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A Systematic Review on the Antioxidant and Antiiflammatory Properties of Zingiberaceae Plants

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Abstract: *For the last few decades, plant-based medicines, e.g. Zingiberaceae, have regained human interests in disease treatments. Zingiberaceae plants have been proven in possessing many pharmacological activities, thus they can be proposed as antioxidant, antiinflammatory, antibacterial, antiemetic, and antidiabetic. This systematic review discusses about the benefits of Zingiberaceae plants as antioxidant and antiinflammatory agents. We assessed 31 articles as evidence-based source from total of 44 articles. Eleven articles discussed on the antioxidant activity and the rest were the antiinflammatory activity. We indicated that Zingiberaceae have antioxidant and antiinflammotry activity. Its antioxidant activity work by inhibiting of oxidation process in the body by scavenging free radicals and transforms them into less reactive forms. Its antiinflammatory activity can be showed with supressor and inhibitor of inflammation reaction especially activation and production of pro-inflammatory agents; NF-κB or cytokines. Results showed Zingiberaceae can be used as alternative agent to conquer oxidant and inflammation in the body.*

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I. Introduction

Zingiberaceae in one of the largest family in the order of Zingiberales. This family aprproximately represent 57 genera and 1500 species which are distributed in many tropical areas in center of Asia[1].These plants are known to have many pharmacological acitvities by their identified-isolates or their secondary metabolite compounds[2]as its antioxidant and anti-inflammatory agents[3,4].

Antioxidants agents have the ability to reducing or scaveging free radicals especially reactive oxygen species (ROS) which been produced in oxyadation process inside many cells in the body[5]. The utility of phytoconstituents as natural antioxidants are safer than synthetic antioxidants[6].

Inflammation is marked with specific signs such as rubor (redness), calor (heat), tumor (swelling), dolor (pain), and function laesa (loss of function). Immune system included antibody cells and complementary protein with two mechanism of action; (1) relieve stimulant of inflammation, and (2) initiate activation of memory cells in immune systems. Stimulant of pro-inflammatory cytokines; interleukin (IL)-1β,tumor necrosis factor (TNF-α), and damage-associated molecular patterns (DAMPs) or pathogen-associated molecular patterns (PAMPs) will interact with its receptors hence lead to activation of nuclear factor-K-light-chain-enhancer of activated B cells (NF-κB or NF-kappaB) transcription in cytoplasm of cells[7]. Many anti-inflammatory agents perform by inhibiting activation or production of pro-inflammatory substituents.

In this paper, we assessed literature studies about the antioxidant and anti-inflammatory potential of Zingiberaceae plants to provide comprehensive information of its benefits.

II. Methods

The following chart of our literature search shown in Figure 1. The sources were: PubMed, GoogleScholar, ScienceDirect dan ResearchGate for anti-oxidant and anti-inflammatory activity of Zingiberace plants. The databases were collected from March/2019 until May/2019 by using the following keywords: "antioxidants"[Pharmacological Action] or "antioxidants"[MeSH Terms] or "antioxidants"[All Fields] or "antioxidant"[All Fields] and "zingiberaceae"[MeSH Terms] or "zingiberaceae"[All Fields], "anti-inflammatory agents"[Pharmacological Action] or "anti-inflammatory agents"[MeSH Terms] or "anti-inflammatory"[All Fields] and "agents"[All Fields] or "anti-inflammatory agents"[All Fields] or "antiinflammatory"[All Fields])

and "zingiberaceae"[MeSH Terms] or "zingiberaceae"[All Fields] in international and national journal released between 2000 until 2019. All journals in English and Indonesian were used. A total of 44 articles were determined, of which 31 articles met the inclusions criteria by excluding paper released before 2000, other pharmacological activities, plants besides Zingiberaceae family, paper with uncomplete result and discussion, and paper that could not be accessed.

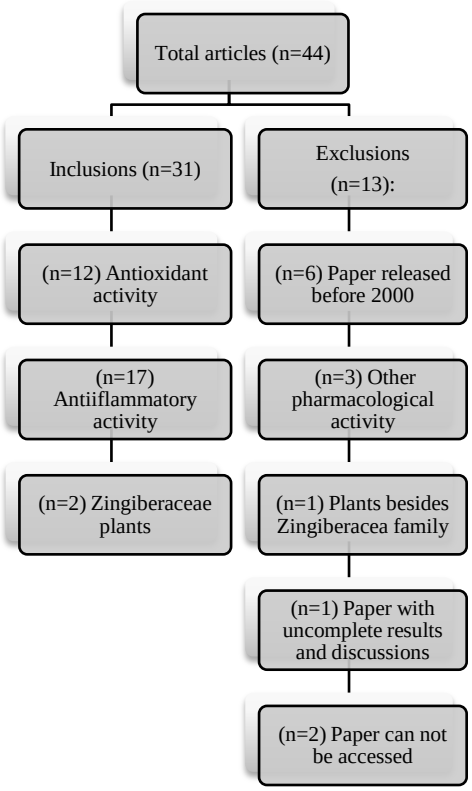

Figure 1. Flowchart of Literature Search

III. Result

The use of different part of plants and different solvent of the extract produce different active compounds resulting in different mechanism action of antioxidant and antiinflammatory activities. Brief explanation of its activities from few plants of Zingiberaceae family shown in Table no 1 and Table no 2.

Table no 1 : Antioxidants Activity in Zingiberaceae Plants

Plant	Part of Plant	Sample	Mechanism of Action	Active Compounds
Amomum subulatum	Seeds	Chloroform : methanol fraction (1:1)	- Increasing catalase and glutathione (GSH) that will lead to protection form oxidative stress in living cell[8] - Reducing lipid peroxidation[8]	N/A
Elleteriarepens	N/A	Hexane extracts	- Protecting DNA, protein, lipid damage[9] - Inhibiting lipid peroxidation[9] - Reconditioning levels of GSH, SOD, and catalase[9]	Polyphenols and flavonoids
Etlingera elatior (Jack) R.M. Smith	Leaves	Methanol extracts	- Inhibiting lipid peroxidation - Scaveging free radicals[10] - Having possibilities of reducing ferric ions in metal chelation[10]	Phenolic compounds
Zingiber officinale Roscoe	Rhizome	Ethanolic extracts	Scaveging free radical to controlling oxidative stress[11]	Polyphenols
	Rhizome	Isolates	- Scaveging free radical[12] - Chelating metal and reducing ferric ions[12]	10-shogaol
	Rhizome	Pure plant extracts	- Scaveging free radical[13] - Chelating metal and reducing ferric ions[13]	Polyphenols
Curcuma longa L.	Rhizome	Ethanolic	Scaveging free radical to controlling	Polyphenols

		extracts	oxidative stress[11]	
Curcuma domestica	Rhizome	Methanolic extracts	Scaveging free radical[14]	Polyphenols
	Rhizome	Pure plant extracts	- Scaveging free radical[13] - Chelating metal and reducing ferric ions[13]	Polyphenols
Polygonum minus	Rhizome	Pure plant extracts	- Scaveging free radical[13] - Chelating metal and reducing ferric ions[13]	Polyphenols
Hedychium coronarium Koenig	Rhizome	Methanolic extracts	Scaveging free radical[14]	Polyphenols
Vanoverberghia sasakiana	Rhizome	Methanolic extracts	Scaveging free radical[14]	Polyphenols
Alpinia officinarum	Rhizome	Methanolic extracts	Scaveging free radical[14]	Polyphenols

Table no 2 : Antiinflammatory Activity in Zingiberaceae Plants

Plant	Part of Plant	Sample	Mechanism of Action	Active Compounds
Zingiberofficinale Roscoe	Crude ginger	Dichloromethane extracts	Protection from chronic joint inflammation by controlling T cells function[15]	17B-estradiol and ginger essential oils (GEO)
	Rhizome	Aquaeos extracts	- Inhibition of TNF-α and PGE2 production and COX-2 expression in human synoviocytes[16] - Regulate activation of NF-κB activation and degradation of its inhibitor IκBα[16]	N/A
	Rhizome	Freeze-dried aqueous extracts	- Reduce production of prostaglandin[17]	Terpenoids and flavonoids
Curcuma longa L.	Rhizome	Isolates	Suppress activation of NF-κB-induced-nuclear factor[18]	Bisdemethylcurcumin
	Rhizome	Curcumin isolates	Inhibit pathways of LOX and COX resulting in the blockade of LTB4 and PGE2 production in injured joints[19]	Curcumin
	Rhizome	Extracts	- Inhibit expression of COX2 in human articular chondrocytes[20] - Suppress regulation of NF-κB, MMPs, and TNF-α in primary chondrocytes[20]	Curcumin, bisdemethoxycurcumin, demethoxycurcumin
	Rhizome	Ethanolic extracts	Inihibit the expressions of COX-2[21]	N/A
	Rhizome	Extracts	- Reduce the incident of angiogenesis (formation of new blood vessels)[22] - Prevent fluid from blood vessels to leak out and cause edema [22]	Curcumin, bisdemethoxycurcumin, demethoxycurcumin
Alpiniagalanga	Rhizome	Aqueous acetone extracts	- Inhibition of beta-hexosaminidase, as marker of IgE-antigen mediated degranulation in RBL-2H3 cells[23] - Inhibit production of IL-4[23]	1′*S*-1′-acetoxychavicol acetate and 1′*S*-1′-acetoxyeugenol acetate
	Rhizome	Aqueous acetone extracts	Inhibit activation of NF-κB by supperessing activation of IKKα/β[24]	1'S-1'-acetoxychavicol acetate
	Rhizome	Ethanolic extracts	- Reduce production of proinflammatory cytokines by blocking activation of NF-κB[25] - Blockage of prostaglandins synthesis[25]	Flavonoids
	Rhizome	Methanolic extract	Reduce activation of cyclooxygenase hence inhibition of prostaglandins synthesis[26]	N/A
Kaempferiagalanga	Rhizome	Aqueous extracts	Inhibit activation of COX[27]	N/A
Elletaria cardamom	Seeds	Oil	Reduce production of IL-1, IL-6, and TNF-α hence inhibition of COX-2[28]	N/A
Elleteriarepens	-	Hexane extracts	- Inhibit activation od cytokines such as COX-2, IL-6, and TNF-α[9] - Inhibition expressions of NO and	N/A

			iNOs[9]	
Etlingeraelatior(Jack.) R. M. Smith	Flowers	Ethanolic extracts	- Inhibit infiltration of inflammatory cells such as neutrophils, limphocytes, and plasma cells[7] - Inhibit activation of NF-κB[7]	Flavonoids

IV. Discussion

Many plants of Zingiberaceae contain secondary metabolite compounds such as phenolic compounds (phenolic acid, flavonoids, quinone, coumarine, gingerol, shogaol etc) showed antioxidant activity[29]. Those compounds take part in antioxidant function in many different ways. Some compounds works by scavenging free radicals, chelating metals and reducing ferric ions[13,14]. One of the most common methods used in estimating antioxidant activity is DPPH method. This method based on calculating reduction of DPPH to form non-radical form DPPH-H by 50% of its concentration in alcoholic solution. Reduction of ferric ions also can be one of the parameters because of iron can oxidative damage in lipids, proteins and other components[30]. It also can stimulate Fenton reaction lead to decomposing lipid hydro-peroxides to peroxyl and alkoxyl radicals in lipid peroxidation process. Some compounds such as polyphenols and flavonoid group also have ability to inhibiting lipid peroxidation that can lead to protection from DNA damage[9].

In general, antiinflammatory activities can be divided into few pathways, such as inhibition of phospholipase A_2, cyclooxigenase (COX), lipoxsigenase (LOX), nitric-oxide synthase (NOS) and NF-KappaB activation. NF-KappaB is located in cytoplasma with its protein inhibitors, IkappaB (IκBα, IκBβ, and IκBε). Inihibition activation of NF-KappaB consist of several stages, such as 1) NF-KappaB upstream stage, 2) IkappaB fosforilation stage, 3) IkappaB degradation stage, 4) Translocaton NF-KappaB to nucleus, and 5) NF-KappaB bound to DNA[7]. This activity can be supported by the presence of active compounds; curcumin and its derivatives[18], sesquiterpen, camphene, cineol, terpineol, terpenes, zingiberol[20], flavonoids[17]and phenylpropanoate[31].

V. Conclusion

Zingiberaceae plants have wide range of mechanism action as antioxidant and antiinflammatory agents with its secondary metabolite compounds as their controller. One compound possesses different mechanism action from the others. Zingiberaceae plants can be used as alternative therapy in managing oxidative stress and inflammations.

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