	***Caryota mitis***
KINGDOM	Plantae
PHYLUM	Tracheophyta
CLASS	Equisetopsida,
SUBCLASS	*Magnoliidae*
ORDER	*Arecales*
FAMILY	*Arecaceae*
GENUS	*Caryota*
SPECIES	*Caryota mitis*

Morphological Description

Leaves: The large, bipinnate leaves of *C. mitis* have a harsh taste and no distinct smell. Each secondary axis ends in a complete leaflet, while the main rachis terminates in two leaflets. As illustrated in Figure 1, the leaflets resemble fishtails, characterized by several prominent ribs but lacking a distinct midrib. The upper surface of the leaflets is slightly darker than the lower surface. These leaves grow along a central rachis that branches into subsidiary axes and feels fibrous to the touch (10).

Flower: The blooms of *C. mitis* range from green to yellowish-green when in the shade, transitioning to yellowish, purple, or crimson as they fully open. Male flowers are approximately 10 mm long, while female flowers are smaller, measuring about 5 mm in length (11).

Stem: The stems of *C. mitis* is typically multi-stemmed and can grow up to 10 meters in height. They are upright, cylindrical, and range in diameter from 5 to 15 cm. The upper surface of the stems is a bright green, while the lower surface tends to be pale brown or grey (10).

Fruit: The fruits of *C. mitis* are spherical in shape with approximately 2 cm in diameter. When they are fully mature, they produce one or two dark red to purple seeds (10).

Inflorescence: The plant is classified as homothallic if it simultaneously produces male and female flowers. The basipetal succession is displayed during flowering, with more mature blossoms appearing higher up the stem and smaller buds and blooms farther down. The 70 – 80 cm inflorescence grows from beneath or in between the leaves and droops downward (10).

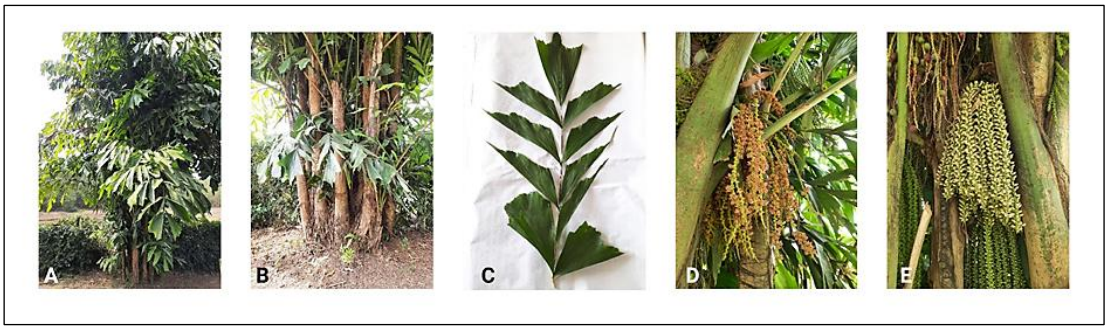

Figure 1: Plant morphology A. *Caryota mitis* tree, B. *Caryota mitis* stem, C. Inflorescence and fruits, D. Leaf of *Caryota mitis*, E. Flower of the plant

Traditional uses and Ethnopharmacology

Plant parts are collected and directly used as medicines, which have been used for thousands of years. These practices are based on indigenous knowledge and cultural beliefs rather than contemporary scientific concepts. This ancient practice is broadly scripted in Ayurveda, Unani, and Traditional Chinese Medicine. *C. mitis* has been used as a folk agent to treat disease elements, including migraine headaches, gastrointestinal-associated diseases, snake bite poisoning, wounds, promoting hair growth, diarrhoea, inflammation, tooth ailments, lesions, bronchitis, emetic, demulcent, diabetes, fever, asthma, rheumatic swellings, Gonorrhoea, and decreased total cholesterol (8, 10-15).

Phytochemical Profile

Palm species contain a variety of primary and secondary metabolites that offer to cure a wide range of disease elements (16). The phytochemical investigation of *C. mitis* revealed that the leaf extracts included varied amounts of alkaloids, flavonoids, Triterpenoids, steroids, fatty acids, and other compounds. The identified compounds are represented in Table 2.

Table 2: Phytochemicals Compound Isolated from *C. mitis*

Classification	Sl. No.	Chemical Component	Chemical Formula	Part of Plant	References
Alkaloids	1	Nicotine	$C_{10}H_{14}N_2$	Leaves	(17)
	2	Methyl N-methyl piperidine-3-carboxylate	$C_8H_{15}NO_2$	Leaves	(17)
	3	Propyl N-methyl piperidine-3-carboxylate	$C_{10}H_{19}NO_2$	Leaves	(17)
	4	Ethyl N-methyl piperidine-3-carboxylate	$C_9H_{17}NO_2$	Leaves	(17)
	5	Guvacoline	$C_7H_{11}NO_2$	Leaves	(17)
	6	Ethyl N-methyl-l, 2,5,6-tetrahydro-pyridine-3-carboxylate	$C_9H_{15}NO_2$	Leaves	(17)
	7	Arecoline	$C_8H_{13}NO_2$	Leaves	(17)
	8	Ethyl nicotinate	$C_8H_9NO_2$	Leaves	(17)
Flavonoids	9	Quercetin	$C_{15}H_{10}O_7$	Leaves	(18, 19)
	10	Kaempferol	$C_{15}H_{19}O_6$	Leaves	(18, 19)
	11	Astragalin	$C_{21}H_{20}O_{11}$	Leaves	(18)
	12	Isoquercetrin	$C_{21}H_2O_{12}$	Leaves	(18)
	13	Nicotiflorin	$C_{27}H_{30}O_{15}$	Leaves	(18)
	14	Rutin	$C_{27}H_{30}O_{16}$	Leaves	(18)
	15	Catechin hexoside	$C_{21}H_{23}O_{11}$	Leaves	(18)
	16	Catechin	$C_{15}H_{13}O_6$	Leaves	(18)
	17	Quercetin-*O*-sophoroside	$C_{27}H_{29}O_{17}$	Leaves	(19)

Triterpenoids and steroids	18	β-amyrin	$C_{30}H_{50}O$	Leaves	(18)
	19	β-sitosterol	$C_{29}H_{50}O$	Leaves	(18)
Fatty acids	20	Methyl decanoate	$C_{11}H_{22}O_2$	Leaves	(20)
	21	Dimethyl octanedioate	$C_{10}H_{18}O_4$	Leaves	(20)
	22	Methyl dodecanoate	$C_{13}H_{26}O_2$	Leaves	(20)
	23	Dimethyl nonanedioate	$C_{11}H_{20}O_4$	Leaves	(20)
	24	Methyl tridecanoate	$C_{14}H_{28}O_2$	Leaves	(20)
	25	Methyl tetradecanoate	$C_{15}H_{30}O_2$	Leaves	(20)
	26	Dimethyl undecanedioate	$C_{13}H_{24}O_4$	Leaves	(20)
	27	Methyl- 4,8,12-trimethyl tridecanoate	$C_{17}H_{34}O_2$	Leaves	(20)
	28	Methyl pentadecanoate	$C_{16}H_{32}O_2$	Leaves	(20)
	29	Methyl-5,9,13-trimethyl tetradecanoate	$C_{18}H_{36}O_2$	Leaves	(20)
	30	Methyl-9-hexadecenoate	$C_{17}H_{32}O_2$	Leaves	(20)
	31	Methyl hexadecanoate	$C_{17}H_{34}O_2$	Leaves	(20)
	32	Methyl-10-heptadecenoate	$C_{18}H_{34}O_2$	Leaves	(20)
	33	Methyl heptadecanoate	$C_{18}H_{36}O_2$	Leaves	(20)
	34	Methyl-11-eicosenoate	$C_{21}H_{40}O_2$	Leaves	(20)
	35	Methyl eicosanoate	$C_{21}H_{42}O_2$	Leaves	(20)
	36	Linoleic acid	$C_{18}H_{31}O_2$	Leaves	(20)
	37	Tetradecanamide	$C_{14}H_{30}NO$	Leaves	(20)
	38	Palmitamide	$C_{16}H_{34}NO$	Leaves	(20)
Others	39	chlorogenic acid methyl ester	$C_{17}H_{20}O_9$	Leaves	(18)
	40	Hexonic acid	$C_6H_{11}O_7$	Leaves	(19)
	41	Quinic acid	$C_7H_{11}O_6$	Leaves	(19)
	42	Iso/Citric acid	$C_6H_7O_7$	Leaves	(19)
	43	Dihydroxybenzoic acid-*O*-hexoside	$C_{13}H_{15}O_9$	Leaves	(19)

Medicinal/Pharmacological Activities

Only a few scientific validations and pharmacological studies have been conducted on *C. mitis.* Reportedly, *C. mitis* shows anti-bacterial, antioxidant, thermolytic properties, anti-fungal, anti-tumour, cytotoxicity activity, anti-inflammatory, anti-asthmatic, analgesic activity, and antipyretic. A summarise the evaluations conducted on the therapeutic efficacy of *C. mitis* is summarized in Table 3 and Figure 2.

Anti-microbial Activity

Bacteria interact with host organisms and are responsible for causing various diseases. They may be exotoxins, endotoxins, antigenic variation, or invasion produced by the bacteria. *Klebsiella pneumoniae* (*Klebsiella sp.*) is responsible for causing pneumonia, urinary tract infections (UTI), sepsis, and liver abscesses—*Escherichia coli* (*E. coli*) causes gastrointestinal tract (GIT) infections and meningitis. *Micrococcus sp*. causes skin infections, and *staphylococcus aureus* (*S. aureus*) is responsible for bone joint infections, pneumonia, and skin infections. Seed oil extract of *C. mitis* shows prominent bactericidal effects against the four bacteria species with a zone of inhibition (ZOI) 12-17 at (minimum inhibitory concentration MIC: 50-100 mg ml -1), 5-11 at (MIC: 25-100 mg ml^{-1}), 4-9 at (MIC: 25-100 mg ml^{-1}) and 4-9 at (MIC: 25-100 mg ml^{-1}). Furthermore, the Oil extract was explored for anti-fungal activity. Where the oil extract of *C. mitis* seed shows resistance against the *Aspergillus niger* (*A. niger)* notable anti-fungal activity against the *C. albicans* with ZOI 12.5-17 at (MIC: 25-100 mg ml^{-1}) (21).Furthermore, the antimicrobial activity of *C. mitis* was explored against bacterial strains such as *E. coli* and *S. aureus* and the fungal strain *C. albicans* using agar well diffusion and microtiter

broth dilution methods. The ethyl acetate fraction exhibited the most potent antibacterial effect against *S. aureus*, resulting in a 20 mm ZOI with MIC 2.5 mg/ml. It also displayed a moderate level of activity against *E. coli*. The n-butanol fraction demonstrated a bactericidal solid effect against both bacterial strains with ZOI 17-19, MIC: 2.5 mg/ml. Meanwhile, *C. albicans*, the n-butanol, and aqueous fractions are more prominent with ZOI 12 mm, with MIC 5 mg/ml against anti-fungal activity (18). In another study, the *C. mitis* leaves were crushed, defatted, and the alkaloids extracted using an acid-base method, tested against *S. aureus*, *E. coli*, and *C. albicans* using diffusion method by utilizing agar and microtiter broth methods to explore the antimicrobial activity. In this study, Ampicillin (10 µg/ml), Gentamicin (5 µg/ml), and Clotrimazole (5 µg/ml) are considered as the reference drug. The n-butanol and alkaloid fraction demonstrated potent antibacterial properties, with 14 to 19 mm inhibition zones and MIC values of 2.5 to 5 mg/ml. The alkaloid fraction exhibited a significant antifungal effect, with a 16 mm inhibition zone and a 2.5 mg/ml MIC (17).

Anti-inflammatory Activity

To investigate the anti-inflammatory activity of *C. mitis* leaf extracts, carrageenan-induced paw edema model. Different fractions of 400 mg/kg were extracted intraperitoneally from other groups of rats. The right hind paw was injected with carrageenan to cause inflammation, and the thickness of the paw was measured after five hours of injection. The data demonstrate that the n-butanol fraction had the least anti-inflammatory effect. In contrast, the aqueous and ethyl acetate fractions had the highest activity levels. The effects begin with 1 hour and continue for 5 hours (10). Furthermore, the anti-inflammatory effect of the methanolic extract of *C. mitis* was examined using the protein denaturation technique. The extract solutions were tested at a 62.5-1000 µg/mL concentration against the diclofenac sodium (1000 µg/mL). The extent of protein denaturation inhibition was quantified by measuring the % using a UV-visible spectrophotometer at a wavelength of 416 nm. The results showed that the extracts effectively and progressively reduced protein denaturation dose-dependently. The findings indicate that the most significant inhibition achieved was 45.45% at a concentration of 1000 µg/mL, which was lower than the inhibition of 85.48% observed with diclofenac sodium. These findings indicate that the extract's anti-inflammatory activities are attributed to secondary metabolites, specifically flavonoids and alkaloids (22).

Analgesic and Anti-Pyretic Activity

C. mitis, the analgesic and antipyretic activity, was explored *in-vivo* models. For antipyretic activity, they plotted yeast to induce hyperthermia in rats; different fractions of extract 400 mg/kg were given and compared against indomethacin (8 mg/kg). The n-hexane and aqueous 400 mg/kg fractions exhibited significant antipyretic effects, with the maximum effect observed at the 3rd-hour post-administration, which continued until the 5th hour. Furthermore, the analgesic effect was explored in mice models induced by acetic acid and tested against ketoprofen (10 mg/kg) to compare the efficacy of plant extracts. The ethanolic extracts and ethyl acetate fractions at a dose of 400 mg/kg exhibited a high percentage of inhibition in writing (10).

Antioxidant Activity

The Ferric Reducing Antioxidant Power (FRAP) assay quantifies the capacity of the sample medication to reduce ferric ions to ferrous ions, hence measuring its reducing power. That indicates the antioxidant potential. In contrast, 2,2-diphenyl-1-picrylhydrazyl (DPPH assay) measures the radical scavenging potential of the sample. In 2020, Dawood and his team investigated the oil extract from the fruits of *C. mitis* by using the two above assays. The oil extract shows the FRAP value of 0.0707 µmol at 2000 ug/ml. additionally, the DPPH assay shows notable concentration-dependent scavenging activity with inhibition of 79.86 % at 2000 µg/ml. The author claimed that the presence of polysaccharides in fruits contributes to the antioxidant effect (23). In addition, the DPPH assay is carried out to assess the antioxidant properties of the leaf extract. The results indicate that the ethanolic extract quenched free radicals effectively with a 98.47 % inhibition at 100 µg/ml concentration and an EC50 value of 22.5µg/ml. The author also suggested flavonoids, quercetin, and kaempferol derivatives support the antioxidant activity (19). Moreover, the antioxidant properties of *C. mitis* have been evaluated in a study using DPPH assay. The

findings showed that the plant extracts and fractions, particularly the ethyl acetate, quercetin-3-O-β-D-glucoside, and rutin, exhibit extremely strong antioxidant activity when compared to ascorbic acid as a reference standard (24)

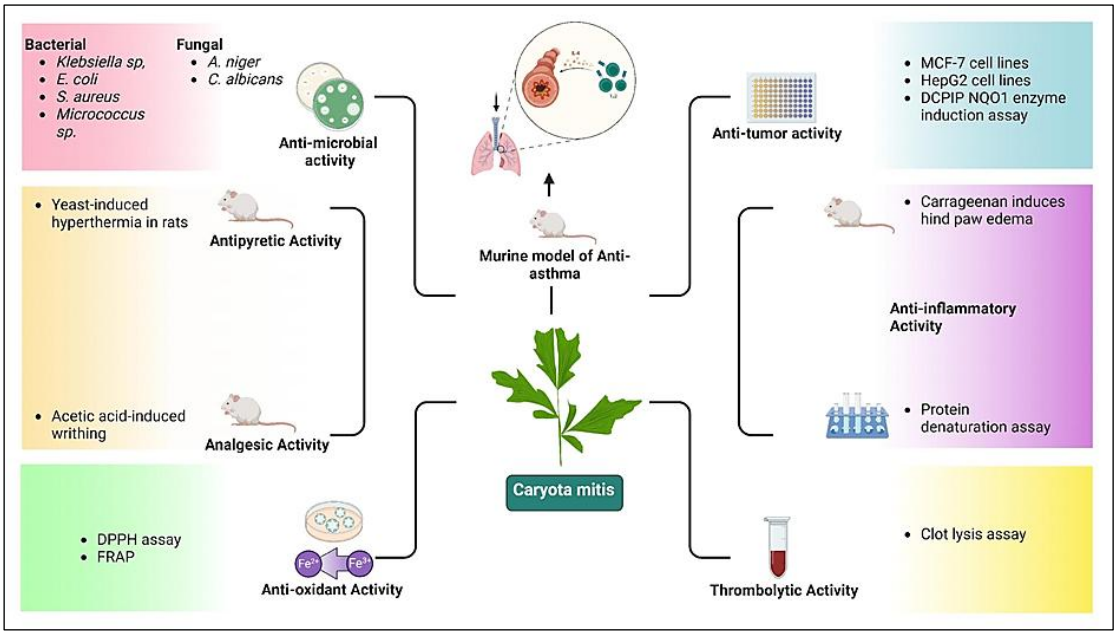

Figure 2: A comprehensive visual representation of the pharmacological activities of *C. mitis*

Figure 2 highlights it's anti-microbial (anti-bacterial and anti-fungal), anti-tumor, anti-inflammatory, antipyretic, analgesic, antioxidant, and thrombolytic effects, along with its role in reducing asthma-related symptoms in murine models.

Thrombolytic Activity

Various pathological conditions trigger thrombosis formation. This thrombosis formation leads to blocking the blood flow into the heart muscle, leading to myocardial infarction. This can be functioning by the blood clotting system. So, there is a need to explore the thrombolytic activity. The methanolic extract *C. mitis* was analyzed using a clot lysis assay. The clots were exposed to 100 µL of methyl extract, streptokinase as a positive control, and distilled water as a negative control at 37 °C for 90 minutes. The *C. mitis* extract demonstrated a notable clot dissolution rate of 24.29 % compared to 75.35 % achieved by streptokinase and 3.78 % achieved by distilled water. Flavonoids and phenolic substances achieve notable thrombolytic action, which disrupts platelet activation (22).

Cytotoxicity Activity

The brine shrimp lethality assays carried out the cytotoxicity study, and the cytotoxicity of *C. mitis* methanolic extract was determined. After developing, nauplii of Artemia salina shrimp were treated with different extract solution doses ranging from 31.25 to 1000 µg/mL. The positive control was vincristine-sulfate (1.63µg/mL). Following 24 hours, the death rate was noted, and the LC50 value for *C. mitis* was found to be 550.57 µg/mL, showing modest toxicity. The Finding also suggested that the cytotoxic activity is likely due to the presence of alkaloids (22).

Antitumor Activity

The antitumor activities of the *C. mitis* plant were explored by Dawood H. and their team in 2020. The authors isolated crude heteropolysaccharides from its fruits and investigated through the *in-vitro* model, such as HepG2 and MCF-7 cell lines and 5-Flurouracil used as a standard drug. The polysaccharide obtained from *C. mitis* exhibited concentration-dependent antitumor effects with IC50 values of 13.6µg/ml and 46.4µg/ml for HepG2 and MCF-7 cells (23). NQO1, a carcinogenesis marker, is a detoxifying enzyme that plays a crucial role in Phase II, detoxifying quinones and their derivatives. A study of the anti-cancer activity of *C. mitis* leaf extract in-vitro on murine hepatoma cell line Hepa-1c1c7 focuses on NQO1 enzyme induction. Different leaf extract fractions were explored, and it was indicated that the petroleum ether extracts exhibited significant

enzyme activity and showed a 2.75-fold increase over the control. This finding was further supported by the Western blot analysis, which confirmed the inducing activity of extracts concentration of 100 µg/mL (20). Furthermore, the chemo-preventive activity of plant extract was investigated through DCPIP assay in Hepa-1c1c7 cell culture in-vitro to observe the induction of phase II cyto protective enzyme NQO1. The results show that the NQO1 enzyme induction improved 4.5 times compared to the vehicle group, indicating that *C. mitis* is a promising chemo-preventive action (19).

Antiallergic and anti-asthmatic

Polylactic co-glycolic acid (PLGA) loaded *C. mitis* extracts nanoparticle (NP) shows promising effects against allergic asthma. In 2013, Xiao and his group explored the adjuvant for asthma in a murine model in BALB/c mice. In this study, different parameters are used to examine the activity. The PLGA-loaded extract mitigates the airway hyper responsive assay. Furthermore, it was also seen that the PLGA-loaded Extracts induce IgG and IgG2a antibodies and inhibit IgE antibodies. The cytokines assay reveals that it suppresses the IL4 expression and increases the expression of IFN-gamma and IL10 (25).

Table 3: Summary of Pharmacological Activities of *C. mitis* Extracts

S. No	Pharmacological Activity	Plants Parts	Dose	Experimental Methods		Outcomes	References
				in-vitro	***in-vivo***		
1	Anti-fungal activity	Leaves	20 mg/ml	Agar plate assays against *C. albicans* and Clotrimazole (5 µg/ml) as the positive control	-	Alkaloid fractions show potent anti-fungal activity against *C. albicans* with ZOI 16 mm, MIC 2.5 mg/ml.	(17)
		Leaves	5 mg/ml	Agar well diffusion against *C. albicans* and Clotrimazole (5µg/ml) as positive control	-	N-butanol and aqueous fractions show potent anti-fungal activity with ZOI 12 mm, MIC- 5 mg/ml.	(18)
		Fruits	25-100 mg ml^{-1}	Agar well diffusion against the *C. albicans* and *A. niger* and Clotrimazole (10 mg ml^{-1}) as referenced drug	-	Seeds oils extracts show significant show resistance against *A. niger* and show significant concentration dependant anti-fungal activity against *C. albicans* ZOI 12.5-17 MIC 25- 100 mg ml^{-1}	(21)
2	Anti-bacterial activity	Leaves	20 mg/ml	Agar plate assays against the	-	N-butanol and alkaloid fraction show robust	(17)

				S. aureus and *E. coli*. Ampicillin (10 µg/ml) and Gentamicin (5 µg/ml) are the standrad drug.		bactericidal activity against *S. aureus* and *E. coli*, having ZOI 17-19 mm and 14-18 mm, MIC 2.5 mg/ml and 5 mg/ml.	
		Leaves	2.5 - 5 mg/ ml	Agar well diffusion against *S. aureus* and *E. coli*. Ampicillin (10µg/ml) and Gentamicin (5µg/ml) as standard drug	-	Significant bactericidal activity against *S. aureus* and *E. coli* is demonstrated by the N-butanol fraction, ZOI 17 mm and 14 mm, with MIC 2.5 mg/ml and 5 mg/ml. Ethyl acetate fraction shows strong bactericidal against the *S. aureus* ZOI 20 mm, MIC 2.5 mg/ml and moderate against the *E. coli* ZOI 11 mm, ZOI 5mg/ml.	(18)
		Fruits	25 - 100 mg ml-1	Agar wall diffusion against the *E. coli, S. aureus, Klebsiella sp., Micrococcus sp.* And Gentamicin (10 mg ml^{-1}) as the positive control	-	Seed oils extract shows activity against all four bacteria with ZOI *Klebsiella sp*. 7-12 mm, *E. coli* 5-18 mm, Micrococcus sp. 4- 10 mm, and *S. aureus* 4-9 mm.	(21)
3	Anti-inflammatory	Leaves	400 mg/ kg	-	Carrageenan induces hind paw edema, and Indomethacin 8mg/kg is a standard	Aqueous fraction shows a robust anti-inflammatory effect, beginning with 1 hr to 5 hrs. Where n-butanol shows the most	(10)

					drug.	minor activity.	
		Leaves	62.5 - 1000 µg/ mL	Protein denaturation assay compared against the Diclofenac (1000 µg/mL)	-	The extract shows concentration dependant inhibition of the protein, and % of inhibition lies between (6.06-45.45 %)	(22)
4	Antipyretic Activity	Leaves	400 mg/ kg	-	Yeast-induced hyperthermia in rats and Indomethacin 8 mg/kg as standard drug	n-hexane and aqueous fractions show significant antipyretic activity. The activity of the effect reached its maximum at 3 hrs and continued till 5 hrs.	(10)
5	Analgesic Activity	Leaves	400 mg/ kg	-	Acetic acid-induced writhing in mice and Ketoprofen (10 mg/kg) as a standard drug.	Ethanolic extract and ethyl acetate extract show a higher percentage of analgesic activity.	(10)
6	Anti-oxidant Activity	Leaves	100 µg/ ml	DPPH assay	-	Ethanolic extract shows significant anti-oxidant activity with 98.87 % inhibition with EC50 22.5 µg/ml.	(19)
		Fruits	250 - 2000 µg/ ml	DPPH	-	Oil extract resulted in a concentrate-dependent anti-oxidant activity with inhibition of 79.86 % at 2000 µg/ml with IC 50 422.11 µg/ml.	(23)
			250 - 2000 µg/ ml	FRAP	-	The oil extract shows anti-oxidant activity with an FRAP value of 0.0707	
		Leaves	62.5 µg/ ml^{-1} mg/ ml	DPPH assay	-	The ethyl acetate fraction shows the highest scavenger activity compared to the ascorbic	(24)

						acid.	
7	Thrombolytic Activity	Leaves	100 µL	Clot lysis assay	-	The plant extracts show significant clot lysis activity with a percentage of 24.29 %	(22)
8	Cytotoxicity Activity	Leaves	31.25-1000 µg/mL	Brine shrimp lethality bioassays against the vincristine sulfate.	-	The methanolic extract decreased mortality with lower LC50-550.57 µg/ml concentrations.	(22)
9	Antitumor Activity	Leaves	100 µg/ml	DCPIP NQO1 enzyme induction assay in Hepa-1c1c7	-	Ethanolic extract shows promising anti-tumor activity via induction of NQO1 enzyme 4-5 fold compared to the control.	(19)
		Leaves	100 µg/ml	induction assay in Hepa-1c1c8	-	Petroleum ether shows promising chemo-preventive activity via NQO1 enzyme induction with 2.75 times than the control.	(20)
		Fruits	6.25 - 100 µg/ml	MCF-7 cell lines tested against the 5-fluorouracil	-	Concentrate-dependant antitumor activity with IC 50 value of 46.4 µg/ml	(23)
			6.25 - 100 µg/ml	HepG2 cell lines tested against the 5-fluorouracil	-	Concentrate-dependant antitumor activity with IC 50 value 13.6 µg/ml	
10	Anti-Allergic Asthma	-	50 µg	-	Murine model of allergic asthma BALB/c mice	↓ IL4, ↓ IgE, ↓ Th2 expressions ↑IFN-γ, ↑ IL10, ↑ IgG, ↑ IgG2a, ↑ Th1 ↓ airway hyper responsiveness	(25)

Toxicity Study and Adverse Effects

C. mitis is used in traditional medicine. Although, the safety needs to be assessed. The acute toxicity test of different extracts of *C. mitis* leaves was performed using the method proposed by D Lorke. Eighteen albino mice, split into six groups of three mice each, received intraperitoneal doses of the various fractions of *C. mitis* leaf extract at 100 to 5000 mg/kg. For six and twenty-four hours, the toxicity and mortality indications were noted. No dose-related mortality or side effects were recorded, and no targeted organ was identified (10).

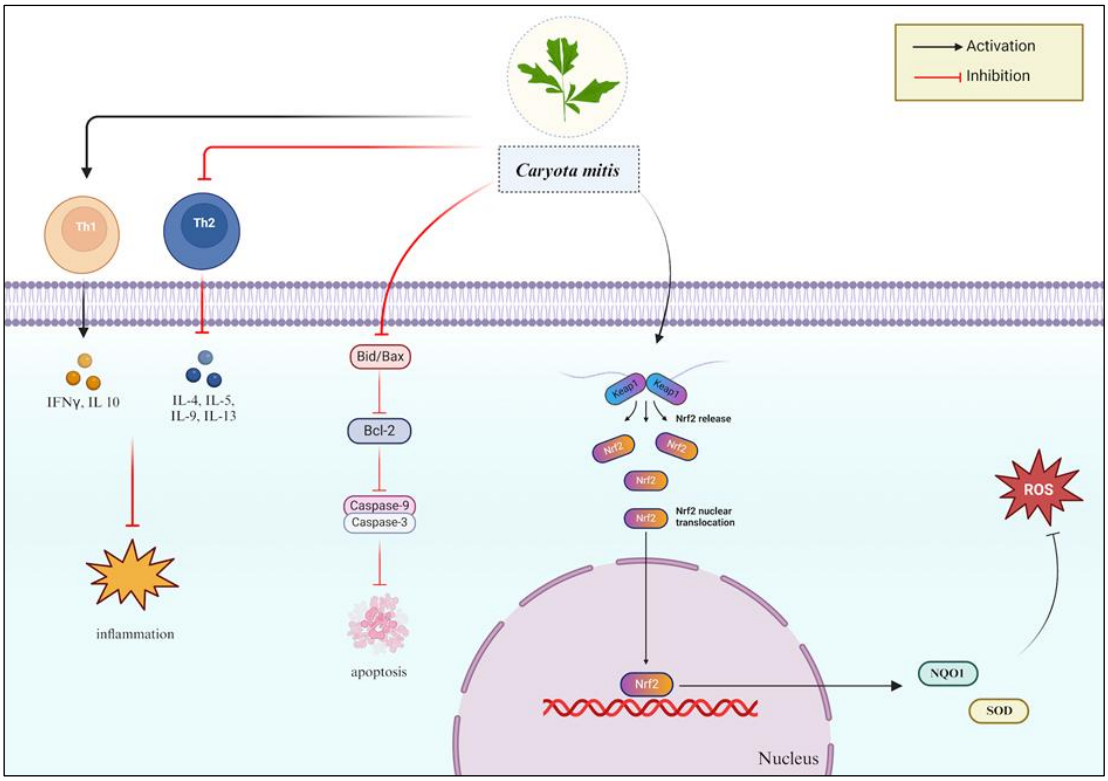

Figure 3: Possible Mechanism Representation of Anti-Inflammatory and Antioxidant of *C. mitis*

Figure 3 shows, *C. mitis* modulate Th1 and Th2 immune responses and inhibit inflammation. It may also regulate the apoptosis through Bid/Bax and caspase pathways. *C. mitis* activate the Nrf2-Keap1 pathway to counter oxidative stress by promoting the expression of antioxidant enzymes like NQO1 and SOD.

Discussion

C. mitis is a valuable medicinal resource with a noteworthy heritage in history. It is widely utilized in medicines, food, and ornamental applications, highlighting its significant economic significance. Our study is a comprehensive review of the ethnopharmacology, phytochemistry, therapeutic activities, and toxicology associated with the plant. The phytochemistry analysis reveals that over 43 chemical compounds have been isolated, where flavonoids, terpenoids, steroids, alkaloids, and fatty acids are the main active components. Our findings outlined that the leaf extracts play a positive role in microbial infection and have analgesic, antipyretic, antioxidant and thrombolytic activities. Although a few studies focused on using fruits/ seeds, it has been reported that the oil extract shows significant activity against microbial infections, anti-tumour and antioxidant activity. Among isolated phytochemicals, the flavonoids in *C. mitis* such as quercetin, kaempferol, astragalin, isoquercetrin, nicotiflorin, rutin, catechin hexoside, catechin, quercetin-O-sophoroside may offer potential therapeutic benefits such as antioxidant, anti-allergic, anti-inflammatory, anti-cancer, anti-diabetic, cardioprotective, and anti-obesity (26, 27). The presence of alkaloids such as Nicotine, Methyl N-methyl piperidine-3-carboxylate, Propyl N-methyl piperidine-3-carboxylate, Ethyl N-methyl piperidine-3-carboxylate, guvacoline, Ethyl N-methyl-l, 2, 5, 6-tetrahydro-pyridine-3-carboxylate, Arecoline, Ethyl nicotinate may offer to treat neurodegenerative disorders, cardiovascular disorders, and inflammatory disorders. Managing various diseases now significantly relies on the fundamental process of anti-inflammatory and antioxidant mechanisms (28). Figure 3 suggests the possible anti-inflammatory and antioxidant mechanism of *C. mitis*. Despite these results, more research is necessary to understand the plant's potential thoroughly. 1; The crude extracts of *C. mitis* exhibit a broad spectrum of biological activities, yet their specific active components have not been fully identified. Bioassay-guided isolation is required to address this, and their mechanisms of action, which remain poorly understood, should

be explored in greater depth through further investigation. 2; most pharmacological activity validation of *C. mitis* has concentrated on preliminary *in-vitro* and *in-vivo* studies; questions have been raised about their clinical relevance. Consequently, future studies should concentrate on an *in-vivo* investigation to offer tremendous evidence potential. 3; There is a dearth of research on other parts of the plants in traditional medicine. Most of the research was carried out on the leaf and seeds of this plant. So, further investigation should be undertaken to utilize other parts in the context of the medicinal and pharmacological aspects. 4; Fruit/Seed extract demonstrates promising early anticancer bioassay results, but in-depth studies like cell migration assay, Annexin V, and cell cycle analysis study remain unaccomplished (19, 20, 23). 5; Pharmacokinetic study is important to understand the relationship between the body's physiology and drugs. This study also mitigates or limits the toxicity and improves the efficacy. There is no such evidence of the pharmacokinetic data to date, so it's urgent to establish the pharmacokinetics data. 6; Toxicology studies are important to find undesirable and adverse side effects. Abd Elhakim and their team validated the acute toxicity study on albino mice and showed no toxicity, mortality, or targeted organ defect (10). However, acute toxicity study only provides information about the short-term effects of substances after a single/multiple exposure with in time frame of 24 to 48 hrs. This only helps to identify typically harmful effects such as irritation, lethality and acute organ damage; it does not account for long-term risk and safety. So, it is necessary to explore further the long-term toxicity and side effects of *C. mitis* through well-designed preclinical studies to ensure their safety, efficacy, and sustainable therapeutic uses.

Conclusion

In summary, *C. mitis* exhibits a significant medicinal and commercial value. Several ethnomedicine studies show that people use *C. mitis* to treat different ailments. In this review, *C. mitis* demonstrates a wide range of pharmacological activities, showcasing its potential as a source of bioactive compounds for therapeutic applications. The leaves exhibit significant anti-fungal, anti-bacterial, anti-inflammatory, analgesic, antioxidant, thrombolytic, cytotoxic, anti-tumour, and anti-allergic asthma activities, while the fruits are particularly effective in anti-fungal, anti-bacterial, antioxidant, and anti-tumour activity. These findings highlighted the versatility of *C. mitis* in addressing various health conditions. However, further studies, including detailed mechanistic investigations, pharmacokinetics, toxicology, safety assessments, clinical validations, and quality control, are essential to exploring and fully utilizing its therapeutic potential for modern medicine.

Abbreviations

C. mitis: *Caryota mitis,* DPPH: 2,2-diphenyl-1-picrylhydrazyl, FRAP: Ferric Reducing Antioxidant Power, MIC: Minimum Inhibitory Concentration, NP: Nanoparticle PLGA: Poly lactic co-glycolic Acid, ZOI: Zone of Inhibition.

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Author Contributions

Sandesh Pattanaik: Conceptualization, writing, review, data curation, writing original manuscript. Sudipta Jena: Review and editing. Diptirani Rath: Conceptualization, review, and editing.

Conflicts of Interest

The author has no financial or other conflicts of interest that might affect the impartiality of this publication.

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Not Applicable.

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