Indonesian Food Science and Technology Journal
IFSTJ : Vol 3 no 1 December 2019
ISSN : 2615-367X

BIOACTIVITY OF CINNAMON *(Cinamomum* sp)

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***Abstract*-Cinnamon has been widely used as a spice in food and medicine. Cinnamon grow in the Asian region. Indonesia is one of the cinnamon producing countries. The chemical composition of cinnamon plants varies according to the variety, the part of the plant, the place and the climate to grow. The main bioactive component in cinnamon bark is cynnamaldehide. Cynnamaldehide in cinnamon has good physiological effects on body health such as antioxidants, anticancer, anti-inflammatory, antidiabetic, antidyslipidemic anti-hyperuricemia, and antimicrobial properties. Research is generally still conducted in vitro, clinical trial limited.**

***Keywords*— cinnamon; antioxidant; anticancer; cynnamaldehyde.**

INTRODUCTION

Cinnamon is a spice that it has been known for a long time. It has been widely used as a spice in food and medicine. Cinnamon belongs to the family Lauraceae and genus Cinnamomum. The genus Cinnamomum has approximately 250 species, many of which grow in the Asian region. Indonesia is one of the cinnamon producing countries. *Cinnamomum burmanii* the mostly was planted. The production centers are Jambi and West Sumatra Other types widely traded *are C. zeylanicum* from South India, Sri Lanka and Madagascar, *C. cassia* from South China, Myanmar, and Vietnam, C. *loureirii* from Vietnam, Cambodia and Laos, and *C. syntoms* from Malaysia [1] and *C. osmophoeum* from Taiwan [2].

Part of the cinnamon plant traded for a long time was cinnamon bark. Cinnamon bark is processed into many essential oils which are then applied for various purposes such as flavor, cosmetics and medicine. The main component of cinnamon bark is cynnamaldehide [3]. FEMA sets GRAS status for cinnamaldehyde as flavor ingredient [4]. Apart from the actual skin of other parts of cinnamon, leaves and roots also contain many active components that function for health.

THE CHEMICAL COMPOSITION OF CINNAMON

The main bioactive component in cinnamon bark is cynnamaldehide, but there are also types of cinnamon whose main component is not cynnamaldehyde. Cynnamaldehyde in plants is in the pathic sikimat acid which functions to form lignin. Cynnamaldehide is formed from phenyl alanine through cinnamic acid, and subsequently turns into cynnamil alcohol in the process of lignin formation [3].

The chemical composition of cinnamon plants varies according to the variety, the part of the plant, the place and the climate to grow. The amount and type of compounds identified in the essential oils of the 5 types of cinnamon leaves were different depending on the variety. Consequently the amount of compounds in the essential oils of leaves of *C. cassia, C. zeylanicum, C. pauciflorum, C. tamala, and C. burmannii* are 22, 22, 21, 13, and 6. The main volatile components in *C. cassia* leaves aretrans-cynnamaldehyde (30.36%), 3-Methoxy, 1-2, propanediol (29.30%), and o-Methoxhy cynnamaldehyde (25.39%), *C. zeylaicum* are eugenol (79.75 %) and trans- cynnamaldehide (16.25 %), *C. pauciflorum* are eugenol (54.74 %), 5-(2-Propenyl),1-3,benzodioxole (17.23 %) and trans-cynnamaldehide (12.80 %), *C. tamala* are 5-(2-Propenyl),1-3,benzodioxole (28.67 %) dan trans-cynnamaldehide (15.90 %), dan *C. burmanii* adalah trans- cynnamaldehide (60.17 %) dan eugenol (17.62 %) [4]. Cinnamon leaves has phenolic and flavonoid content [5]. The yield of cinnamon oil is influenced by the type of variety. The highest yields of cinnamon leaf essential oils from highest to lowest were *C. cassia* (1.54%), *C. zeylanicum* (1.50%), *C. pauciflorum* (1.36%), *C. burmannii* (0.78%). and *C. tamala* (0.72%) [4]. Toxicity tests show that trans-cinnamaldehyde does not damage cells [2].

The main components of essential oils from cinnamon bark are cinnamal dehyde (76.34%), 2 propenal, 3-2-methoxyphenyl (11.02%) and propanone 1-4-methoxyphenyl [6]. The plant age affects the yield of cinnamon bark essential oil. High yields are produced in cinnamon plants that are harvested with more than 12 years of age. The yield and composition of cinnamon bark essential oils on the top, middle and bottom in plants of the same age are different. The highest yield was generated at the top (2.61%) followed by the middle (2.10%) and bottom (2.06%). Extraction of the upper and middle bark are more beneficial than extracting all the components of the bark [7].

ANTIOXIDANT ACTIVIY OF CINNAMON

Cinnamon plants have been known as plants whic contain antioxidants. Antioxidant components are found in leaves, bark, roots and fruit. Different varieties and climate will cause differences in the antioxidant activity. Ethanol extracts from 5 types of cinnamon leaves that grow in China, namely *C. burmanii*, *C. cassia, C. pauci fl orum, C. tamala,* and *C. zeylanicum* have different antioxidant activities. *C. zeylanicum* leaf extract has the highest DPPH radical scavenging and total antioxidant activity, while *C. tamala* has the highest superoxide anion scavenging activity [5].

Cynnamaldehide Indian bark *C. verum* and *C. burmanii* from Indonesia have antioxidant abilities [3]. Cynnamaldehide is able to suppress DPPH radicals, chelate metals and inhibit peroxidase activity [8]. The active component of butanol fraction from *C. osmophloeum* bark from Taiwan is kaempferol-7-O-rhamnoside. Its antioxidant activity has an EC_{50} value of 26 μM with the DPPH method and 68.1 μM with the superoxide scavenger method. This result is better when compared with cathecin which has an EC_{50} value of 20 μg / ml. The butanol fraction has an EC_{50} of 5 μg / ml, it is better than the active component [9].

ANTIDIABETES ACTIVIY OF CINNAMON

Water extract of *C. tamala* leaves (CTE) from India has the ability as an antidiabetic. The active components in *C. tamala* leaves are phenol (20.83 mg /g db), ascorbate (22.30 mg /g db), and caratenoid (0.82 mg / g db). Research on mice showed that after taking CTE at a dose of 250 mg / kg / day for 20 days, the level of sugar in the blood of mice changed from 375 mg / dL to 75 mg / dL (normal). The content of gluthatione in the liver increases from 25.66 mM / 100g to 45.00 mM / 100g (normal). Next, the contennt of glycogen t increases from 21.18 mg / 100g to 44.05 mg / 100 g, normal mice have glycogen 40.65 mg / 100 g. CTE reduced Thiobarbituric Acid Reactive Sub-Stances (TBARS) content in the liver of diabetic rats from 1.84 mM / 100g to 1.01 mM / 100g, normal rat TBARS was 0.82 mM / 100 [10].

Consumption of foods containing *C. zeylanicum* oil 5% reduced glucose levels in the blood of streptozotocin-induced mice from 354.82 to 182.00 mg / dl, triglycerides from 152.04 to 128.16 mg / dl, cholesterol from 102.36 to 76.34 mg / dl and LDL from 52.72 ± 1.0 to 32.95 mg/dl. The essential oil of *C. zeylanicum* decreased AST (alanine aminotransferase) from 119.3 to 84.2 U / L and decreased ALT (alanine aminotransferase) from 88.8 to 54.8 U / L. AST and ALT activity in blood is increased in diabetic mice. The main compounds in *C. zeylanicum* oil are cinnamaldehyde 62.7%, β-caryophyllene 6.5%, eugenol 5.25%, α-terpineol 2.8% and cinnamyl alcohol 0.18% [11].

The research showed consumption of *C. cassia* bark powder in people with type II diabetes can reduce blood sugar content. The study was conducted on 60 people with diabetes II from Pakistan (30 men and 30 women), age of 52.2 years and had suffered diabetic for 6.73 years. The results showed consumption of 1, 3, 6 g per day for 40 consecutive days reduced blood glucose levels in patients with a range that was not much different, namely 18-29%. Consumption of 1 g / day of *C. cassia* powder for 40 days, the patient's sugar levels dropped from 11.6 to 8.7 mmol / L on day 40 and 9.7 mmol / L on day 60 (20 days after consuming). In addition cinnamon powder also reduces cholesterol levels in the blood of diabetics by 13-26%, triglycerides 23-30% and LDL 10-24%. The decrease was still significant after 20 days consuming *C. cassia* (Khan et al., 2003). Consumption of cassia powder in patients with type II diabetes for 40 days at a dose of 4 times 2 g / day (after breakfast, lunch, afternoon and evening) blood sugar levels in patients dropped from 187.66 mg / dl (day 0) to 172.93 mg /dl. Addition of *C. verum* water extract to bioyogurts increases the total phenol content and antioxidant activity. Inhibiting the activity of α-amylase and α-glucosidase enzymes during storage at 4 ° C for 21 days.It is suitable for diabetics drinks [12].

ANTICANCER ACTIVIY OF CINNAMON

Water extract from cinnamon bark C. cassia has been tested for its ability to inhibit cervical cancer cells in vitro. Extracts (80 μg / ml) can reduce the growth of cancer cells up to three times. Giving the extract causes reduced cancer cell migration, due to the downregulation of MMP-2 expression. Increased cervical cancer cells are comparable to over-expression of Her-2 oncoprotein. Cinnamon extract significantly decreases the expression of Her-2 oncoprotein. In addition, the extract also induces apoptosis in cervical cancer cells through increased intracellular calcium signaling and loss of mitochondrial membrane potential (Koppikar, 2010). Lignant ester compound ((7′S, 8′R, 8R) -lyoniresinol-9,9′-di-O- (E) -feruloyl ester) was isolated from the stem and roots of *C. osmophloeum* namely. It can suppress cancer cells liver in humans, namely HepG2 (human hepatoma cell line) and Hep3B (human hepatocellular carcinoma) and oral cancer cells Ca9-22 (gingival cancer) with IC_{50} values 7.87, 4.31, and 2.51 μg / mL [13].

One of mechanism of cinnamon leaves as an anticancer through apoptosis. Apoptosis plays an important role in the development of multicellular organisms, regulating and maintaining the balance of cell populations in tissue. Apoptosis induction shows that these compounds can function to prevent the development of cancer. Apoptotic cells are characterized by a shrinking cell nucleus [14].

Cynnamaldehyde can induce apoptosis. Giving cynnamaldehide from *C. osmophloeum* leaves can induce apoptosis of K562 cells (leukemia cells) with concentrations up to 200 μM. Cynnamaldehyde dehyde induces cell death by altering core morphology, DNA fragmentation, and changing cell morphology (plasma membrane blebbing and cell shrinking). Cynnamaldehyde causes potential loss of mitochondrial transmembrane, stimulates the production of reactive oxygen species (ROS), releases mitochondrial cytochrome into cytosol and subsequently induces procaspase-9 and procaspase-3 processes. Increasing ROS

and decreasing glutathione are suspected cynnamaldehyde mechanisms in inducing K526 cells [15].

ANTI-INFLAMMATORY OF CINNAMON

Cinnamon is used as an anti-inflammatory and has an effect on nitric oxide (NO), nuclear factor kappa-b (NF-kB) and PGE2. NO is a free radical synthesized from L-arginine by nitric oxide synthase (NOS) in mammalian cells or tissues. NO are needed to regulate physical homeostasis, but large increases in NO are associated with various diseases and inflammation. NO production is related to the accumulation of PGE2 which will affect pathogenesis. NF-κB induces inflammation through induction of transcriptional code for inflammatory mediator genes. Cynnamaldehyde in *C. cassia* extract inhibits inflammation by inhibiting NO production and NF-kB transcription activity [16].

Trans-cinnamaldehyde from *C. osmophloeum* twig essential oil from Taiwan has the ability to suppress NO synthase (IC_{50} 88.4 µM). Giving trans-cinnamaldehyde 10 µg / ml can inhibit NO 59.9%. Whereas using essential oils from *C. osmophloeum* twig at a concentration of 10 µg / ml NO production can be inhibited by 48.3%. This result is lower than that of curcumin as a comparison, where curcumin 10 µg / ml inhibits NO about 80%. The administration of *C. osmophloeum* 10 µg / ml essential oil can inhibit the accumulation of PGE2 in 65% cells, this result is lower when compared with indomethacin (commercial drugs) which is 98%. Other components of *C. osmophloeum essential* oil can suppress NO. At a concentration of 10 µg / ml caryophyllene inhibits NO by 54.0%, L-borneol 46.1%, L-bornyl acetate 45.7%, eugenol 46.2%, b-caryophyllene 40.9%, E-nerolidol 40 7%, a-terpineol 38.1% and p-allylanisole 30.9% lower than MCO [2].

As an anti-inflammatory cynnamaldehyde can inhibit the secretion of interleukin-1beta and tumor necrosis factor alpha in lipopolysaccharides (LPS) or liplipoteicoic acid (LTA) which stimulates murine J774A.1 macrophages. Cynnamaldehide also suppresses the production of cytokines from LPS. Furthermore ROS released from the LPS that stimulates J774A.1 macrophages can be reduced by cynnamaldehyde. Cynnamaldehyde inhibits extracellular posporilation regulated by signal kinase 1/2 and c-Jun N-terminal kinase 1/2 on LPS [17].

ANTIDYSLIPIDEMIC OF CINNAMON

The active component of *C. osmophloeum* (COE) hot water extract is kaemferol 3-O-β-D-apiofuranosyl- (1-2) -α-L-arabinofuranosyl-7-O-αL-rhamnopyranoside (7.56%). Consumption of COE in hamsters with a high fat diet has been shown to reduce the content of total cholesterol (TC), triglycerides (TS) and low density lipoprotein (LDL-C). Consumption of COE 100 mg / kg for 5 weeks was reduced TC 12.63% and TG 34.25%. Consumption for 10 weeks decreased TC 33.88%, TG 36.88%. LDL 27.77%, without damage to the hamster's kidneys and liver. The content of glutamate oxaloacetate transaminase (GOT) and glutamic pyruvic transaminase (GPT) in blood does not differ between normal hamsters and those consuming COE (Lin et al. 2011). Consumption of water extract of *C. tamala* leaves from India 400 mg / kg for 10 days reduced TC 20.01%, TS 19, 68%, and LDL-C 28.9% in high fat diet albino rats [18].

ANTI-HYPERURICEMIA OF CINNAMON

Cinnamaldehyde from essential oils from *C. osmophloeum* leaves can reduce uric acid content in the blood. Giving cinnamaldehyde in mice suffering from hyperuricemic at a dose of 150 mg / kg reduced uric acid rats by 84.48%. Cinnamaldehyde can inhibit the activity of the enzyme xanthine oxidase (XOD) with an IC50 value of 8.4 µg / ml. XOD is an enzyme that catalyzes the oxidation reaction of hypoxanthine and xanthine to gout. Inhibition of XOD activity will inhibit the biosynthesis of gout [19].

ANTIMICROBIAL OF CINNAMON

The main components essential oils from *C. cassia* leaves from China are cinnamaldehyde (65%) and methoxy-cinnamaldehyde (21%). This essential oil can inhibit the growth of pathogenic bacteria in vitro. The pathogenic bacteria that were inhibited were *Escherichia coli* O157: H7 with MIC value of 0.05% and MCT 0.013%, *Salmonella typhimurium* SL 134 with MIC value of 0.025% and MCT 0.013%, Staphylococcus aureus with MIC value of 0.025% and MCT 0.013%, and against Listeria monocytogenes with MIC values 0.05%and MCT 0.025%. Antimicrobial activity is high if MIC ≤ 0.01% and MTC ≤ 0.025% [20].

The main components essential oils from *C. verum* leaves from Madagascar are eugenol (63%) and carryophyllene (5%). This essential oil can inhibit the growth of *E. coli* O157: H7 with MIC value of 0.1% and MCT 0.013%, *S. typhimurium* SL 134 with a MIC value of 0.1% and MCT 0.013%, *S. aureus* with a MIC value of 0.05 % and MCT 0.013%, and against *L. monocytogenes* with MIC values 0.2%, MCT 0.006% [19]. (Oussalah et al., 2007). Application of 0.3% cinnamon in pasteurized apple juice can activate the growth of *S. typhimurium*, Y. and *S. aureus* when stored at 5 and 20 ° C for 20 days [21].

Cinnamon oil 3% can inhibit the growth of *Rhizopus nigricans* with MIC value of 0.16% (Xing et al., 2010). While the essential oil of *C. jensenianum* 8 µl / ml can inhibit 100% of the process of germination of spores from *Aspergilus flavus* [22]. (Tian et al., 2011). Essential oils made from cinnamon waste (*C. zeylanicum*) with main compounds are cynnamaldehide (66.62%), sinamil acetate (13.89%), linalool (4.96%) and β-caryophilen (4.45%). This oil can inhibit *Colletohricum musa* with MIC value 0.86 mg / ml and MLC of 1 mg / ml, *Fusarium proliferatum* with MIC value 0.64 mg / ml and MLC of 0.86 mg / ml in vitro. This compound is able as an antimicrobial to extend the shelf life of bananas. Cynnamal dehyde most strongly inhibits growth of fungi [23].

The essential oil of *C. zeylanicum* can inhibit the growth of *C. coccodes*, *Botrytis cinerea*, *Cladosporium herbarum*, and *A. niger* at concentrations of 25-500 ppm in vitro [24], *A. flavus* and , *A. ochraceus* [25]. *C. zeylanicum* bark extract can inhibit the growth of *Candida albicans* and *Saccharomyces cerevisiae*, the inhibition zone is much greater than the standard antifungal drug amphotericin B [26].

CONCLUSIONS

The main component of cinnamon is cynnamadehid. This component has many benefits against cardiovascular diseases such as antidiabetic, uric acid, and cancer. Research has been done in vitro and in vivo, while clinical trials are still limited

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