



## The Herbal Potential of Ginger (*Zingiber officinale* Roscoe) and Guava (*Psidium guajava* L.) as Supplements for the Management of Coronavirus Disease 2019 (COVID-19)

Rachmat Hidayat<sup>1\*</sup>, Patricia Wulandari<sup>2</sup>

<sup>1</sup>Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

<sup>2</sup>Cattleya Mental Health Center, Palembang, Indonesia

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#### \*Corresponding author:

Rachmat Hidayat

#### E-mail address:

[dr.rachmat.hidayat@gmail.com](mailto:dr.rachmat.hidayat@gmail.com)

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### ABSTRACT

Increasing the body's immunity is one of the efforts to prevent infection with COVID-19. This literature review aims to describe the potential of ginger (*Zingiber officinale roscoe*) and guava (*Psidium guajava* L.) as supplements for the management of COVID-19. Grated ginger (*Zingiber officinale roscoe*) is used as a topical medication to treat swelling, rheumatism, and headaches. In vivo tests in rats that were immunosuppressed using cyclophosphamide showed that ginger essential oil given once a day orally for a week could increase the humoral immune response. Meanwhile, guava has high levels of polyphenols such as myricetin and apigenin compounds, ellagic acid, and anthocyanins. The high vitamin C content in guava contributes to immune defense by supporting various cellular functions of both the innate and adaptive immune systems.

### 1. Introduction

COVID-19 (Coronavirus disease 2019) is a new type of disease caused by a virus from the coronavirus group, namely the severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2.<sup>1</sup> COVID-19 can cause respiratory system disorders, ranging from mild symptoms such as flu to lung infections, such as pneumonia. Starting in December 2019, precisely on December 29, 2019, the first five cases of pneumonia patients were found in Wuhan City, Hubei Province, China. Five people were hospitalized with acute respiratory distress syndrome, and one of them died.<sup>2</sup> About 66% of patients were exposed to the

Hunan fish market or seafood market (wet market) in Wuhan city. On January 13, 2020, Thailand was the first country to have confirmed Covid-19 outside of China. Also, on January 30, 2020, WHO sounded the health emergency alarm public health emergency of international concern (PHEIC).<sup>2</sup>

Indonesia is a country with the second largest biodiversity in the world. This potential is one of the great capital to be utilized for the benefit of mankind.<sup>3,4</sup> Biodiversity is one of the potential developments of herbs that are useful in overcoming various human health disorders, including overcoming health

problems due to COVID-19. This literature review aims to describe the potential of ginger (*Zingiber officinale* roscoe) and guava (*Psidium guajava* L.) as a supplement to the management of COVID-19.

### **Benefits of ginger (*Zingiber officinale* Roscoe)**

*Zingiber officinale* Roscoe or often called ginger, has a chemical content of essential oils (1-4%): (-)-zingiberene; (+)-ar-curcumene; (-)- $\beta$ -Sesquiphellandrene; and  $\beta$ -bisabolene; [3-6]-, and spicy substances with the main components [8]-,[10]-, and [12]-gingerol; as well as *shogaols*. Grated ginger rhizome is used as a topical medication to treat swelling, rheumatism, and headaches. The Malay community uses the juice of the rhizome to cure colic. Meanwhile, Javanese people use sunthi ginger rhizome, which is squeezed to treat wounds caused by thorns, nail abrasions, wounds from snake bites, itching, and swelling. In ancient Chinese literature, ginger is useful for treating kidney inflammation and stomach cramps during menstruation and facilitating menstruation. It is also used to treat nausea, vomiting, coughing, dropsy (swelling caused by excess fluid in body tissues), and diarrhea and is often used to treat flatulence as a stimulant and diuretic.

In vivo tests in rats that were immunosuppressed using cyclophosphamide showed that ginger essential oil given once a day orally for a week could increase the humoral immune response. Humoral immunity involves interaction between B-cells and antigens for subsequent proliferation and differentiation into plasma cells that secrete antibodies.<sup>5,6</sup>

In vitro and in vivo studies to test the anti-inflammatory activity of ginger have been carried out. In vivo research using rats with foot edema method showed that administration of the ginger extract at a dose of 200 mg/kg significantly reduced the production of PGE<sub>2</sub>, TNF- $\alpha$ , IL-6, monocyte chemoattractant protein-1 (MCP-1), regulation of activation, expressed normal T cells and secreted (RANTES) myeloperoxidase. Activity (MPO). Ginger extract at 100 and 200 mg/kg was equivalent to indomethacin in reducing the amount of NO and

increasing the total antioxidant capacity. Anti-inflammatory activity test of ginger water extracts doses of 100 and 1,000 mg/kg BW orally for three days in ICR strain mice given before inflammation induction on day 3 using lipopolysaccharide intraperitoneally in the liver significantly reduced pathological liver changes and pro-inflammatory cytokines. (IFN $\gamma$  and IL-6) in serum. In addition, the extract can inhibit NF- $\kappa$ B activation by preventing I $\kappa$ B- $\alpha$  degradation, as well as phosphorylation of ERK1/2, SAPK/JNK, and p38 MAPKs. This represents a decrease in the expression of inducible nitric oxide synthase. (iNOS) and cyclooxygenase-2 (COX-2).<sup>7,8</sup>

A double-blind, randomized trial to determine the effect of ginger on pro-inflammatory cytokines (IL-6 and TNF- $\alpha$ ) and hs-CRP protein in 64 patients with type 2 diabetes mellitus who received 2 g of fresh ginger rhizome powder per day for 2 months showed that the administration of ginger significantly reduced the levels of TNF- $\alpha$  ( $p= 0.006$ ), IL-6 ( $p= 0.02$ ) and hs-CRP ( $p= 0.012$ ) compared to pre-treatment, so from these results it is known that the administration of ginger can reduce inflammation in patients with type 2 diabetes mellitus.<sup>9,10</sup>

How to use ginger is described as follows; ginger powder as much as 2-4 g / day. For the preparation of the infusion, mix boiling water with 0.5 to 1 gram of powder and let stand for 5 minutes. The main side effects reported are Mild-moderate gastrointestinal complaints, such as bad taste in the mouth, diarrhea, stomach discomfort, reflux, and heartburn. It is reported that giving 6 g of dry ginger or more can increase the exfoliation of gastric cells, which triggers gastric ulcers. It is recommended that the dose in patients on an empty stomach be limited to a maximum of 6 g. Clinical trials of giving ginger to children showed no reported side effects. The use of large doses of ginger (12-14 g) is not recommended together with anticoagulant drugs because it can increase the effect of hypothermia (blood is difficult to clot).

### **Benefits of guava (*Psidium guajava* L.)**

Guava has the scientific name *Psidium guajava* L. Synonyms: *P. cujavillus* Burm f., *P. pomiferum* L., *P. pumilum* Vahl, *P. pyreferum*. The chemical content of guava fruit is vitamin C, vitamin A, iron, phosphorus, calcium, flavonoids, and polyphenol groups. Guava fruit has high levels of polyphenols such as myricetin and apigenin compounds, ellagic acid, and anthocyanins. In addition, it contains terpenoids (triterpenes and carotenoids), flavonols, tannins, and phenolic acid derivatives. Based on the results of HPLC-MS, GC-MS, and NMR analysis, the chemical compounds of kojic acid and 5-hydroxymethylfurfural were found. Other ingredients are saponins, oleonic acid, lyxopyranoside, arabopyranoside, guajavarin, quercetin, caryophyllene oxide, and p-seline. Guava fruit is known as a famous tropical fruit in Asia. Guava fruit has antioxidant, anti-inflammatory, and anti-diabetic properties. In Indonesia, guava fruit is commonly used to increase platelets in dengue hemorrhagic fever. Guava is used traditionally in China for diabetes.<sup>11,12</sup>

In *in vivo* studies to test the antioxidant effect using mice, administration of red guava fruit juice can reduce the damage to the tracheal epithelium of mice due to exposure to cigarette smoke. The effective dose of guava juice to reduce tracheal damage is 0.26 ml/mouse/day, or the equivalent of consuming 100 grams of guava fruit for humans every day. Guava contains vitamin C and vitamin A, where the vitamin C content in guava is four times higher than the vitamin C content in oranges. Vitamin C helps in boosting immunity, maintain a healthy body, and protect against pathogens that cause infection. Vitamin C contributes to immune defense by supporting various cellular functions of both the innate and adaptive immune systems. Polyphenol compounds in guava fruit and leaf extracts can act as immunostimulants that can cause an increase in the immune system so that it can protect the body from various infectious diseases. A properly functioning immune system is essential to staying healthy.

Administration of guava juice (*Psidium guajava* L)

orally at a dose of 9 g/15 ml per day (divided into 3 doses) for 14 days has an effect on histopathological parameters of chronic inflammation (decrease in the size of the depth of cartilage destruction, the number of mononuclear inflammatory cells, and the number of inflammatory cells). synovial stromal capillaries) And capillary vascular endothelial growth factor (VEGF) expression in the joint tissue of adjuvant-induced arthritis in Wistar rats with 0.1 ml Complete Freund's Adjuvant (CFA). In another study, oral administration of lycopene (from guava fruit extract) can inhibit inflammation in the footprints of mice induced by carrageenan. Purified lycopene isolate (12.5 mg/kg po) could significantly inhibit edema formation caused by phlogistic and immunostaining agents for iNOS, COX-2, and NF- $\kappa$ B. Neutrophil migration in the tissue of the footprints, peritoneal cavity, and myeloperoxidase (MPO) activity decreased while glutathione (GSH) levels increased. This shows that the administration of lycopene from guava fruit extract is beneficial for acute inflammation and can protect against oxidative stress by down-regulating inflammatory mediators and inhibiting the expression of genes involved in inflammation.

How to use guava is described as follows; 100 grams of guava fruit (about 1 large fruit) or 55 grams of guava fruit (about 1 medium fruit). The content of vitamin C is 228.3 mg in 100 grams of fruit. It can also be consumed by: one half-ripe guava, cut into quarters, and boiled with 1 L of water until it boils, then filtered to take the water. This herb is taken 2 times a day in the morning and evening. Unwanted effects can cause constipation. Theoretically, the use of guava extract together with anti-cholesterol, antidepressant, and diabetic agents can increase the potency of these drugs.

### **2. Conclusion**

Ginger and guava have the potential to boost the system and are useful as supplements for the treatment of COVID-19.

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