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Traditional Medicines Prescription and the Potential of Original Indonesian Herbs as Natural Immunomodulators

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Abstract

Traditional medicine is an ingredient or a recipe for components in the form of plant ingredients, animal ingredients, mineral substances, galenic preparations, or mixtures of these ingredients that have been used for treatment from generation to generation and can be applied by the prevailing norms in society. Traditional medicinal herbs can be an option for health maintenance, disease prevention, and health care and strengthening a person's immune system. With low prices and easy-to-find raw materials, traditional medicinal ingredients can be made and consumed at home. This review aims to provide information that native Indonesian herbs act as traditional medicines and also have potential as immunomodulators. The way to get this information is by searching through Google Scholar. The results show that many native Indonesian herbs act as natural immunomodulators. Therefore, it can be concluded that native Indonesian herbs can be developed into phytopharmaca as immunomodulators.

Keywords: Traditional medicinal ingredients, native Indonesian herbs, immunomodulators.

1. Introduction

Original Indonesian herbs are medicinal plants grown and cultivated in Indonesia and are used from generation to generation for health purposes [1]. Since ancient times, the Indonesian people have used traditional Indonesian medicinal ingredients to maintain health, prevent disease, and health care. Indonesian traditional medicinal ingredients can come from plants, animals, and minerals, but generally, those used come from plants. Traditional medicinal ingredients are one or more types of plants with other additives inert/neutral [2].

Immunity consists of 2 types: natural immunity (in native/native) and adaptive immunity (specific/acquired). Natural immunity is the body's first defense mechanism against infection. This immune response immediately kills microbes, stimulates adaptive immunity, and provides a signal essential for initiating B and T lymphocyte responses to specific antigens. Adaptive immunity develops more slowly than natural, requiring lymphocyte proliferation and differentiation to adapt to microbial invasion to produce a more efficient response when faced with the same microbial exposure. Immunomodulators are all drugs that can modify the immune response, stimulate natural and adaptive defense mechanisms, and can function as both immunosuppressants and immunostimulants. The body's defense system can be activated by administering immunomodulators to increase a person's immune response [3,4].

Traditional medicinal herbs can be an option to strengthen a person's immune system. With low prices and easy-to-find raw materials, traditional medicinal ingredients can be made and consumed at home. The Ministry of Health of the Republic of Indonesia advises the public to take advantage of traditional herbs to maintain health, prevent disease, and maintain endurance [5]. Currently, immunomodulators made from local Indonesian plants are continuously being developed by experts. This review discusses traditional medicinal

herbs and the potential of native Indonesian herbs as natural immunomodulators, including *Cinnamomum burmanii* (cinnamon), *Curcuma longa* (turmeric), *Phyllanthus niruri* (meniran), *Zingiber officinale* (ginger).

2. Methods of data collection

In compiling this review article, the technique used is to use literature studies by searching for sources or literature in primary data in official books and international journals in the last ten years (2011-2021). This review article's preliminary reference search is through trusted websites such as ResearchGate, Google Scholar, Elsevier, and other published and trustworthy journals.

3. Indonesian traditional medicinal herbs

Since ancient times, the Indonesian people have used traditional Indonesian medicinal ingredients to maintain health, prevent disease, and health care. Indonesian traditional medicinal ingredients can come from plants, animals, and minerals, but generally, those used come from plants. The following is a list of some traditional medicinal plants (Table 1), which contains the region's name, the part used, the traditional use, and herbs' preparation from several native Indonesian herbs [2].

Table 1: Some of the medicinal plants used in the manufacture of native Indonesian herbal recipes

No.	Medicinal plants	Region name	The part used	Benefits	How to make a recipe
1	<i>Cinnamomum burmanii</i> (cinnamon)	a) Sumatra: Holim, modang siak-siak (Batak), kanigar, madang kulit manih (Minang); b) Javanese: Huru mentek, kiamis (Sundanese), kanyengar (Kangean); c) Nusa Tenggara: Kesingaar, cingar (Bali), onte (Sasak), kaninggu (Sumba), puundinga (Flores).	Bark	Menstrual pain Diabetes	Boil 2 g of ingredients with 2 cups of water to 1 cup left, cool, strain, and divide into two parts. A total of 2 g of the material is crushed into a powder, brewed with 1 cup of boiling water, let stand, strain, drink while warm.
2	<i>Curcuma domestica</i> (turmeric)	a) Sumatra: kunyet (Aceh), hunik (Batak); b) Kalimantan: janar (Banjar), cahang (Dayak Panyabung); c) Javanese: koneng, temu kuning (Sundanese), kunir (Javanese), konye, temo koneng (Madura); d) Nusa Tenggara: Kunyik (Sasak); Sulawesi: hamu (Sangir), alawahu (Gorontalo); Maluku: kumino, unin (Ambon)	Rhizome	Stiff pains Back pain Childbirth	A total of 20 g of ingredients is brewed with 1 cup of boiling water; let stand, strain, and drink while warm. As much as 3 g of the material is shredded, attached to the affected part, and left to dry. A total of 1 handful of

					mashed rhizomes, boil in 3 cups of water to become 1 cup, cool, strain, drink by adding lime juice, honey, or brown sugar to taste, drink while warm.
3	<i>Phyllanthus niruri</i> (meniran)	a) Sumatra: sidukuang anak (Minang); b) Javanese: meniran green, meneniran (Sundanese), meniran (Javanese); c) Ternate: gosau ma dungi.	Herba	Mumps	A total of 10 g of ingredients are boiled in 2 cups of water to 1 cup, cool, filter, and drink all at once
4	<i>Zingiber officinale</i> Rosc. (ginger)	a) Sumatra: halia (Aceh), sipodeh (Minangkabau), jahi (Lampung); b) Javanese: jae (Javanese), jhai (Madura); c) Borneo: lai (Dayak); d) Nusa Tenggara: jae (Bali), reja (Bima); e) Sulawesi: melito (Gorontalo), song (Bugis); f) Maluku: sehi (Ambon), siwei (Buru), gerak (Ternate), gora (Tidore); g) Papua: lali (Kalana fat), manman (Kapaur)	Rhizome	Back pain Colds Antinausea - vomiting	The ingredients are shredded and mixed with tamarind; apply on the part that hurts. The ingredients are burned until fragrant, crushed; pour 1 cup of boiling water, let stand, and enough palm sugar and drink while warm. The ingredients are refined; pour them with boiling water; you can add honey or brown sugar according to your taste, drink while warm.

4. Natural immunomodulators

Immunomodulators are certain compounds that can increase the body's defense mechanism, both specifically and non-specifically, through cellular and humoral defense mechanisms. Immunomodulators function to repair impaired immune systems (immune restoration), suppressor normalizes abnormal immune reactions

(immunosuppressants), increase the immune response (immunostimulants) [4]. Immunomodulators with natural ingredients can be obtained from native Indonesian herbal plants. Here are some explanations of some native Indonesian herbal plants used as immunomodulators, such as cinnamon, turmeric, meniran, and ginger.

4.1 Cinnamon (*Cinnamomum burmannii*)

Cinnamomum burmannii (Figure 1) is a type of herb from the Lauraceae family. Commonly known as cinnamon, it is found in Southeast Asia and Indonesia, used as a spice in cooking and traditional medicine [6]. *Cinnamomum burmannii* contains tannins and volatile oil up to 4%: Cinnamaldehyde (60–75%), benzaldehyde and cumin aldehyde; phenols (4-10%) including eugenol, and methyl eugenol, pinene, phellandrene, cymene, and caryophyllene (hydrocarbons), eugenol acetate, cinnamyl acetate and benzyl benzoate (ester), linalool (alcohol). Cinnamon oil has antifungal, antiviral, bactericidal, and larvicidal, antiseptic, astringent pharmacological activity [7].



Figure 1: *Cinnamomum burmannii*

C. burmannii extract has the active compound cinnamaldehyde, which acts as an immunomodulator. Pratiwi *et al.* (2016) reported that *C. burmannii* extract increases granulocyte receptors and secretes IFN- γ , which activates macrophages to increase phagocytic activity. This activity was able to kill *Salmonella enteritidis* bacteria in thirty infected Wistar rats [4].

Astika *et al.* (2020) reported a study using 25 male Wistar rats randomly divided into five groups. The CN-G group was given standard feed, and the CP-G group was given an everyday meal and 2.5 mg/kg of levamisole; the CBE-100, CBE-200, CBE-400 groups were given standard feed and 100 mg of cinnamon extract, respectively. / kg BW, 200 mg/kg BW, and 400 mg/kg BW. The treatment was given for seven days, and on the 8th day, the rats were injected intraperitoneally with *S. aureus* suspension. The results showed that the neutrophil and lymphocyte count was found to be significantly different in the CBE-100 group compared to the other groups. An increase in the value of neutrophils in leukocytes is also known as neutrophilic leukocytosis. This condition results from a normal immune response during bacterial or viral infections, injury, and inflammation. The above studies' results indicate that the ethanol extract of *C. burmannii* can be used as an immunomodulator that increases the immune response [8].

4.2 Turmeric (*Curcuma longa*)

Turmeric or *Curcuma longa* from the Zingiberaceae family is locally known as "kunyit or kunir" (Figure 2). Turmeric has a distinctive aroma and yellowish red color. The curcuminoids in turmeric, the most prominent being the unsaturated β -diketone curcumin (curcumin) which, together with desmethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC), make up 50-60% of the curcuminoids present in the spice [9]. Its pharmacological activities include anti-inflammatory, antimicrobial, antiviral, antifungal, antioxidant, chemosensitizing, wound healing. Curcumin modulates T-cell proliferation and activation [10].



Figure 2. *Curcuma longa*

The immunomodulatory activity of the hot water extract fraction of *Curcuma longa* was investigated using peripheral blood mononuclear cells (PBMC). This study indicates that the polar fraction of the hot water extract of *C. longa* has a stimulating effect on the proliferation of PBMCs. Hot water extract of *C. longa* can be used as a supporting supplement for cancer patients undergoing chemotherapy. Patients with cancer also experience decreased immunity [11, 12].

4.3 Meniran (*Phyllanthus niruri*)

Phyllanthus niruri (meniran) (Figure 3) from the Phyllanthaceae family contains chemicals such as flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannins, coumarins, and saponins.

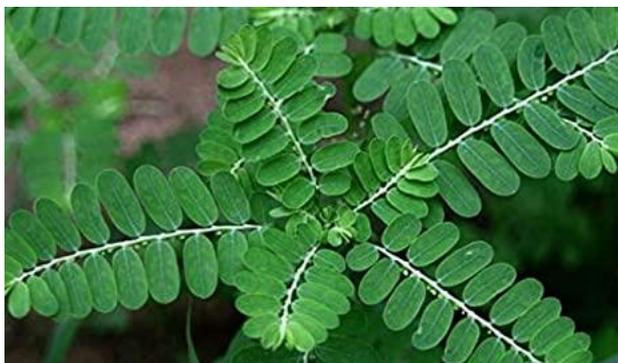


Figure 3. *Phyllanthus niruri*

In clinical studies, *P. niruri* has proven its ability to modulate and activate the immune system. *P. niruri* has medicinal effects on conditions such as dysentery, influenza, vaginitis, tumors, diabetes, diuretics, jaundice, kidney stones, dyspepsia, anti-hepatotoxic, anti-hepatitis B, and antihyperglycemic. *P. niruri* also has antiviral activity against the human immunodeficiency virus [13]. *P. niruri* extract showed significant anti-tumor activity. Flavonoids in *P. niruri* act as immunomodulators, especially as immunostimulators, because they can increase phagocytic activity and capacity as well as antibody titers [14].

4.4 Ginger (*Zingiber officinale*)

Zingiber officinale (Figure 4) is a type of medicinal plant from the Zingiberaceae family used as a cooking spice [15]. *Zingiber officinale* has secondary metabolic, including phenolic compounds such as gingerol,

shogaol, and paradol, showing antioxidant, anti-inflammatory, and antiobesity properties. This plant also contains sesquiterpenes such as bisabolene, zingiberene, zingiberol, sesquiphellandrene, and curcumin [15, 16].



Figure 4: *Zingiber officinale*

Gingerol compounds are promising drug candidates for treating various diseases associated with inflammation, cancer, and viral infections. Traditionally, *Zingiber officinale* is formulated as a decoction and processed into ginger oil which is indicated to treat coughs, asthma, gout, anti-inflammatory, headaches and arthritis. Research of the chemical compound found in ginger is 6-gingerol. The bioactive compound from phenol found in the ginger rhizome, 6-gingerol, binds to the COVID 19 virus RNA protein to form hydrogen-bonding interactions. The energy binding affinities are -11.4082 and -12.9523 KJ/Mol. This bond energy reflects the good inhibitory activity against the COVID 19 virus [17].

5. Conclusion

The community has long used Indonesian native herbs, including *Cinnamomum burmannii* (cinnamon), *Curcuma longa* (turmeric), *Phyllanthus niruri* (meniran), *Zingiber officinale* (ginger), as health care, disease prevention. Its potential as an immunomodulator has been proven both preclinically and clinically through several studies. Immunomodulators are needed, especially in the current state of the COVID 19 pandemic.

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A Brief Author Biography



Prof. Dr. Harrizul Rivai, M.S., was born in Payakumbuh, West Sumatra, on 4 September 1953. His father is Rivai Said, and his mother is Saridahanum Syofyan. The Author obtained a Bachelor of Pharmacy from the Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Padjajaran University, Bandung (1976), a Master of Science degree from the Bandung Institute of Technology (1984), and a Doctorate from the Department of Chemistry, Faculty of Mathematics and Natural Sciences, Andalas University, Padang (2011). Now the Author is a Professor and Researcher at the Faculty of Pharmacy, Andalas University, Padang. The Author also serves as Deputy Chair of Academic Affairs at the YPTIK Padang College of Pharmacy (STIFARM). The Author wrote the book "Principles of Chemical Examination" (Publisher UI-Press, 1995), translated the book "Pharmaceutical Statistics" (EGC Medical Book Publishers, 2010), and wrote "Chapter 4" in the book "Recent Research Advances in Biology Vol. 4" (International Book Publisher, India, and United Kingdom, 2020). The Author has also written articles in various international journals in various science fields, such as chemistry, biology, and pharmacy.