



Potential of Meniran (*Phyllanthus niruri* L.) and Sambiloto (*Andrographis paniculata*) as a Supplement to the Management of Coronavirus Disease 2019 (COVID-19)

Rachmat Hidayat^{1*}, Patricia Wulandari²

¹Department of Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

²Cattleya Mental Health Center, Palembang, Indonesia

ARTICLE INFO

Keywords:

Andrographis paniculata

COVID-19

Immunomodulator

Phyllanthus niruri

*Corresponding author:

Rachmat Hidayat

E-mail address:

dr.rachmat.hidayat@gmail.com

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

<https://doi.org/10.37275/ehi.v3i2.58>

ABSTRACT

COVID-19 infection with moderate or severe symptoms can cause pneumonia with an opaque appearance that can be detected on a chest CT scan, pulmonary edema, and accumulation of pleural fluid in the lungs. The use of herbs as health drinks is thought to play a role in increasing the body's immunity. Meniran plant (*Phyllanthus niruri*) contains tannins and flavonoids, which are efficacious as immunomodulators. Meanwhile, sambiloto also contains chemical compounds of alkaloids, carbohydrates, resins, saponins, flavonoids, steroids, glycosides, and tannins. Meniran and sambiloto herbs have the potential to increase the system potential to be developed as a supplement to treat COVID-19.

1. Introduction

In December 2019, there was a report of the Coronavirus from the city of Wuhan, Hubei province, China. This virus has become a pandemic that has spread throughout the world to this day. The name COVID-19 stands for coronavirus diseases 2019 or also known as SARS-Cov-2. While this research was being conducted, COVID-19 cases were increasing, reaching 96.2 million in the world, 977 thousand positive cases in Indonesia, and 13,599 thousand positive cases in South Sumatra. COVID-19 infection, both moderate and severe symptoms, can cause pneumonia with an opaque appearance that can be

detected on a chest CT scan, pulmonary edema, and accumulation of pleural fluid in the lungs. The genetic sequence of SARS-CoV-2 showed that COVID-19 belongs to the -coronavirus genus, with 79% nucleotide identity to SARS-CoV and 51.8% identity to MERS-CoV. Inoculation with SARS-CoV-2 of human airway epithelial cells in vitro caused a cytopathic effect and cessation of ciliary movement of respiratory epithelial cells, similar to the cytopathic effect observed in SARS-CoV infection.¹

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. The use of herbs is 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.^{2,3} Various plants with health potential have been studied regarding their use in improving the body's health status, including triggering the body's immune power in dealing with COVID-19.

2. Benefits of Meniran (*Phyllanthus niruri* L.)

Phyllanthus niruri L. often called *meniran*, *didukung anak*, *daun gendong anak*, *gosau ma dung-dung*. This plant contains chemical tannins, resins, potassium, flavonoids (quercetin, quercitrin, isoquercitrin, astragalol, rutin; *kaemferol-4-ramnopyranoside*, *eridiktol-7-ramnopyranoside*), and lignans (cubebin dimethyl ether, urinatetralinurine, nirurine, phyllanthuric acid). hypophyllanthine, triterpene lup-20-en-3-ol. The leaves, roots, and all parts of this plant can be used empirically for the treatment of epilepsy, malaria, constipation, high blood pressure, irregular menstruation, thrush (leaves), heartburn, tooth pain (roots), poor urination, gonorrhoea, syphilis, kidney pain, diarrhoea, fever, tetanus, dirty blood, convulsions gagau, egg white in urine, urinary stones (all parts) and others.⁴

In testing the immunostimulant effect of meniran water extract in vivo using tilapia fish (*Oreochromis mossambicus*) at a dose range of 0.002 – 20 mg, it showed a significant increase in neutrophil activation and antibody response. Based on observations, fish with a test dose of 20 mg/kg BW showed a maximum increase in primary and secondary antibody responses, and a dose of 0.002 mg/kg showed higher neutrophil activation than the control group. The results of this test indicate that meniran extract has potential as an immunostimulant.⁵

Research in vitro using PBMC (peripheral blood

mononuclear cells) and macrophage cells of TB patients showed that aqueous extract of *Phyllanthus niruri* L. leaves had immunomodulatory with increased PBMC cell proliferation, increased phagocyte activity, and increased release of NO macrophages (dose-dependent effect). Clinical trials have also been carried out in a number of hospitals in Jakarta and Surabaya. It is reported that adjuvant therapy or complementary therapy is a drug that is consumed as a supporter of the main drug effect because it is known to increase the potency of the main drug. Meniran extracts succeeded in shortening the duration of treatment in several diseases such as TB, hepatitis, and candidiasis vaginalis. The addition of meniran extract to anti-tuberculosis drugs for post-primary can encourage changes in acid-fast bacilli (BTA) three times greater. The results of clinical testing showed that patients who received anti-tuberculosis drugs along with 50 mg of meniran extract, recovered at week 6 while patients who only received anti-tuberculosis drugs recovered at week 14. Furthermore, it was reported that there was no significant difference in side effects between the two treatments. In other words, giving meniran extract combined with standard anti-tuberculosis drugs was quite safe.⁶

Based on antiviral activity testing in mice, it was found that intraperitoneal administration of *Phyllanthus niruri* L. aqueous extract was effective in inhibiting Woodchuck hepatitis virus (WHV), in which 3 out of 4 test animals decreased and eliminated surface antigen titer and DNA polymerase activity in serum for 3-6 weeks, and no more WHV was detected at week 45 after previously discontinued administration at week 10.

Based on the tests carried out on mice, it was found that the administration of hexane extract, lignan-rich fraction, or phytylteralin lignin Meniran orally provides consistent antioxidant effects against inflammatory agents in rat paws characterized by inhibition of the increase in IL-1 β .

Based on the results of in vivo testing on mice (oxidative stress induced by nimesulide), it was found that the administration of aqueous extract had

antioxidant activity and protected the liver from damage caused by nimesulide by regulating oxidative stress in the liver. Administration Intraperitoneal showed more effective results than oral administration. Other tests in vivo showed the antioxidant activity of meniran water extract against paracetamol-induced liver damage in rats. The mechanism was through a decrease in glutamate oxaloacetate transaminase (GOT) and glutamate pyruvate transaminase. (GPT) serum, and increased catalase activity in the liver of the test group.

The use of meniran as a decoction, 15-30 g of meniran herb in 250 mL of water, taken 2-3 times per day. Dekokta is a liquid preparation made by extracting herbal preparations with water at a temperature of 90°C for 30 minutes. Meniran side effects in the form of hypoglycemia, hypotension, and electrolyte and mineral imbalances. Meniran can interact in the form of increasing the effectiveness of insulin and diabetes drugs if used together. Meniran contains geraniin reported to have negative inotropic, negative chronotropic, hypotensive, and ACE inhibitor effects. Therefore, it may enhance the effect of antihypertensive drugs α -blockers and heart medication. Meniran herb ethanol extract can inhibit cytochrome P450 enzymes in vivo and in vitro. Meniran has a synergistic effect with antimicrobial drugs and antagonists with corticosteroids (immunosuppressant agents).

Benefits of Sambiloto (*Andrographis paniculata*)

Sambiloto belongs to the *Andrographis* tribe *Acanthaceae*. The scientific name of the sambiloto medicinal plant is *Andrographis paniculata*. The popularity of the sambiloto plant in Indonesia has caused several regions/ethnicities in Indonesia to have different names, for example in Java it is known as Ki oray, ki peurat, takilo (Sundanese), bidara, sadilata, sambilata, takila (Javanese). While the name sambiloto in English is *green chireta*, *king of bitters*, while in Thailand it is called *fa thalaai*, in the Philippines it is called *aluy* and in France it is known as *roi des amers*. The chemical content of sambiloto

simplicia includes lactone terpenoids which include andrographolide, deoxyandrographolide, 11, 12-didehydro-14-deoxyandrographolide, neoandrographolide, andrographicide, deoxyandrographicide, and andropanoside. With andrographolide identity compounds. Sambiloto also contains chemical compounds of alkaloids, carbohydrates, resins, saponins, flavonoids, steroids, glycosides and tannins. The use of herbs described in the pharmacopoeia and certain official documents, namely: for bacillary dysentery, bronchitis, ulcers, colitis, coughs, dyspepsia, fever, hepatitis, malaria, mouth sores, wounds, tuberculosis, and venomous snakebites; In traditional medicine, it is used for colic, otitis media, vaginitis, pelvic inflammatory disease, chickenpox, eczema, and burns. This plant is used for tonsillitis, ulcers, typhoid, fever, itching, bitten by insects or poisonous snakes, diabetes, dysentery, ear inflammation, appendicitis, colds, and dirty blood.⁷

Sambiloto herb (*Andrographis paniculata* Burm. Nees) contains many components of chemical compounds that have been widely studied with activity as a hepatoprotection, and one of the active substances is *andrographolide*. The study aimed to determine the activity of *A. paniculata*, which has acted as an immunomodulator and hepatoprotection against Balb/c mice that had been induced by the hepatitis B vaccine. The three most active fractions of n-hexane showed an increase in the amount of IgG from the highest to the lowest, namely: F2 (containing groups of terpenoid compounds, steroids and flavonoids) IgG levels of 0.569 mg/20 g body weight in mice, F1 (containing groups of terpenoid compounds) IgG levels 0.126 mg/20 g BW of mice, F4 (containing groups of alkaloids and terpenoids) levels of IgG 0.094 mg/20 g BW of mice. Research has been carried out on the immunomodulatory effect of andrographolide on innate and adaptive immune responses using mice at a dose of 1 mg/kg. The results showed that there was a decrease in the production of anti-HBs antibodies and the number of splenocytes producing IL-4. Andrographolides can modulate innate and adaptive immune responses by regulating macrophage

phenotypic polarization and antibody Ag-specific^{8,9}

A double-blind, randomized controlled trial of *A. paniculata* in patients with uncomplicated upper respiratory tract infection, with a total of 223 patients divided into two groups (placebo, and *A. paniculata* (200 mg/day)). From clinical research, it was shown that extract of *A. paniculata* is effective for reducing symptoms of upper respiratory tract infection, with effectiveness 2.1 times (52.7%) higher than placebo. An andrographolide clinical trial was conducted to examine 13 HIV-positive patients and five healthy volunteers who were HIV-negative. The study started with a dose of 5 mg/kg for the first 3 weeks, then increased to 10 mg/kg for 3 weeks, and then increased to 20 mg/kg for the last 3 weeks. Andrographolide administration significantly increased the CD4+ lymphocyte count from an initial mean of 405 to 501 in HIV-positive patients. There was no statistically significant change in the mean blood level of HIV-1 viral load. A recent study summarized that andrographolide derivatives might be promising candidates for preventing HIV infection, suggesting that andrographolides inhibit gp120-mediated fusion of HL2/3 cells with T2M-bl cells.^{10,11}

Several studies have reported the antioxidant activity of *A. paniculata* and its constituents.^{9,10} Aqueous extract of *A. paniculata* significantly increased the activity of antioxidant defense enzymes such as catalase, superoxide dismutase, and *glutathione-S-transferase* and reduced glutathione content. This extract significantly inhibited lipid peroxidation by lowering the levels of thiobarbituric acid reactive substances in the liver and kidneys of diabetic rats (compared to normal rats) and also significantly increased hepatic glutathione concentration levels. *Pre-treatment* of andrographolide was reported to significantly attenuate the accumulation of phorbol-12-myristate-13-acetate- (PMA-) induced ROS formation and N-formyl-methionyl-leucyl-phenylalanine- (fMLP-) that induces mouse neutrophil adhesion. It was shown that *in vivo* that administration of andrographolide sulfonate (using a water-soluble andrographolide),

intraperitoneally reduced the severity of colitis in 2-4 trinitrobenzene-induced rats (TNBS).^{12,13}

Usage: 3-9 g of dried herbs or 25-75 g of fresh herbs as a single dose as needed. A total of three grams of dry ingredients or 25 grams of fresh ingredients are boiled and taken 2 times a day before eating. Undesirable effects of using high doses of sambiloto herbs can cause stomach discomfort, vomiting, nausea, and loss of appetite. This is due to the sambiloto taste of andrographolide, while in women, it can cause antifertility effects. It has been reported (very rarely) the occurrence of itching (chills/urticaria) and swelling of the eyes after drinking sambiloto stew. It is recommended to avoid this plant during pregnancy due to its ovulation prevention effect. Individuals who are allergic to plants can even develop anaphylactic reactions. Avoid long-term use concurrently with immunosuppressant drugs. Sambiloto herb extract may have a synergistic effect with isoniazid. Sambiloto has a hypotensive and antiplatelet effect, so it can increase the effect of antihypertensive and antiplatelet drugs.

2. Conclusion

Meniran and sambiloto herbs have the potential to increase the immune system potential to be developed as a supplement for the management of COVID-19.

3. References

1. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. *Clin Immunol.* 2020; 215:108427.
2. Saleh MI, Hidayat R, Febriyanto G, Parisa N. Potential of karamunting (*Rhodomlyrtus tomentosa*) fraction against kidney damage in diabetic rats. *Polonica Herbs.* 2021; 67(2).
3. Carrasco R, Schmidt G, Romero AL, Sartoretto JL, Caparroz A, 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.

4. Chatterjee M, Sil PC. Hepatoprotective effect of aqueous extract of *Phyllanthus niruri* on nimesulide-induced oxidative stress in vivo. *Indian Journal of Biochemistry and Biophysics*. 2006; 43(5):299–305.
5. 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.
6. Chung WY, Park JH, Kim MJ, Kim HO, Hwang JK, et al. Xanthorrhizol inhibits 12-O-tetradecanoylphorbol-13-acetate-induced acute inflammation and two-stage mouse skin carcinogenesis by blocking the expression of ornithine decarboxylase, cyclooxygenase-2 and inducible nitric oxide synthase through mitogen-acti. *Carcinogenesis*. 2007; 28(6): 1224–31.
7. Jayakumar T, Hsieh CY, Lee JJ, Sheu JR. Experimental and clinical pharmacology of *Andrographis paniculata* and its major bioactive phytoconstituent andrographolide. *Evidence-Based Complementary and Alternative Medicine*, 2013.
8. Jolliffe DA, Griffiths CJ, Martineau AR. Vitamin D in the Prevention of Acute Respiratory Infection: Systematic Review of Clinical Studies. *Journal of Steroid Biochemistry and Molecular Biology*. 2013; 136(1):321–9.
9. Kassuya CAL, Leite DFP, De Melo LV, Rehder, VLC, Calixto JB. Anti-inflammatory properties of extracts, fractions, and lignans isolated from *Phyllanthus amarus*. *Planta Medica*, 2005; 71(8):721–6.
10. Putri DU, Rintiswati N, Soesatyo MHNE, Haryana SM. Immune modulation properties of herbal plant leaves: *Phyllanthus niruri* aqueous extract on immune cells of tuberculosis patient - in vitro study. *Natural Product Research*. 2018; 32(4):463–7.
11. Rahayu MP. Immunomodulator activity of n-hexane fraction from Sambiloto herb (*Andrographis paniculata*, (Burm. F) Nees) Against Hepatitis B Vaccine Induced Mice with Ig G Parameter. *Journal of Pharmascience*, 2015; 2(1):35–43.
12. Sabir SM, Rocha JBT. Water-extractable phytochemicals from *Phyllanthus niruri* exhibit distinct in vitro antioxidant and in vivo hepatoprotective activity against paracetamol-induced liver damage in mice. *Food Chemistry*. 2008; 111(4):845–51.
13. Saxena RC, Singh R, Kumar P, Yadav SC, Negi MPS, et al. A randomized double-blind placebo controlled clinical evaluation of extract of *Andrographis paniculata* in patients with uncomplicated upper respiratory tract infection. *Phytomedicine*. 2010; 17(3–4), 178–85.