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Traditional uses, phytochemistry and pharmacology of three medicinally potential Curcuma species

Abstract The leaves and rhizomes of certain species of Curcuma are extensively used in Ayurvedic medicine and as traditional remedies against various ailments. Curcuma longa, C. caesia and C. amada are three important species of the genus Curcuma, with wide range of medicinal properties. Biological activities, including antioxidant, antibacterial, and anti-inflammatory properties, as well as presence of several bioactive components have been reported in various discrete literatures. Here we have prepared a comprehensive document to summarize the ethnomedicinal uses, phytochemical constituents, and major pharmacological activities of C. longa, C. amada, and C. caesia, by pulling together the published information from various authentic sources. Keywords: C. longa, C. amada, C. caesia, curcumin, ethnomedicine, bioactivity.

#### 1. Introduction

In India, various plant species are being used medicinally for centuries due to their therapeutic qualities. India is home to numerous traditional medicinal systems including Siddha, Unani, Ayurveda, with a broad diversity of ethnomedicinal resources. Almost all civilizations have history of using plant-based treatments and many nations devote 40% to 50% of their whole health budget to the development of new medications (Fuloria et al., 2022). The Curcuma genus belongs to Zingiberaceae family, is a rhizomatous annual or perennial herb. Linnaeus created the genus Curcuma in his 1753 book Species Plantarum (Sudeepthi et al., 2014). The majority of the 120 species of this genus have already been mentioned in various literatures (Kress et al., 2022). Curcuma longa L., C. aromatica Salisb, C. angustifolia Roxb, C. zanthorrhiza Roxb., C. amada Roxb., C. caesia Roxb. and Curcuma zedoaria (Christm.) Roscoe, are common species that can be found distributed around India and the world. Many species in this genus have significant therapeutic potential that can be used to treat a wide range of medical conditions, including those involving the

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spleen, enlar	ged liver, hepatic disorders, skin conditions, chest	pain,	cough, diabetes, rheumatism, and blood purification (

Saikia and Borthakur, 2010). C.

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longa, commonly known as turmeric or haldi in India, is known for its natural yellow color attributed to the presence of curcumin and its analogs (Siju et al., 2010).

The world's tropics and subtropics are home to the turmeric plant. Although the origin of the plant is unknown, it is said to have started in South-east Asia, most likely in India (Fuloria et al., 2022). The plant is cultivated throughout India. More than 80% of the world's output of turmeric is produced in India, which is followed by China, Myanmar, Nigeria, and Bangladesh. These nations are known

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for producing high-quality turmeric with higher concentrations of essential oils and curcumin (Dei and Ghidoni 2019). Due to its medicinal

qualities, turmeric is highly valued in India (Campbell et al., 2019). C. caesia, also referred to as black turmeric (English) or kali haldi (Hindi), thrives on moist, rich, clayey soils. It came from the Himalayan region, including South East Asia and India. Due to high therapeutic value, C. caesia has been exploited indiscriminately from their natural habitat which has pushed it under the category of critically endangered species (Behar et al., 2014; Kumar et al., 1998). C. amada having physical characteristics with ginger (Zingiber officinale), tastes more like raw mango (Mangifera indica). C. amada is cultivated in a variety of climates, although the hot climate is ideal for the plant's optimum growth. Keeping in view the tremendous pharmacological potentials of Curcuma spp, we have prepared a precise review of the ethnomedicinal uses, phytochemical constituents, and major pharmacological activities of three medicinally potential Curcuma species, viz. C. longa, C. amada, and C. caesia.

C. longa C. amada C. caesia

2. Traditional uses C. longa is used traditionally to treat dental problems, digestive disorders like indigestion, ulcers, and upper abdominal discomfort or pain, as well as to lessen the hallucinogenic effects of hashish and other psychoactive drugs (Fuloria et al., 2022). C. longa is also well-described in Indian material medicine (Dravyaguna Shastra), where Hindu girls apply it daily on their foreheads as part of their beauty routine. One of the most important aspects of Hindu ritual is the application of C. longa paste on the bride (Paranjpe and Pranjpe, 2001). Tribal women from Assam apply a fresh rhizome paste to treat skin infections as well as to brighten their skin. C. longa helps to lower blood clotting and blood sugar level (Zhang et al., 2013). Turmeric powder mixed with calcium hydroxide is indeed a popular home remedy for treating sprains and swelling induced by wounds that can be applied directly to the injury site (Fuloria et al., 2022). Numerous species in this genus are valuable as medicines, dyes, and spices. The oldest healthcare system in India, Ayurveda, attributes numerous benefits to C. amada rhizomes as a carminative, digestive, stomachic, demulcent, vulnerary, febrifuge, diuretic, expectorant, anti-inflammatory, appetizer, alexeteric, antipyretic, aphrodisiac, and laxative (Warrier, 1993).

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Additional health benefits of C. amada including bioactivity against biliousness, itching, asthma, and inflammation due to injuries

were reported (Sastri, 1950).

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The C. amada rhizome's effectiveness against inflammation in the mouth and ears, gleet, ulcers on the male genitalia, scabies, lumbago and stomatitis

have been documented in numerous reports (Kirtikar and Basu, 1984; Hussain et al., 1992; Warrier et al., 1994). The herbal systems of Ayurveda, Unani, and Siddha have documented C. caesia as a medicinal herb (Ranemma and Reddy, 2017). The fresh leaves of C. caesia are eaten directly or given as a drink to treat cough (Awang-Kanak et al., 2018). It is mixed with milk or honey to be consumed twice daily for treatment of infertility, irregular menstrual cycle, and weakness and to induce longevity (Verma et al., 2010). Bites from snakes or scorpions can also be treated with rhizome paste of C. caesia (Bhardwaj et al., 2023). During marriage and engagement rituals, tribal women use powdered C. caesia rhizome as a face mask to enhance beauty (Paliwal et al., 2011). Crushed fresh rhizome is applied as a paste for strains and bruises and as a migraine remedy (Sahu and Saxena, 2018). Additionally, it is eaten orally with water to treat bloating and stomach pain (Sahu and Saxena, 2018). An extract made from dried rhizomes is consumed for asthma treatment (Pandey and Lal, 1999).

#### 3. Phytochemistry

From 32 Curcuma spp. 719 components, including terpenoids, flavonoids, phenylpropene derivatives, alkaloids, diphenylalkanoids, steroids, and other substances, have so far been extracted and identified (Sun et al., 2017). Over 235 phytoconstituents, mostly polyphenols and terpenoids, were discovered in the rhizome (Table 1). The most prevalent polyphenols are curcuminoids, which are composed primarily of curcumin (80%). There are 14 more ingredients in addition to the 109 sesquiterpenes, 68 monoterpenes, 22 diarylheptanoids and diarylpentanoids, 8 phenolics, 5 diterpenes, 4 sterols, 3 triterpenoids, and 2 alkaloids (Fuloria et al., 2022). Table 1: Qualitative phytochemical evaluation of C. longa, C. amada and C. caesia (Borah et al., 2016 ; Eze-Steven et al., 2021 ; Grover et al., 2021 ; Hait and Deepal., 2018 ; Sutar et al., 2020 ; Ysdav and Saravanan, 2019). Plant Extraction solvent Alkaloid Flavonoid Saponin Tannin Glycosides Terpenoids Phenol Steroid C. longa Methanol + + + + + +

Ethanol + - + + + + - -Acetone + + + + + + + -Ethyl acetate + + + + + + + + Chloroform - - + - + + - + Hydroalcohol + + + + + + + + C. amada Methanol - + + - - + - + Ethanol + + + + + + + + +Ethyl acetate - + - + - + - + Chloroform - - - + - + - + Aqueous - + + + - + - -Petroleum ether + - + + - + - +Acetone + + + + + + + - C. caesia Metanol - + + + + + + + Ethanol + + + + + + NA -Ethyl acetate - + - NA - NA - NA Chloroform - + - + + + - + Aqueous + - + + + + - - (+) Indicates 'Presence'; (-) Indicates 'Absence' 4. Pharmacological activities

4.1 Antioxidant activity Antioxidants shield the body from free radical damage. Curcumin and its three derivatives (dimethoxy curcumin, bisdemethoxycurcumin, and diacetyl curcumin) were reported for their antioxidant properties (Faizal et al., 2009). The curcumin component of C. longa and its water and fat-soluble derivatives show powerful anti-oxidant capacity, comparable to vitamins C and E. According to previous study curcumin is eight times more effective than vitamin E at reducing lipid peroxidation (Toda et al., 1985). The ability to scavenge H2O2 was the highest in

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the methanolic extract of both leaves and rhizomes of C. amada,

followed by chloroform and aqueous extracts. Rhizomes demonstrated more activity. Chloroform and aqueous extracts were the most effective at inhibiting the production of nitric oxide and superoxide in vitro, followed by methanolic extracts of both leaves and rhizomes of C. amada (Sudeepthi et al., 2014). Methanolic

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extract of C. caesia rhizome is a good source of natural antioxidant (

Liu et al., 2013). When compared to C. zedoaria, protein extracts from C. caesia rhizomes showed lower inhibitory concentrations (IC50 values), indicating stronger antioxidant activity (Angel et al., 2013). Additionally, methanolic extract (50% concentration) of C. caesia leaves showed antioxidant activity, with thiobarbituric acid-reactive substances (TBARS) inhibition levels ranging from 47.24 to 73.30% (Ho et al., 2018). The ability of a methanolic extract of the C. caesia rhizome to act as an antioxidant by effectively scavenging free radicals in Wistar rat models of diabetes induced by streptozotocin (STZ) was also reported (Majumder et al., 2017). 4.2 Anticancer activity Curcumin slowed down tumour growth and cell division in prostate and colon cancer. Additionally, curcumin of C. longa could reduce the activity of a number of common carcinogens and mutagens in various cell types in both in vivo and in vitro investigations (Dorai et al., 2001). Methanolic extract of leaves and rhizomes of C. amada were tested for studying anti- cancer activity against breast cancer. The diphenylamine method for testing the anti-cancer activity revealed that the C. amada

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rhizomes and	d leaves triggered cell death in breast cancer lines	(both MCF-7 and MDA MB 231). Steroid and terpenoid compounds
might be res	ponsible for anticancer activity (	

Sivaprabha et al., 2015) C. caesia methanolic extract of rhizomes showed positive anticancer activity against Ehrlich's ascites carcinoma (EAC) in mice by notably reducing the tumor weight, tumor volume, viable cell count and rising the lifespan percentage (57.14 and 88.09 %) of EAC-treated mice (Karmakar et al., 2013).

4.3 Antimicrobial activity The C. longa treated rabbit group had a significantly greater mean value for wound contraction, and therefore, revealed decreased inflammation and a rising tendency in collagen formation. Another study identified the phytoconstituents such as alkaloid, flavonoid, anthocyanin, steroids, and coumarin in C. longa extracts and demonstrated the synergistic combinatorial impact of copper metal ions with aqueous extracts of C. longa against Paenibacillus popilliae, a known food spoilage bacterium (Jassal et al., 2015). Methanol, hexane, ethylacetate, chloroform and acetone extracts of C. amada were found to be highly antibacterial against pathogenic bacteria Salmonella typhi,

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Bacillus cereus, Micrococcus luteus, Staphylococcus aureus, Listeria monocytogenes and Enterococcus fecalis (Policegoudra et al., 2007a & 2007b).

Some components of C. amada volatile oils like, pinene and myrcene showed antifungal activity against Fusarium. falcatum, F. moniliforme, Aspergillus niger, A. terreus and Curvularia palliscens (Singh et al., 2002). Acetone extract of C. caesia showed the highest activity against S. aureus, while chloroform extract showed the highest inhibitory action against Serratia marcescens (Jose and Thomas, 2014). Mycobacterium tuberculosis (Mtb H37Rv) and six multidrug-resistant (MDR) clinical strains of Mtb, which were isolated from sputum samples of pulmonary tuberculosis (TB) patients, were successfully eradicated by an ethanolic extract of C. caesia rhizome (Gupta et al., 2018).

4.4 Antidiabetic activity Compared to curcuminoids or sesquiterpenoids alone, the ethanolic extract of C. longa with both of these compounds was found to be more hypoglycemic (Nishiyama et al., 2005). Human pancreatic amylase was blocked by both the isopropanol and the acetone extract of C. longa, which lessened starch breakdown and lowered blood glucose levels (Ponnusamy et al., 2010). Mice treated with



fasting blood glucose (FBG), glycosylated haemoglobin (HbA1c), and oral glucose tolerance test (OGTT) level towards normal (

Majumder et al., 2017). 4.5 Anti-inflamation activity Curcumin from C. longa has been demonstrated to have anti-inflammatory properties in conditions such as chronic anterior uveitis, inflammatory bowel disease, and pancreatitis (Hewlings and Kalman, 2017). An oil-free aqueous extract (COFAE) of C. longa showed significant anti-inflammatory effects against acute and chronic inflammation. An extract of C. longa was given to rats with arthritis due to collagen dysfunction, and it stopped the degenerative changes in their bones and joints (Sun et al., 2017). C. amada ethanolic extract showed the presence of various chemical constituents with the presence of carbonyl, ester, hydroxyl and olefinic groups. The extract showed dose-dependent anti-inflammatory activity, which

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was found to be statistically important at greater concentration in acute carrageenan-induced rat paw edema model.

The extract showed anti-inflammatory activity during different acute stages of inflammation and on the formation of granular tissue (Majumdar et al., 2000). The strongest albumin denaturation inhibitory action was shown by the leaf essential oil of C. caesia, which also had a lower IC50 value (182.5 g/mL) than the typical sodium diclofenac (906.5 g/mL). Inflammatory disease can be decreased or delayed by inhibition of cyclooxygenase (COX) enzymes linked with inflammatory intermediates such as thromboxanes and prostaglandin. Hexane and methanolic extracts of C. caesia have been demonstrated to have anti-inflammatory effect by selectively inhibiting COX-2 and mildly inhibiting COX-1 (Angel et al., 2013).

4.6 Other activities C. longa rhizome powder is added to cow's urine to treat dermatitis and internal itching, while rhizome juice is used as an antiparasitic agent in the treatment of several skin disorders (Paranjpe and Pranjpe, 2001). Curcumin from C. longa, with proven antimutagenic, antioxidant, free radical scavenging, anti-inflammatory, and anti-carcinogenic abilities, protect the skin from detrimental UV-induced impacts (Binic et al., 2013). Aqueous rhizomes extract of C. amada applied to the rabbits, in 200 mg/kg dose, showed significant antipyretic activity (Kumar et al., 2015). C. amada also showed other activities like anti-ulcer, anti-tubercular, anti-hyperglycemic, and analgesic activity (Kanase and Khan, 2018). C. amada was found to act as Central nervous system (CNS) depressant, because of its ability to slow down the brain activity making them useful for treating anxiety, panic, acute stress reactions and sleep disorder. In addition, C caesia was reported to purify blood, to treat cancer, inflammatory illnesses, ulcers, dermatitis, excessive cholesterol, diabetes, irregular menstruation, stomach pain, and ulcerative colitis (Arulmozhi et al., 2006 ; Pandey and Chowdhury, 2003 ; Sarangthem and Haokip, 2010; Kagyung et al., 2010 ; Hait et al., 2019).

5. Conclusion Most of the traditional claims regarding the pharmacological properties of C. longa, C. amada, and C. caesia have now been validated in various scientific investigations both in vitro and in vivo. The rhizomes of the all three Curcuma spp. have remarkable bioactive properties. Due to its possible health advantages, all three species of Curcuma genus are now gaining attention from the researchers. These three species of Curcuma have the potential to be investigated as a natural complementary and alternative health therapy with promising prospective for the pharmaceutical industries. Here, we have precisely documented the medicinal properties and phytochemistry of these three species based on published information. However, there is considerable research gap in the investigation of stress response of these species in changing climate. Specific reaction of these species towards various stress factors in terms of growth and production of pharmacologically potential secondary metabolites as well as their bioactivity are yet to be known sufficiently.

6. Reference

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rhizomes and leaves triggered cell death in breast cancer lines (both MCF-7 and MDA MB 231). Steroid and terpenoid compounds might be responsible for anticancer activity (				rhizomes and leaves of mango ginger induce cell death in breast cancer lines MDA MB 231 and MCF-7. Terperniods and steroids compounds might be responsible for anticancer activity [19].				
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the plant extract had no deleterious side effects even at a high dose (650 mg/kg								
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the rhizome of C. caesia was found to be potential antidiabetic agent.								
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