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Review Article

Curcuma zedoaria Rosc. (white turmeric): a review of its chemical, pharmacological and ethnomedicinal properties

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Abstract

Objectives *Curcuma zedoaria* Rosc is a perennial herb found in tropical countries, such as India, Japan and Thailand. Various parts of this plant are used in Ayurveda and other folk medicines for the treatment of different ailments such as diarrhoea, cancer, flatulence and dyspepsia. This study is an attempt to compile an up-to-date and comprehensive review of *C. zedoaria* that covers its traditional and folk medicinal uses, phytochemistry and pharmacology.

Key findings Research carried out using different in-vitro and in-vivo techniques of biological evaluation supports most of the claims.

Summary This review presents the botany, chemistry, traditional uses and pharmacological data of the plant.

Keywords antifungal; *Curcuma zedoaria;* white turmeric; Zingiberaceae

Introduction

Curcuma zedoaria Rosc, also known as white turmeric, zedoaria or gajutsu,[1] is a perennial rhizomatous herb that belongs to the Zingiberaceae family. The plant is indigenous to Bangladesh, Sri Lanka and India, and is also widely cultivated in China, Japan, Brazil, Nepal and Thailand. In India it is known by its several vernacular names, the most commonly used ones being Krachura (Sanskrit), Gandamatsi (Hindi) and Sutha (Bengali).[2] It is used traditionally for the treatment of menstrual disorders, dyspepsia, vomiting[3] and for cancer.[4] Rural people use the rhizome for its rubefacient, carminative, expectorant, demulcent, diuretic and stimulant properties while the root is used in the treatment of flatulence, dyspepsia, cold, cough and fever.[1]

Zedoaria is a herbaceous and rhizomatous perennial plant composed of an upright pseudostem, a corm and underground cylindrical branches or rhizomes and fleshy roots. Some roots develop terminal storage structures (rounded to elongated tuber-like roots called t-roots). From March to April the axillary buds of the corm and apical buds of the third-order rhizomes emerge above the ground as inflorescences. This basal flower spike, which grows about 30 cm tall, appears just before the foliage. On the node closest to the flower spike, a vegetative shoot always develops. No additional floral buds sprout but more vegetative shoots develop. New branches start to develop on corms of recently formed aerial shoots. By autumn, the above-ground foliage dies back. From November to December storage roots are formed, having a high (> 70%) carbohydrate content.[5]

The pharmacognostical study of the rhizomes finds place in the Ayurvedic Pharmacopoeia of India. This study is an attempt to compile an up-to-date and comprehensive review of *C. zedoaria* that covers its traditional and folk medicinal uses, phytochemistry and pharmacology.

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Ethnomedicinal or Traditional Uses

C. zedoaria is a well known ethnomedicinal plant that is also used in Ayurveda. Its use in the Indian traditional folk medicine is also well documented. Table 1 indicates the use of different parts of *C. zedoaria* in traditional systems of medicine.[2,3,6,7]

Table 1 Ethnomedicinal uses of *C. zedoaria*

Plant parts	Traditional uses
Oil of rhizome	Stomachic, emmenagogic, vomiting, menstrual haematometra[3]
Fresh roots	Treatment of leucorrhoeal discharge[6]
Tuber juice	Treatment of worms in children[2]
Powdered rhizome	Antiallergant[6]
Leaf juice	Treatment of dropsy[2]
Leaf juice	Treatment of leprosy[7]
Leaf paste	As plasters in lymphangitis, furunculosis[7]

Phytochemistry

C. zedoaria is a rich source of essential oils:, starch, curcumin (**1**) arabin, gums, etc.[2] Makabe *et al.*[8] have isolated more than 10 sesquiterpenes from the rhizome of *C. zedoaria* and were able to structurally characterize 15 such compounds, namely furanodiene (**2**), furanodienone (**3**), zedorone (**4**), curzerenone (**5**), curzeone (**6**), germacrone (**7**), 13-hydroxy germacrone (**8**), dihydrocurdione (**9**), curcumenone (**10**) and zedoarondiol (**11**).

Phytochemical analysis was carried out by Navarro *et al.*[9] using air-dried rhizomes (3 kg). The powder was extracted twice with dichloromethane at room temperature for five days, and then with ethyl acetate and methanol, respectively. The extracts were then concentrated under reduced pressure to give the respective fractions. A part of the dichloromethane fraction (50 g) was chromatographed using a silica gel column eluted with a mixture of hexane–ethyl acetate in increasing polarity. The fraction F1 (3.5 g), obtained from the above, was rechromatographed over a silica gel column and, when eluted with benzene–acetone (9 : 1), yielded about 500 mg of compound **1** and 150 mg of compound **2**. Spectroscopic data (IR and NMR) confirmed identity of compound **1** as curcumenol and compound **2** was a mixture of phytosterols (especially sitosterol and stigmasterol 2 : 1).

Christiane *et al.*[10] described the seasonal variation of curcumenol (**12**) and dihydrocurdione, two active terpenoids from different parts (roots, mother rhizome and rugous rhizome) of *C. zedoaria* grown in Brazil. The analysis was carried out by high resolution gas chromatography, using external standards for determination. The results showed that both terpenoids are present in all the parts studied. However, *C. zedoaria* exhibited about three times more terpenoids in the mother rhizome in autumn than in other parts and seasons studied.

A new eudesmane-type sesquiterpene, zedoarofuran, and six new guaiane or secoguaiane-type sesquiterpenes, 4-epicurcumenol, neocurcumenol, gajutsulactones A and B and zedoarolides A and B, were isolated from the aqueous acetone extract of zedoaria rhizome together with 36 known sesquiterpenes and two diarylheptanoids. Their stereostructures were elucidated on the basis of chemical and physicochemical evidence.[11] Two guaiane derivatives were isolated from the rhizomes of *C. zedoaria*. Their structures, zedoalactone A and zedoalactone B, were established by ^{1}H and ^{13}C NMR spectroscopic studies and by comparison with closely related compounds.[12] Zedoarol (**13**), 13-hydroxygermacrone and curzeone were isolated and structurally elucidated by Shiobara *et al.*[13] using *C. zedoaria*.

Three sesquiterpenoids, curcumenone, curcumanolide-A (**14**) and curcumanolide-B (**15**), were isolated from the dried rhizome of *C. zedoaria* by Shiobara *et al.*[14] Ethyl paramethoxycinnamate (**16**) was isolated from the methanolic extract of *C. zedoaria* by chromatography on neutral alumina and silica gel.[15] In the course of searching for biologically active sesquiterpenoids from the *Curcuma* genus, two sesquiterpenoids were isolated from the rhizome of *C. zedoaria*. Their structures were identified as α-turmerone (**17**) and β-turmerone (**18**). The structural elucidation of these compounds was carried out by comparison of their physical and spectral data with previously reported values.[16] Mau *et al.*[17] isolated essential oils from the rhizomes. They isolated a total of 36 compounds but were only able to structurally characterize epicurzerenone (**19**) and curzerene (**20**).

The essential oil obtained by hydrodistillation of the rhizome of *C. zedoaria* native to north-east India has been analysed by gas chromatography (GC) and gas chromatography–mass spectrometry (GC-MS). Thirty-seven constituents representing about 87.7% of the total oil have been identified. Curzerenone (22.3%) was the major component, followed by 1,8-cineole (**21**) (15.9%) and germacrone (9.0%).[18] The chemical investigation on essential oils of rhizomes of *C. zedoaria*, done by GC and GC-MS, revealed the presence of 1,8-cineole (18.5%), cymene (18.42%), α-phellandrene (14.9%) (**27**) and β-eudesmol (**22**) (10.6%).[19]

The essential oil produced by hydrodistillation of *C. zedoaria* leaves was investigated by GC and GC-MS. Twenty-three compounds were identified, accounting for 75% of the oil. The oil of *C. zedoaria* was made up mainly of mono- and sesquiterpenoids, monoterpene hydrocarbons (2.3%), oxygenated monoterpenes (26%), sesquiterpene hydrocarbons (38%) and oxygenated sesquiterpenes (13.5%). The major constituents of the leaf oil were α-terpinyl acetate (8.4%), isoborneol (7%) and dehydrocurdione (9%).[20]

Chemical analysis of the volatile oil from *C. zedoaria* using GC-MS technique revealed the presence of β-tumerone (19.88%), 1,8-cineole (8.93%) and zingiberene (**23**) (7.84%) as major constituents.[21]

The essential oil of the dried rhizome was isolated using simultaneous steam distillation and solvent extraction and its fractions were prepared by silica gel column chromatography. In total, 36 compounds were identified in the essential oil, including 17 terpenes, 13 alcohols and 6 ketones. Epicurzerenone and curzerene were found in the first and second highest amounts (24.1 and 10.4%).[17]

Curcumin, dihydrocurcumin (**24**), tetrahydrodemethoxycurcumin and tetratetrahydrobisdemethoxycurcumin were isolated together with two bisabolane-type sesquiterpenes from 80% aqueous acetone extract of the rhizome of *C. zedoaria*. Bioassay-directed fractionation of an ethanol extract of *C. zedoaria* led to the isolation of an active curcuminoid, which was identified as demethoxycurcumin by comparison of its ^{1}H and ^{13}C NMR spectra with literature data and by direct comparison with synthetic material. Curcumin and bisdemethoxycurcumin were also obtained.[22]

The variation of curcuminoids in the ethanolic extract of *C. zedoaria* was measured by using high-performance liquid chromatography (HPLC). The analysis was carried out at

425 nm using a BDS Hypersil C18 column as a stationary phase, 0.1% acetic acid aqueous solution and acetonitrile as mobile phase. Ethanolic extracts of *C. zedoaria* rhizomes collected from various parts of Thailand contained curcumin, demethoxycurcumin and bisdemethoxycurcumin in the range of 1.46 ± 0.45 to 5.73 ± 0.11% w/w (average 2.73 ± 1.24% w/w), 3.15 ± 0.15 to 10.98 ± 0.28% w/w (average 7.37 ± 2.71% w/w) and 0.49 ± 0.02 to 2.99 ± 0.20% w/w (average 1.40 ± 0.82% w/w), respectively. The highest average total curcuminoid content in the extracts was found to be 16.83 ± 0.62% w/w while the lowest content was 6.09 ± 1.79% w/w. This information will be useful as a guide for further standardization of *C. zedoaria* extracts for which the content has not been reported elsewhere (Figure 1).[23]

Figure 2 gives the structures of a few biologically active compounds that have been isolated from *C. zedoaria*. Table 2 shows the percentage of various phytoconstituents present in *C. zedoaria*.

Pharmacological Properties

Several workers have reported the different biological actions of *C. zedoaria* in various in-vitro and in-vivo test models. Different parts of this plant have been found to exhibit antimicrobial, anticancer, antiallergic and analgesic activity. These are described in greater detail in the following sections.

Antimicrobial and antifungal activity

The antimicrobial activity of extracts of *C. zedoaria* tubers was tested against six bacterial and two fungal strains using the agar well diffusion and broth dilution methods. Petroleum ether, hexane, chloroform, acetone and ethanol extracts exhibited antibacterial as well as antifungal activity. Acetone and hexane extracts of the tubers showed comparable antimicrobial activity as indicated by minimum inhibitory concentration (MIC) values. The MIC values for different strains and extracts ranged from 0.01 to 0.15 mg/ml. The findings also support the use of *C. zedoaria* tubers in traditional medicine for the treatment of bacterial and fungal infections.[1]

The antimicrobial activity of oils obtained from *C. zedoaria* in Nepal was examined using the Petri plate–paper disk method. The microorganisms tested were *Staphylococcus aureus* (IFO14462), *Corynebacterium amycolatum* (IFO 15207), *Escherichia coli* (IFO 15034), *Candida albicans* (IFO 1594) and *Aspergillus ochraceus* (IFO 31221). All the examined oils indicated antimicrobial activity at similar levels. Hence, it was revealed that oils produced in Nepal could be effectively applicable to a variety of uses in terms of antimicrobial activity.[24]

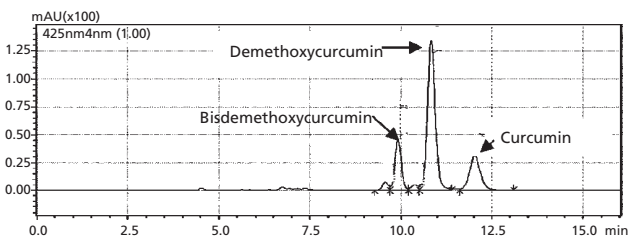

Figure 1 Chromatogram of 70% ethanolic extract of *C. zedoaria* rhizome.

Essential oils were obtained from *Curcuma* species, viz. *C. aromatica*, *C. longa*, *C. zedoaria* and fermented turmeric. Except for fermented turmeric, the essential oils were extracted from homogenates of fresh tubers by the steam distillation method, and were then sterilized by filtration before antibacterial tests. Antibacterial activity was examined against four Gram-negative (non-01 *Vibrio cholerae* (NVC), *Salmonella enteritidis* (SE), enterotoxigenic *E. coli* (ETEC), enterohaemorrhagic *E. coli* O157 (EHEC)) and two Gram-positive (*S. aureus* and *Bacillus cereus* ATCC 11707 (BC)) bacteria, including foodborne pathogenic bacteria. The broth dilution method was used for evaluating the antibacterial activity of the essential oils. In the broth dilution method, the MIC of *C. zedoaria* against *B. cereus* was found to be 0.035% v/v. The antibacterial activity of these oils against the other bacteria, except for *B. cereus*, was moderate. In addition, the effect of heating the essential oils on their antibacterial activity was also examined. The activity against *B. cereus* remained unaffected after heating at 121°C for 20 min.[25]

The antimicrobial activity of *C. zedoaria* extract against some oral microorganisms was compared with the antimicrobial activity of five commercial mouthrinses to evaluate the potential of the plant extract to be incorporated into the formulae for improving or creating antiseptic activity. The in-vitro antimicrobial efficacy of plant extracts and commercial products was evaluated against *Streptococcus mutans, Enterococcus faecalis, S. aureus* and *C. albicans* using a linear regression method to evaluate the microbial reduction obtained as a function of the exposure time, considering effectiveness as a 99.999% reduction in count of standardized microbial populations within 60 s. The results showed that the antimicrobial efficacy of *C. zedoaria* extract was similar to that of commercial products, and its incorporation into a mouthrinse could be an alternative for improving the antimicrobial efficacy of the oral product.[26]

Ficker *et al.*[27] used extracts from 11 plant species belonging to the Zingiberaceae for the testing of antifungal activity using disc diffusion bioassays. Among 11 extracts, the extract of *C. zedoaria* was found to have pronounced inhibitory activity against a wide variety of human pathogenic fungi, including strains resistant to the common antifungals amphotericin B and ketoconazole, thus proving the claims made by people of Kenyah (Indonesian Borneo) for the use of *C. zedoaria* as an antifungal agent.

Antiamoebic activity

Alcoholic extract of rhizome of *C. zedoaria* was able to inhibit the growth of *Entamoeba histolytica* at a concencentration of 1–10 mg/ml.[28]

Larvicidal effect

Zedoary oil and its formulated preparation, zedoary oil-impregnated sand granules, were tested for larvicidal efficacy against *Aedes aegypti* mosquitoes and compared with that of Abate (temephos). Zedoary oil exhibited pronounced

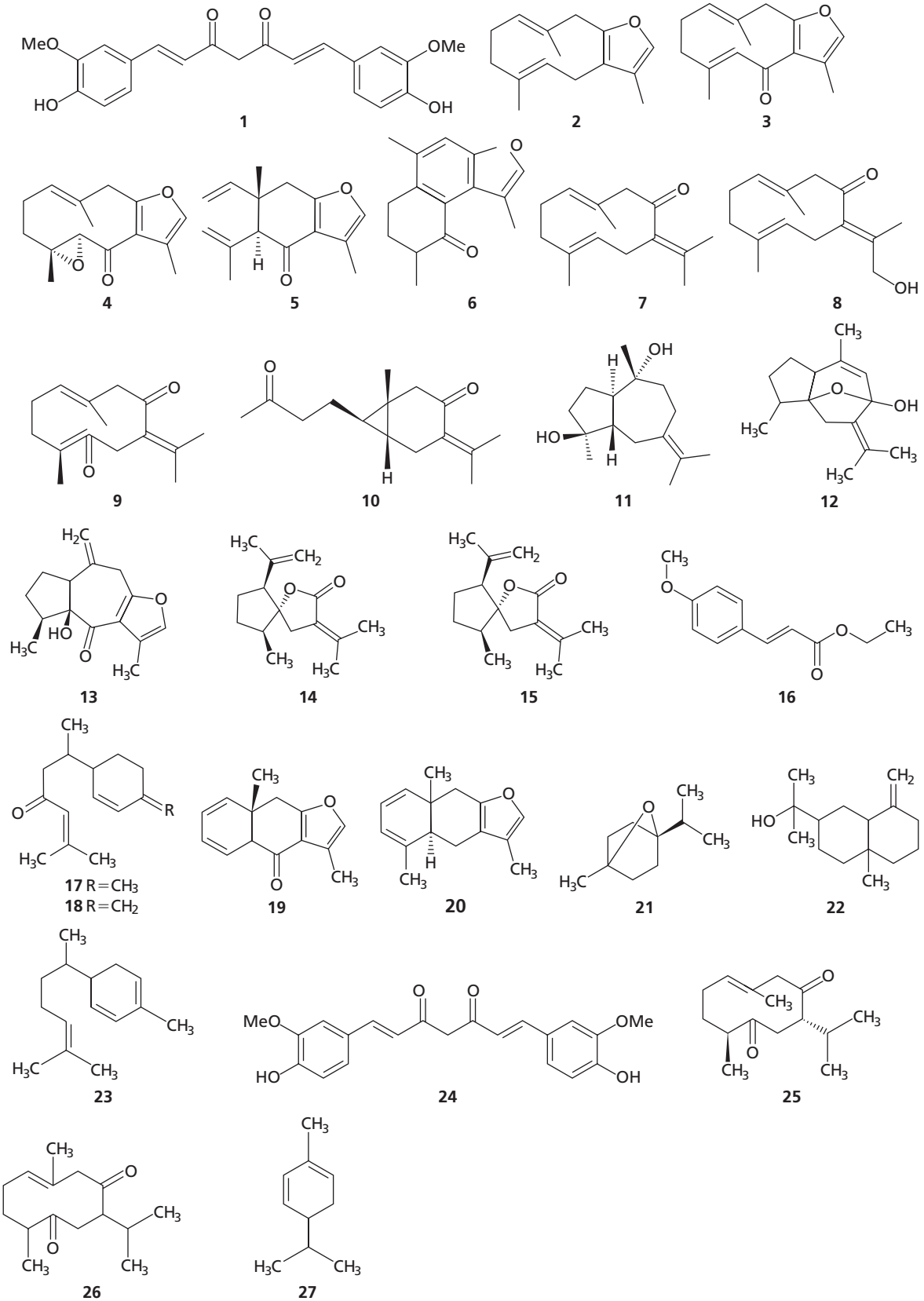

Figure 2 Structures of the biologically active compounds isolated from *C. zedoaria*. **1**, Cucrumin; **2**, furanodiene; **3**, furanodienone; **4**, zedorone; **5**, curzerenone; **6**, curzeone; **7**, germacrone; **8**, 13-hydroxygermacrone; **9**, dihydrocurdione; **10**, curcumenone; **11**, zedoaronediol; **12**, curcumenol; **13**, zedoarol; **14**, curcumanolide-A; **15**, curcumanolide-B; **16**, ethyl para-methoxycinnamate; **17**, **18**, β-turmerone; **19**, epicurzerenone; **20**, curzerene; **21**, 1,8-cineole; **22**, β-eudesmol; **23**, zingiberene; **24**, dihydrocurcumin; **25**, curdione; **26**, neocurdione; **27**, α-phellandrene.

Table 2 Percentage of various phytoconstituents present in *C. zedoaria*

Source	Active constituents	Percentage (%)
Oil from *C. zedoaria* rhizome[18]	Curzerenone	22.3
	1,8 Cineole	15.9
	Germacrone	9.0
Oil from *C. zedoaria* rhizome[19]	Cymene	18.42
	α-Phellandrene	14.90
	β-Eudesmol	10.60
Oil from *C. zedoaria* leaves[20]	Monoterpene hydrocarbon	2.3
	Oxygenated monoterpene	26.0
	Sesquiterpene hydrocarbon	38.0
	Oxygenated sesquiterpene	13.5
	α-Terpinyl acetate	8.4
	Isoborneol	7.0
	Dehydrocurdione	9.0
Volatile oil from *C. zedoaria*[17]	Epicurzerenone	24.1
	Curzerene	10.4

potential against *A. aegypti* with a 50% and 99% lethal dose (LD50 and LD99, respectively) of 33.45 and 83.39 ppm, respectively.[29]

Toxic effect of *C. zedoaria* on rats and chicks

A flour was prepared from rhizomes of *C. zedoaria* in such a way that most of the protein was retained. The crude protein (nitrogen × 6.25) content in this product was 155 g/kg, compared with approximately 10 g/kg in commercial *C. zedoaria* flour.

The high-protein flour proved highly toxic to 5-week-old rats and caused 100% mortality within six days when given at 320 g/kg diet. Fresh rhizomes were minced and dried and the resulting meal was given to weanling rats at 400 g/kg diet. All the rats lost weight rapidly, and two of the five rats died within 4 days.

This same *C. zedoaria* meal was given to one-day-old chicks at 100 and 200 g/kg diet. All the chicks survived the test period (20 days), but body weight, food intake and efficiency of food conversion decreased with increase in the level of *C. zedoaria* meal in the diet.[30]

Analgesic activity

Navarro *et al.*[9] investigated the analgesic activity of *C. zedoaria* rhizomes grown in Brazil. From the rhizome's hydroalcholic extract, different fractions (dichloromethane, ethyl acetate, methanol) were prepared and tested for analgesic activity along with curcumenol. Aspirin and dipyrone were used as standard drugs. The activity was investigated using several models of pain in mice, including writhing, formalin and capsaicin. Curcumenol presented promising analgesic effects, being several times more potent than the reference drugs evaluated in the same experimental models. The calculated 50% inhibitory dose (ID50) values were 22 and 12 μmol/kg when evaluated in writhing and capsaicin tests, respectively, and 29 μmol/kg in relation to the second phase of the formalin model. The lack of effect in the hot-plate test suggests that curcumenol acts by a mechanism that does not involve the participation of the opioid system. All the fractions were pharmacologically analysed. The results indicate that the dichloromethane extract caused a dose-dependent analgesic effect when given by the intraperitoneal route, inhibiting acetic acid-induced writhing responses in mice. It presented a calculated ID50 value of 3.6 mg/kg, with maximum inhibition of 69.5%, being several times more active than reference drugs aspirin and dipyrone, which presented ID50s of 25 and 57 mg/kg, respectively. When analysed in the formalin test, the dichloromethane extract showed analgesic activity significantly in a dose-dependent manner. The results confirm and justify the popular use of this plant for the treatment of dolorous processes.[9]

Antinociceptive activity

The antinociceptive activity of the dichloromethane extracts from different parts (roots, mother rhizome and rugous rhizome) collected in different seasons was studied using the acetic acid-induced abdominal constriction model in mice. The extracts obtained from mother rhizome collected in autumn and winter at doses of 10 mg/kg intraperitoneally caused considerable antinociceptive activity, inhibiting 91.1 and 93.4% of the abdominal constrictions, respectively, whereas compounds curcumenol and dihydrocurdione caused inhibitions of 64.0 and 46.0%, respectively. These results confirm that both compounds contribute towards antinociceptive and analgesic activity.[10]

Antiallergic activity

The 80% aqueous acetone extract of the rhizomes of *C. zedoaria* cultivated in Thailand (Thai zedoary) was found to inhibit the release of beta-hexosaminidase, as a marker of antigen-IgE-mediated degranulation, in RBL-2H3 cells and passive cutaneous anaphylaxis reaction in mice. From the active fraction, four curcuminoids (curcumin, dihydrocurcumin, tetrahydrodemethoxycurcumin and tetrahydrobisdemethoxycurcumin) were isolated together with two bisabolane-type sesquiterpenes. The effect of four curcuminoids (curcumin, dihydrocurcumin, tetrahydrodemethoxycurcumin and tetrahydrobisdemethoxycurcumin) and several related compounds isolated therefrom were studied for degranulation. Among them, curcumin showed the highest activity against beta-hexosaminidase release having a 50% inhibitory concentration (IC50) of 5.3 μM, followed by bisdemethoxycurcumin (IC50 11 μM). With regard to the structural requirements of curcuminoids for the activity, the conjugated olefins at the 1–7 positions and the 4′-or 4″-hydroxy groups of curcuminoids were suggested to be essential for strong activity, whereas the 3′-or 3″-methoxy group only enhanced the activity. Furthermore, the effects of curcumin and bisdemethoxycurcumin on calcium ionophore (A23187 and ionomycin)-induced degranulation and antigen-induced release of tumour necrosis factor (TNF)-α and interleukin (IL)-4 were examined.[31]

Antiulcer activity

C. zedoaria is the chief ingredient in several Unani preparations used to treat peptic ulcer. The effect of root powder (200 mg/kg, p.o.) on the volume of gastric juice, gastric pH, total acid, free acid and ulcer index in pyloric-ligated rats

was studied. The root powder at a dose level of 200 mg/kg reduced the gastric pH, free acid, total acid and ulcer index significantly and the results were comparable with that of the standard drug omeprazole (30 mg/kg, i.p.), thereby providing justification that the root is effective in affording protection against hyperacidity and gastric ulcers.[29]

Platelet activating activity

The freeze-dried form of aqueous extract of *C. zedoaria* was studied for its inhibitory effect on platelet activating factor using a radioligand. It was found that *C. zedoaria* inhibited 50.60% platelet activating factor binding to rabbit platelets at a concentration of 200 μg/ml.[32]

Hepatoprotective activity

Hepatoprotective sesquiterpenes were isolated from the aqueous acetone extract of the rhizome of *C. zedoaria*. Principal sesquiterpenes, furanodiene, germacrone, curdione (**25**), neocurdione (**26**), curcumenol, isocurcumenol, aerugidiol, zedoarondiol, curcumenone and curcumin were found to show potent protective effect on D-galactosamine (D-GalN)/lipopolysaccharide (LPS)-induced acute liver injury in mice. Possible mechanisms for their hepatoprotective activity were based on the inhibitory effect on D-GalN-induced cytotoxicity in primary cultured rat hepatocytes, LPS-induced nitric oxide (NO) production in cultured mouse peritoneal macrophages, and D-Gal N/TNF-α-induced liver injury in mice.[33]

A study was carried out to assess the effect of *C. zedoaria* on the growth of cultured human hepatic myofibroblast cells (hMF). During the course of liver fibrogenesis, hMF, mostly derived from hepatic stellate cells, proliferate and synthesize excessive amounts of extracellular matrix components. A water extract of Zedoariae rhizoma was evaluated for its antiproliferative effect on the growth inhibition of hMF, since proliferation of hMF is known to be central for the development of fibrosis during liver injury and factors that may limit their growth are potential antifibrotic agents. hMF were obtained by outgrowth from human liver explants. Zedoariae rhizoma markedly reduced serum-driven cell proliferation, as assessed by nuclear autoradiography experiments and measurement of actual cell growth. Growth inhibition was totally reversed after removal of the Zedoariae rhizoma. Zedoariae rhizoma potently inhibited hMF growth (IC50 8.5 μg/ml), in a pertussis toxin-insensitive manner. Analysis of the mechanisms involved in growth inhibition revealed that Zedoariae rhizoma rapidly increased prostaglandin E2 production and, in turn, cAMP, which inhibited hMF proliferation but did not affect cAMP levels. Production of cAMP by Zedoariae rhizoma was abolished by NS-398, a selective inhibitor of cycloxygenase (COX)-2. Also, Zedoariae rhizoma potently induced COX-2 protein expression. Blocking COX-2 by NS-398 blunted the antiproliferative effect of Zedoariae rhizoma. Hence it can be concluded that Zedoariae rhizoma inhibits proliferation of hMF, probably via an intracellular mechanism, through early COX-2 dependent release of prostaglandin E2 and cAMP and delayed COX-2 induction. Results indicated a novel role for Zedoariae rhizoma as a growth-inhibitory mediator and pointed out its potential involvement in the negative regulation of liver fibrogenesis. The results that Zedoariae rhizoma exhibits potent antiproliferative and antifibrogenic effects toward hMF indicated that Zedoariae rhizoma might have therapeutic implications in chronic liver disease.[34]

Antivenom activity

Aqueous extract of *C. zedoaria* was investigated for inhibitory activity by binding of anti-cobra venom antibody to antigen of cobra venom by using the 96-well plate enzyme linked immunosorbent assay (ELISA) method. In this study the extract was allowed to react with immobilized venom before the addition of antivenom antibody. The extract of *C. zedoaria* showed clear inhibitory activity. It was found that the extract targeted neurotoxin and protein-degrading enzyme present in venom, thus suggesting use of aqueous extract as antivenom.[35]

Anti-inflammatory activity

C. zedoaria showed promising anti-inflammatory activity in experimental models. Compounds curzenone and dehydrocurdione obtained from methanolic extract of the rhizomes suppressed 12-*O*-tetradecanoylphorbol-13-acetate (TPA) by 75% and 53%, respectively, at a dose of 1 μmol application.[8]

Chihiro *et al*.[21] have also studied the anti-inflammatory property of the methanolic extract of *C. zedoaria* using the adjuvant arthritis mouse model. However, it did not show any significant activity.

Hemagglutinating activity

Hemagglutinating activity has been shown in extract of the *C. zedoaria*. Crude proteins obtained by Mg/NP-40 extraction from *Curcuma* species exhibited agglutination activity against rabbit erythrocytes.[36]

Antimutagenic activity

Thirty-six commonly used anticancer crude drugs from Chinese herbs were studied for their antimutagenic activity, by using the *Salmonella*/microsomal system in the presence of picrolonic acid or benzo[a]pyrene to test whether they contained direct or indirect antimutagens. Each crude drug was extracted with boiling water for 2 h (i.e. the method commonly used by Chinese people to prepare the drug for oral intake). *C. zedoaria* was found to possess moderate activity against against benzo[α]pyrene.[37]

Cytotoxic activity

Water and ethanolic extracts of 12 Thai medicinal plants used as the ingredients of a southern Thai traditional formula for cancer treatment were tested for cytotoxic activity against two types of human cancer cell lines (large cell lung carcinoma (CORL-23) and prostate cancer (PC3)) and one type of normal human cell line (fibroblast cells (10FS)). The sulforhodamine B assay was used to test cytotoxic activity against all the cell types. One concentration (50 μg/ml) of two different extracts was tested first against cell lines and the active plant extracts were diluted further and tested for calculating IC50. The ethanolic extracts of *C. zedoaria* showed cytotoxic activity against CORL-23 and PC3 but less

cytotoxic activity against 10FS (IC50: 6.05, 17.84 and 55.50 μg/ml, respectively). The water extract of the plant exhibited no activity against any of the human cells studied. Ethanolic plant extract of *C. zedoaria* showed specific activity against lung cancer cell lines and less cytotoxic activity against normal cells.[38]

Myoungae *et al.*[39] investigated the effect of hexane extract and its fractions on the proliferation of SiHa, SNU-1 and HepG2 cell lines. Among these fractions, final fraction H2-3-1 ((−)-α-curcumene) and H2-3-3 (β-tumerone) showed a cytotoxic effect on SiHa and HepG2 cell lines. The hallmark of apoptosis, DNA fragmentation, also appeared in the final fractions (−)-α-curcumene and β-tumerone after 24° h treatment in SiHa cell line. Furthermore, these fractions were shown to be able to induce cell death in a [^{3}H]thymidine incorporation test. From these results, it is speculated that the hexane extract of *C. zedoaria* has a good cytotoxic effect.

Matthes *et al.*[40] reported that zerumbone, zerumbone epoxide, diferuloylmethane and di-p-coumaroylmethane isolated from the rhizomes of *C. zedoaria* possessed cytotoxic effects.

Anticancer activity

The inhibitory effect of water extract of *C. zedoaria* on experimental pulmonary metastasis of B16 melanoma cells was investigated. The intake of water extract at doses of 250 and 500 mg/kg for 42 days from 14 days before tumour inoculation significantly reduced the number of metastatic surface nodules in the lung, resulting in an extended life span. When the duration of water extract intake was examined, survival time was not affected by pre-intake before B16 melanoma cell inoculation and was slightly extended by post-intake after B16 melanoma cell inoculation, although the life span was prolonged by intake throughout the experiment. The intake of water extract for 42 days increased NO production by macrophages following stimulation with LPS in a dose-dependent manner. The elevated NO was found to serve as a cytotoxic mediator against B16 melanoma cells in co-culture with macrophages. On the contrary, B16 melanoma-conditioned medium reduced NO production by macrophages. However, water extract treatment significantly reversed the reduction in NO production by the conditioned medium. These findings indicate that water extract possesses anti-migratory effects on B16 melanoma cells and that the macrophage function-modulating activity by water extract appears to underlie its anti-metastatic activity, which leads to a decrease in the number of lung metastatic surface nodules and the extension of life span. This suggests that the water extract of *C. zedoaria* may play an important role in the inhibition of cancer metastasis.[41]

A study conducted by Hong *et al.*[42] found that the methanolic extract of *C. zedoaria* had both anticancer and anti-inflammatory activity. The inhibitors of prostaglandin biosynthesis and NO production have been considered as potential anti-inflammatory and cancer chemopreventive agents. Methanolic extracts of *C. zedoaria* showed potent inhibition of COX-2 activity (> 80% inhibition at the test concentration of 10 μg/ml).

Curcuminoids were synthesized and demonstrated to be cytotoxic against human ovarian cancer OVCAR-3 cells. The observed curative dose at 50% (CD50) for curcumin, demethoxycurcumin and bisdemethoxycurcumin was 4.4, 3.8 and 3.1 μg/ml, respectively.[22]

Antioxidant activity

At 20 mg/ml, the essential oil of *C. zedoaria* was moderate to good in antioxidant activity, good in reducing power and excellent in scavenging effect on 1,1-diphenyl-2-picrylhydrazyl radical but low in chelating effect on ferrousion.[17]

Micropropagation and Callogenesis of *C. zedoaria*

In-vitro micropropagation and callogenesis of *C. zedoaria* served as an alternative to improve plant production. Micropropagation by using shoot apexes produced by rhizome and from in-vitro plants were carried out on Murashige & Skoog medium supplemented with 2.0 mg/l benzyl amino purine and 30 g/l sucrose. Plantlets were satisfactorily acclimatized to greenhouse conditions by using a plastic cover for at least 10 days. Treatment with endomycorrhiza at the ex-vitro transferring time was beneficial to acclimatization, improving plant growth and development. Callus induction and growth were obtained by inoculating root segments on Murashige & Skoog medium supplemented with 1.0 mg/l naphthalene acetic acid and incubation in the dark at 25 ± 2°C. Cell suspension cultures were established on liquid medium of the same chemical composition and same culture conditions to obtain a growth curve.[43]

Table 3 lists the reported activity for phytochemical constituents isolated from *C. zedoaria* and Table 4 shows a summary of significant research findings on *C. zedoaria*.

Conclusions

Curcuma zedoaria is a well-known plant used in the Indian system of medicine, besides which folklore medicine also claims

Table 3 List of reported activities for phytochemical constituents isolated from *C. zedoaria*

Phytochemical constituents	Activity
Curcumenol, dihyrocurdione	Analgesic, antinociceptive[10]
Curcumin, dihydrocurcumin, tetrahyrodemothxycurcumin, tetrahydrobismethoxycurcumin	Antiallergic[31]
α-Curcumene, β-tumerone	Cytotoxic effect[38]
Zerumbone, zerumbone epoxide, diferuloylmethane, di-p-coumaroylmethane	Cytotoxic effect[39]
Curcumin, demothxycurcumin and bisdemothxycurcumin	Anticancer[22]
Furanodiene, germacrone, curdione, neocurdione, curcumenol, isocurcumenol, aerugidiol, zedoarondiol, curcumenone and curcumin	Hepatoprotective[33]
Curzenone and dehydrocurdione	Anti-inflammatory[8]

Table 4 Summary of significant research findings on *C. zedoaria*

Source	Activity	Observations
C. zedoaria tuber extracts (petroleum ether, hexane, chloroform, acetone, ethanol)	Antimicrobial and antifungal	All the extracts of the tubers showed both antifungal and antimicrobial activity. Hexane and acetone extract showed comparable better activity than other extract[1]
Oil of tubers from *C. zedoaria* of Nepal	Antimicrobial	Oil showed marked activity against wide range of microorganisms like *S. aureus*, *E. coli*, *C. albicans*, and *A. ochraceus*[19]
Comparison of oil from tubers of different curcuma species with *C. zedoaria*	Antimicrobial	*C. zedoaria* showed better activity against *B. cereus* compared with oils obtained from other species[25]
C. zedoaria tuber extract	Antimicrobial	*C. zedoaria* extract was compared with five commercial mouth-rinses. It was observed that the products had equal efficacy in inhibiting the oral microrganism[26]
C. zedoaria tuber extract	Antimicrobial	Extract of *C. zedoaria* exhibited pronounced inhibitory activity against human pathogenic fungi, including strain resistant to ketocanazole and amphotericin B[27]
Alcholic extract of *C. zedoaria* rhizome	Antiamoebic	Inhibited the growth of *E. histolytica*[28]
Comparison of zedoary oil and its formulated preparation for larvicidal activity	Larvicidal	Zedoary oil exhibited good efficacy against *A. aegypti* compared with formulated preparation[29]
Different fractions of hydroalcholic extract of C. *zedoaria* (dichloromethane, ethyl acetate, methanol) and using aspirin and dipyrone as standard	Analgesic	Dichloromethane fraction of the extract showed promising dose dependent analgesic activity compared with the standard in acetic acid induced writhing responses in mice[9]
Activity of dichloromethane extract prepared from underground parts collected in different seasons	Antinociceptive	Extract prepared from mother rhizome collected in autumn and winter showed better activity compared with the extract prepared from other parts[10]
C. zedoaria root powder and standard drug omeprazole	Antiulcer	Powder reduced gastric pH, free acid, total acid and ulcer index significantly when compared with the standard[36]
C. zedoaria freeze dried aqueous extract	Platelet activating activity	Extract inhibited 50–60% platelet activating factor in rabbit platelet[32]
Water extract of rhizome of zedoaria was evaluated for its use in chronic liver disease	Hepatoprotective	Zedoaria rhizome exhibited potent antiproliferative and antifibrogenic effect toward human hepatic myofibroblast cell[34]
Aqueous extract of *C. zedoaria* rhizome	Antivenom	Potent activity was observed by targeting neurotoxin and protein degradative enzyme present in venom[35]
Comparison of water and ethanolic extract of *C. zedoaria*	Cytotoxic	Ethanolic extract showed better activity against two human cancer cell lines whereas no activity was observed against normal human cell line by both water and alcholic extract[38]
Water extract of *C. zedoaria* rhizome	Anticancer	Water extract of *C. zedoaria* exhibited role in inhibition of cancer metastasis[41]
Methanolic extract of *C. zedoaria*	Anticancer	Extract exhibited potent inhibition of COX-2 activity[42]
Essential oil of *C. zedoaria* rhizome	Antioxidant	Oil showed good to moderate antioxidant activity in DPPH model[7]

its use in cancer, ulcer, diarrhoea, dysentery, toothache, etc. Research carried out using different in-vitro and in-vivo techniques of biological evaluation support most of these claims.

C. zedoaria is cultivated in India, Sri Lanka and China for its starch-rich tubers, known in the trade as zedoary root. This root is the source of 'Shoti Starch', which is used as a substitute for arrowroot and barley. Zedoary is also used in the manufacture of liquors, stomach essences and bitters and for the production of perfumes and cosmetics.[18]

Presently there is an increasing interest worldwide in herbal medicines accompanied by increased laboratory investigation into the pharmacological properties of the bioactive ingredients and their ability to treat various diseases.[44–46] Numerous drugs have entered the international market through exploration of ethnopharmacology and traditional medicine. Although scientific studies have been carried out on a large number of Indian botanicals, a considerably smaller number of marketable drugs or phytochemical entities have entered the evidence-based therapeutics. Efforts are therefore needed to establish and validate evidence regarding safety and practices of Ayurvedic medicines.[47]

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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