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A Review of an Important Medicinal Plant: *Alpinia galanga* (L.) Willd

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ABSTRACT

Middle class people who live in rural or urban areas often find it difficult to access modern health services, so they more often use traditional medicines obtained from herbal plants that grow around them. *Alpinia galanga* (Zingiberaceae), often referred to as galangal, is one type of herbal plant that is widely grown in Asia. Many developing countries cultivate this plant, including Indonesia. This plant has a variety of benefits, ranging from being used as a food flavoring, which creates a distinctive aroma in cooking. This plant can also be used as a treatment for various diseases. Although the galangal rhizome is the most widely used and studied part of the plant, the flower on the galangal plant can also provide additional benefits because these flowers have antimicrobial and antioxidant properties, although their chemical composition is different from parts of the galangal rhizome. This study, therefore, aimed to describe the traditional use of rhizome galangal, its phytochemistry, its phytoconstituents, and its future prospects for identifying effective therapeutic compounds.

Keywords: *Alpinia galanga*, Medicinal plant, Traditional use, Phytochemistry, Phytoconstituent

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INTRODUCTION

Middle class people who live in rural or urban areas often find it difficult to get modern health services, so they more often use traditional medicines obtained from herbal plants that grow around them. Treatment with herbs can be an alternative treatment when modern treatments are difficult to obtain [1, 2]. Treatment with herbal plants is widely used in developing countries, especially in those countries whose communities have a poor economy [3].

Herbal medicines are either organic or natural. Pure herbal medicine is obtained from plant extracts that have medicinal benefits, without a mixture of artificial chemicals (synthetic) and without a mixture of animal components. There is currently a rapidly increasing demand for the use of medicines from herbal plants throughout the world [4]. Africans and Asians use the most herbs, followed by Australians and North Americans. Around 100 million Europeans have started using herbal plants as alternative medicines [5].

Alpinia galanga (Zingiberaceae), often referred to as galangal, is one type of herbal plant that is widely grown in Asia. Many developing countries cultivate this plant, including Indonesia. This plant has a variety of benefits, ranging from being used as a food flavoring to create a distinctive aroma in cooking. This plant can also be used as a treatment for various diseases [6].

Galangal is widely used to treat breathing diseases, stomach diseases, diarrhea, and stomach cramps. Galangal can also function as an antimicrobial replacement for antibiotics [7, 8]. Galangal is also effective for treating fever, abnormal menstruation, and to increase male fertility [9]. Galangal rhizome began to be used in several formulations to prevent cancer and tumors and is also used for the treatment of other diseases such as rheumatism, inflammation, diabetes, and neurological disorders [10-14]. Galangal is a mixture that has begun to be used by the community to overcome several chronic diseases [15].

In the galangal rhizome, there are various compounds, namely essential oils, flavonoids, phenolic acids, saponins, and terpenoids [16, 17], while there are main active compounds found in the galangal rhizome, namely galangal acetate, kaempferol, and 1,8-cineole [14, 18-21].

Although the galangal rhizome is the most widely used and studied part of the plant, the flowers on the galangal plant can also provide additional benefits because they have antimicrobial and antioxidant properties, although their chemical composition is different from parts of the galangal rhizome [22]. This study therefore aimed to describe the traditional use of rizhome galangal, its phytochemistry, its phytoconstituents, and its future prospects for developing effective therapeutic compounds.

TAXONOMY

Kingdom: Plantae
Divisio: Magnoliophyta
Class: Liliopsida
Subclass: Zingiberidae
Order: Zingiberales
Family: Zingiberaceae
Subfamily: Alpinioideae
Tribe: Alpinieae
Genus: Alpinia
Species: *Alpinia galanga* [23]

PLANT DESCRIPTION

Alpinia galanga is a herb that can grow up to 3.5 centimeters, with underground rhizomes and minor adventitious roots. The rhizomes have a red-brown color on the surface, while the inside of the rhizome is brown, orange. They are 2.5–10 cm long with a pseudo-stem that

is erect and covered with leaves. Size and shape of the leaves are 3.8–11.5 cm, oblong-lanceolate, glabrous, distichous, and acute. Flowers are compound and 3–4 long with a pleasant smell, with flower crowns green at the base and white buds. The fruit is ellipsoidal and capsule-shaped, with a diameter of 1.5 cm, and colored orange to red. Galangal has a 2n chromosome number of 48 [24]. There are species variations, and the plant is easy to grow in countries that have appropriate agro-ecological conditions.

There are pink galangal rhizomes and whitish yellow galangal rhizomes. Pink galangal rhizomes have a diameter of 8–10 cm, with a pseudo-stem length of 3 m. The yellowish white galangal rhizome has a smaller diameter of 1–2 cm, and the length of the pseudo-stem is 1–1.5 m. *Alpinia galanga* is easy to grow in various regions of Indonesia, especially on the islands of Kalimantan and Java [25]. The morphology of galangal plants is shown in Fig. 1.

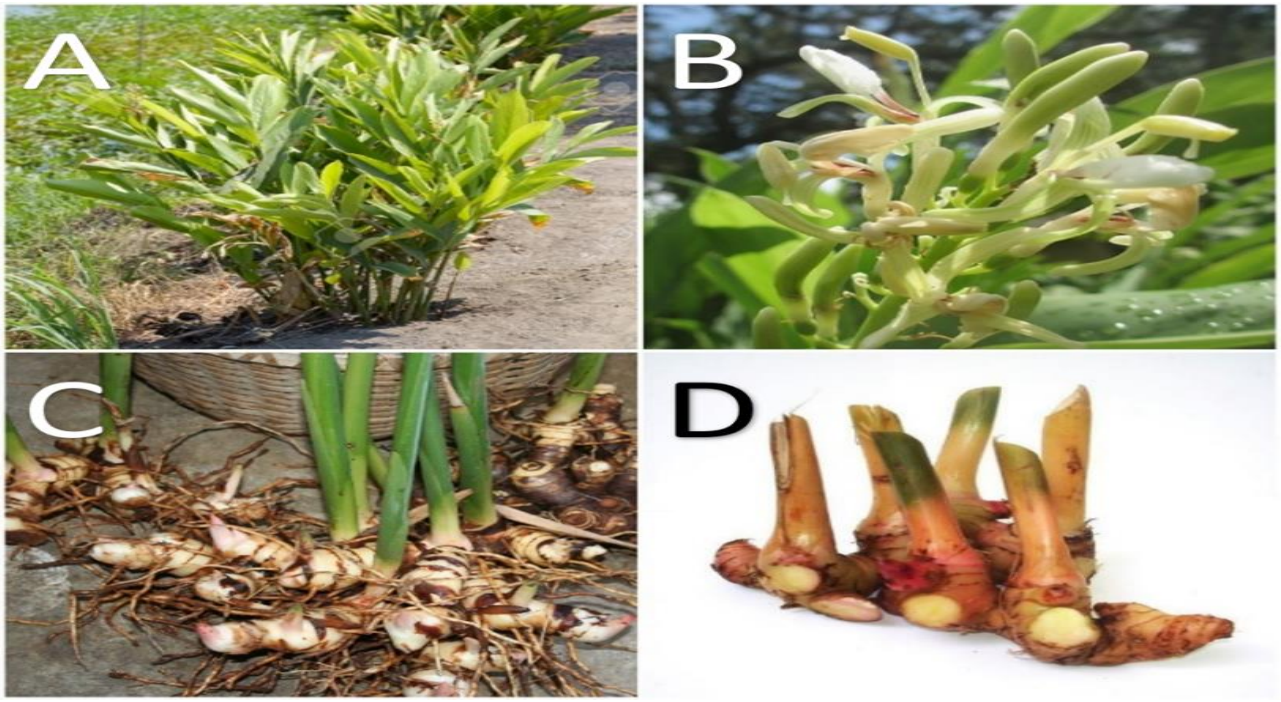

Figure 1. (A) The whole plant of *Alpinia galanga*, (B) flower of *Alpinia galanga*, (C) rhizome of *Alpinia galanga,* and (D) a dried rhizome of *Alpinia galanga* [25].

GEOGRAPHICAL DISTRIBUTION

Alpinia galanga grows in many Asian countries such as India, Arabia, China, Sri Lanka, and Indonesia. It favours hot places exposed to extensive sunlight, but it can also grow in shrubs, forests, and open spaces [26]. In India, galangal plants are exported to the Western Ghats and Himalayan regions [27].

TRADITIONAL USE

The galangal rhizome is effectively used as a therapeutic treatment for various diseases, because it contains anti-bacterial, anti-fungal, anti-inflammatory, anti-hepatotoxic, antioxidant, immunodulator, anti-ulcerative, anti-tumor, and anti-allergic activities [27]. It can be used to treat stomach pain, back pain, rheumatism, asthma, diabetes, heart disease, disorders of the liver, kidney disease, and to increase the appetite [28]. Galangal rhizome can also be used as a substitute for antibiotics, disinfectants, and food seasonings [29]. Galangal seed can be used as a gastric therapy and to treat cardiotonic lesions, and has diuretic, antiplatelet, antifungal, and anti-tumor activities [30]. The tuber of the galangal plant is often used as a cough therapy in young children with asthma, fever, dyspepsia, bronchitis, diabetes mellitus, and irritations [31].

PHYTOCHEMISTRY OF GALANGAL

Alpinia galanga and *Alpinia officinarum* are the two species of galangal plants that are the most common and widely studied, because they have medicinal and ethnobotanical properties [9]. *Alpinia galanga* has pharmacological properties related to phytochemicals in different types of galangal. Phytochemicals are heterogeneous compounds that have a variety of structures and a wide structural distribution. Judging from the mechanism of metabolic biosynthesis, many phytochemicals can be divided into three classes: terpene compounds, phenolics, and alkaloids [32, 33]. Phytochemicals in the species *Alpinia galanga* mostly are comprised of terpene and phenolic compounds. The geographical distribution of *Alpinia galanga* dispersion is also very influential on the distribution of terpenes and phenolic compounds [32, 34].

PHENOLIC COMPOUNDS

Phenolic compounds are phenylpropanoids synthesized from shikimate metabolism. These compounds are the result of metabolites from the secondary metabolism of galangal plants [35]. Phenolic compounds have a variety of distributions, molecular weights, and complexities. All phenolic compounds have one OH-bound group with aromatic arene (phenyl) rings [32]. Phenolic compounds obtain the activity of phenolic hydroxyl groups from their aromatic rings and are often regarded as weak acids. These compounds can also be classified depending on the amount and composition of carbon atoms in the molecules and their chemical diversities [36]. Based on the composition and number of carbon atoms, phenolic compounds are classified into four groups: flavonoids,

phenolic acids, stilbenes, and lignins. Flavonoids are classified as isoflavonoids, flavonoids, flavones, flavan-3-ols, proanthocyanidins, anthocyanins, and condensed tannins, whereas phenolic acids are classified as derivatives of hydroxybenzoic acid and hydroxycinamic acid [32, 36-38]. Some structures of phenolic compounds are shown in Fig. 2. In the galangal rhizome, several phenolic compounds and their derivatives have been identified, including ferulic acid, apigenin, vanillic acid, kaempferol, kaempferol-3-O-methylether, luteolin, chrysin, 1'-acetoxyeugenol acetic acid, and p-hydroxybenzoic acid [39, 40].

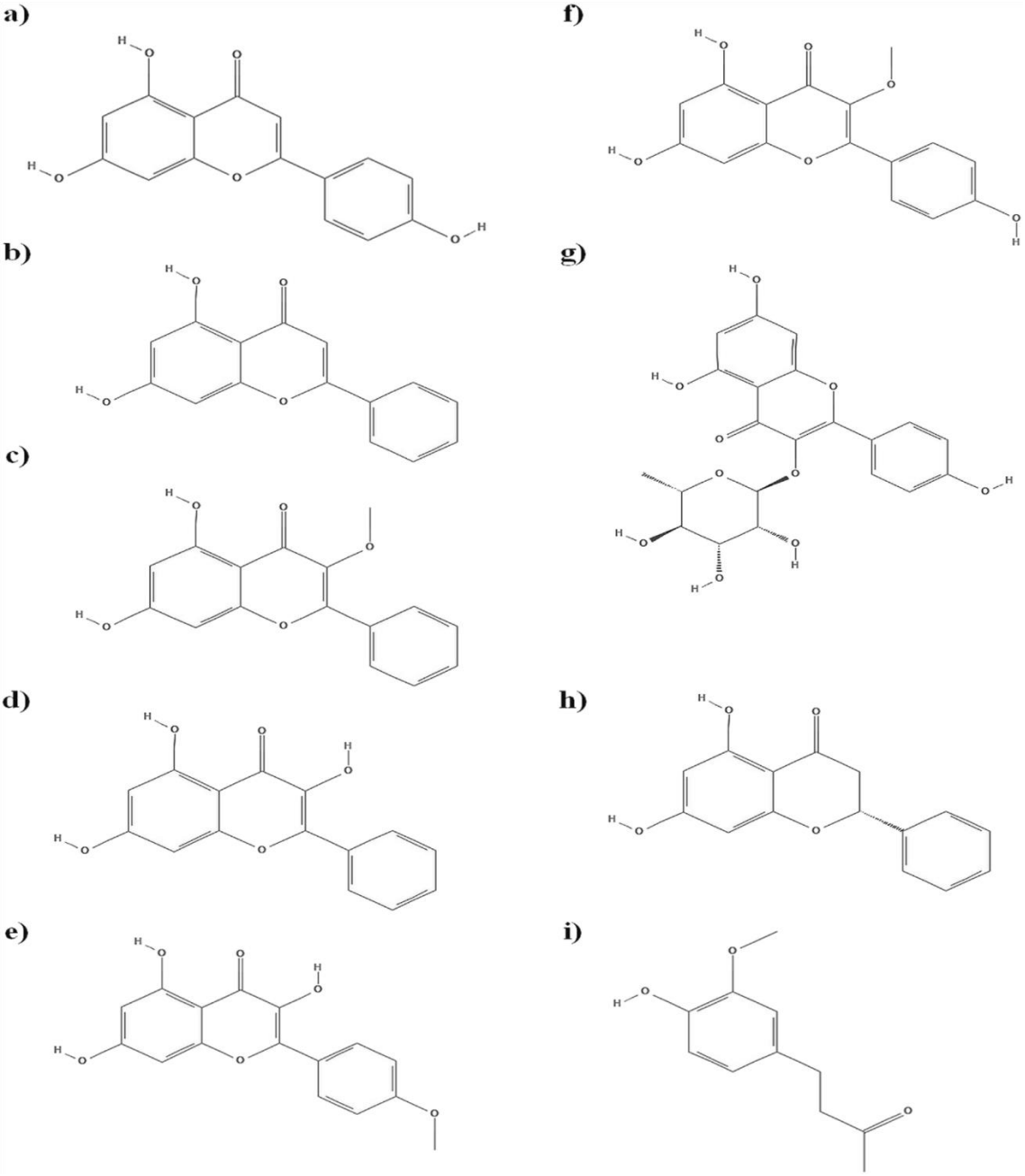

Figure 2. The structure of phenolic compounds that have been identified in the species, *Alpinia galanga* and *Alpinia officinarum*. a) Apigenin, b) chrysin, c) galangin-3-methylether, d) galangin, e) kaempferide, f) kaempferol-3-methylether, g) kaempferol-3-rhamnoside, h) pinocembrin, and i) zingerone.

TERPENES

Terpenes, commonly referred to as terpenoids, comprise a group of about 30,000 secondary metabolites formed from molecules of five carbon isopentane units, commonly referred to as isoprene units. This molecule is the result of biosynthesis of the mevalonate pathway by the cytochrome P450s enzymes and the terpene synthase enzymes. Terpenes can be classified depending on the amount of carbons, for example, 5-carbon terpenoids are referred to as hemiterpenoids, 10 carbon terpenoids are referred to as monoterpenes, 15 carbon terpenoids are referred to as sesquiterpenes, 20 carbon terpenoids are referred to as terpenes, and 30 carbon terpenoids are referred to as terpenes [32, 41, 42]. Terpenes are associated with pharmacological properties of herbal plants, one of which is galangal, because it is known to have antimicrobial, anti-inflammatory, antidiabetic, and anti-cancer activities [22, 43]. Some terpenoid compounds found in *Alpinia galanga* and *Alpinia officinarum* include galangal diterpen A, galangal diterpen B, 1,8-cineole, and

α-pinene [44-47]. The structure of these compounds is shown in Fig. 3.

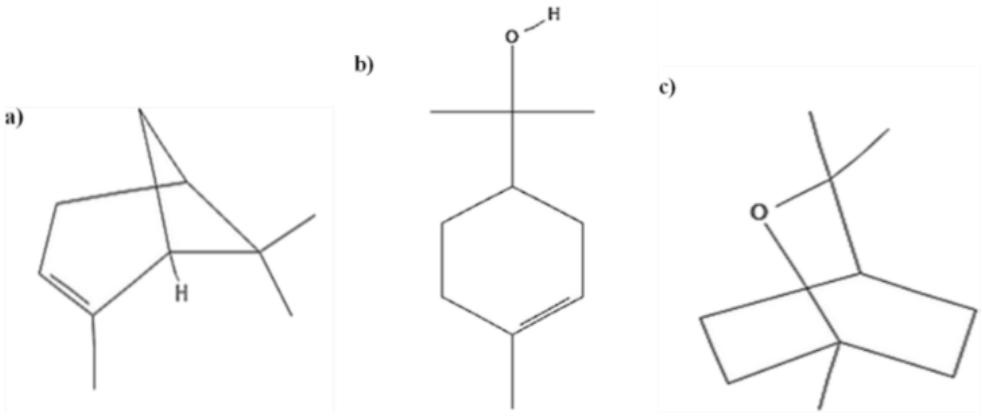

Figure 3. The structure of terpenes found in the species, *Alpinia galanga* and *Alpinia officinarum*. a) α-pinene, b) α-terpineol, and c) 1,8-cineole.

PHYTOCONSTITUENTS OF GALANGAL

The constituents identified in the galangal rhizome include alpinine, kaempferide, methyl cinnamate, camphor, pinene, galangin, pineol, 3-dioxy 4-methoxy flavone, p-methane-1,8-epoxy-acethoxychavicol acetate, (1'S)-l-1'-acetoxyeugenol acetate, 1'-acetoxyeugenol acetate, (1'S)-1'-acetoxychavicol acetate, 1'-acetoxychavicol acetate, chavicol acetate, chavicol, D-camphor, (1R, 3S, 4S)-trans-3-hydroxy-1,8-cineole-D-glucopyranoside, (1R, 2R, 4S) 1,8-cineole, 3-hydroxy-1, 8-cineole glucopyranosides, 8-cineole-D-glucopyranosides, (4R, 1S, 2S) -trans-2-hydroxy-1, trans-p-coumaryldiacetate, trans coniferyldiacetate, di- (p-hydroxy-cisstyryl) methane, trans β-faranesene, 1'-hydroxychavicol acetate, 4-hydoxybenzyldehyde, 7-hydroxy-cytylid) 3-dethethoxy flavone, p-hydroxycinammaldehyde, kaempferol-4'-methylether, kaempferol-7'-methylether, methylcinnamate, isorhamnetin, kaempferol, eugenol acetate, campeene, borneol, zerumbone, α-terpinee, α-terpinee, 4-α-erinep α-thene -menmen, α-humulene, fenchyl acetate, and bornyl acetate [48]. Two diterpens called galangal A and B, two labdane diterpens, called galanolactone and (E) -β (17), 12-labdiene-15,16-dial, were isolated from *Alpinia galanga* followed by (E)-(17)-β epoxylabd-12-ene 15.16-dial. The aromatic component of the galangal rhizome is 1'-acetoxychavicol acetate [49]. The mechanism of action and biomolecules identified from *Alpinia galanga* can are listed in Table 1.

Table 1. The mechanism of action of the main biomolecules found in *Alpinia galanga*.

Name of compound	Type of the compound	Pharmacological activity	References
(BHPHTO) 1,7-bis(4hydroxyphenyl)-1,4, 6-heptatrien-3-one and (BDMC) bisdemethoxycurcumin	Curcuminoid (Natural phenols)	In cell viability testing, it can inhibit proliferation of human melanoma A2058.	[50]
1'-acetoxychavicol acetate	Phenylpropanoid	In myeloid leukemia cells, apoptosis is induced by ACA. In NB4 cells, ACA that induces apoptosis is related to caspase-9 activation and restores the potential of mitochondrial transmembrane, thus tracking mitochondrial oxygen pressure mediates ACA-induced blood signaling. However, apoptosis is activated by ACA with activated activity casapse-8 induced by Fas.	[51]
1'S-1'-acetoxyeugenol acetate	Phenylpropanoid	It has an important role in the final phase I type allergic reaction, which occurs in RBL-2H3 cells.	[52]
p-hydroxycinnamaldehyde	Phenylpropanoid	It has a chondrocyte effect that can be used as a potential therapy in the treatment of osteoarthritis.	[53]
1'S-1'-acetoxychavicol acetate	Phenylpropanoid	It is a potential therapy in the discovery of anti-TB and plays an important role in fighting against the resistance of mycobacterium bacteria because of the way it inhibits the efflux pump.	[54]

1'S-1'-acetoxychavicol acetate (ACA)	Phenylpropanoid	It has an important role in inhibiting the activation of NF-κB.	[55]
1'S-1'-acetoxychavicol acetate (ACA)	Phenylpropanoid	It works as an antiplasmid against bacteria that are resistant to various antibiotics (multi-drug resistant).	[56]

BIOLOGICAL AND PHARMACOLOGICAL ACTIONS

Alpinia galanga has currently become a popular herbal plant for research, so *Alpinia galanga* has been studied for its pharmacological effects. Some of the health benefits of *Alpinia galanga* are described below.

Antimicrobial Activity

The extracts from *Alpinia galanga* have shown significant results in inhibiting the growth of *Escherichia coli, Staphylococcus aureus*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, and *Klebsiella pneumonia*, but are not effective in inhibiting bacteria such as *Staphylococcus epidermidi* [57]. Essential oil compounds in the galangal rhizome have significant activity in inhibiting the growth of bacteria such as *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus suis*, *Pasteurella multocida*, *Arcanobacterium pyogenes*, and *Erysipelothrix rhusiopathiac*. The effect is associated with bisase, 4-ally phenylacetate, and 1,8-cineole [58]. While the results of ethanol extraction from galangal flowers have shown significant effects in inhibiting *Staphylococcus aureus*, seen in the diffusion tests or minimum inhibitory concentrations (MIC) of galangal flower extracts as 0.352–0.547 mg/ml and inhibition zones around 26–31 mm, the ethanol extracts from galangal flowers have not shown significant results in inhibiting the growth of Salmonella bacteria and *Escherichia coli* [59].

The ethanol extract of *Alpinia galanga* significantly inhibited the bacterium, *Staphylococcus aureus*. Using the diffusion test or MIC (minimum inhibitory concentration), the galangal rhizome extract MIC was 0.325 mg/ml and MBC (the minimum bactericidal concentration) was 1.3 mg/ml. Observations using electron microscopy showed that the galangal rhizome extracts cause damage to the outer and inner membranes of bacteria, and there is cytoplasmic coagulation. Nucleic acid damage results from the removal of cell material from the cytoplasmic by coagulation activity [60].

Alpinia galanga is has antifungal activity and can replace antifungal products such as Ketoconazole and Amphotericin B [61]. *Alpinia galanga* is is effective in inhibiting the growth of yeast such as *Candida albicans* [62]. The ethanol extracts of *Alpinia galanga* have phytotoxic effects against *Lemna minor* and have antifungal effects on the growth of the fungus, *Trichophyton longifusus* [63]. *Alpinia galanga* ethanolic extracts at a concentration of 10 mg/ml are also able to inhibit the growth of the phytopathogenic fungi, *Candida albicans*, *Fusariumoxy sporum*, and *Colletotric hummusae* [64]. Methanol extracts of *Alpinia galanga* inhibited the development of human cytomegalovirus and human immunodeficiency virus type 1. Chloroform extracts of *Alpinia galanga* at a concentration of 1 µg/ml showed inhibition of the growth of *Entamoeba histolytica.* Extraction galangal rhizome also inhibits the growth of *Giardia intestinalis* at MIC (minimum inhibitory concentration) of 125 µg/ml [65, 66]. extraction of the galangal rhizome using chloroform, ethyl acetate and hexane showed inhibition of the growth of promastigote, *L. donovani in vitro* [67].

Antifungal Activity

Ethanolic extracts from *Alpinia galanga* have antifungal activity, showing significant results in inhibiting the growth of the fungus, *Trichophyton longifusus* [63]. Diterpen compounds in *Alpinia galanga* (E), such as -8β, 17-epoxylabd-12-ene-15, and 16-dial synergistically play important roles in the antifungal activities of chalcones and quercetins against the growth of *Candida albicans* [68]. A high antifungal activity of DCM and n-hexane extracts of *Alpinia galanga* have been observed using diffusion tests or inhibition zone tests. *Alpinia galanga* contains flavonoids and phenolic compounds, which also play roles in counteracting free radicals [69].

Anti-inflammatory Activity

Acetone extracts from the galangal rhizomes play an important role in inhibiting the release of beta-hexominidase, and also play a role in RBL-2H3 cells, which can act as a marker for degranulation by antigen mediation [70]. The galangal rhizome has anti-inflammatory potential, and total aqueous extracts (TAQs) and total alcoholic extracts (TAEs) evaluations have been conducted on the galangal rhizome. The anti-inflammatory properties of a TAQ extract of galangal and TAE from galangal rhizomes were evaluated in sub-acute (M2; cotton-pellet-induced granuloma) and acute (M1; carrageenan-induced paw edema) rat models [71]. Analgesic and anti-inflammatory activities of the galangal rhizomes extract have been shown with topical preparations. Evaluation of anti-inflammatory activity has been reported against carrageenan-induced edema in experimental rats and in formalin tests. Methyl salicylate ointment and piroxicam gel have been studied as positive controls for analgesic and anti-inflammatory activities. The rate of edema inhibition with preparations containing extracts at 1–5% w/w showed significant results that varied from controls. The anti-inflammatory effect of SN at a dose of 4-5% is in accordance with the effect of Piroxicam after 3 hours of carrageenan injection [72]. Anti-inflammatory and anti-diabetic activities have been reported for methanolic and phenolic extracts from the galangal rhizomes [73]. The effect of p-hydroxycinnamaldehyde from *Alpinia galanga* acetate extract has been reported in cases of chondrocytes in humans. Osteoarthritis is a disease that is often found in humans. Significant side effects occurred in patients who were given nonsteroidal anti-inflammatory therapy [74].

Anti-hepatotoxic Activity

Paracetamol hepatotoxicity treatment has been reported in rats using an *Alpinia galanga* extract. This study was carried out using *Alpinia galanga* extract at concentrations of 200 and 400 mg/kg in order to detect hepatoprotective effects on hepatotoxicity in rats induced by paracetamol [62].

Antioxidant Activity

Alpinia galanga extract has antioxidant activity. A water extract containing 50% ethanol was studied for its antioxidant activity, and its composition compared with

two other samples, namely essential oils and water extracts. Antioxidant activity was measured using the oxygen radical absorption capacity (ORAC) and 2,2-diphenyl-1-picrillhidrazil (DPPH). It has been reported that an ethanol extract had the highest free radical DPPH neutralizing ability. The ORAC value of the ethanol extract had the highest value compared to essential oils and water extracts [75]. It has been reported that galangal rhizome has antioxidant activity when extracted with 1-acetoxychavicol acetate and its compounds [76]. A methanol extract from *Alpinia galanga* has has been evaluated for its antioxidant activity (AOA) and total phenolic content using the DPPH test, chelating iron ions, reducing power (RP), and the AOA β-carotene bleaching tests [77].

Immunomodulatory Activity
A study on mice reported immunostimulant activity in a solution of polysaccharide extract in warm water from *Alpinia galanga* [78].

Anti-diabetic Activity
The galangal rhizome extracts have shown hypoglycemic activity on rabbit blood glucose levels [79]. The results of the treatment using galangal rhizome powder, and methanolic and water extracts showed significant results in reducing blood glucose levels in healthy rabbits and improving the lipid profile in rats with diabetes and euglycemia [80]. A methanolic extract derived from the galangal rhizome also inhibited the glycosylation of hemoglobin. Galangal rhizome significantly has anti-diabetic activity through in vitro, by inhibiting dose-dependent α-amylase and α-glucosidase activity [81].

Anti-ulcer Activity
An *Alpinia galanga* ethanolic extract has anti-ulcer, anti-gastric secretion, and cytoprotective properties in rats. The galangal rhizome is also widely used to treat stomach disorders. An *Alpinia galanga* ethanolic extract showed significant results in reducing gastric secretion and was cytoprotective; therefore, *Alpinia galanga* also had anti-ulcer activity [82]. It was reported that the galangal rhizome ethanolic extracts caused cytological and biochemical changes in rats induced by cyclophosphamide. The galangal rhizome, in addition to being a spice, is also used in medicine to treat stomach aches, gastralgia, dyspepsia, digestive disorders, sea ailments, tonics, and ulcers [83].
There are also anti-feedants and lethal substances in the galangal rhizome extract. An active compound in the galangal rhizome extract shows insecticidal activity; the compound is acetate 1'-acetoxicaviol, which has the molecular formula: $C_{13}H_{14}O_4$. Some other galangal species also contain compounds that are anti-feedants [84].

Anti-tumor Activity
The galangal rhizome contains bisdemethoxycurcumin (BDMC) and 1,7-bis (4-hydroxyphenyl) -1,4,6-heptatrien-3-one (BHPHTO) compounds, which were investigated to determine their effectiveness in the human melanoma cell line, A2058, which showed that the compounds inhibited cell proliferation. Furthermore, studies of B16-F10 cells showed reduction of melanin content and inhibition of tyrosinase cellular activity [50].

Anti-allergic Activity
The galangal rhizome has anti-allergic properties and is an effective allergy treatment. In a rat model, the galangal rhizome active compounds inhibited the release of IgE that was mediated in passive skin anaphylaxis reactions [52].

Anti-HIV Activity
The galangal rhizome extract contains the active compound, 1'S-1'acetoxychavicol acetate, which plays an important role in blocking reverse transport replication of anti-human immunodeficiency virus type 1 [85].

Anti-SARS-CoV-2 Sctivity
The use of herbal treatments increased rapidly during the 2020 coronavirus pandemic (Covid-19). In Indonesia, each ethnic group has its own medicinal herbs, which are mostly obtained from local plants. Herbal plants in the Zingiberaceae family include *Alpinia*, *Kaemferia*, *Curcuma*, *Zingiber*, *Costus*, and *Elattaria*, which contain compounds often used as herbal treatments [86]. Utomo et al (2020) demonstrated the potential inhibitory effect of *Citrus*, *Curcuma*, *Caesalpinia*, and *Alpinia* on SARS-CoV-2 infection, so their development may provide novel treatment and prevention strategies for COVID-19 treatment. One of the phytocomponents of *Alpinia galanga* has been predicted as a possible potent antiviral agent against SARS-CoV-2 [87].

CONCLUSION
Alpinia galanga is a common herbal plant, is widely used as a treatment for various diseases, and has a diverse pharmacological spectrum. *Alpinia galanga* contains a variety of chemical compounds that have pharmacological properties as herbal medicines. We suggest that *Alpinia galanga* might be useful as a treatment for COVID-19, although further studies should be conducted to confirm the results of computational studies.

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