



Curcuma zedoaria (Christm.) Roscoe (Benefits And Bioactivity)

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ABSTRACT

Curcuma zedoaria (Christm.) Roscoe or temu putih is native plant in India, have been long cultivated in Indonesia. By the local communities in Java, its have been used as component of the jamu and the traditional maedicine. This article is based on literature offline andonline media. Offline literature used the books, whereas online media used Web, Scopus, Pubmed, and scientific journals. Based on a study of ethnobotany Curcuma zedoaria used as medicine and spices. The main of secondary metabolites of Curcuma zedoaria rhizomes are terpenoids especially seskui-terpenoid and monoterpenoid. Curcuma zedoaria have bioactivities as anticholesterol, anti tumor/ canker, anti inflammation, demam, antipiretik, 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, has about 80 species, which are distributed throughout tropical Asia from India, South China, Southeast Asia, Papua New Guinea, and North Australia (Srigusa et al., 2007). 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 (Srigusa et al., 2007). Apart from being economically important in the tropics, some of the genus *Curcuma* are used as ornamental plants (Leong-Škorničková et al., 2008) such as *Curcuma xanthorrhiza* (ginger), *Curcuma zedoaria* (white turmeric), and *Curcuma longa* (turmeric).

Species in the genus *Curcuma* have similar morphological structures, especially leaf parts, so that

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 (Škorničková and Sabu, 2005). 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 (Srigusa et al., 2007).

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 (Srigusa et al., 2007). In the treatment of *Curcuma zedoaria*, it has long been used by various

ethnic groups in Indonesia, Malaysia and India (Malek et al., 2004). In Malaysia, *Curcuma zedoaria* is widely consumed as a spice and food for postpartum mothers (Malek et al., 2004).

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

2. Research Methods

The writing of this article is based on literature studies obtained both on and off line. *Online* articles in the form of journals and research results. *Offline* is based on various literature books such as *Plants Resources of South East Asian* and other books. The *online* media is based on the Web, Scopus, Pubmed, and *on-line* media which are used for publications of various *Scientific journals*.

3. Results and Discussion

Description of *Curcuma zedoaria* (Christm.) Roscoe

Phylogenetically, Zingiberales belongs to the group of eumnocots. *Zingiberaceae* is the largest family in the order *Zingiberales* compared to *Musaceae*, *Strelitziaceae*, and *Heliconiaceae* (Kress, 1990). *Zingiberaceae* are 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 (Kress et al., 2002). *Zingiberaceae* has a genus of 53 genera and more than 1200 species (Kress, 1990). *Curcuma* is one of the genera in the *Zingiberaceae* family with about 80 species (Srigusa et al., 2007). 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 (Srigusa et al., 2007).

Curcuma zedoaria or often referred to as temu putih is a *native species* of India, which has been cultivated throughout Southeast Asia (Srigusa et al., 2007), 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, has a height of one meter, the main rhizome is ovoid, and the inside of the tuber is pale yellow (Srigusa et al., 2007). Leaf blade *Curcuma zedoaria* is 80 cm long, usually with purple blotches along the midrib on both leaf surfaces. When young (small), the color of the rhizomes of *C. zedoaria* is similar to that of *Curcuma aeruginosa* and *Curcuma mango* (Hamdi et al., 2014). *Curcuma zedoaria* (Christm.) Rosc.

Secondary Metabolites *Curcuma zedoaria* (Christm.)

Roscoe

Plants are the source Phytochemical compounds are widely used in chemotherapy treatment, and most of them are still extracted (Dias et al., 2012). The potential of secondary metabolite compounds can be used as 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.

Curcuma zedoaria has main secondary metabolites in the form of terpenoids (Azam et al., 2014; Tariq et al., 2016) especially sesquiterpenoids (Ma et al., 1995; Syu et al., 1998; Tariq et al., 2016), phenolic (Azam et al., 2014; Tariq et al., 2016), tannins, saponins, alkaloids, terpinoids, and steroids (Azam et al., 2014). Terpenoids are compounds where terpenes are a chemical compound composed of the isoprene molecule $\text{CH}_2 = \text{C}(\text{CH}_3) - \text{CH} = \text{CH}_2$ and the carbon framework is built by joining two or more C5 units (Harborne, 1987). Five sesquiterpenes were isolated on the rhizome of *Curcuma zedoaria*, namely three types of guaiane sesquiterpene (curcumenol, isoprocucumenol and procucumenol), one type of caraborane sesquiterpene (curcumenone), and one type of germacrane sesquiterpene. (zederone) (Tariq et al., 2016). The main sesquiterpene compounds in *Curcuma zedoaria* include furanodiene, furanodiene, germacrone, curdione, neocurdione, curcumenol, isocurcumenol, aerugidiol,

zedoarondiol, curcumenone and curcumin (Matsuda et al., 1998).

The extracted secondary metabolites in plants are influenced by the extracting compound. The rhizoma extract of *Curcuma zedoaria* using hexane and dichloromethane contained compounds (**Fig. 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 (Hamdi et al., 2014). 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 terpene (zerumin A) (Hamdi et al., 2015).

Makabe et al. (2006) have successfully isolated more than 10 sesquiterpenes from *Curcuma zedoaria* rhizomes, including: furanodiene, furanodienone, zedorone, curzerenone, curzeone, germacrone, 13-hydroxygermacrone, dihydrocurdione, curcumenone and zedoarondiol. Rahman et al. (2012) succeeded in isolating at least 27 compounds from *Curcuma Zedoaria*, including: curcumin, furanodiene, furanodienone, zedorone, curzerenone, curzeone, germacrone, 13-hydroxygermacrone, dihydrocurdione, curcumenone, zedoarondiol, curcumenol, curcumanolide, curcumanolide, ethylparmethoxycinnamate, 18, β -turmerone, epicurzerenone, curzerene, 1,8-cineole, β - eudesmol, zingiberene, dihydrocurcumin, curdione, neocurdione, α -phellandrene.

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 of traditional dishes, and as a food for postpartum mothers (Malek et al., 2004). *Curcuma zedoaria* has

properties as cholesterol (Matsuda et al., 1998; Khare et al., 2008; Duangjai et al., 2011; Srividya et al., 2012; Tariq et al., 2016), anti-tumor / cancer (Kim et al., 2000; Lobo et al 2009; Hamdi et al., 2014; Handajani et al., 2003; Murwanti et al., 2004; Shin and Lee, 2013), anti-inflammatory (Kaushik and Jalalpur, 2011), fever, antipyretics, and analgesics (Navarro et al., 2002; Chattopadhyay et al., 2005; Azam et al., 2014), antimicrobes (Rita et al., 2010; Shahriar, 2010; Das and Rahman, 2012).

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 antihyperlipidemic activity (Srividya et al., 2012). *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 choleric effect (Khare et al., 2008). 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 (Matsuda et al., 1998). *Curcuma zedoaria* rhizome has a protective role against hypercholesterolemic and lipidemic conditions (Tariq et al., 2016). The proper treatment of the different components of the metabolic syndrome such as hypercholesterolemia and hypertriglyceridemia requires some synthetic drug prescription for prevent or reduce the risk of morbidity and cardiovascular mortality (Tariq et al., 2016). *Curcuma zedoaria* suggests the consumption of this plant for possible treatment of hyperlipidemia, hypercholesterolemia and / or atherosclerosis (Pizziolo et al., 2011). *Curcuma zedoaria* is one of the plants that is responsible for their cholesterol-lowering effect in an in-vivo model (Duangjai et al., 2011).

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 (Kaushik and Jalalpur, 2011).

Anti cancer

Compounds used as cancer drugs are compounds that can inhibit cell growth. The anti-cancer effects and biological properties of *C. zedoaria* rhizome have been widely reported by Lobo *et al.*, (Lobo *et al.*, 2009; Hamdi *et al.*, 2014). 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) (Hamdi *et al.*, 2014). Its anti-cancer properties are due to the protein-bound polysaccharides of *C. zedoaria* which can inhibit growth sarcoma-180 (Kim *et al.*, 2000).

The rhizome of *C. zedoaria* is known as one of the simplicia which can protect and cure many diseases, especially tumors and cancer (Handajani *et al.*, 2003; Murwanti *et al.*, 2004; Shin and Lee., 2013). Temu putih extract has been shown to be able to inhibit the growth of lung tumors (Murwanti *et al.*, 2004), ovarian cancer (Syu *et al.*, 1998). Several *C. zedoaria* compounds reported to have anti-cancer activity include α -curcumene (Shin and Lee, 2013) and curcumin (Syu *et al.*, 1998). Shin and Lee (2013) reported that *C. zedoaria* rhizome extract with a concentration of 200 mg / kg body weight was able to inhibit mitotic activity. A different matter was reported by Murwanti *et al.* (2004) that the ethanol extract of temu putih rhizome can inhibit the growth of lung tumors in female mice and 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%) (Murwanti *et al.*, 2004). He further said that the damage to sub-diploid cells increases depending on the concentration (Shin and Lee, 2013).

The active compound in the form of α -curcumene 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 (Shin and Lee, 2013). 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 caspase-3 via cytochrome release mitochondria c (Shin and Lee, 2013). The ethanol extract of temu putih rhizome showed inhibiting activity of OVCAR-3 cells, namely human ovarian cancer cell line (Syu *et al.*, 1998). Curcumin has been shown to be able to suppress cancer cell proliferation through the mechanism of inducing apoptosis (Surh, 1999), inhibiting prostaglandin synthetase, leukotriene biosynthesis, and blocking the action of the arachidonic 5-lipooksigenase enzyme (Kiuchi, 1992).

Leukemia is a disease caused by uncontrolled growth of white blood cells that is often referred to as blood cancer. Among the sesquiterpenes tested, the curcumenone 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 μ M, 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 μ M (Hamdi and Satti, 2017).

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 caused secondary to infection, tissue damage, swelling, transplant rejection, malignancy or other conditions. 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. Synthesis of prostaglandin E2 (PGE2) will trigger the hypothalamus to raise body temperature (Saper and Breder, 1994). 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) (Azam *et al.*, 2014).

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. (Azam *et al.*, 2014). Most of the 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 less side effects. For pro-inflammatory mediators a number of plant extracts have studied modulate the cyclooxygenase pathway that inhibits the synthesis of leukotrienes and prostaglandins by inhibiting the COX-1 and COX-2 pathways (Oh *et al* 2007; Alberto *et al*, 2009).

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 91, 67%)

Anti Microbial

Anti-microbial is a compound that can inhibit microbial growth. Rhizoma extract of *C.zedoaria* has anti-bacterial activity (Rita, 2010; Das and Rahman, 2012; Shahriar 2010) and anti-fungal (Das and Rahman 2012). Bacteria growth that can be inhibited by *C.zedoaria* can be in the form of gram-positive bacteria (*Bacillus sereus*, *Bacillus megaterium*, *Bacillus subtilis*, *Staphylococcus aureus*, *Sarcina lutea*) and gram-negative bacteria (*Salmonella paratyphi*, *Salmonella typhi*, *Vibrio parahemolyticus*, *Vibrio minicus*, *E. coli*, *Shigella dysenteriae*) (Das and Rahman, 2012). *Pseudomonas aureus*, *Shigella boydii*, *Candida albicans*, *Aspergillus niger* are types of fungi whose growth is inhibited by *C. zedoaria* extract (Das and Rahman, 2012). Shahriar (2010) 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*, *Sarcina lutea* (Shahriar, 2010).

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 (Rita, 2010). Crude methanol extract has antimicrobial activity against gram-positive, gram-negative bacteria, and fungi comparable to the drug kanamycin standard (Das and Rahman, 2012). 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) (Das and Rahman, 2012).

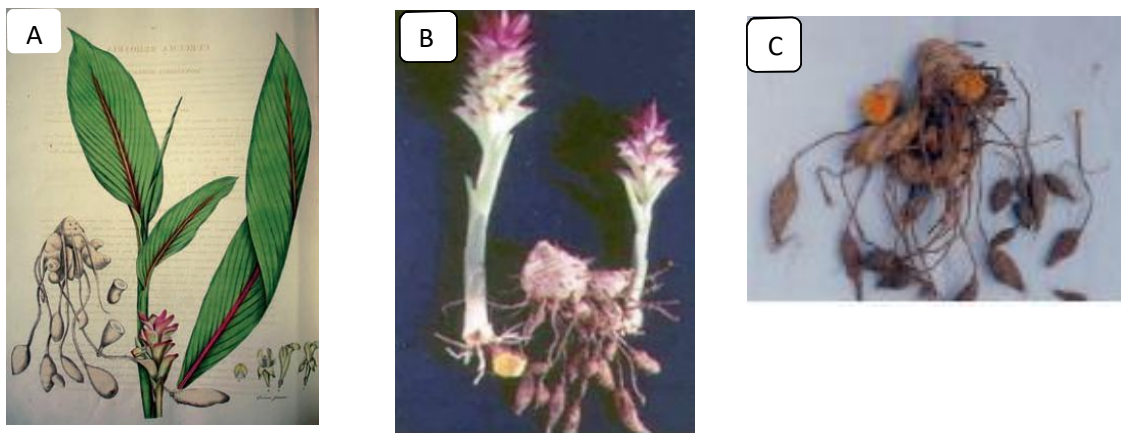
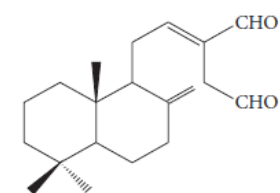
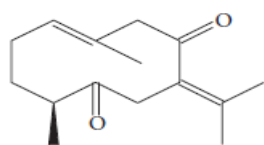


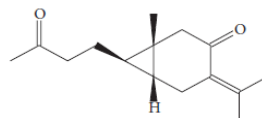
Figure 1. *Curcuma zedoaria* (Christm.) Roscoe A. Illustration (Leong-Škorničková et al., 2008); B. flowering stalk with rhizomes; C. rhizomes with sessile umbil (Srivastava et al., 2011).



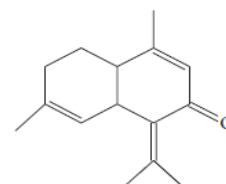
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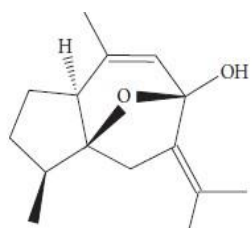
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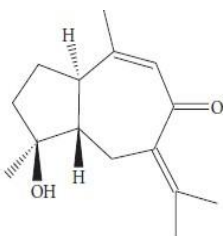
curcumenone



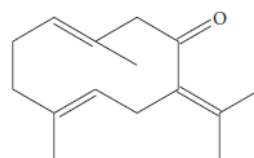
comosone II



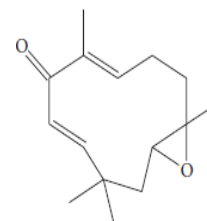
curcumenol



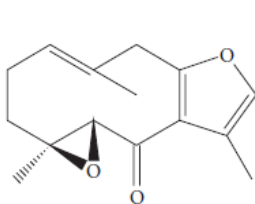
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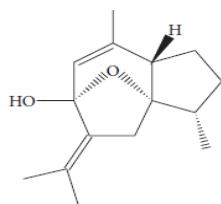
germacrone



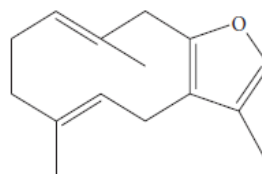
zerumbone epoxide



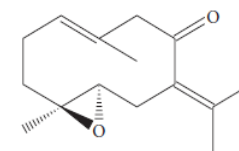
zederone



9-isopropylidene-2,6-dimethyl-11-oxatricyclo[6.2.1.0^{1,5}]undec-6-en-8-ol



furanodiene



germacrone-4,5-epoxide

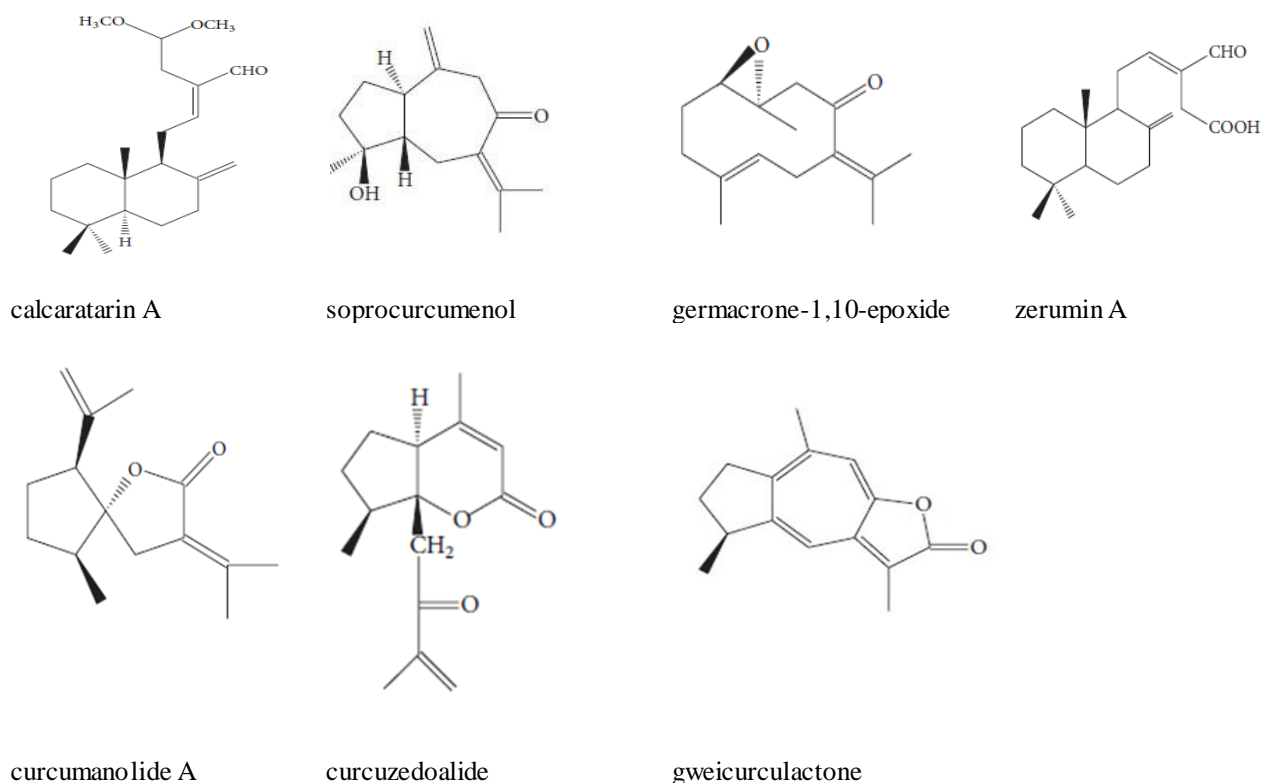


Figure 2. Structure of various compounds that have been isolated from rhizoma *Curcuma zedoaria* (Hamdi et al., 2014)

4. CONCLUSION

1. Terpenoids, especially sesquiterpenoids and monoterpenoids, are the main secondary metabolites found in *C. zedoaria* rhizomes.
2. *Curcuma zedoaria* has properties as cholesterol, anti-tumor / cancer, anti-inflammatory, fever, antipyretic, analgesic and anti-microbial.
3. Secondary metabolite compounds *C. Zedoaria* which have properties include the main sesquiterpene compounds in *Curcuma zedoaria* including furanodiene, furanodiene, germacrone, curdione, neocurdione, curcumenol, isocurcumenol, aerugidiol, zedoarondiol, curcumenone and curcumin.

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