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Research Paper

Potency of Medicinal Plants as Immunostimulants

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ABSTRACT
Introduction: *Medicinal plants are plants that have medicinal properties and are used as medicine in the healing and prevention of disease*
Objective: *To find out medicinal plants that can be efficacious as immunostimulants that can boost the immune system.*
Methods: *The method used was a literature study. Data sources came from research journals on the efficacy of plants that can boost the body's immune system from various national and international sources. The data search strategy used was to search directly for gray literature through the Google search engine and use the Google Scholar, Pubmed and Science Direct databases. Inclusion criteria included national journals on the efficacy of sungkai plants with Sinta accreditation 1-6, and Scopus indexed international journals with Q1-Q4 rankings. Exclusion criteria included journals that did not focus on discussing the efficacy of plants as immunostimulants, unaccredited journals, and research journals with review methods.*
Results: *From the national and international journals that have been reviewed, it was found that there are many types of plants that act as immunomodulators with different mechanisms of action.*
Conclusion: *plants can act as immunostimulants because of the content of secondary metabolites contained therein that can increase the body's immune system through an immune system enhancement mechanism.*

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I. INTRODUCTION

Medicinal plants are plants that have medicinal properties and are used as medicine in the healing and prevention of disease (1). Indonesia is one of the countries known as a storehouse of medicinal plants. There are about 30,000 species of flora found in Indonesia's tropical forests. About 9,600 species have been recognized as medicinal. Since ancient times, medicinal plants processed into drugs have been widely used by the Indonesian people, both in the form of single fresh, mixed, and herbaceous which is better known as traditional medicine (2).

The immune system is a very important system for the body to avoid and fight various diseases. The balance of the immune system can be influenced by internal factors in the body and external factors that need to be maintained to keep the body healthy. Active compounds contained in plants that trigger the immune system in recent years have been used as immunotherapy, which is a treatment method that combines conventional medicine with traditional medicine to obtain maximum treatment results against various diseases (3).

The immune system can protect humans from foreign substances and pathogens such as viruses, bacteria, parasites and fungi. There are two types of immune responses, namely specific and non-specific immune responses. Non-specific immune responses work quickly to protect humans from microorganisms while specific immune responses show specific responses to certain microbes. Immunostimulants can boost the body's defense mechanisms. In general, immunostimulants are defined as compounds that can enhance the body's specific and non-specific defense mechanisms through cellular or humoral responses. Certain plants contain compounds that exhibit immunostimulatory activity (4). Some plants used by the community to increase endurance used by the community are Gambir (*Uncaria gambir* Roxb.), Pegagan Embun (*Hydrocotyle sibthorpioides* Lam), Sungkai (*Peronema canescens* Jack), and Mengkudu (*Morinda citrifolia* L.).

Immunostimulation works in improving the function of the immune system by using materials that can stimulate and improve the function of the immune system, for example Levamisol. Levamisol works to increase T cell proliferation and cytotoxicity and restore anergy in some patients with cancer (non-specific immunostimulation). Immunostimulators can be divided into two, namely biological and synthetic. In its

development, there are various kinds of products to increase immunity that have been widely circulated in the market and have been approved by the Food and Drug Administration (BPOM). One of them as used as a comparison in this study is Stimuno. Stimuno has indications of strengthening the body's immune system, and increasing the production of antibodies so that immunity is stronger (4). Stimuno is made from *Phyllanthus niruri* L. (meniran) plant extract. Meniran contains many chemical elements such as lignin which consists of *phyllanthine, hypophyllanthine, phyltetralin, lintretalin, nirathin, nitretalin, nirphylline, nirurin,* and *niruriside*. Flavonoids consist of *quercetin, quercitrin, isoquercitrin, astragalin, rutine,* and *physetinglucoside*. Terpenes consist of *limonene, lupeol acetate, lupeol* and *cymene*. Lipids consist of *ricinoleic acid, dotriancontanoic acid, linoleic acid,* and *linolenic acid*. Benzenoids are *methylsalicilate. Alkaloids consist of norsecurinine, 4-methoxy-norsecurinine, entnorsecurinina, nirurine, phyllanthine,* and *phyllochrysine*. Steroids in the form of *betasitosterol* (5).

Stimuno works directly to strengthen the immune system by multiplying antibodies to defend the body (immunomodulator) in addition to other properties, namely as adjuvant therapy in the treatment of tuberculosis (5). Giving *Phyllanthus niruri* (meniran) extract can increase the phagocytic activity of macrophage cells and increase the number of lymphocyte cells. *Phyllanthus niruri* (meniran) is also able to increase non-specific immune responses in the form of increased macrophage chemotaxis, neutrophil chemotaxis, and increased NK cell cytotoxis (6). Stimuno medicine consists of two variants, namely capsules and syrup. In Stimuno capsules in one box consists of 10 capsules / blister. Each Stimuno capsule contains 50 mg of *Phyllanthus niruri* L. extract. Whereas the Stimuno syrup in one bottle consists of 60 ml and every 5 ml contains 25 mg of *Phyllanthus niruri* L. extract (4).

II. METHODOLOGY

The method used was a literature study. Data sources came from research journals on the efficacy of plants that can boost the body's immune system from various national and international sources. The data search strategy used was to search directly for gray literature through the Google search engine and use the Google Scholar, Pubmed and Science Direct databases. Inclusion criteria included national journals on the efficacy of sungkai plants with Sinta accreditation 1-6, and Scopus indexed international journals with Q1-Q4 rankings. Exclusion criteria included journals that did not focus on discussing the efficacy of plants as immunostimulants, unaccredited journals, and research journals with review methods.

III. DISCUSSION

From the results of research on the identification of traditional medicinal plants of the Lembak Eight tribe in Bengkulu, it is known that young leaves of Peronema canescens Jack are the raw material for herbal medicines to reduce heat and in the treatment of the Serawai tribe, Sungkai leaves are pounded and slapped for bruises, Sungkai stem water is drunk as a smallpox medicine. The Sungkai plant is traditionally used by the Dayak tribe in East Kalimantan as a medicine, among others, for colds, fever, ringworms, as a bath for women after childbirth and as a mouthwash to prevent toothache. Sungkai leaf decoction is also traditionally used by local people in the Curup area, Bengkulu Province as a cure for malaria. In the treatment of the Dayak Tunjung tribe in East Kalimantan, young Sungkai leaves are used as a fever remedy while the roots are used as a diuretic and for body aches.

The ethanol fraction of Sungkai leaves is proven to be able to inhibit the growth of Plasmodium berghei parasites in the red blood cells of male white mice, where at a dose of 0.084 g / kgbw has the greatest percentage of inhibition compared to other treatment groups, reaching 54.06%. It can be concluded that the ethanol fraction of Sungkai leaves at a dose of 0.084 g / kgbw is the most effective dose and can have potential as an antimalarial. The results showed that the ethanol fraction of Sungkai leaves has the ability to inhibit the growth of Plasmodium berghei parasites in the blood of male white mice better than the synthetic drug chloroquine (7).

Sungkai plant (*Peronema canescens* Jack) is one of the medicinal plants that has been widely used as medicine such as medicine for malaria, antiplasmodium, pesticides, antipyretics, immunity, and teratogenicity. The content of secondary metabolite compounds contained in sungkai leaf extract is such as alkaloid, terpenoid, steroid, flavonoid, and tannin compound groups, and there are seven types of clerodane diterpenoid compounds contained, namely peronemin A2, A3, B1, B2, B3, C1, and D1 (8).

On the skin, sungkai can be used as a natural antioxidant and sungkai leaves can boost the immune system. So that this traditional treatment can be used in the health care system and in accordance with the rules of formal health services, which must be medically accountable. In addition, sungkai skin also has potential as a natural antioxidant (9).

Empirically, the sungkai plant has been used as a fever reducer, toothache, and malaria. In previous research, this sungkai leaf has been tested and proven to have an antibacterial effect. Then in preclinical testing,

sungkai leaves have the potential as antihyperuricemia, namely by reducing blood uric acid levels in mice. Young sungkai leaf extract also has the potential to improve health (10).

According to Pindan 2021, ethanol extracts from sungkai leaves have been shown to contain alkaloids, flavonoids, steroids, triterpenoids, phenolics and saponins. The flavonoid compound here acts as an analgesic by reducing the production of prostaglandins, where the mechanism of the flavonoid compound is to inhibit the action of the cyclooxygenation enzyme so that it can reduce pain (11). Sungkai leaves contain bioactive compounds such as triterpenoids, alkaloids, flavonoids, phenolics, steroids and saponins, which are believed to have antioxidant activity (10).

The types of secondary metabolites found in sungkai leaves in crude extracts are alkaloids, flavonoids, phenolics, steroids and saponins. In the n-hexane fraction there are compounds such as steroids, flavonoids and triterpenoids. Furthermore, the ethyl acetate fraction contained compounds such as alkaloids, triterpenoids and steroids and in the remaining ethanol fraction, namely alkaloids, flavonoids, phenolics, steroids and saponins (9).

Pegagan embun (*Hydrocotyle sibthorpioides* Lam.) is a plant that has many pharmacological activities, has been used traditionally to relieve swelling, diuretic, expectorant, inflammation, and neutralize toxins (detoxification) (12). The immunostimulant activity of gotu kola dew is evident from the flavonoid chemical content in its ethanol extracts (13).

Hydrocotyle sibthorpioides Lam. is a widespread herb in the world. In China this medicinal plant is often used to treat immune disorders and liver disorders. In addition, the plant is effective in the treatment of rheumatism, dysentery, jaundice, and exerts a strong inhibitory effect on tumor growth (14). Pegagan embun also has activities to cure fever, relieve swelling, diuretic, expectorant, anti-inflammatory, antibiotic, and neutralize toxins (detoxification). (12).

In Indonesia gambir is often used as a food supplement, tanner and traditional medicine. Along with technological advances, gambir is now widely used in the pharmaceutical, cosmetic, food, textile and ink industries (15). Plant species of the Rubiaceae family have important roles in daily life, one of which is the source of many products including, Uncaria gambir which is a source of tannin, Calycophyllum, and Neolamarckia Chinensis as a source of wood. Gambir is a natural product from the leaves of *Uncaria gambir* and has economic value as a leather tanning agent. Many other gambir species are also found with similar uses based on their polyphenolic content (16).

Gambir species are widely used as traditional medicine for the treatment of many diseases such as wounds, ulcers, fever, headaches, gastrointestinal diseases, microbial infections, hypertension, and nervous disorders. Many species of the genus *Uncaria*, such as *Uncaria gambir, Uncaria guianensis, Uncaria hirsuta, Uncaria glabrata, Uncaria macrophylla, Uncaria quadrangularis, Uncaria rhynchophylla, Uncaria sinensis, and Uncaria tomentosa* have been used as traditional medicine for the treatment of such diseases (16).

The main components of gambir are cathecin (catechin acid or cathecu acid) and catechin tannate (cathecin anhydride). Gambir also contains a small amount of quarcetine, which is a coloring material that has a yellow color. Cathecin when subjected to prolonged heating or heating with alkaline solutions will easily become cathecin tannate, due to its own condensation and easily dissolves in cold water or hot water (17). Catechins are compounds found in tannins that are flavan-3-ol while leukoanthocyanidins are flavan-3-4-diol. Both phenolics are often associated with carbohydrates or protein molecules to produce more complex tannin compounds (18).

Traditionally steeped fresh gambir leaves are used to treat loose stools, dysentery, and as a gargle for a sore throat. Meanwhile, gambir extract is used to treat burns, sciatica, and lumbago (19). According to Ermiati (2004), gambir can be used as a mixture of drugs for burns, headaches, skin pain medications, diarrhea, mouth ulcers, dysentery, and complementary to consuming betel nut, even gambir has developed into the needs of various types of industries, such as the pharmaceutical industry, cosmetics, batik, paints, tanners, biopesticides, growth hormones, pigments and as a complementary food mixture. In addition, according to Amalia (2009), gambir extract can act as an immunomodulator and according to Sari (2010) gambir is also proven as an analgesic, anti-inflammatory and hypoglycemic drug (20). Gunawijaya (1996) reported that the administration of gambir with various dose levels can inhibit the increase in cholesterol in mice. This is because gambir contains compounds that are antioxidants and one of the active compounds is catechin. This is in accordance with the theory that catechins are strong antioxidants that have the ability to overcome free radicals originating from oxygen including reactive OH (20).

Based on research conducted by Aminah (2010), the test of immunomodulatory effects of combined water extracts of betel leaf (*Piper betle*) and gambir (*Uncaria gambir* Roxb) by measuring the activity and phagocytosis capacity of mice peritoneal fluid in ingesting Staphylococcus epidermidis bacteria and its effect on changes in acid phosphatase enzyme levels in mice peritoneal macrophage cells in vivo. Of the three doses given for the ability of activity and capacity as well as its effect on acid phosphatase enzyme levels showed a significant change at a dose of 200 mg / kgbw (21).

Immunomodulatory effects of a combination of catechins from the ethyl acetate phase of gambir (*Uncaria gambir* Roxb.) and eugenol by carbon clearance method in vivo. It was concluded that the combination of catechins from the ethyl acetate phase of gambir and eugenol (1:2 ratio) doses of 100 mg/kgBW and 200 mg/kgBW was a strong immunomodulator (22).

IV. CONCLUSIONS

Plants can act as immunostimulants because of the content of secondary metabolites contained therein that can increase the body's immune system through an immune system enhancement mechanism.

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REFERENCES

[1]. Novitasari AE, Putri DZ. Maserasi. J Sains - Isolasi dan Identifikasi Sapon Pada Ekstrak Daun Mahkota Dewa dengan Ekstrak Maserasi. 2016;6(No. 12):10–4.

[2]. Afriwardi, Nazmi R, Dillasamola D, Badriyya E, Aldi Y. Anti-inflammatory activity of Pegagan Embun (Hydrocotyle sibthorpioides Lam.) plant extract on topical application. Pharmacogn J. 2021;13(2):411–7.

[3]. Effendi N. Identifikasi Aktivitas Imunoglobulin M (IG.M) Ekstrak Etanol Cuplikan (Physalis minima Linn.) Pada Mencit. J Kesehat. 2014;7(2):353–60.

[4]. BPOM. Formularium Ramuan Etnomedisin Obat Asli Indonesia. Jakarta: BPOM RI; 2013.

[5]. Widaryanto E AN. Prospektif Tanaman Obat Berkhasiat. Malang: UB Press; 2018.

[6]. Aldi Y, Rasyadi Y, Handayani D. Aktivitas Imunomodulator dari Ekstrak Etanol Meniran (Phyllanthus niruri Linn.) terhadap Ayam Broiler. J Sains Farm Klin. 2015;1(1):20.

[7]. Prasiwi D, Sundaryono A, Handayani D. Aktivitas Fraksi Etanol dari Ekstrak Daun Peronema canescens terhadap Tingkat Pertumbuhan Plasmodium berghei. Alotrop. 2018 May;2(1).

[8]. Bahri S, Ambarwati Y, Mahendra PT, Kimia J, Matematika F, Ilmu D, et al. Uji Daya Imunitas Sediaan Daun Sungkai (Peronema canescens Jack) Pada Mencit (Mus. musculus). 2022;122–33.

[9]. Pindan NP, Daniel, Saleh C, Magdaleni AR. Uji Fitokimia Dan Uji Aktivitas Antioksidan Ekstrak Fraksi N-Heksana, Etil Asetat Dan Etanol Sisa Dari Daun Sungkai (Peronema canescens Jack.) Dengan Metode DPPH. J At. 2021;6(1):22–7.

[10]. Okfrianti Y, Irnameria D, Bertalina B. Aktivitas Antioksidan Ekstrak Etanol Daun Sungkai (Peronema canescens Jack). J Kesehat. 2022;13(2):333.

[11]. Pratami Br Sinaga M, Elysa Putri Mambang D, Sari Lubis M, Yuniarti R. Uji Aktivitas Analgesik Ekstrak Daun Sungkai (Peronema canescens Jack.) Terhadap Mencit Jantan (Mus musculus) Analgesic Activity Test Of Sungkai Leaf (Peronema canescens Jack.) Extract On Male Mice (Mus musculus). Agustus. 2022;2(1):100–10.

[12]. Afriwardi, Fitri A, Husni E, Badriyya E, Aldi Y. Immunostimulant activity of pegagan embun herbs extract (Hydrocotyle sibthorpioides Lam.) with carbon clearance method towards male white mice. Pharmacogn J. 2021;13(6):1472–7.

[13]. Huang SS, Huang GJ, Ho YL, Lin YH, Hung HJ, Chang TN, et al. Antioxidant and antiproliferative activities of the four Hydrocotyle species from Taiwan. Bot Stud. 2008;49(4):311–22.

[14]. Ge L, Shen L, Chen Q, Li X, Zhang L. The complete chloroplast genome sequence of Hydrocotyle sibthorpioides (Apiales: araliaceae). Mitochondrial DNA Part B Resour. 2017;2(1):29–30.

[15]. Muchtar, H., Yusmeiarti YG. Pengaruh jenis absorban dalam proses isolasi katechin gambir. J Ris Ind. 2008;2.

[16]. Ravipati AS, Reddy N, Koyyalamudi SR. Biologically active compounds from the genus Uncaria (Rubiaceae). 1st ed. Vol. 43, Studies in Natural Products Chemistry. Elsevier B.V.; 2014. 381–408 p.

[17]. Nainggolan P. Teknologi Perbenihan Tanaman Gambir (Uncaria gambir Roxb). Medan: Balai Pengkajian Teknologi Pertanian Sumatera Utara; 2013.

[18]. Yeni G, Syamsu K, Mardliyati E, Muchtar H. Penentuan Teknologi Proses Pembuatan Gambir Murni dan Katekin Terstandar dari Gambir Asalan. J Litbang Ind. 2017;7(1):1.

[19]. Lucida H, Amri Bakhtiar dan Wina Astari Putri. Formulasi sediaan antiseptik mulut dari katekin gambir Jurusan Farmasi FMIPA Universitas Andalas Padang. 2006;12(1).

[20]. Frinanda D, Efrizal, Rahayu R. Efektivitas Gambir (Uncaria gambir Roxb .) sebagai Anti Hiperkolesterolemia dan Stabilisator Nilai Darah pada Mencit Putih (Mus musculus) Jantan Effectivity of Gambier (Uncaria gambir Roxb .) as Anti Hypercholesterolemic and Stabilizer of Blood Value. J Biol Univ Andalas (J Bio UA. 2014;3(3):231–7.

[21]. Aminah N. Uji efek imunomodulator ekstrak air kombinasi daun sirih (Piper betle) dan gambir (Uncaria gambir Hnuter) Roxb) dengan pengukuran aktivitas dan kapasitas fagositosis serta pengaruhnya terhadap perubahan kadar enzim asam fosfatase pada sel makrofag periton. Jakarta: UIN Syarif Hidayatullah; 2010.

[22]. Zilhadia, Nurmeilis A. Uji Efek Imunomodulator Kombinasi Katekin Dari Fase Etil Asetat Gambir (Uncaria gambier, Roxb.) Dan Eugenol Menggunakan Parameter Bersihan Karbon Secara In Vivo. UIN Syarif Hidayatullah Jakarta. UIN Syarif Hidayatullah Jakarta; 2012.