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Khrishna Murti, PhD

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Submitted to the journal “Eureka Herba Indonesia (July 19th, 2022)

Turmeric Potential (*Curcuma longa* L.) and Temulawak (*Curcuma xanthorrhiza* Roxb.) in Handling Corona Virus Disease 2019 (COVID-19)

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Abstract

One of the efforts to prevent COVID-19 that can be done is to increase individual immunity. The effort that can be done is to use herbal ingredients as health drinks. *Curcuma longa* L. or turmeric has long been known as one of the ingredients used to treat some complaints. Turmeric has a chemical content, namely carbohydrates (69.4%); curcuminoids and essential oils (5.8%). Turmeric and curcumin are nonmutagenic and no reproductive toxicity has been observed. *Curcuma xanthorrhiza* Roxb also called temulawak, contains curcuminoids (1-2%) and essential oils with xanthorrhizol components (31.9%), β -curcumene (17.1%), arcurcumene (13.2%), camphor (5.4%), γ -curcumene (2.6%), (Z)- γ -bisabolene (2.6%), and (E)- β -farnesene (1.2%). Empirically temulawak has been used for generations in Indonesia to treat various digestive disorders, complaints on the skin, liver and bile disorders.

Keywords: *Curcuma longa*, *Curcuma xanthorrhiza*, COVID-19, Curcuminoid.

1. Introduction

The novel coronavirus (COVID-19) has now become a pandemic and become a world health problem. Covid-19 cases began with information from the World Health Organization (WHO) on December 31, 2019, which stated that there were cases of pneumonia clusters with unclear etiologies in Wuhan City, Hubei Province, China. This case continued to grow until it was finally discovered that the cause of this pneumonia cluster was the novel coronavirus. The case continued to grow until there were reports of deaths and importations outside China. On January 30, 2020, WHO designated COVID-19 as a public health emergency of international concern

(PHEIC). On February 12, 2020, WHO officially designated this novel coronavirus disease in humans as Coronavirus Disease (COVID-19). In Indonesia itself, the first case of COVID-19 was reported on March 2, 2020. The area of spread of COVID-19 in Indonesia is widespread in almost all provinces. The number of patients infected with COVID-19 also continues to grow. Over the next few months the Indonesian nation will face major problems caused by COVID-19, if not handled appropriately.

Faced with a situation like this, efforts to control and prevent COVID-19 are needed. One of the prevention efforts that can be done is to increase community resilience, through the health of individual bodies. Endurance can be maintained and improved, especially through healthy living habits including maintaining cleanliness, good nutritional intake, coupled with the use of health supplements and herbal ingredients / traditional medicines. Indonesia is one of the countries with a large diversity of biological wealth. No less than 30,000 species of plants exist in the tropical forests of Indonesia. Of these, around 9,600 species are known to have medicinal properties but not all of them are optimally utilized as herbal medicine.^{1,2} The use of herbs is as a medicine in the form of steeping herbs, herbs, standardized herbal medicines and phytopharmaceuticals. Jamu is the cultural heritage of the Indonesian nation, which has traditionally and for generations been used to improve the degree of health.

2. Benefits of kunyit (*Curcuma longa* L.)

Curcuma longa L. or turmeric has long been known as one of the ingredients used to treat some complaints. Turmeric has a chemical content, namely carbohydrates (69.4%); curcuminoids (a mixture of curcumin, demetoxicurcumin and bisdemetoxicurcumin); and essential oils (5.8%). Rhizomes mixed with warm milk are used to cure colds, bronchitis and asthma. While fresh squeezed rhizomes can be applied to skin infections. Turmeric rhizomes are also mentioned to have the property of relieving various inflammations, rheumatism, abdominal pain, liver diseases, kidney stones and cleansing menstruation.³

Research on immunomodulatory activity in vivo using poly d,l-lactic-co-glycolic acid entrapped curcumin nanoparticle in albino mice sensitised with goat red blood cells (SRBCs) showed that nano curcumin at doses of 5 mg/kg and 10 mg/kg improved the immune response mediating the initial response of cells compared to controls. Similar results also occurred in secondary humoral antibodies, where white blood cell production and lymphoid organ weight also increased

in the group given 10 mg/kg of nano curcumin. Other studies have been conducted to determine the effect of postpartum-supplied phytonutrient administration in dairy cows. Phytonutrients used such as curcuma oleoresins (2 g/cow); onion extract (2 g/cow); oleoresin capsicum (2 g/cow). From a 23-day study, results were obtained that all phytonutrients exert an immunostimulant effect by activating and inducing CD4 cell expansion. ^{4,5}

In vivo studies of the combination of 30% ethanol extract from *Artemisia capillaris*, *Sanguisorba officinalis*, and *Curcuma longa* in hydrodynamically induced mice of HBV (Hepatitis B Virus) genomes showed that both the combination of the three extracts and those administered together with entecavir were able to suppress HBV replication and the production of inflammatory cytokines without showing toxicity. ^{6th}

Research on the anti-inflammatory activity in vivo of oil-free water-extracts from turmeric using mice (ear edema with induction using xylene) and rats (cotton pellet granuloma model) showed that water-free oil extracts from turmeric at three dose levels (Doses for mice: 90, 180 and 360 mg/kg bw; Doses for rats : 45, 90 and 180 mg/kg bw) significantly ($P \leq 0.05$) inhibited inflammation in both study models, as evidenced by a reduction in ear weight and a decrease in wet and dry weight of cotton pellets, when compared with controls. The oil-free water-extract of turmeric exhibits an anti-inflammatory effect against acute and chronic inflammation comparable to the effects of curcuminoids and tumerones (essential oils).

Administration of turmeric rhizome extract in rats induced acute liver stress with CCl₄ showed a significant decrease in lipid peroxidation of membranes in the liver. Extracts of turmeric rhizomes and curcumin showed significant protection against liver injury by increasing hepatic superoxide dismutase; glutathione peroxidase activity, and glutathione amounts in the treatment group, which led to a decrease in lipid peroxidase levels. Therefore, turmeric and curcumin rhizome extracts are potential antioxidant agents against acute hepatotoxicity.

The method of use is as follows; as much as 25 g of fresh turmeric, thoroughly washed, grated, squeezed, filtered, plus 1 tablespoon of honey then taken 2 times a day. Dry matter: 3-9 grams per day; Powder: 1.5- 3.0 g/day; oral infusion: 0.5 – 1 gram three times a day. The powder should be consumed 2 to 3 times a day after meals; tea (2 to 3 cups) is consumed between meals. To make tea, heat 0.5 to 1 gram of the drug in boiling water, cover, wait 5 minutes.

Turmeric and curcumin are nonmutagenic and no reproductive toxicity has been observed. The FDA classifies turmeric as Generally Recognized As Safe (GRAS). No major side effects

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3. Benefits of temulawak (*Curcuma xanthorrhiza* Roxb.)

Curcuma xanthorrhiza Roxb also called temulawak, contains curcuminoids (1-2%) and essential oils with xanthorrhizol components (31.9%), β -curcumene (17.1%), arcurcumene (13.2%), camphor (5.4%), γ -curcumene (2.6%), (Z)- γ -bisabolene (2.6%), and (E)- β -farnesene (1.2%). Empirically temulawak has been used for generations in Indonesia to treat various complaints of stomach and liver disorders, fever and constipation, galactagogue, bloody diarrhea, dysentery, inflammation of the rectum, hemorrhoids, stomach disorders which are 30 caused by cold, infected wounds, skin eruptions, acne vulgaris, eczema, smallpox and anorexia as well as to reduce uterine inflammation after childbirth.^{5,6}

The administration of 2% temulawak powder on the controlled diet of Sprague Dawley rats for 3–5 weeks showed temulawak was able to increase the proportion of spleen T cells during the experimental period, but had a variable effect on B cells and a subset (part) of T cells, namely an increase in the proportion of B cells in temulawak administration for 3 weeks and helper (Th) T cells in temulawak administration for 4 weeks without an increase in the proportion of T cells suppressor (Ts). The effect of this medicinal plant on the proportion of macrophages of the spleen and peripheral blood is inconsistent. Thus, this study shows that Temulawak shows the activity of activating immune function mediated by T cells and B cells.^{7,8}

Pre-implementation of the temulawak hexan fraction dose of 500 mg/kgbb peroral in male Sprague Dawley rats for 7 consecutive days followed by hepatotoxic induction with CCl₄ can increase levels of *glutathione peroxidase* (GPx), superoxide dismutase (SOD), *glutathione reductase* (GR), catalase (CAT), and total protein (TP) levels and can reduce *malondialdehyde* levels (MDA) on the hepar rather than the control. This shows that temulawak can act as an

antioxidant and can prevent lipid peroxidation caused by CCl₄. Pre-implementation of temulawak ethanol extract dose 500 mg / kgbb peroral in male Sprague Dawley rats for 7 consecutive days followed by hepatotoxic induction with ethanol reduces the symptoms of fatty liver and significantly ($p < 0.05$) inhibits the increase in levels of antioxidant enzymes that play a role in liver disease, namely alanine transaminases (ALT), aspartate transaminases (AST) and alkaline phosphatase (ALP).^{9,10pm}

Pre-treatment with 0.1 - 2.0 μ mol xanthorrhizol/50 μ l of topically administered DMSO-acetone inhibits edema in the ear of a TPA-induced IDR mice (12-O-tetradecanoylphorbol-13-acetate), which has a direct correlation with inflammation. Administration of the hexan fraction of temulawak rhizomes at a dose of 75 mg / kg bb in edema-induced rats with carrageenan and acetic acid-induced mice showed inhibition in the formation of edema and was associated with the presence of non-phenolic linear diarilheptanoids in temulawak. Administration of temulawak extract (50 and 100 mg / kg bb / day) and xanthorrhizol (10 and 25 mg / kg bb / day) in obesity-induced mice with a high-fat diet showed a decrease in the fat of the sole epididymis of the feet successively extracts (25.8% and 22.5%) as well as xanthorrhizol (26.6% and 20.1%). Extracts and xanthorrhizol can also inhibit the production of pro-inflammatory cytokines such as TNF- α , IL-6, IL-1 β , and C-reactive protein (CRP) in adipose tissue (27.8-82.7%), liver (43.9-84.7%), and muscle (65.2-92.5%).

Empirical use in Indonesia, especially to relieve liver function disorders, can be done by boiling 25 g of fresh temulawak slices with 500 mL of water to stay 300 mL, drunk for a day. Another way can be done by taking 25 g of fresh rhizomes, grated, squeezed, filtered divided in half and drunk for a day.

The European Medicine Agency reports no serious side effects have been reported as of now.^{4,5} Further the chemical composition of temulawak does not give a reason for safety concerns. The use of temulawak in pregnant women and during breastfeeding is not recommended until there is data that curcumin and/ or its metabolites can be transferred through lactation. Use in patients with blockage of the bile ducts, cholangitis, gallstones or other bilestone diseases should consult a doctor.

4. Conclusion

Turmeric and temulawak herbs empirically and scientifically have the potential to increase the body's immunity in the face of COVID-19.

5. References

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Submission acknowledgement

Dear author(s),

Rachmat Hidayat*, Patricia Wulandari has submitted the manuscript "Potency of Turmeric (*Curcuma longa* L.) and Temulawak (*Curcuma xanthorrhiza* Roxb.) in Handling 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**



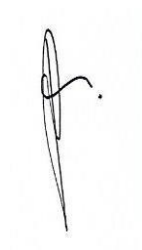
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Peer Review Results

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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 2: Revision required

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- 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

Turmeric Potential (*Curcuma longa* L.) and Temulawak (*Curcuma xanthorrhiza* Roxb.) in Handling Corona Virus Disease 2019 (COVID-19) →¹

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Abstract→³

One of the efforts to prevent COVID-19 that can be done is to increase individual immunity. The effort that can be done is to use herbal ingredients as health drinks. *Curcuma longa* L. or turmeric has long been known as one of the ingredients used to treat some complaints. Turmeric has a chemical content, namely carbohydrates (69.4%); curcuminoids and essential oils (5.8%). Turmeric and curcumin are nonmutagenic and no reproductive toxicity has been observed. *Curcuma xanthorrhiza* Roxb also called temulawak, contains curcuminoids (1-2%) and essential oils with xanthorrhizol components (31.9%), β -curcumene (17.1%), arcurcumene (13.2%), camphor (5.4%), γ -curcumene (2.6%), (Z)- γ -bisabolene (2.6%), and (E)- β -farnesene (1.2%). Empirically temulawak has been used for generations in Indonesia to treat various digestive disorders, complaints on the skin, liver and bile disorders.

Keywords: *Curcuma longa*, *Curcuma xanthorrhiza*, COVID-19, Curcuminoid. →²

1. Introduction→⁴

The novel coronavirus (COVID-19) has now become a pandemic and become a world health problem. Covid-19 cases began with information from the World Health Organization (WHO) on December 31, 2019, which stated that there were cases of pneumonia clusters with unclear etiologies in Wuhan City, Hubei Province, China. This case continued to grow until it was finally discovered that the cause of this pneumonia cluster was the novel coronavirus. The case continued to grow until there were reports of deaths and importations outside China. On January 30, 2020, WHO designated COVID-19 as a public health emergency of international concern

(PHEIC). On February 12, 2020, WHO officially designated this novel coronavirus disease in humans as Coronavirus Disease (COVID-19). In Indonesia itself, the first case of COVID-19 was reported on March 2, 2020. The area of spread of COVID-19 in Indonesia is widespread in almost all provinces. The number of patients infected with COVID-19 also continues to grow. Over the next few months the Indonesian nation will face major problems caused by COVID-19, if not handled appropriately.

Faced with a situation like this, efforts to control and prevent COVID-19 are needed. One of the prevention efforts that can be done is to increase community resilience, through the health of individual bodies. Endurance can be maintained and improved, especially through healthy living habits including maintaining cleanliness, good nutritional intake, coupled with the use of health supplements and herbal ingredients / traditional medicines. Indonesia is one of the countries with a large diversity of biological wealth. No less than 30,000 species of plants exist in the tropical forests of Indonesia. Of these, around 9,600 species are known to have medicinal properties but not all of them are optimally utilized as herbal medicine.^{1,2} The use of herbs is as a medicine in the form of steeping herbs, herbs, standardized herbal medicines and phytopharmaceuticals. Jamu is the cultural heritage of the Indonesian nation, which has traditionally and for generations been used to improve the degree of health.

2. Benefits of kunyit (*Curcuma longa* L.)

Curcuma longa L. or turmeric has long been known as one of the ingredients used to treat some complaints. Turmeric has a chemical content, namely carbohydrates (69.4%); curcuminoids (a mixture of curcumin, demetoxicurcumin and bisdemetoxicurcumin); and essential oils (5.8%). Rhizomes mixed with warm milk are used to cure colds, bronchitis and asthma. While fresh squeezed rhizomes can be applied to skin infections. Turmeric rhizomes are also mentioned to have the property of relieving various inflammations, rheumatism, abdominal pain, liver diseases, kidney stones and cleansing menstruation.³

Research on immunomodulatory activity in vivo using poly d,l-lactic-co-glycolic acid entrapped curcumin nanoparticle in albino mice sensitised with goat red blood cells (SRBCs) showed that nano curcumin at doses of 5 mg/kg and 10 mg/kg improved the immune response mediating the initial response of cells compared to controls. Similar results also occurred in secondary humoral antibodies, where white blood cell production and lymphoid organ weight also increased

in the group given 10 mg/kg of nano curcumin. Other studies have been conducted to determine the effect of postrum-supplied phytonutrient administration in dairy cows. Phytonutrients used such as curcuma oleoresins (2 g/cow); onion extract (2 g/cow); oleoresin capsicum (2 g/cow). From a 23-day study, results were obtained that all phytonutrients exert an immunostimulant effect by activating and inducing CD4 cell expansion. ^{4,5}

In vivo studies of the combination of 30% ethanol extract from *Artemisia capillaris*, *Sanguisorba officinalis*, and *Curcuma longa* in hydrodynamically induced mice of HBV (Hepatitis B Virus) genomes showed that both the combination of the three extracts and those administered together with entecavir were able to suppress HBV replication and the production of inflammatory cytokines without showing toxicity. ^{6th}

Research on the anti-inflammatory activity in vivo of oil-free water-extracts from turmeric using mice (ear edema with induction using xylene) and rats (cotton pellet granuloma model) showed that water-free oil extracts from turmeric at three dose levels (Doses for mice: 90, 180 and 360 mg/kg bw; Doses for rats : 45, 90 and 180 mg/kg bw) significantly ($P \leq 0.05$) inhibited inflammation in both study models, as evidenced by a reduction in ear weight and a decrease in wet and dry weight of cotton pellets, when compared with controls. The oil-free water-extract of turmeric exhibits an anti-inflammatory effect against acute and chronic inflammation comparable to the effects of curcuminoids and tumerones (essential oils).

Administration of turmeric rhizome extract in rats induced acute liver stress with CCl₄ showed a significant decrease in lipid peroxidation of membranes in the liver. Extracts of turmeric rhizomes and curcumin showed significant protection against liver injury by increasing hepatic superoxide dismutase; glutathione peroxidase activity, and glutathione amounts in the treatment group, which led to a decrease in lipid peroxidase levels. Therefore, turmeric and curcumin rhizome extracts are potential antioxidant agents against acute hepatotoxicity.

The method of use is as follows; as much as 25 g of fresh turmeric, thoroughly washed, grated, squeezed, filtered, plus 1 tablespoon of honey then taken 2 times a day. Dry matter: 3-9 grams per day; Powder: 1.5- 3.0 g/day; oral infusion: 0.5 – 1 gram three times a day. The powder should be consumed 2 to 3 times a day after meals; tea (2 to 3 cups) is consumed between meals. To make tea, heat 0.5 to 1 gram of the drug in boiling water, cover, wait 5 minutes.

Turmeric and curcumin are nonmutagenic and no reproductive toxicity has been observed. The FDA classifies turmeric as Generally Recognized As Safe (GRAS). No major side effects

were reported in clinical studies of turmeric extract use and neither was curcumin up to a dosage of 8 g/day for 3 months. In other clinical trials mild side effects such as nausea, diarrhea, headache, fatigue and drowsiness were reported in the turmeric group at a dose of 2 g / day (dry powder of turmeric rhizomes). Should not be used in conjunction with nonsteroidal anti-inflammatory drugs (NSAIDs), antiplatelets, and antihyperlipidemia groups. Use in patients with blockage of the bile ducts, cholangitis, gallstones or other bilestone diseases should consult a doctor Its use is not recommended in pregnant and lactating women due to the lack of relevant data on the safety of use during pregnancy and lactation.

3. Benefits of temulawak (*Curcuma xanthorrhiza* Roxb.)

Curcuma xanthorrhiza Roxb also called temulawak, contains curcuminoids (1-2%) and essential oils with xanthorrhizol components (31.9%), β -curcumene (17.1%), arcurcumene (13.2%), camphor (5.4%), γ -curcumene (2.6%), (Z)- γ -bisabolene (2.6%), and (E)- β -farnesene (1.2%). Empirically temulawak has been used for generations in Indonesia to treat various complaints of stomach and liver disorders, fever and constipation, galactagogue, bloody diarrhea, dysentery, inflammation of the rectum, hemorrhoids, stomach disorders which are 30 caused by cold, infected wounds, skin eruptions, acne vulgaris, eczema, smallpox and anorexia as well as to reduce uterine inflammation after childbirth.^{5,6}

The administration of 2% temulawak powder on the controlled diet of Sprague Dawley rats for 3–5 weeks showed temulawak was able to increase the proportion of spleen T cells during the experimental period, but had a variable effect on B cells and a subset (part) of T cells, namely an increase in the proportion of B cells in temulawak administration for 3 weeks and helper (Th) T cells in temulawak administration for 4 weeks without an increase in the proportion of T cells suppressor (Ts). The effect of this medicinal plant on the proportion of macrophages of the spleen and peripheral blood is inconsistent. Thus, this study shows that Temulawak shows the activity of activating immune function mediated by T cells and B cells.^{7,8}

Pre-implementation of the temulawak hexan fraction dose of 500 mg/kgbb peroral in male Sprague Dawley rats for 7 consecutive days followed by hepatotoxic induction with CCl₄ can increase levels of *glutathione peroxidase* (GPx), superoxide dismutase (SOD), *glutathione reductase* (GR), catalase (CAT), and total protein (TP) levels and can reduce *malondialdehyde* levels (MDA) on the hepar rather than the control. This shows that temulawak can act as an

antioxidant and can prevent lipid peroxidation caused by CCl₄. Pre-implementation of temulawak ethanol extract dose 500 mg / kgbb peroral in male Sprague Dawley rats for 7 consecutive days followed by hepatotoxic induction with ethanol reduces the symptoms of fatty liver and significantly ($p < 0.05$) inhibits the increase in levels of antioxidant enzymes that play a role in liver disease, namely alanine transaminases (ALT), aspartate transaminases (AST) and alkaline phosphatase (ALP).^{9,10 pm}

Pre-treatment with 0.1 - 2.0 μ mol xanthorrhizol/50 μ l of topically administered DMSO-acetone inhibits edema in the ear of a TPA-induced IDR mice (12-O-tetradecanoylphorbol-13-acetate), which has a direct correlation with inflammation. Administration of the hexan fraction of temulawak rhizomes at a dose of 75 mg / kg bb in edema-induced rats with carrageenan and acetic acid-induced mice showed inhibition in the formation of edema and was associated with the presence of non-phenolic linear diarilheptanoids in temulawak. Administration of temulawak extract (50 and 100 mg / kg bb / day) and xanthorrhizol (10 and 25 mg / kg bb / day) in obesity-induced mice with a high-fat diet showed a decrease in the fat of the sole epididymis of the feet successively extracts (25.8% and 22.5%) as well as xanthorrhizol (26.6% and 20.1%). Extracts and xanthorrhizol can also inhibit the production of pro-inflammatory cytokines such as TNF- α , IL-6, IL-1 β , and C-reactive protein (CRP) in adipose tissue (27.8-82.7%), liver (43.9-84.7%), and muscle (65.2-92.5%).

Empirical use in Indonesia, especially to relieve liver function disorders, can be done by boiling 25 g of fresh temulawak slices with 500 mL of water to stay 300 mL, drunk for a day. Another way can be done by taking 25 g of fresh rhizomes, grated, squeezed, filtered divided in half and drunk for a day.

The European Medicine Agency reports no serious side effects have been reported as of now.^{4,5} Further the chemical composition of temulawak does not give a reason for safety concerns. The use of temulawak in pregnant women and during breastfeeding is not recommended until there is data that curcumin and/ or its metabolites can be transferred through lactation. Use in patients with blockage of the bile ducts, cholangitis, gallstones or other bilestone diseases should consult a doctor.

4. Conclusion→5

Turmeric and temulawak herbs empirically and scientifically have the potential to increase the body's immunity in the face of COVID-19.

5. References →6

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Potency of Turmeric (*Curcuma longa* L.) and Temulawak (*Curcuma xanthorrhiza* Roxb.) in Handling Coronavirus Disease 2019 (COVID-19)

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ABSTRACT

One of the efforts to prevent COVID-19 that can be done is to increase individual immunity. The effort that can be made is to use herbal ingredients as health drinks. *Curcuma longa* L., or turmeric, has long been known as one of the ingredients used to treat several complaints. Turmeric has a chemical content of carbohydrates (69.4%), curcuminoids, and essential oils (5.8%). Turmeric and curcumin are non-mutagenic, and no reproductive toxicity has been observed. *Curcuma xanthorrhiza* Roxb, also known as temulawak, contains curcuminoids (1-2%) and essential oils with xanthorrhizol components (31.9%), β -curcumene (17.1%), arcurcumene (13.2%), camphor (5.4%), γ -curcumene (2.6%), (Z)- γ -bisabolene (2.6%), and (E)- β -farnesene (1.2%). Empirically, temulawak has been used for generations in Indonesia to treat various digestive disorders, skin complaints, liver and bile disorders.

1. Introduction

Novel coronavirus (COVID-19) has now become a pandemic and a global health problem. COVID-19 cases started with information from the World Health Organization (WHO) on 31st December 2019, which mentioned cluster pneumonia with unclear etiology in Wuhan City, Hubei Province, China. This case continued to grow until it was finally discovered that the cause cluster was the novel coronavirus. This case continued to grow until there were reports of deaths and imports outside China. On 30th January 2020, WHO declared COVID-19 a public health emergency of international concern (PHEIC). On February 12, 2020, WHO officially declared the novel coronavirus disease. In humans, this is called Coronavirus Disease (COVID-

19). In Indonesia itself, the first case of COVID-19 was reported on 2nd March 2020. The area of spread of COVID-19 in Indonesia is widespread in almost all provinces. The number of patients infected with COVID-19 also continues to grow. A few months next, the Indonesian nation will face major problems caused by COVID-19 if not handled properly.

Facing a situation like this, it is necessary to control and prevent COVID-19. One of the prevention efforts that can be done is to increase community resilience through individual body health. The body's immune system can be maintained and improved, mainly through healthy living habits, including maintaining cleanliness, and good nutrition, coupled

with the use of health supplements and herbal ingredients/traditional medicines. Indonesia is one of the countries with great biodiversity. No less than 30,000 species of plants exist in the tropical forests of Indonesia. Of these, around 9,600 species are known to have medicinal properties, but not all of them are used optimally as herbal medicines.^{1,2} Utilization of herbs as medicine in the form of steeping ingredients, herbs, standardized herbal medicines, and phytopharmaceuticals. Herbal medicine is a cultural heritage of the Indonesian people, which has been traditionally and for generations used to improve health status.

Benefits of turmeric (*Curcuma longa* L.)

Curcuma longa L., or turmeric, has long been known as one of the ingredients used to treat several complaints. Turmeric has a chemical content of carbohydrates (69.4%), curcuminoids (a mixture of curcumin, demethoxycurcumin, and bisdemethoxycurcumin), and essential oil (5.8%). Rhizome mixed with warm milk is used to cure colds, bronchitis, and asthma. Meanwhile, fresh rhizome juice can be applied to skin infections. Turmeric rhizome is also said to have properties to relieve various inflammations, rheumatism, stomach pain, liver disease, kidney stones, and cleanse menstruation.³

Research on immunomodulatory activity in vivo by using poly d,l-lactic-co-glycolic acid entrapped curcumin nanoparticles in albino mice desensitized with goat red blood cells (SRBCs) showed that nano curcumin at doses of 5 mg/kg and 10 mg/kg increased the immune response mediating the response. Baseline cells compared to controls. The same results also occurred in secondary humoral antibodies, where the production of white blood cells and lymphoid organ weight also increased in the group given 10 mg/kg nano curcumin. Other studies have been conducted to determine the effect of post-rum-supply phytonutrients in dairy cows. Phytonutrients such as date palm oleoresin (2 g/beef); onion extract (2 g/beef), and oleoresin capsicum (2 g/beef). From a 23-day study, it

was found that all phytonutrients exert an immunostimulating by activating and inducing CD4 cell expansion.^{4,5}

In vivo study of a combination of 30% ethanol extract of *Artemisia capillaris*, *Sanguisorba officinalis*, and *Curcuma longa* in mice hydrodynamically induced by HBV genome (Hepatitis B Virus) showed that both the combination of the three extracts and those given together with entecavir were able to suppress HBV replication, and production of inflammatory cytokines without showing toxicity.⁶

In vivo anti-inflammatory activity studies of oil-free aqueous extract of turmeric using mice (xylene-induced ear edema) and mice (cotton pellet granuloma model) showed that oil-free aqueous extract of turmeric at three dose levels (Dose for mice: 90, 180 and 360 mg/kg bw; Doses for rats: 45, 90 and 180 mg/kg bw) significantly ($P \leq 0.05$) inhibited inflammation in both study models, as evidenced by a reduction in ear weight and a decrease in wet and dry weight. From cotton pellets, when compared with controls. The oil-free aqueous extract of turmeric showed an anti-inflammatory effect against acute and chronic inflammation comparable to that of curcuminoids and turmerones (essential oils).

Administration of turmeric rhizome extract to rats induced by acute liver stress with CCl₄ showed a significant decrease in membrane lipid peroxidation in the liver. Turmeric rhizome extract and curcumin showed significant protection against liver injury by increasing hepatic superoxide dismutase; glutathione peroxidase activity, and the amount of glutathione in the treatment group, which led to a decrease in lipid peroxidase level. Therefore, turmeric rhizome extract and curcumin are potential antioxidant agents against acute hepatotoxicity.

How to use it is as follows; as much as 25 g of fresh turmeric, washed, grated, squeezed, filtered, plus 1 tablespoon of honey, then taken 2 times a day. Dry matter: 3-9 grams per day; Powder: 1.5- 3.0 g/day; oral infusion: 0.5 – 1 gram three times a day. The powder should be taken 2 to 3 times a day after meals; tea (2 to 3 cups) is consumed between meals. To make

tea, heat 0.5 to 1 gram of the drug in boiling water, cover, and wait 5 minutes.

Turmeric and curcumin are non-mutagenic, and no reproductive toxicity has been observed. FDA classifies turmeric as Generally Recognized As Safe (GRAS). No major side effects were reported in clinical studies using turmeric extract and, similarly, curcumin up to a dose of 8 g/day for 3 months. In another clinical trial, mild side effects such as nausea, diarrhea, headache, fatigue, and drowsiness were reported in the turmeric group at a dose of 2 g/day (turmeric rhizome dry powder). It should not be used concurrently with non-steroidal anti-inflammatory drugs (NSAIDs), antiplatelet, and antihyperlipidemic. Its use in patients with bile duct obstruction, cholangitis, gallstones, or other biliary diseases should consult a doctor. Its use is not recommended in pregnant and lactating women due to the lack of relevant data on the safety of use during pregnancy and lactation.

Benefits of Temulawak (*Curcuma xanthorrhiza* Roxb.)

Curcuma xanthorrhiza Roxb also called temulawak, contains curcuminoids (1-2%) and essential oils with xanthorrhizol components (31.9%), β -curcumene (17.1%), arcurcumene (13.2%), camphor (5.4%), γ -curcumene (2.6%), (Z)- γ -bisabolene (2.6%), and (E)- β -farnesene (1.2%). Empirically, temulawak has been used for generations in Indonesia to treat various stomach complaints and liver disorders, fever and constipation, galactagogue, bloody diarrhea, dysentery, rectal inflammation, hemorrhoids, gastric disorders caused by cold, infected wounds, skin eruptions, acne vulgaris, eczema, smallpox and anorexia and to reduce inflammation of the uterus after childbirth.^{5,6}

Giving 2% temulawak powder to a controlled diet of Sprague Dawley rats for 3 – 5 weeks showed that ginger was able to increase the proportion of spleen T cells during the experimental period but gave a variable effect on B cells and a subset of T cells, namely an increase in the proportion of spleen cells. B

on the administration of temulawak for 3 weeks and helper T cells (Th) on the administration of temulawak for 4 weeks without an increase in the proportion of suppressor T cells (Ts). The effects of these medicinal plants on the proportion of macrophages from the spleen and peripheral blood were inconsistent. Thus, this study shows that temulawak exhibits T-cell and B-cell-mediated immune function activation.^{7,8}

Pretreatment of the hexane fraction of temulawak at a dose of 500 mg/kg body weight orally in male Sprague Dawley rats for 7 consecutive days followed by hepatotoxic induction with CCl₄ can increase levels of *glutathione peroxidase* (GPx), superoxide dismutase (SOD), *glutathione reductase* (GR), catalase (CAT), and total protein (TP) and can reduce levels of *malondialdehyde* (MDA) in the liver compared to controls. This shows that temulawak can act as an antioxidant and can prevent lipid peroxidation caused by CCl₄. Pretreatment of ethanol extract of temulawak at a dose of 500 mg/kgbw orally in male Sprague Dawley rats for 7 consecutive days followed by hepatotoxic induction with ethanol reduced the symptoms of fatty liver and significantly ($p < 0.05$) inhibited the increase in levels of antioxidant enzymes that play a role in the disease. Liver, namely alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP).^{9,10}

Pretreatment with 0.1 - 2.0 mol xanthorrhizol/50 l DMSO-acetone applied topically inhibited TPA-induced ear edema in IDR mice (12-O-tetradecanoylphorbol-13-acetate), which had a direct correlation with inflammation. Administration of the hexane fraction of temulawak rhizome at a dose of 75 mg/kg bw to carrageenan-induced edema and mice showed inhibition of edema formation and was associated with the presence of non-phenolic linear diarylheptanoids in temulawak. The administration of temulawak extract (50 and 100 mg/kg bw/day) and xanthorrhizol (10 and 25 mg/kg bw/day) in obese-induced mice with a high-fat diet showed a decrease in the epididymal fat of the soles of the feet, respectively, the extract (25.8% and 22.5%) and xanthorrhizol (26.6% and 20.1%). Extracts and

xanthorrhizol can also inhibit the production of pro-inflammatory cytokines such as TNF- α , IL-6, IL-1 β , and C-reactive protein. (CRP) in adipose tissue (27.8-82.7%), liver (43.9-84.7%), and muscle (65.2-92.5%).

Empirical use in Indonesia, especially to relieve liver function disorders, can be done by boiling 25 g of fresh ginger slices with 500 mL of water until only 300 mL is left, taken for a day. Another way can be done by taking 25 g of fresh rhizome, grated, squeezed, filtered divided into three, and drunk for a day.

European Medicine Agency reported no serious side effects reported to date.^{4,5} Furthermore, the chemical composition of temulawak does not provide a reason for safety concerns. The use of ginger in pregnant women and during lactation is not recommended until there are data that curcumin and/or its metabolites can be transferred through lactation. Use in patients with bile duct blockage, cholangitis, gallstones, or other biliary diseases should consult a doctor.

2. Conclusion

Turmeric and temulawak herbs empirically and scientifically have the potential to increase the body's immunity in dealing with COVID-19.

3. References

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Potency of Turmeric (*Curcuma longa* L.) and Temulawak (*Curcuma xanthorrhiza* Roxb.) in Handling Coronavirus Disease 2019 (COVID-19)

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ABSTRACT

One of the efforts to prevent COVID-19 that can be done is to increase individual immunity. The effort that can be made is to use herbal ingredients as health drinks. *Curcuma longa* L., or turmeric, has long been known as one of the ingredients used to treat several complaints. Turmeric has a chemical content of carbohydrates (69.4%), curcuminoids, and essential oils (5.8%). Turmeric and curcumin are non-mutagenic, and no reproductive toxicity has been observed. *Curcuma xanthorrhiza* Roxb, also known as temulawak, contains curcuminoids (1-2%) and essential oils with xanthorrhizol components (31.9%), β -curcumene (17.1%), arcurcumene (13.2%), camphor (5.4%), γ -curcumene (2.6%), (Z)- γ -bisabolene (2.6%), and (E)- β -farnesene (1.2%). Empirically, temulawak has been used for generations in Indonesia to treat various digestive disorders, skin complaints, liver and bile disorders.

1. Introduction

Novel coronavirus (COVID-19) has now become a pandemic and a global health problem. COVID-19 cases started with information from the World Health Organization (WHO) on 31st December 2019, which mentioned cluster pneumonia with unclear etiology in Wuhan City, Hubei Province, China. This case continued to grow until it was finally discovered that the cause cluster was the novel coronavirus. This case continued to grow until there were reports of deaths and imports outside China. On 30th January 2020, WHO declared COVID-19 a public health emergency of international concern (PHEIC). On February 12, 2020, WHO officially declared the novel coronavirus disease.

In humans, this is called Coronavirus Disease (COVID-19). In Indonesia itself, the first case of COVID-19 was reported on 2nd March 2020. The area of spread of COVID-19 in Indonesia is widespread in almost all provinces. The number of patients infected with COVID-19 also continues to grow. A few months next, the Indonesian nation will face major problems caused by COVID-19 if not handled properly.

Facing a situation like this, it is necessary to control and prevent COVID-19. One of the prevention efforts that can be done is to increase community resilience through individual body health. The body's immune system can be maintained and improved,

mainly through healthy living habits, including maintaining cleanliness, and good nutrition, coupled with the use of health supplements and herbal ingredients/traditional medicines. Indonesia is one of the countries with great biodiversity. No less than 30,000 species of plants exist in the tropical forests of Indonesia. Of these, around 9,600 species are known to have medicinal properties, but not all of them are used optimally as herbal medicines.^{1,2} Utilization of herbs as medicine in the form of steeping ingredients, herbs, standardized herbal medicines, and phytopharmaceuticals. Herbal medicine is a cultural heritage of the Indonesian people, which has been traditionally and for generations used to improve health status.

Benefits of turmeric (*Curcuma longa* L.)

Curcuma longa L., or turmeric, has long been known as one of the ingredients used to treat several complaints. Turmeric has a chemical content of carbohydrates (69.4%), curcuminoids (a mixture of curcumin, demethoxycurcumin, and bisdemethoxycurcumin), and essential oil (5.8%). Rhizome mixed with warm milk is used to cure colds, bronchitis, and asthma. Meanwhile, fresh rhizome juice can be applied to skin infections. Turmeric rhizome is also said to have properties to relieve various inflammations, rheumatism, stomach pain, liver disease, kidney stones, and cleanse menstruation.³

Research on immunomodulatory activity in vivo by using poly d,l-lactic-co-glycolic acid entrapped curcumin nanoparticles in albino mice desensitized with goat red blood cells (SRBCs) showed that nano curcumin at doses of 5 mg/kg and 10 mg/kg increased the immune response mediating the response. Baseline cells compared to controls. The same results also occurred in secondary humoral antibodies, where the production of white blood cells and lymphoid organ weight also increased in the group given 10 mg/kg nano curcumin. Other studies have been conducted to determine the effect of post-rum-supply phytonutrients in dairy cows. Phytonutrients such as date palm

oleoresin (2 g/beef); onion extract (2 g/beef), and oleoresin capsicum (2 g/beef). From a 23-day study, it was found that all phytonutrients exert an immunostimulating by activating and inducing CD4 cell expansion.^{4,5}

In vivo study of a combination of 30% ethanol extract of *Artemisia capillaris*, *Sanguisorba officinalis*, and *Curcuma longa* in mice hydrodynamically induced by HBV genome (Hepatitis B Virus) showed that both the combination of the three extracts and those given together with entecavir were able to suppress HBV replication. and production of inflammatory cytokines without showing toxicity.⁶

In vivo anti-inflammatory activity studies of oil-free aqueous extract of turmeric using mice (xylene-induced ear edema) and mice (cotton pellet granuloma model) showed that oil-free aqueous extract of turmeric at three dose levels (Dose for mice: 90, 180 and 360 mg/kg bw; Doses for rats: 45, 90 and 180 mg/kg bw) significantly ($P \leq 0.05$) inhibited inflammation in both study models, as evidenced by a reduction in ear weight and decrease in wet and dry weight. For cotton pellets, when compared with controls. The oil-free aqueous extract of turmeric showed an anti-inflammatory effect against acute and chronic inflammation comparable to that of curcuminoids and turmerones (essential oils).

Administration of turmeric rhizome extract to rats induced by acute liver stress with CCl₄ showed a significant decrease in membrane lipid peroxidation in the liver. Turmeric rhizome extract and curcumin showed significant protection against liver injury by increasing hepatic superoxide dismutase; glutathione peroxidase activity, and the amount of glutathione in the treatment group, which led to a decrease in lipid peroxidase level. Therefore, turmeric rhizome extract and curcumin are potential antioxidant agents against acute hepatotoxicity.

How to use it is as follows; as much as 25 g of fresh turmeric, washed, grated, squeezed, filtered, plus 1 tablespoon of honey, then taken 2 times a day. Dry matter: 3-9 grams per day; Powder: 1.5- 3.0 g/day; oral infusion: 0.5 – 1 gram three times a day. The

powder should be taken 2 to 3 times a day after meals; tea (2 to 3 cups) is consumed between meals. To make tea, heat 0.5 to 1 gram of the drug in boiling water, cover, and wait 5 minutes.

Turmeric and curcumin are non-mutagenic, and no reproductive toxicity has been observed. FDA classifies turmeric as Generally Recognized As Safe (GRAS). No major side effects were reported in clinical studies using turmeric extract and, similarly, curcumin up to a dose of 8 g/day for 3 months. In another clinical trial, mild side effects such as nausea, diarrhea, headache, fatigue, and drowsiness were reported in the turmeric group at a dose of 2 g/day (turmeric rhizome dry powder). It should not be used concurrently with non-steroidal anti-inflammatory drugs (NSAIDs), antiplatelet, and antihyperlipidemic. Its use in patients with bile duct obstruction, cholangitis, gallstones, or other biliary diseases should consult a doctor. Its use is not recommended in pregnant and lactating women due to the lack of relevant data on the safety of use during pregnancy and lactation.

Benefits of Temulawak (*Curcuma xanthorrhiza* Roxb.)

Curcuma xanthorrhiza Roxb also called temulawak, contains curcuminoids (1-2%) and essential oils with xanthorrhizol components (31.9%), β -curcumene (17.1%), arcurcumene (13.2%), camphor (5.4%), γ -curcumene (2.6%), (Z)- γ -bisabolene (2.6%), and (E)- β -farnesene (1.2%). Empirically, temulawak has been used for generations in Indonesia to treat various stomach complaints and liver disorders, fever and constipation, galactagogue, bloody diarrhea, dysentery, rectal inflammation, hemorrhoids, gastric disorders caused by cold, infected wounds, skin eruptions, acne vulgaris, eczema, smallpox and anorexia and to reduce inflammation of the uterus after childbirth.^{5,6}

Giving 2% temulawak powder to a controlled diet of Sprague Dawley rats for 3 – 5 weeks showed that ginger was able to increase the proportion of spleen T cells during the experimental period but gave a

variable effect on B cells and a subset of T cells, namely an increase in the proportion of spleen cells. B on the administration of temulawak for 3 weeks and helper T cells (Th) on the administration of temulawak for 4 weeks without an increase in the proportion of suppressor T cells (Ts). The effects of these medicinal plants on the proportion of macrophages from the spleen and peripheral blood were inconsistent. Thus, this study shows that temulawak exhibits T-cell and B-cell-mediated immune function activation.^{7,8}

Pretreatment of the hexane fraction of temulawak at a dose of 500 mg/kg body weight orally in male Sprague Dawley rats for 7 consecutive days followed by hepatotoxic induction with CCl₄ can increase levels of *glutathione peroxidase* (GPx), superoxide dismutase (SOD), *glutathione reductase* (GR), catalase (CAT), and total protein (TP) and can reduce levels of *malondialdehyde* (MDA) in the liver compared to controls. This shows that temulawak can act as an antioxidant and can prevent lipid peroxidation caused by CCl₄. Pretreatment of ethanol extract of temulawak at a dose of 500 mg/kgbw orally in male Sprague Dawley rats for 7 consecutive days followed by hepatotoxic induction with ethanol reduced the symptoms of fatty liver and significantly ($p < 0.05$) inhibited the increase in levels of antioxidant enzymes that play a role in the disease. Liver, namely alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP).^{9,10}

Pretreatment with 0.1 - 2.0 mol xanthorrhizol/50 l DMSO-acetone applied topically inhibited TPA-induced ear edema in IDR mice (12-O-tetradecanoylphorbol-13-acetate), which had a direct correlation with inflammation. Administration of the hexane fraction of temulawak rhizome at a dose of 75 mg/kg bw to carrageenan-induced edema and mice showed inhibition of edema formation and was associated with the presence of non-phenolic linear diarylheptanoids in temulawak. The administration of temulawak extract (50 and 100 mg/kg bw/day) and xanthorrhizol (10 and 25 mg/kg bw/day) in obese-induced mice with a high-fat diet showed a decrease in the epididymal fat of the soles of the feet,

respectively, the extract (25.8% and 22.5%) and xanthorrhizol (26.6% and 20.1%). Extracts and xanthorrhizol can also inhibit the production of pro-inflammatory cytokines such as TNF- α , IL-6, IL-1 β , and C-reactive protein. (CRP) in adipose tissue (27.8-82.7%), liver (43.9-84.7%), and muscle (65.2-92.5%).

Empirical use in Indonesia, especially to relieve liver function disorders, can be done by boiling 25 g of fresh ginger slices with 500 mL of water until only 300 mL is left, taken for a day. Another way can be done by taking 25 g of fresh rhizome, grated, squeezed, filtered divided into three, and drunk for a day.

European Medicine Agency reported no serious side effects reported to date.^{4,5} Furthermore, the chemical composition of temulawak does not provide a reason for safety concerns. The use of ginger in pregnant women and during lactation is not recommended until there are data that curcumin and/or its metabolites cannot be transferred through lactation. Use in patients with bile duct blockage, cholangitis, gallstones, or other biliary diseases should consult a doctor.

2. Conclusion

Turmeric and temulawak herbs empirically and scientifically have the potential to increase the body's immunity in dealing with COVID-19.

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CERTIFICATE

O F P U B L I C A T I O N

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