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Curcuma zedoaria (Christm.) Roscoe: Benefits and Bioactivity

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A B S T R A C T

Curcuma zedoaria (Christm.) Roscoe or Temu Putih is a native plant in India and has been long cultivated in Indonesia. By the local communities in Java, it has been used as a component of the Jammu and the traditional medicine. This article is based on literature from offline and online media. Offline literature used the books, whereas online media used Web, Scopus, Pubmed, and scientific journals. Based on a study of ethnobotany Curcuma zedoaria was used as medicine and spices. The main secondary metabolites of *Curcuma zedoaria* rhizomes are terpenoids, especially sesquiterpenoids and monoterpenoids. *Curcuma zedoaria* have bioactivities as anticholesterol, anti-tumor/cancer, anti-inflammation, fever, antipyretic, analgesic dan anti-microbial

1. Introduction

The genus Curcuma L. (Zingiberaceae) is very important economically because it is a tradable commodity. The genus Curcuma L. is one of the largest genera in the Zingiberaceae family and has about 80 species, which are distributed throughout tropical Asia from India, South China, Southeast Asia, Papua New Guinea, and North Australia. It is estimated that 50% of the species of the Curcuma genus are used by humans and more than 50% of the Curcuma species are unknown. Apart from being economically important in the tropics, some of the genus Curcuma are used as ornamental plants such as Curcuma xanthorrhiza (ginger), *Curcuma zedoaria* (white turmeric), and Curcuma longa (turmeric).[1,2]

Species in the genus Curcuma have similar morphological structures, especially leaf parts so it is difficult to distinguish from one species to another. To identify species of the Curcuma genus, various characters are used, including rhizome color, inflorescence, bractea shape and color, and other flower parts. Taxonomic knowledge of the genus Curcuma is needed to correctly determine which species are used commercially as spices, ornamental plants, and medicines. Initially, Curcuma was a member of the Hedychiceae family but was subsequently revised and included in the Zingiberaceae family.[2-4]

Curcuma zedoaria or also known as turmeric / temu putih is one of the Curcuma genus which is widely used as a medicine and as an ingredient in cooking. In Indonesia, *Curcuma zedoaria* leaves are

used as an additional spice to enhance the taste of fish and other foods. In the treatment of *Curcuma zedoaria,* it has long been used by various ethnic groups in Indonesia, Malaysia, and India. In Malaysia, *Curcuma zedoaria* is widely consumed as a spice and food for postpartum mothers.[3]

The use of plants as medicine is related to their secondary metabolite content. This article will discuss in more detail the relationship between the secondary metabolite content of *Curcuma zedoaria* with its utilization and bioactivity.

2. Methods

The writing of this article is based on literature studies obtained both on and offline. Online articles in the form of journals and research results. Offline is based on various literature books such as Plants Resources of Southeast Asia and other books. The online media is based on the Web, Scopus, Pubmed, and online media which are used for publications of various scientific journals.

3. Results and Discussion

Description of *Curcuma zedoaria* (Christm.) Roscoe

Phylogenetically, Zingiberales belong to the group of monocots. Zingiberaceae is the largest family in the order Zingiberales compared to Musaceae, Strelitziaceae, and Heliconiaceae. Zingiberaceae is pantropically distributed with one genus (Renealmia) found in the Neotropics, four genera (Aframomum, Aulotandra, Siphonochilus, and Renealmia) found in Africa, and the rest of the genera distributed in East Asia and the Pacific Islands. Zingiberaceae has a genus of 53 genera and more than 1200 species. Curcuma is one of the genera in the Zingiberaceae family with about 80 species. It is estimated that 50% of the species of the Curcuma genus are used by humans and more than 50% of the Curcuma species are unknown.[5-7]

Curcuma zedoaria or often referred to as Temu Putih is a native species of India, which has been cultivated throughout Southeast Asia, including Indonesia. The name of the white meeting for *Curcuma zedoaria is* thought to be related to the presence of white tubers, even though the rhizomes are yellow. *Curcuma zedoaria* (Figure 1) is a perennial herb, that has a height of one meter, the main rhizome is ovoid, and the inside of the tuber is pale yellow. Leaf-blade *Curcuma zedoaria* is 80 cm long, usually with purple blotches along the midrib on both leaf surfaces.[8]

Secondary Metabolites *Curcuma zedoaria* (Christm.) Roscoe

Plants are the source of Phytochemical compounds that are widely used in chemotherapy treatment, and most of them are still extracted. The potential of secondary metabolite compounds can be used for cancer, diabetes mellitus, heart, and cholesterol. Secondary metabolites are compounds produced from secondary metabolic processes by using intermediates from primary metabolic reactions which are widely used as medicinal substances. Secondary metabolic types and concentrations vary between plant species. Secondary metabolites are used by plants as a defense against an unfavorable environment but are sometimes used as a marker for plant identification.[9,10]

Curcuma zedoaria has main secondary metabolites in the form of terpenoids especially sesquiterpenoids, phenolic, tannins, saponins, alkaloids, terpenoids, and steroids. Terpenoids are compounds where terpenes are a chemical compound composed of the isoprene molecule CH2 = C (CH3) - CH = CH2 and the carbon frame is built by joining two or more C5 units. Five sesquiterpenes were isolated on the rhizome of *Curcuma zedoaria,* namely three types of guaiane sesquiterpene (curcumenol, isoprocurcumenol and procurcumenol), one type of caraborane sesquiterpene (curcumenone), and one type of germacrane sesquiterpene. (zederone). The main sesquiterpene compounds in *Curcuma zedoaria* include furanodiene, furanodiene, germacrone, curdione, neocurdione, curcumenol, isocurcumenol, aerugidiol, zedoarondiol, curcumenone and curcumin.[11,12]

The extracted secondary metabolites in plants are

influenced by the extracting compound. The rhizoma extract of Curcuma zedoaria using hexane and dichloromethane contained compounds (Figure 2) namely: labda-8,12diena-15,16 dial dehydrocurdione, curcumenone, comosone II, curcumenol, procurcumenol, germacrone, zerumbone epoxide, zederone, 9- isopropilidene -2,6-dimethyl-11-oxatricyclo [6.2.1.01, 5] undec-6-en-8-ol, furanodiena, germacrone -4,5- epoxide, calcaratarin A, isoprocurcuminol, germacrone -1,10-epoxide, zerumin A, curcumanolide A, curcuzedoalide, and gweicurculactone. The structure of the compounds extracted from *Curcuma zedoaria* can be seen in Figure 2. Rimpan *Curcuma zedoaria* successfully isolated nine sesquiterpenes (germacrone, dehydrocurdione, curcumenol, isoprocurcumenol, curcumenone, procurcumenol, zerumbone epoxide, zederone), gweicurculactone, and one labdane tertpene (zerumin A).[12,13]

Other studies have successfully isolated more than 10 sesquiterpenes from *Curcuma zedoaria* rhizomes, including furanodiene, furanodie none, zedorone, curzerenone, curzeone, germacrone, 13-hydroxygermacrone, dihydrocurdione, curcumenone, and zedoaronediol. Another study succeeded in isolating at least 27 compounds from Curcuma zedoaria including curcumin, furanodiene, furanodienone, zedorone, curzerenone, curzeone, germacrone,13-hydroxygermacrone, dihydrocurdione, curcumenone, zedoaronediol, curcumin, curcumanolide, curcuminoids. Ethylpara methoxycinnamate, 18, β-turmerone, epicurzerenone, curzerene, 1,8-cineole, β - eudesmol, zingiberene, dihydrocurcumin, curdione, neocurdione, α-phellandrene.[13]

Benefits of *Curcuma zedoaria* (Christm.) Roscoe

Curcuma zedoaria has been around for a long time used as food and medicinal ingredients. *Curcuma zedoaria* is widely consumed as a spice, such as the taste in traditional dishes, and as a food for postpartum mothers. *Curcuma zedoaria* has properties such as cholesterol, anti-tumor / cancer, anti-inflammatory, fever, antipyretics, and analgesics, anti-microbes.[14]

Anti-Cholesterol

Cholesterol is a circulatory system disorder with excessive blood fat content. *Curcuma zedoaria* extract at a dose of 200-400 mg/kg was found to be effective in reducing total cholesterol levels (17.1% -19.65%) after 12 days of pre-treatment which showed antihilperidemic activity. Curcuma's cholesterol-lowering actions include disrupting intestinal cholesterol absorption, increasing the conversion of cholesterol to bile acids, and increasing the excretion of bile acids through its choleretic effect. The main sesquiterpene compounds, including furanodiene, furanodiene, germacrone, curdione, neocurdione, curcumenol, isocurcumenol, aerugidiol, zedoarondiol, curcumenone, and curcumin, have shown potential to protect against liver injury-induced d-galactosamine or lipopolysaccharide in mice. *Curcuma zedoaria* rhizome has a protective role against hypercholesterolemic and lipidemic conditions. The proper treatment of the different components of the metabolic syndrome such as hypercholesterolemia and hypertriglyceridemia requires some synthetic drug prescription to prevent or reduce the risk of morbidity and cardiovascular mortality. *Curcuma zedoaria* suggests the consumption of this plant for possible treatment of hyperlipidemia, hypercholesterolemia, and / or atherosclerosis. *Curcuma zedoaria* is one of the plants that is responsible for their cholesterol-lowering effect in an in-vivo model.[15-17]

Anti-inflammatory

Curcuma zedoaria is traditionally used in the treatment of inflammation or anti-inflammatory. Petroleum ether extract, chloroform from rhizoma C. zedoaria showed significant p <0.001 anti-inflammatory, when compared with controls with standard drugs (Indomethacin 10 mg / kg.i.p and Rumalaya forte 200 mg / kg). Petroleum ether extract 200 and chloroform 400 mg/kg of C. zedoaria extract showed maximum anti-inflammatory activity at 2 to 6

hours.[18]

Anticancer

Compounds used as cancer drugs are compounds that can inhibit cell growth. Extracts from C. zedoaria rhizomes using hexane and dichloromethane have anti-cancer activity against four cancer cell lines (Ca Ski, MCF-7, PC-3, and HT-29). Its anti-cancer properties are due to the protein-bound polysaccharides of C. zedoaria which can inhibit the growth sarcoma-180.[19]

The rhizome of C. zedoaria is known as one of the simplicia which can protect and cure many diseases, especially tumors and cancer. Temu Putih extract has been shown to be able to inhibit the growth of lung tumors and ovarian cancer. Several C. zedoaria compounds reported having anti-cancer activity include α-curcumin and curcumin. Another study reported that C. zedoaria rhizome extract with a concentration of 200 mg/kg body weight was able to inhibit mitotic activity. The ethanol extract of temu Putih rhizome can inhibit the growth of lung tumors in female mice with a concentration of 250 mg/kg BW (49.63%), a dose of 500 mg / kgBW (73.33%)), and a dose of 750 mg/kg (77.78%). He further said that the damage to sub- diploid cells increases depending on the concentration.[18-20]

The active compound in the form of α-curcumin can inhibit the viability of SiHa cells > 73% for 48 hours of incubation. The ability of α- curcumene to inhibit cancer through fragmentation of nucleosomal DNA. Mitochondrial cytochrome c activation and in vitro caspase -3 activity assay showed that caspases activation accompanies the apoptotic effect of α-curcumene, which mediates cell death. These results indicate that the apoptotic effect of α-curcumene on SiHa cells can be activated by caspase -3 via cytochrome-release mitochondria c. Activation and in vitro caspase -3 activity assay showed that caspases activation accompanies the apoptotic effect of α-curcumene, which mediates cell death. These results indicate that the apoptotic effect of α-curcumene on SiHa cells can be activated by caspase -3 via cytochrome-release mitochondria c. The ethanol extract of Temu Putih rhizome showed inhibiting activity of OVCAR-3 cells, namely human ovarian cancer cell line. Curcumin has been shown to be able to suppress cancer cell proliferation through the mechanism of inducing apoptosis, inhibiting prostaglandin synthetase, leukotriene biosynthesis, and blocking the action of the arachidonic 5-lipooksigenase enzyme.[19]

Leukemia is a disease caused by the uncontrolled growth of white blood cells that is often referred to as blood cancer. Among the sesquiterpenes tested, the curcuminoid compound from C. zedoaria showed the strongest cytotoxic properties against WEHI-3 and HL-60 cells with IC50 values of 25.6 and 106.8 μM, for the WEHI-3 and HL-60 cell lines. respectively (Figure 2). Curcumenone compounds also showed cytotoxicity against normal human umbilical vein endothelial (HUVEC) cells with an IC50 value of 69.6 μM .[21]

Fever, Antipyretics and Analgesics

Fever is the body's natural defense creating an environment in which infectious agents or damaged tissue cannot survive. Paracetamol is a commercial synthetic drug that is used to reduce fever. Long-term use of synthetic drugs will result in organ damage. Fever or pyrexia is caused secondary to an infection, tissue damage, swelling, transplant rejection, malignancy, or other conditions. Among other diseases (Chattopadhyay et al., 2005). Usually, infected or damaged tissue initiates pro-inflammatory mediator-enhanced formation (cytokines such as interleukin 1β, α, β, and tumor necrosis factor- α), which increase prostaglandin E2 (PGE2) synthesis near the preoptic hypothalamic area. The synthesis of prostaglandin E2 (PGE2) will trigger the hypothalamus to raise body temperature. The results showed that the ethanol extract of C. zedoaria significantly reduced yeast-induced body temperature in rats in a dose-dependent manner and the antipyretic effect at a dose of 750 mg/kg was comparable to the standard antipyretic paracetamol (10 mg/kg).[18]

Antipyretics are compounds that function to reduce pain, which is caused by disturbances in the human body. Phytochemical screening of ethanol extract shows the presence of tannins, flavonoids, saponins, alkaloids, terpenoids, carbohydrates, and steroids as the main constituents of C. zedoaria extract, some of which have antipyretic activity. Most antipyretic drugs inhibit the expression of cyclooxygenase -2 (COX-2) to reduce body temperature which increases the inhibition of PGE2 biosynthesis. In addition, this synthetic agent irreversibly inhibits COX-2 with high selectivity but is toxic to liver cells, glomerulus, brain cortex, and heart muscle, whereas natural COX-2 inhibitors have lower selectivity with fewer side effects. For pro-inflammatory mediators, a number of plant extracts have been studied to modulate the cyclooxygenase pathway that inhibits the synthesis of leukotrienes and prostaglandins by inhibiting the COX-1 and COX-2 pathways.[17-19]

Methanolic rhizome extract has mild analgesic properties (with 66.67% writhing inhibition). The ether extracts from rhizomes, leaves, and stems showed moderate analgesic properties (with writhing inhibition of 70.24%, 75%, 71.43% respectively), while the ether extracts from the leaves showed significant analgesic properties (with 91 writhing inhibition, 67%) Methanolic rhizome extract has mild analgesic properties (with 66.67% writhing inhibition). The ether extracts from rhizomes, leaves, and stems had shown moderate analgesic properties (with writhing inhibition of 70.24%, 75%, 71.43% respectively), while the ether extracts from the leaves showed significant analgesic properties (with writhing inhibition of 91, 67%).[20]

Anti-Microbial

Anti-microbial is a compound that can inhibit microbial growth. Rhizoma extract of C.zedoaria has anti-bacterial activity and is anti-fungal. Bacteria growth that can be inhibited by C.zedoaria can be in the form of gram-positive bacteria (Bacillus cereus, Bacillus megaterium, Bacillus subtilis, Staphylococcus aureus, Sarcina lutea) and gram-negative bacteria (Salmonella paratyphi, Salmonella typhi, Vibrio parahemolyticus, Vibrio minicus, E. coli, Shigella dysenteriae). Pseudomonas aureus, Shigella boydii, Candida albicans, and Aspergillus niger are types of fungi whose growth is inhibited by C. zedoaria extract. Another study stated that gram-negative bacteria S. typhi, S. paratyphi A, S. paratyphi B, Escherichia coli, Shigella boydii, Shigella dysenteriae, Shigella sonei but insensitive to Vibrio cholerae, Vibrio mimicus, Klebsiella sp. Pseudomonas aeruginosa and also insensitive to gram-positive bacteria such as Staphylococcus aureus, B. subtilis, B. cereus, B. megaterium, and Sarcina lutea.

Extracts from C. zedoaria contain triterpenoids that can inhibit the growth of Staphylococcus aureus and E. coli bacteria with weak inhibition at concentrations of 500 ppm and 1000 ppm. Crude methanol extract has antimicrobial activity against gram-positive, gram-negative bacteria, and fungi comparable to the drug kanamycin standard. The stem extract showed mild sensitivity to several gram-positive, gram-negative bacteria and fungi (inhibition zone 7 mm). The ether leaf extract and the methanol leaf extract also showed mild sensitivity to some gram-positive, gram-negative bacteria and fungi (10-12 mm and 11-12 mm each). Methanolic rhizome extract showed significant sensitivity to several gram-positive, gram-negative bacteria and fungi (inhibition zone 13-15 mm).[21-23]

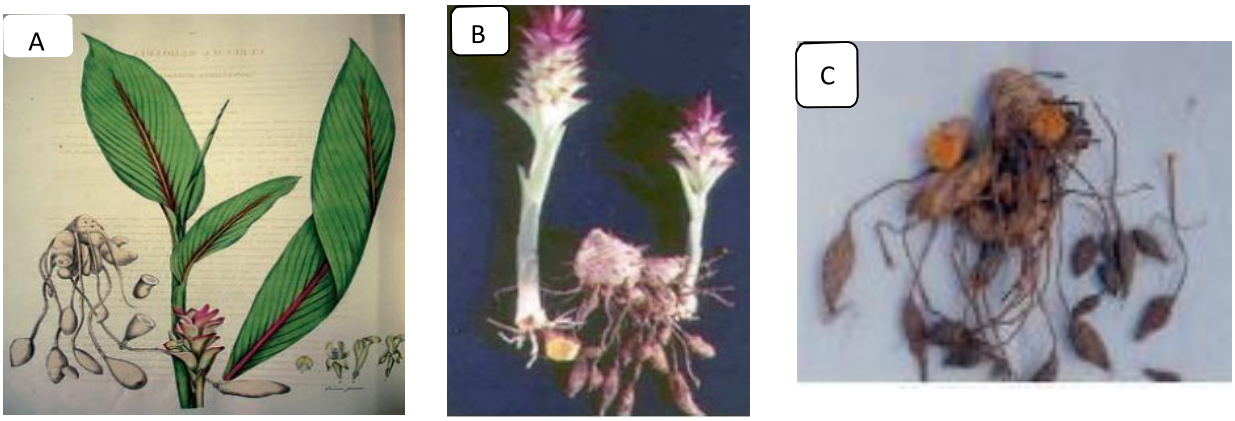
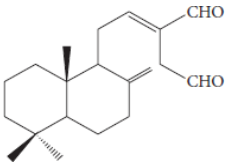
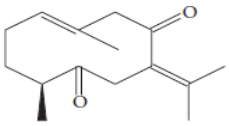


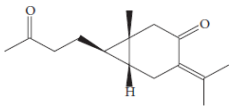
Figure 1. *Curcuma zedoaria* (Christm.) Roscoe A. Illustration; B. flowering stalk with rhizomes; c. rhizomes with sessile umbil.



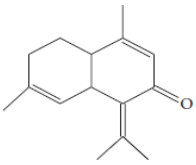
labda-8(17),12 diene-15,16 dial



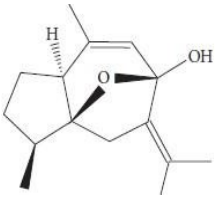
dehydrocurdione



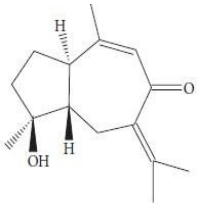
curcumenone



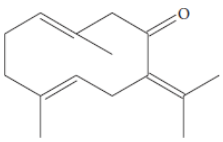
comosone II



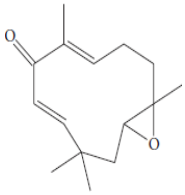
curcumenol



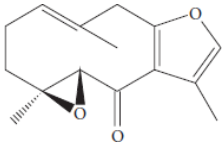
procurcumenol



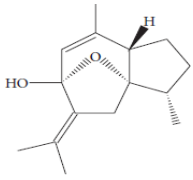
germacrone



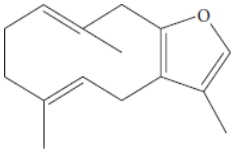
zerumbone epoxide



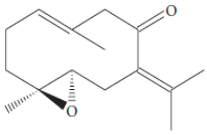
zederone



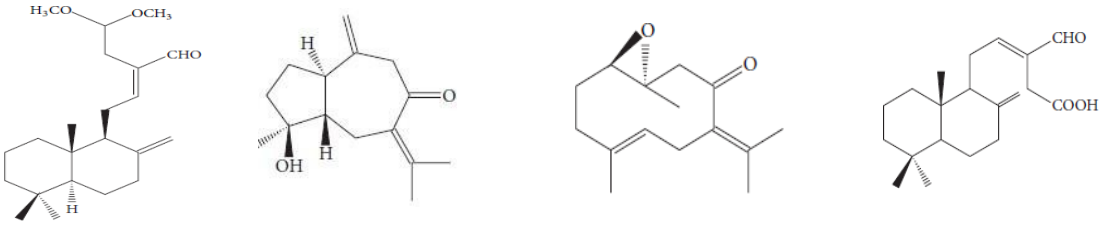
9-isopropylidene-2,6-dimethyl-11-oxatricyclo [6.2.1.01,5]undec-6-en-8-ol



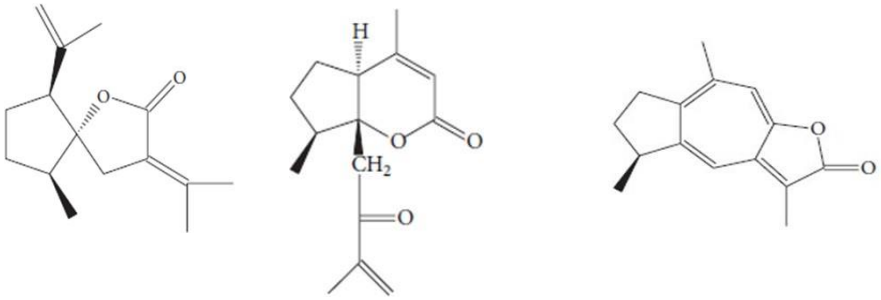
furanodiene



germacrone-4,5- epoxide



calcaratarin A soprocurcumenol germacrone-1,10-epoxide zerumin A



curcumanolide A curcuzedoalide gweicurculactone

Figure 2. Structure of various compounds that have been isolated from rhiizoma *Curcuma zedoaria*

4. Conclusion

Curcuma zedoaria has properties such as cholesterol, anti-tumor/cancer, anti-inflammatory, fever, antipyretic, analgesic, and anti-microbial.

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