

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

1. Proofread document received (September 16<sup>th</sup>, 2022)
  - Document from proofreading service
2. Submitted to the journal "Eureka Herba Indonesia (September 21<sup>th</sup>, 2022)
3. Peer Reviewer results: Revision Required (September 30<sup>th</sup>, 2022)
4. Revised version received by journal (September 11<sup>th</sup>, 2022)
5. Paper Accepted for publication (October 13<sup>th</sup>, 2022)
6. Galley proof (October 15<sup>th</sup>, 2022)
7. Paper published (October 17<sup>th</sup>, 2022)

September 16<sup>th</sup>, 2022

**HM Publisher**

Jl Sirnaraga No 99, 8 Ilir, Ilir Timur 3, Palembang, South Sumatra, Indonesia

**CONFIDENTIAL**  
September 16<sup>th</sup>, 2022

**Certificate Service Confirmation**

To whom it may concern,

HM Publisher provided comprehensive editing services for manuscript entitled The Herbal Potential of Ginger (*Zingiber officinale Roscoe*) and Guava (*Psidium guajava L.*) as Supplements for the Management of Coronavirus Disease 2019 (COVID-19). The edit has achieved Grade A: priority publishing; no language polishing required after editing. Should you require any additional information, please do not hesitate to contact me.

Regards,



Khrishna Murti, PhD  
Head of Language Institute-HM Publisher  
Email: khrishnamurti@gmail.com

**Submitted to the journal “Eureka Herba Indonesia (September 21<sup>th</sup>, 2022)**

**Herbal Potential of Ginger (*Zingiber officinale* Roscoe) and Guava (*Psidium guajava* L.) as  
a Supplement to 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

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

**Abstract**

Increasing the body's immunity is one of the efforts to prevent being infected with COVID-19. This literature review aims to describe the potential of ginger (*Zingiber officinale* roscoe) and guava (*Psidium guajava* L.) as covid-19 management supplements. Grated rhizomes of ginger (*Zingiber officinale* roscoe) are used as a smear remedy to treat swelling, rheumatism and headaches. An in vivo test on immune-suppressed mice using cyclophosphamide, showed that ginger essential oil given once a day orally for a week can enhance the humoral immune response. Meanwhile, guava has high levels of polyphenols such as mirisetin and apigenin compounds, elagat acid, and anthocyanins. The high content of vitamin C in guava contributes to the body's immune defense by supporting various cellular functions both innate and adaptive immune systems.

**Keywords.** *Psidium guajava*, *Zingiber officinale*, Essential oils, Vitamin C.

**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 virus. <sup>1</sup> COVID-19 can cause respiratory system disorders, ranging from mild flu-like symptoms, to lung infections, such as pneumonia. Starting in December 2019 to be precise on December 29, 2019, the first five cases of pneumonia patients were found in Wuhan City, Hubei Province, China. Five of the people were hospitalized with acute respiratory distress syndrome and one of them died. <sup>2</sup> About 66% of sufferers are exposed to human's fish market or seafood market in Wuhan city. On January 13, 2020, Thailand was the first canyon to be confirmed with Covid-19 outside of China. On January 30, 2020, WHO also sounded the public health emergency alarm that is of

concern to the whole world, namely the public health emergency of international concern (PHEIC).

2

Indonesia is the country with the second largest biodiversity in the world. This potential is one of the big capitals to be utilized for the benefit of humans.<sup>3,4</sup> Biodiversity is one of the potential development of herbs that are useful in overcoming various human health disorders, including to overcome health disorders due to COVID 19. This literature review aims to describe the potential of ginger (*Zingiber officinale* roscoe) and guava (*Psidium guajava* L.) as covid-19 management supplements.

## **2. Benefits jahe (*Zingiber officinale* Roscoe)**

*Zingiber officinale* Roscoe or often called Ginger, has a chemical content, namely essential oils (1-4%): (-)-zingiberene; (+)-ar-curcumene; (-)- $\beta$ -Sesquiphellandrene; and  $\beta$ -bisabolene; [3-6]-, and a spicy substance with the main components [8]-, [10]-, and [12]-gingerol; as well as *shogaols*. Grated rhizomes of ginger are used as a smearing drug to treat swelling, rheumatism and headaches. The Malays use rhizome juice for colic medicine. Meanwhile, Javanese people use the rhizome of sunthi ginger which is squeezed to treat wounds caused by being pierced by thorns, abrasioned nails, wounds caused by snake bites, itching and swelling. In the ancient Chinese literature, ginger was useful for treating inflammation of the kidneys, abdominal cramps during menstruation and facilitating menstruation. It is also used to treat nausea-vomiting, cough, dropsy (swelling caused by excess fluid in body tissues), diarrhea and is often used to treat flatulence, as a stimulant and diuretic.

An in vivo test on immune-suppressed mice using cyclophosphamide, showed that ginger essential oil given once a day orally for a week can enhance the humoral immune response. Humoral immunity involves the interaction between B-cells and antigens for subsequent proliferation and differentiation into plasma cells that secrete antibody.<sup>5,6</sup>

In vitro and in vivo studies to test the anti-inflammatory activity of ginger have been carried out. In vivo studies using rats with the foot edema method showed that the administration of ginger extract at a dose of 200 mg / kg significantly decreased production from PGE2, TNF- $\alpha$ , IL-6, monocyte chemoattractant *protein-1* (MCP-1), activation regulation, expressed and secreted normal T cells (RANTES), myeloperoxidase activity (MPO). Ginger extract at 100 and 200 mg/kg of equiptitence with indomethacin in reducing the amount of NO and increasing the total antioxidant capacity. Anti-inflammatory activity test of ginger water extract at doses of 100 and

1,000 mg/kg peroral BB for three days on mice of ICR strains administered before inflammatory induction on day 3 using lipopolysaccharides intraperitoneally in the liver significantly decreased changes in liver pathology and pro-inflammatory cytokines (IFN- $\gamma$  and IL-6) in serum. In addition, the extract can inhibit the activation of NF- $\kappa$  B by preventing I $\kappa$ B- $\alpha$  degradation, as well as phosphorylation of ERK1/2, SAPK/JNK and p38 MAPKs. This describes a decrease in the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2).<sup>7,8</sup>

In a double randomized clinical trial disguised to determine the effect of ginger on pro-inflammatory cytokines (IL-6 and TNF- $\alpha$ ) and hs-CRP protein in 64 type 2 diabetes mellitus patients who received 2 g of fresh ginger rhizome powder per day for 2 months showed ginger administration significantly lowered 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 ginger administration can reduce inflammation in patients with type 2 diabetes mellitus.<sup>9,10pm</sup>

The way of use of ginger is described as follows; serbuk ginger as much as 2-4 g / day. For infusion preparation, mix boiling water with 0.5 to 1 gram of powder and let stand for 5 minutes. The side effects reported are mainly: Mild-moderate gastrointestinal complaints, such as bad taste in the mouth, diarrhea, stomach discomfort, reflux and heartburn. It is reported that the administration of 6 g of dried ginger or more can increase the exfoliation of gastric cells, which provokes the onset of peptic ulcers. It is recommended that the dosage in patients on an empty stomach be limited to a maximum of 6 g. Clinical trials of ginger administration in 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 enhance the effect of hypothermia (blood is difficult to clot).

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

Guava has the scientific names *Psidium guajava* L. Synonyms: *P. cujavillus* Burm f., *P. pomiferum* L., *P. pumilum* Vahl, *P. pyreferum*. The chemical content in guava fruit is vitamin C, vitamin A, iron, phosphorus, calcium, flavonoids and polyphenol groups. Guava fruits have high levels of polyphenols such as the compounds mirisetin and apigenin, elagate acid, and anthocyanins. Additionally it contains terpenoids (triterpenes and carotenoids), flavonols, tannins and phenolic acid derivatives. Based on the results of the analysis of HPLC-MS, GC-MS and NMR, chemical compounds of kojat acid and 5-hydroxymethylfurfural were found. Other

ingredients are saponins, oleonic acid, lyxopyranoside, arabopyranoside, guaijavarin, quercetin, caryophyllene oxide and p-seline. Guava fruit is known as a famous tropical fruit in Asia. Guava fruits have antioxidative, anti-inflammatory and antidiabetic 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 an in vivo study to test the antioxidant effects using mice, giving red guava fruit juice can reduce damage to the epithelium of the mice trachea due to exposure to cigarette smoke. The effective dose of guava fruit juice to reduce tracheal damage is 0.26 ml / mice / day or the equivalent of consuming 100 gr of guava fruit for humans every day. Guava contains vitamin C and vitamin A, where the vitamin C content in guava is four times that of vitamin C in oranges. Vitamin C helps in improving immunity, maintaining a healthy body and protecting against pathogens that cause infections. Vitamin C contributes to the body's immune defenses by supporting various cellular functions both innate and adaptive immune systems. Polyphenol compounds in guava fruit extracts and leaves 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.

Oral administration of guava juice (*Psidium guajava* L) at a dose of 9 g/15 ml per day (divided into 3 doses) for 14 days affects the histopathological parameters of chronic inflammation (decrease in the size of the depth of cartilage digestion, the number of mononuclear inflammatory cells, and the number of capillary blood vessels of the synovium stroma) and the expression of VEGF (vascular endothelial growth factor) of capillary blood vessels in adjuvant-induced joint tissues Wistar rat arthritis with Complete Freund's Adjuvant (CFA) 0.1 ml. In other studies, oral administration of lycopene (from red guava fruit extract) may inhibit inflammation of the footprints of carrageenan-induced mice. Purified lycopene isolates (12.5 mg/kg p.o) can significantly inhibit the formation of edema caused by phlogistic and immunostaining agents for iNOS, COX-2 and NF- $\kappa$ B. Migration of neutrophils in the tissues of the footprints, peritoneal cavity, myeloperoxidase (MPO) activity decreased while glutathione (GSH) levels increased. This suggests that the administration of lycopene from red guava fruit extract is beneficial for acute inflammation, can protect against oxidative stress by downregulating inflammatory mediators and inhibiting the expression of genes involved in inflammation.

The way of use of guava is described as follows; 100 grams of guava fruits (about 1 large fruit) or 55 grams of guava fruits (about 1 medium-sized fruit). The content of vitamin C amounted to 228.3 mg in 100 grams of fruit. It can also be consumed by: one half-cooked guava, halved and boiled with 1 L of water until boiling, then filtered for water to be taken. This decoction diminum 2 times a day morning and evening. Undesirable effects can lead to constipation. Theoretically, the use of guava extract simultaneously with antiolesterol agents, antidepressants and diabetes, can increase the potency of such drugs.

#### 4. Conclusion

Ginger and guava herbs have the potential to spur the immune system and are useful as a therapeutic supplement for COVID 19.

#### 5. References

1. Steardo L, Steardo Jr L, Zorec R, Verkhatsky A. Neuroinfection may contribute to pathophysiology and clinical manifestations of COVID-19. *Acta Physiol (Oxf)*. 2020;229(3):e13743.
2. Parasher A. COVID-19: Current understanding to its pathophysiology, clinical presentation and treatment. *Postgraduate Med J*. 2020;97(1147).
3. Sholikhah EN. Indonesian medicinal plants as sources of secondary metabolites pharmaceutical industry. *J Med Sci*. 2016;48(4).
4. Falah F, Hadiwibowo N. Species identification of traditional medicine plants for women's health in East Kalimantan: Lesson learned from local wisdom. *Indo J Forestry Res*. 2017;4(1):49-68.
5. Afolayan FID, Erinwusi B, Oyeyemi OT. Immunomodulatory activity of curcumin-entrapped poly d-l-lactic-co-glycolic acid nanoparticles in mice. *Integrative Med Res*. 2018; 4-11.
6. Agrawal, R. C., Pandey, P. Screening of *Andrographis paniculata* extract for antioxidant and genotoxic activities. *Int J Res Granthaalayah*. 2019; 7:132–142.
7. Bager, S. (2012). Assessment Report on *Zingiber officinale* Roscoe Rhizoma. Committee on Herbal Medicinal Products (HMPC), 44(March), 43.

8. Carrasco, R., Schmidt, G., Romero, A. L., Sartoretto, J. L., Caparroz-assef, S. M., et al. (2009). Immunomodulatory activity of *Zingiber officinale* Roscoe, *Salvia officinalis* L. and *Syzygium aromaticum* L. essential oils: evidence for humor- and cell-mediated responses. *J Pharmacy Pharmacol*, (61), 961–967.
9. Choi, Y. Y., Kim, M. H., Hong, J., Kim, S. H., & Yang, W. M. (2013). Dried ginger (*Zingiber officinalis*) inhibits inflammation in a lipopolysaccharide-induced mouse model. *Evidence-Based Complementary and Alternative Medicine*, 2013.
10. Ezzat, S. M., Ezzat, M. I., Okba, M. M., Menze, E. T., & Abdel-Naim, A. B. (2018). The hidden mechanism beyond ginger (*Zingiber officinale* Rosc.) potent in vivo and in vitro anti-inflammatory activity. *J Ethnopharm*. 214, 113–123.
11. Febrianti, N., & Suryati, R. Y. (2014). Effect of Red Guava Fruit Juice (*Psidium guajava* L) on The Histopathological Picture of Tracheal Mice (*Mus musculus*) Swiss Strain Exposed to Cigarette Smoke. *Biodeukatika*, 2(1), 16–18.
12. Herlina, A. E., Wijaya, I., & Wijayahadi, N. (2013). Effect of Guava Juice Administration (*Psidium guajava* L), on histopathological parameters of chronic inflammation and vascular endothelial growth factor expression: an experimental study on adjuvant-induced arthritis in wistar rats. *Media Medika Indonesia*, 47(1).
13. Hoseinifar, S. H., Sohrabi, A., Paknejad, H., Jafari, V., Paolucci, M., et al. (2019). Enrichment of common carp (*Cyprinus carpio*) fingerlings diet with *Psidium guajava*: The effects on cutaneous mucosal and serum immune parameters and immune related genes expression. *Fish and Shellfish Immunology*, 86(2019), 688–694.
14. Jang, M., Jeong, S. W., Cho, S. K., Ahn, K. S., Lee, J. H., et al. (2014). Anti-inflammatory effects of an ethanolic extract of guava (*Psidium guajava* L.) leaves in vitro and in vivo. *Journal of Medicinal Food*, 17(6), 678–685.

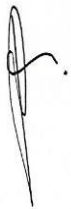


**Submission acknowledgement**

Dear author(s),

Rachmat Hidayat\*, Patricia Wulandari has submitted the manuscript "The Herbal Potential of Ginger (*Zingiber officinale Roscoe*) and Guava (*Psidium guajava L.*) as Supplements for the Management of Coronavirus Disease 2019 (COVID-19)" to Eureka Herba Indonesia. The paper will be screened by editor and reviewed by peer review.

Cordially,



Prof. Paula Magnano, PhD

Editor



**HM Publisher**

**Eureka Herba Indonesia**



**Peer Review Results**

Dear author(s),

Rachmat Hidayat\*, Patricia Wulandari has submitted the manuscript "The Herbal Potential of Ginger (*Zingiber officinale Roscoe*) and Guava (*Psidium guajava L.*) as Supplements for the Management of Coronavirus Disease 2019 (COVID-19)" to Eureka Herba Indonesia. The decision : Revision Required.  
Cordially,

A handwritten signature in black ink, appearing to be "P. Magnano", is positioned to the left of the editor's name.

Prof. Paula Magnano, PhD

Editor



**HM Publisher**

***(\*) Corresponding author***

## Reviewer 1: Revision required

### **Herbal Potential of Ginger (*Zingiber officinale* Roscoe) and Guava (*Psidium guajava* L.) as a Supplement to The Management of Coronavirus Disease 2019 (COVID-19)** →1

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

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

### **Abstract** →3

Increasing the body's immunity is one of the efforts to prevent being infected with COVID-19. This literature review aims to describe the potential of ginger (*Zingiber officinale* roscoe) and guava (*Psidium guajava* L.) as covid-19 management supplements. Grated rhizomes of ginger (*Zingiber officinale* roscoe) are used as a smear remedy to treat swelling, rheumatism and headaches. An in vivo test on immune-suppressed mice using cyclophosphamide, showed that ginger essential oil given once a day orally for a week can enhance the humoral immune response. Meanwhile, guava has high levels of polyphenols such as mirisetin and apigenin compounds, elagat acid, and anthocyanins. The high content of vitamin C in guava contributes to the body's immune defense by supporting various cellular functions both innate and adaptive immune systems.

**Keywords.** *Psidium guajava*, *Zingiber officinale*, Essential oils, Vitamin C. →2

### **1. Introduction** →4

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 virus. <sup>1</sup> COVID-19 can cause respiratory system disorders, ranging from mild flu-like symptoms, to lung infections, such as pneumonia. Starting in December 2019 to be precise on December 29, 2019, the first five cases of pneumonia patients were found in Wuhan City, Hubei Province, China. Five of the people were hospitalized with acute respiratory distress syndrome and one of them died. <sup>2</sup> About 66% of sufferers are exposed to human's fish market or seafood market in Wuhan city. On January 13, 2020, Thailand was the first canyon to be confirmed with Covid-19 outside of China. On January 30, 2020, WHO also sounded the public health emergency alarm that is of

concern to the whole world, namely the public health emergency of international concern (PHEIC).

2

Indonesia is the country with the second largest biodiversity in the world. This potential is one of the big capitals to be utilized for the benefit of humans.<sup>3,4</sup> Biodiversity is one of the potential development of herbs that are useful in overcoming various human health disorders, including to overcome health disorders due to COVID 19. This literature review aims to describe the potential of ginger (*Zingiber officinale* roscoe) and guava (*Psidium guajava* L.) as covid-19 management supplements.

## 2. Benefits jahe (*Zingiber officinale* Roscoe)

*Zingiber officinale* Roscoe or often called Ginger, has a chemical content, namely essential oils (1-4%): (-)-zingiberene; (+)-ar-curcumene; (-)- $\beta$ -Sesquiphellandrene; and  $\beta$ -bisabolene; [3-6]-, and a spicy substance with the main components [8]-, [10]-, and [12]-gingerol; as well as *shogaols*. Grated rhizomes of ginger are used as a smearing drug to treat swelling, rheumatism and headaches. The Malays use rhizome juice for colic medicine. Meanwhile, Javanese people use the rhizome of sunthi ginger which is squeezed to treat wounds caused by being pierced by thorns, abrasioned nails, wounds caused by snake bites, itching and swelling. In the ancient Chinese literature, ginger was useful for treating inflammation of the kidneys, abdominal cramps during menstruation and facilitating menstruation. It is also used to treat nausea-vomiting, cough, dropsy (swelling caused by excess fluid in body tissues), diarrhea and is often used to treat flatulence, as a stimulant and diuretic.

An in vivo test on immune-suppressed mice using cyclophosphamide, showed that ginger essential oil given once a day orally for a week can enhance the humoral immune response. Humoral immunity involves the interaction between B-cells and antigens for subsequent proliferation and differentiation into plasma cells that secrete antibody.<sup>5,6</sup>

In vitro and in vivo studies to test the anti-inflammatory activity of ginger have been carried out. In vivo studies using rats with the foot edema method showed that the administration of ginger extract at a dose of 200 mg / kg significantly decreased production from PGE2, TNF- $\alpha$ , IL-6, monocyte chemoattractant *protein-1* (MCP-1), activation regulation, expressed and secreted normal T cells (RANTES), myeloperoxidase activity (MPO). Ginger extract at 100 and 200 mg/kg of equiptitence with indomethacin in reducing the amount of NO and increasing the total antioxidant capacity. Anti-inflammatory activity test of ginger water extract at doses of 100 and

1,000 mg/kg peroral BB for three days on mice of ICR strains administered before inflammatory induction on day 3 using lipopolysaccharides intraperitoneally in the liver significantly decreased changes in liver pathology and pro-inflammatory cytokines (IFN- $\gamma$  and IL-6) in serum. In addition, the extract can inhibit the activation of NF- $\kappa$  B by preventing I $\kappa$ B- $\alpha$  degradation, as well as phosphorylation of ERK1/2, SAPK/JNK and p38 MAPKs. This describes a decrease in the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2).<sup>7,8</sup>

In a double randomized clinical trial disguised to determine the effect of ginger on pro-inflammatory cytokines (IL-6 and TNF- $\alpha$ ) and hs-CRP protein in 64 type 2 diabetes mellitus patients who received 2 g of fresh ginger rhizome powder per day for 2 months showed ginger administration significantly lowered 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 ginger administration can reduce inflammation in patients with type 2 diabetes mellitus.<sup>9,10pm</sup>

The way of use of ginger is described as follows; serbuk ginger as much as 2-4 g / day. For infusion preparation, mix boiling water with 0.5 to 1 gram of powder and let stand for 5 minutes. The side effects reported are mainly: Mild-moderate gastrointestinal complaints, such as bad taste in the mouth, diarrhea, stomach discomfort, reflux and heartburn. It is reported that the administration of 6 g of dried ginger or more can increase the exfoliation of gastric cells, which provokes the onset of peptic ulcers. It is recommended that the dosage in patients on an empty stomach be limited to a maximum of 6 g. Clinical trials of ginger administration in 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 enhance the effect of hypothermia (blood is difficult to clot).

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

Guava has the scientific names *Psidium guajava* L. Synonyms: *P. cujavillus* Burm f., *P. pomiferum* L., *P. pumilum* Vahl, *P. pyreferum*. The chemical content in guava fruit is vitamin C, vitamin A, iron, phosphorus, calcium, flavonoids and polyphenol groups. Guava fruits have high levels of polyphenols such as the compounds mirisetin and apigenin, elagate acid, and anthocyanins. Additionally it contains terpenoids (triterpenes and carotenoids), flavonols, tannins and phenolic acid derivatives. Based on the results of the analysis of HPLC-MS, GC-MS and NMR, chemical compounds of kojat acid and 5-hydroxymethylfurfural were found. Other

ingredients are saponins, oleonic acid, lycopyranside, arabopyranoside, guaijavarin, quercetin, caryophyllene oxide and p-seline. Guava fruit is known as a famous tropical fruit in Asia. Guava fruits have antioxidative, anti-inflammatory and antidiabetic 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 an in vivo study to test the antioxidant effects using mice, giving red guava fruit juice can reduce damage to the epithelium of the mice trachea due to exposure to cigarette smoke. The effective dose of guava fruit juice to reduce tracheal damage is 0.26 ml / mice / day or the equivalent of consuming 100 gr of guava fruit for humans every day. Guava contains vitamin C and vitamin A, where the vitamin C content in guava is four times that of vitamin C in oranges. Vitamin C helps in improving immunity, maintaining a healthy body and protecting against pathogens that cause infections. Vitamin C contributes to the body's immune defenses by supporting various cellular functions both innate and adaptive immune systems. Polyphenol compounds in guava fruit extracts and leaves 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.

Oral administration of guava juice (*Psidium guajava* L) at a dose of 9 g/15 ml per day (divided into 3 doses) for 14 days affects the histopathological parameters of chronic inflammation (decrease in the size of the depth of cartilage digestion, the number of mononuclear inflammatory cells, and the number of capillary blood vessels of the synovium stroma) and the expression of VEGF (vascular endothelial growth factor) of capillary blood vessels in adjuvant-induced joint tissues Wistar rat arthritis with Complete Freund's Adjuvant (CFA) 0.1 ml. In other studies, oral administration of lycopene (from red guava fruit extract) may inhibit inflammation of the footprints of carrageenan-induced mice. Purified lycopene isolates (12.5 mg/kg p.o) can significantly inhibit the formation of edema caused by phlogistic and immunostaining agents for iNOS, COX-2 and NF- $\kappa$ B. Migration of neutrophils in the tissues of the footprints, peritoneal cavity, myeloperoxidase (MPO) activity decreased while glutathione (GSH) levels increased. This suggests that the administration of lycopene from red guava fruit extract is beneficial for acute inflammation, can protect against oxidative stress by downregulating inflammatory mediators and inhibiting the expression of genes involved in inflammation.

The way of use of guava is described as follows; 100 grams of guava fruits (about 1 large fruit) or 55 grams of guava fruits (about 1 medium-sized fruit). The content of vitamin C amounted to 228.3 mg in 100 grams of fruit. It can also be consumed by: one half-cooked guava, halved and boiled with 1 L of water until boiling, then filtered for water to be taken. This decoction diminum 2 times a day morning and evening. Undesirable effects can lead to constipation. Theoretically, the use of guava extract simultaneously with antiolesterol agents, antidepressants and diabetes, can increase the potency of such drugs.

#### 4. Conclusion →5

Ginger and guava herbs have the potential to spur the immune system and are useful as a therapeutic supplement for COVID 19.

#### 5. References →6

1. Steardo L, Steardo Jr L, Zorec R, Verkhatsky A. Neuroinfection may contribute to pathophysiology and clinical manifestations of COVID-19. *Acta Physiol (Oxf)*. 2020;229(3):e13743.
2. Parasher A. COVID-19: Current understanding to its pathophysiology, clinical presentation and treatment. *Postgraduate Med J*. 2020;97(1147).
3. Sholikhah EN. Indonesian medicinal plants as sources of secondary metabolites pharmaceutical industry. *J Med Sci*. 2016;48(4).
4. Falah F, Hadiwibowo N. Species identification of traditional medicine plants for women's health in East Kalimantan: Lesson learned from local wisdom. *Indo J Forestry Res*. 2017;4(1):49-68.
5. Afolayan FID, Erinwusi B, Oyeyemi OT. Immunomodulatory activity of curcumin-entrapped poly d-l-lactic-co-glycolic acid nanoparticles in mice. *Integrative Med Res*. 2018; 4-11.
6. Agrawal, R. C., Pandey, P. Screening of *Andrographis paniculata* extract for antioxidant and genotoxic activities. *Int J Res Granthaalayah*. 2019; 7:132–142.
7. Bager, S. (2012). Assessment Report on *Zingiber officinale* Roscoe Rhizoma. Committee on Herbal Medicinal Products (HMPC), 44(March), 43.

8. Carrasco, R., Schmidt, G., Romero, A. L., Sartoretto, J. L., Caparroz-assef, S. M., et al. (2009). Immunomodulatory activity of *Zingiber officinale* Roscoe, *Salvia officinalis* L. and *Syzygium aromaticum* L. essential oils: evidence for humor- and cell-mediated responses. *J Pharmacy Pharmacol*, (61), 961–967.
9. Choi, Y. Y., Kim, M. H., Hong, J., Kim, S. H., & Yang, W. M. (2013). Dried ginger (*Zingiber officinalis*) inhibits inflammation in a lipopolysaccharide-induced mouse model. *Evidence-Based Complementary and Alternative Medicine*, 2013.
10. Ezzat, S. M., Ezzat, M. I., Okba, M. M., Menze, E. T., & Abdel-Naim, A. B. (2018). The hidden mechanism beyond ginger (*Zingiber officinale* Rosc.) potent in vivo and in vitro anti-inflammatory activity. *J Ethnopharm*. 214, 113–123.
11. Febrianti, N., & Suryati, R. Y. (2014). Effect of Red Guava Fruit Juice (*Psidium guajava* L ) on The Histopathological Picture of Tracheal Mice (*Mus musculus*) Swiss Strain Exposed to Cigarette Smoke. *Biodeukatika*, 2(1), 16–18.
12. Herlina, A. E., Wijaya, I., & Wijayahadi, N. (2013). Effect of Guava Juice Administration (*Psidium guajava* L), on histopathological parameters of chronic inflammation and vascular endothelial growth factor expression: an experimental study on adjuvant-induced arthritis in wistar rats. *Media Medika Indonesia*, 47(1).
13. Hoseinifar, S. H., Sohrabi, A., Paknejad, H., Jafari, V., Paolucci, M., et al. (2019). Enrichment of common carp (*Cyprinus carpio*) fingerlings diet with *Psidium guajava*: The effects on cutaneous mucosal and serum immune parameters and immune related genes expression. *Fish and Shellfish Immunology*, 86(2019), 688–694.
14. Jang, M., Jeong, S. W., Cho, S. K., Ahn, K. S., Lee, J. H., et al. (2014). Anti-inflammatory effects of an ethanolic extract of guava (*Psidium guajava* L.) leaves in vitro and in vivo. *Journal of Medicinal Food*, 17(6), 678–685.

### **Reviewer Comment:**

- 1→ Title of Manuscripts should be explained main review and declared type of literature review: narrative or systematic review.
- 2→ Keywords should be showed the main words of the study, the authors can use MeSH to develop keywords.
- 3→ Abstract should be showed the main of background, main of review and conclusion of study.



4→Introduction should be showed the urgency of study (epidemiology data), biological plausibility concept, and lack of knowledge in the study.

5→ Conclusion should more specific and not more showed more review.

6→ Authors must check the references for make update references. References should no more than 10 years.

## Reviewer 2: Revision required

### **Herbal Potential of Ginger (*Zingiber officinale* Roscoe) and Guava (*Psidium guajava* L.) as a Supplement to The Management of Coronavirus Disease 2019 (COVID-19)** →1

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

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

### **Abstract** →3

Increasing the body's immunity is one of the efforts to prevent being infected with COVID-19. This literature review aims to describe the potential of ginger (*Zingiber officinale* roscoe) and guava (*Psidium guajava* L.) as covid-19 management supplements. Grated rhizomes of ginger (*Zingiber officinale* roscoe) are used as a smear remedy to treat swelling, rheumatism and headaches. An in vivo test on immune-suppressed mice using cyclophosphamide, showed that ginger essential oil given once a day orally for a week can enhance the humoral immune response. Meanwhile, guava has high levels of polyphenols such as mirisetin and apigenin compounds, elagat acid, and anthocyanins. The high content of vitamin C in guava contributes to the body's immune defense by supporting various cellular functions both innate and adaptive immune systems.

**Keywords.** *Psidium guajava*, *Zingiber officinale*, Essential oils, Vitamin C. →2

### **1. Introduction** →4

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 virus. <sup>1</sup> COVID-19 can cause respiratory system disorders, ranging from mild flu-like symptoms, to lung infections, such as pneumonia. Starting in December 2019 to be precise on December 29, 2019, the first five cases of pneumonia patients were found in Wuhan City, Hubei Province, China. Five of the people were hospitalized with acute respiratory distress syndrome and one of them died. <sup>2</sup> About 66% of sufferers are exposed to human's fish market or seafood market in Wuhan city. On January 13, 2020, Thailand was the first country to be confirmed with Covid-19 outside of China. On January 30, 2020, WHO also sounded the public health emergency alarm that is of

concern to the whole world, namely the public health emergency of international concern (PHEIC).

2

Indonesia is the country with the second largest biodiversity in the world. This potential is one of the big capitals to be utilized for the benefit of humans.<sup>3,4</sup> Biodiversity is one of the potential development of herbs that are useful in overcoming various human health disorders, including to overcome health disorders due to COVID 19. This literature review aims to describe the potential of ginger (*Zingiber officinale* roscoe) and guava (*Psidium guajava* L.) as covid-19 management supplements.

## **2. Benefits jahe (*Zingiber officinale* Roscoe)**

*Zingiber officinale* Roscoe or often called Ginger, has a chemical content, namely essential oils (1-4%): (-)-zingiberene; (+)-ar-curcumene; (-)- $\beta$ -Sesquiphellandrene; and  $\beta$ -bisabolene; [3-6]-, and a spicy substance with the main components [8]-, [10]-, and [12]-gingerol; as well as *shogaols*. Grated rhizomes of ginger are used as a smearing drug to treat swelling, rheumatism and headaches. The Malays use rhizome juice for colic medicine. Meanwhile, Javanese people use the rhizome of sunthi ginger which is squeezed to treat wounds caused by being pierced by thorns, abrasioned nails, wounds caused by snake bites, itching and swelling. In the ancient Chinese literature, ginger was useful for treating inflammation of the kidneys, abdominal cramps during menstruation and facilitating menstruation. It is also used to treat nausea-vomiting, cough, dropsy (swelling caused by excess fluid in body tissues), diarrhea and is often used to treat flatulence, as a stimulant and diuretic.

An in vivo test on immune-suppressed mice using cyclophosphamide, showed that ginger essential oil given once a day orally for a week can enhance the humoral immune response. Humoral immunity involves the interaction between B-cells and antigens for subsequent proliferation and differentiation into plasma cells that secrete antibody.<sup>5,6</sup>

In vitro and in vivo studies to test the anti-inflammatory activity of ginger have been carried out. In vivo studies using rats with the foot edema method showed that the administration of ginger extract at a dose of 200 mg / kg significantly decreased production from PGE2, TNF- $\alpha$ , IL-6, monocyte chemoattractant *protein-1* (MCP-1), activation regulation, expressed and secreted normal T cells (RANTES), myeloperoxidase activity (MPO). Ginger extract at 100 and 200 mg/kg of equiptitence with indomethacin in reducing the amount of NO and increasing the total antioxidant capacity. Anti-inflammatory activity test of ginger water extract at doses of 100 and

1,000 mg/kg peroral BB for three days on mice of ICR strains administered before inflammatory induction on day 3 using lipopolysaccharides intraperitoneally in the liver significantly decreased changes in liver pathology and pro-inflammatory cytokines (IFN- $\gamma$  and IL-6) in serum. In addition, the extract can inhibit the activation of NF- $\kappa$  B by preventing I $\kappa$ B- $\alpha$  degradation, as well as phosphorylation of ERK1/2, SAPK/JNK and p38 MAPKs. This describes a decrease in the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2).<sup>7,8</sup>

In a double randomized clinical trial disguised to determine the effect of ginger on pro-inflammatory cytokines (IL-6 and TNF- $\alpha$ ) and hs-CRP protein in 64 type 2 diabetes mellitus patients who received 2 g of fresh ginger rhizome powder per day for 2 months showed ginger administration significantly lowered 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 ginger administration can reduce inflammation in patients with type 2 diabetes mellitus.<sup>9,10 pm</sup>

The way of use of ginger is described as follows; serbuk ginger as much as 2-4 g / day. For infusion preparation, mix boiling water with 0.5 to 1 gram of powder and let stand for 5 minutes. The side effects reported are mainly: Mild-moderate gastrointestinal complaints, such as bad taste in the mouth, diarrhea, stomach discomfort, reflux and heartburn. It is reported that the administration of 6 g of dried ginger or more can increase the exfoliation of gastric cells, which provokes the onset of peptic ulcers. It is recommended that the dosage in patients on an empty stomach be limited to a maximum of 6 g. Clinical trials of ginger administration in 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 enhance the effect of hypothermia (blood is difficult to clot).

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

Guava has the scientific names *Psidium guajava* L. Synonyms: *P. cujavillus* Burm f., *P. pomiferum* L., *P. pumilum* Vahl, *P. pyreferum*. The chemical content in guava fruit is vitamin C, vitamin A, iron, phosphorus, calcium, flavonoids and polyphenol groups. Guava fruits have high levels of polyphenols such as the compounds mirisetin and apigenin, elagate acid, and anthocyanins. Additionally it contains terpenoids (triterpenes and carotenoids), flavonols, tannins and phenolic acid derivatives. Based on the results of the analysis of HPLC-MS, GC-MS and NMR, chemical compounds of kojat acid and 5-hydroxymethylfurfural were found. Other

ingredients are saponins, oleonic acid, lyxopyranoside, arabopyranoside, guaijavarin, quercetin, caryophyllene oxide and p-seline. Guava fruit is known as a famous tropical fruit in Asia. Guava fruits have antioxidative, anti-inflammatory and antidiabetic 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 an in vivo study to test the antioxidant effects using mice, giving red guava fruit juice can reduce damage to the epithelium of the mice trachea due to exposure to cigarette smoke. The effective dose of guava fruit juice to reduce tracheal damage is 0.26 ml / mice / day or the equivalent of consuming 100 gr of guava fruit for humans every day. Guava contains vitamin C and vitamin A, where the vitamin C content in guava is four times that of vitamin C in oranges. Vitamin C helps in improving immunity, maintaining a healthy body and protecting against pathogens that cause infections. Vitamin C contributes to the body's immune defenses by supporting various cellular functions both innate and adaptive immune systems. Polyphenol compounds in guava fruit extracts and leaves 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.

Oral administration of guava juice (*Psidium guajava* L) at a dose of 9 g/15 ml per day (divided into 3 doses) for 14 days affects the histopathological parameters of chronic inflammation (decrease in the size of the depth of cartilage digestion, the number of mononuclear inflammatory cells, and the number of capillary blood vessels of the synovium stroma) and the expression of VEGF (vascular endothelial growth factor) of capillary blood vessels in adjuvant-induced joint tissues Wistar rat arthritis with Complete Freund's Adjuvant (CFA) 0.1 ml. In other studies, oral administration of lycopene (from red guava fruit extract) may inhibit inflammation of the footprints of carrageenan-induced mice. Purified lycopene isolates (12.5 mg/kg p.o) can significantly inhibit the formation of edema caused by phlogistic and immunostaining agents for iNOS, COX-2 and NF- $\kappa$ B. Migration of neutrophils in the tissues of the footprints, peritoneal cavity, myeloperoxidase (MPO) activity decreased while glutathione (GSH) levels increased. This suggests that the administration of lycopene from red guava fruit extract is beneficial for acute inflammation, can protect against oxidative stress by downregulating inflammatory mediators and inhibiting the expression of genes involved in inflammation.

The way of use of guava is described as follows; 100 grams of guava fruits (about 1 large fruit) or 55 grams of guava fruits (about 1 medium-sized fruit). The content of vitamin C amounted to 228.3 mg in 100 grams of fruit. It can also be consumed by: one half-cooked guava, halved and boiled with 1 L of water until boiling, then filtered for water to be taken. This decoction diminum 2 times a day morning and evening. Undesirable effects can lead to constipation. Theoretically, the use of guava extract simultaneously with antiolesterol agents, antidepressants and diabetes, can increase the potency of such drugs.

#### **4. Conclusion**→5

Ginger and guava herbs have the potential to spur the immune system and are useful as a therapeutic supplement for COVID 19.

#### **5. References**→6

1. Steardo L, Steardo Jr L, Zorec R, Verkhatsky A. Neuroinfection may contribute to pathophysiology and clinical manifestations of COVID-19. *Acta Physiol (Oxf)*. 2020;229(3):e13743.
2. Parasher A. COVID-19: Current understanding to its pathophysiology, clinical presentation and treatment. *Postgraduate Med J*. 2020;97(1147).
3. Sholikhah EN. Indonesian medicinal plants as sources of secondary metabolites pharmaceutical industry. *J Med Sci*. 2016;48(4).
4. Falah F, Hadiwibowo N. Species identification of traditional medicine plants for women's health in East Kalimantan: Lesson learned from local wisdom. *Indo J Forestry Res*. 2017;4(1):49-68.
5. Afolayan FID, Erinwusi B, Oyeyemi OT. Immunomodulatory activity of curcumin-entrapped poly d-l-lactic-co-glycolic acid nanoparticles in mice. *Integrative Med Res*. 2018; 4-11.
6. Agrawal, R. C., Pandey, P. Screening of *Andrographis paniculata* extract for antioxidant and genotoxic activities. *Int J Res Granthaalayah*. 2019; 7:132–142.
7. Bager, S. (2012). Assessment Report on *Zingiber officinale* Roscoe Rhizoma. Committee on Herbal Medicinal Products (HMPC), 44(March), 43.

8. Carrasco, R., Schmidt, G., Romero, A. L., Sartoretto, J. L., Caparroz-assef, S. M., et al. (2009). Immunomodulatory activity of *Zingiber officinale* Roscoe, *Salvia officinalis* L. and *Syzygium aromaticum* L. essential oils: evidence for humor- and cell-mediated responses. *J Pharmacy Pharmacol*, (61), 961–967.
9. Choi, Y. Y., Kim, M. H., Hong, J., Kim, S. H., & Yang, W. M. (2013). Dried ginger (*Zingiber officinalis*) inhibits inflammation in a lipopolysaccharide-induced mouse model. *Evidence-Based Complementary and Alternative Medicine*, 2013.
10. Ezzat, S. M., Ezzat, M. I., Okba, M. M., Menze, E. T., & Abdel-Naim, A. B. (2018). The hidden mechanism beyond ginger (*Zingiber officinale* Rosc.) potent in vivo and in vitro anti-inflammatory activity. *J Ethnopharm.* 214, 113–123.
11. Febrianti, N., & Suryati, R. Y. (2014). Effect of Red Guava Fruit Juice (*Psidium guajava* L) on The Histopathological Picture of Tracheal Mice (*Mus musculus*) Swiss Strain Exposed to Cigarette Smoke. *Biodeukatika*, 2(1), 16–18.
12. Herlina, A. E., Wijaya, I., & Wijayahadi, N. (2013). Effect of Guava Juice Administration (*Psidium guajava* L), on histopathological parameters of chronic inflammation and vascular endothelial growth factor expression: an experimental study on adjuvant-induced arthritis in wistar rats. *Media Medika Indonesia*, 47(1).
13. Hoseinifar, S. H., Sohrabi, A., Paknejad, H., Jafari, V., Paolucci, M., et al. (2019). Enrichment of common carp (*Cyprinus carpio*) fingerlings diet with *Psidium guajava*: The effects on cutaneous mucosal and serum immune parameters and immune related genes expression. *Fish and Shellfish Immunology*, 86(2019), 688–694.
14. Jang, M., Jeong, S. W., Cho, S. K., Ahn, K. S., Lee, J. H., et al. (2014). Anti-inflammatory effects of an ethanolic extract of guava (*Psidium guajava* L.) leaves in vitro and in vivo. *Journal of Medicinal Food*, 17(6), 678–685.

### **Reviewer Comment:**

- 1→ Title of Manuscripts should be explained main review and declared type of literature review: narrative or systematic review.
- 2→ Keywords should be showed the main words of the study, the authors can use MeSH to develop keywords.
- 3→ Abstract should be showed the main of background, main of review and conclusion of study.

4→Introduction should be showed the urgency of study (epidemiology data), biological plausibility concept, and lack of knowledge in the study.

5→ Conclusion should more specific and not more showed more review.

6→ Authors must check the references for make update references. References should no more than 10 years.





## 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

### ARTICLE INFO

#### Keywords:

*Psidium guajava*

*Zingiber officinale*

Essential oils

Vitamin C

#### \*Corresponding author:

Rachmat Hidayat

#### E-mail address:

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

All authors have reviewed and approved the final version of the manuscript.

<https://doi.org/10.37275/ehi.v4i1.59>

### 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, guaijavarin, 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.

### 3. References

1. Steardo L, Steardo Jr L, Zorec R, Verkhatsky A. Neuroinfection may contribute to pathophysiology and clinical manifestations of COVID-19. *Acta Physiol (Oxf)*. 2020; 229(3):e13743.
2. Parasher A. COVID-19: Current understanding to its pathophysiology, clinical presentation and treatment. *Postgraduate Med J*. 2020; 97(1147).
3. Sholikhah EN. Indonesian medicinal plants as sources of secondary metabolites pharmaceutical industry. *J Med Sci*. 2016; 48(4).
4. Falah F, Hadiwibowo N. Species identification of traditional medicine plants for women's health in East Kalimantan: Lessons learned from local wisdom. *Indo J Forestry Res*. 2017; 4(1):49-68.
5. Afolayan FID, Erinwusi B, Oyeyemi OT. Immunomodulatory activity of curcumin-entrapped poly dl-lactic-co-glycolic acid nanoparticles in mice. *Integrative Med Res*. 2018; 4-11.
6. Agrawal, RC, Pandey P. Screening of *Andrographis paniculata* extract for antioxidant and genotoxic activities. *Int J Res Granthaalayah*. 2019; 7:132-42.
7. Bager, S. Assessment Report on *Zingiber officinale* Roscoe Rhizoma. Committee on Herbal Medicinal Products (HMPC). 2012; 44(March): 43.
8. Carrasco R, Schmidt G, Romero AL, Sartoretto JL, Caparroz-assef SM, et al. Immunomodulatory activity of *Zingiber officinale* Roscoe, *Salvia officinalis* L. and *Syzygium aromaticum* L. essential oils: evidence for humor- and cell-mediated responses. *J Pharmacy Pharmacol*. 2009; (61), 961-7.
9. Choi YY, Kim MH, Hong J, Kim SH, Yang WM. Dried ginger (*Zingiber officinalis*) inhibits inflammation in a lipopolysaccharide-induced mouse model. *Evidence-Based Complementary and Alternative Medicine*, 2013.
10. Ezzat SM, Ezzat MI, Okba MM, Menze ET Abdel-Naim AB. The hidden mechanism beyond ginger (*Zingiber officinale* Rosc.) potent in vivo and in vitro anti-inflammatory activity. *J Ethnopharm*. 2018; 214: 113-23.
11. Febrianti N, Suryati RY. Effect of red guava fruit juice (*Psidium guajava* L) on histopathological features of the trachea of mice (*mus musculus*) Swiss strain exposed to cigarette smoke. *Biodeutics*. 2014; 2(1):16-18.
12. Herlina AE, Wijaya I, Wijayahadi N. Effect of Guava (*Psidium guajava* L) juice on histopathological parameters of chronic inflammation and vascular endothelial growth factor expression: a laboratory experimental study on adjuvant-induced arthritis in wistar rats. *Media Medika Indonesia*. 2013; 47(1).

**Letter of Acceptance**

Manuscript “The Herbal Potential of Ginger (*Zingiber officinale* Roscoe) and Guava (*Psidium guajava* L.) as Supplements for the Management of Coronavirus Disease 2019 (COVID-19)“ by Rachmat Hidayat\*, Patricia Wulandari, has been accepted to publish in Eureka Herba Indonesia Vol 4 issue 1 in October 2022.

Cordially,



Prof. Paula Magnano, PhD

Editor



**HM Publisher**

**(\*) Corresponding author**

The Corresponding Author can access the account in website :

<https://eurekabiomedical.com/index.php/EHI/login>

User: rachmat

Password: 210587



# Eureka Herba Indonesia

Journal Homepage: <https://eurekabiomedical.com/index.php/EHI>

## 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

### ARTICLE INFO

#### Keywords:

*Psidium guajava*  
*Zingiber officinale*  
Essential oils  
Vitamin C

#### \*Corresponding author:

Rachmat Hidayat

#### E-mail address:

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

All authors have reviewed and approved the final version of the manuscript.

<https://doi.org/10.37275/ehi.v4i1.59>

### 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

Galley Proof

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 ( $p=0.002$ ) 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, guaijavarin, 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 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 decrease while glutathione (GSH) levels increase. 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.



### 3. References

1. Steardo L, Steardo Jr L, Zorec R, Verkhatsky A. Neuroinfection may contribute to pathophysiology and clinical manifestations of COVID-19. *Acta Physiol (Oxf)*. 2020; 229(3):e13743.
2. Parasher A. COVID-19: Current understanding to its pathophysiology, clinical presentation and treatment. *Postgraduate Med J*. 2020; 97(1147).
3. Sholikhah EN. Indonesian medicinal plants as sources of secondary metabolites pharmaceutical industry. *J Med Sci*. 2016; 48(4).
4. Falah F, Hadiwibowo N. Species identification of traditional medicine plants for women's health in East Kalimantan: Lessons learned from local wisdom. *Indo J Forestry Res*. 2017; 4(1):49-68.
5. Afolayan FID, Erinwusi B, Oyeyemi S. Immunomodulatory activity of curcumin-entrapped poly(lactide-co-glycolic acid) nanoparticles in mice. *Innovative Med Res*. 2018; 4-11.
6. Agrawal, RC, Pandey P. Screening of *Andrographis paniculata* extract for antioxidant and genotoxic activities. *Int J Res Granthaalayah*. 2019; 7:132-42.
7. Bager, S. Assessment Report on *Zingiber officinale* Roscoe Rhizoma. Committee on Herbal Medicinal Products (HMPC). 2012; 44(March): 43.
8. Carrasco R, Schmidt G, Romero AL, Sartoretto JL, Caparroz-assef SM, et al. Immunomodulatory activity of *Zingiber officinale* Roscoe, *Salvia officinalis* L. and *Syzygium aromaticum* L. essential oils: evidence for humor- and cell-mediated responses. *J Pharmacy Pharmacol*. 2009; (61), 961-7.
9. Choi YY, Kim MH, Hong J, Kim SH, Yang WM. Dried ginger (*Zingiber officinalis*) inhibits inflammation in a lipopolysaccharide-induced mouse model. *Evidence-Based Complementary and Alternative Medicine*, 2013.
10. Ezzat SM, Ezzat MI, Okba MM, Menze ET, Abdel-Naim AB. The hidden mechanism beyond ginger (*Zingiber officinale* Rosc.) potent in vivo and in vitro anti-inflammatory activity. *J Ethnopharm*. 2018; 214: 113-23.
11. Febrianti N, Suryati RY. Effect of red guava fruit juice (*Psidium guajava* L) on histopathological features of the trachea of mice (*mus musculus*) Swiss strain exposed to cigarette smoke. *Bioinformatics*. 2014; 2(1):16-18.
12. Herlina AE, Wijaya T, Wijayahadi N. Effect of Guava (*Psidium guajava* L) juice on histopathological parameters of chronic inflammation and vascular endothelial growth factor expression: a laboratory experimental study on adjuvant-induced arthritis in wistar rats. *Media Medika Indonesia*. 2013; 47(1).



# CERTIFICATE

OF PUBLICATION

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

Authored by;

Rachmat Hidayat, Patricia Wulandari

Published in

**Eureka Herba Indonesia Volume 4 Issue 1 2023**



Indexed in:

