Exploring the Ethnopharmaceutical Plants of Osing Tribe in Banyuwangi Regency: Potential Application for COVID-19 Therapy

Endah Puspitasari, Alfina Eka Damayanti, Intan Nabila Sufi Zikrina, Dewi Dianasari

Bioactive Natural Product Development Research Group, Faculty of Pharmacy, University of Jember

Endah Puspitasari
Corresponding Author
Bioactive Natural Product Development Research Group, Faculty of Pharmacy, University of Jember, Jember, Indonesia
Email: e.puspitasari@unej.ac.id

Abstract

Ethnopharmacy is the study on herbs or plants that certain ethnic groups practice for treating particular illness. Scientific reporting of beneficial therapeutic plants through this study could promote further development of herbal medicines. We conducted an ethnopharmacy study at several villages of Osing tribe located in Banyuwangi, Indonesia, to identify plants that have the potential to be tested for certain bioactivity, in this case, for COVID-19 therapy. The snowball and purposive sampling methods using qualitative and quantitative research with semi-structured interviews and questionnaires were applied for this study. The parameters used were the Use Value (UV), Informant Consensus Factor (ICF), and Fidelity Level (FL). The plants used in this study were obtained and determined at Balai Konservasi Tumbuhan Kebun Raya Purwodadi, the Indonesian Institute of Science. The results were then followed by the literature study on the plants' potential for COVID-19 therapy. Plant exploration was obtained by considering the results of UV calculation. Based on UV calculations in ethnopharmacy studies, there are several plants that are considered essential and have more efficacies. They are *temulawak,* turmeric*, suruh,*

C|O|P|E COMMITTEE ON PUBLICATION ETHICS

Universiti Sains Islam Malaysia
https://uijournal.usim.edu.my

gigen-gigen, mating, anggrek merpati and *pace*. Three of the eight plants potentially possess immunomodulatory activity that can be used to prevent the infections of SARS-CoV-2. They are the *temulawak (Curcuma xanthorrhiza),* turmeric (*Curcuma domestica)* and *gigen-gigen (Centella asiatica)*.

Keywords: *ethnopharmacy, COVID-19 prevention, Curcuma xanthorrhiza, Curcuma domestica, Centella asiatica*

1. Introduction

The coronavirus disease 2019 (COVID-19) continues to infect and claim lives of humans worldwide. Many patients are infected due to low levels of immunity. As of 14 June 2021, in Indonesia, confirmed COVID-19 cases reached 1,919,547 and number of deaths due to COVID-19 reached 1,751,234 (KPC-PEN, 2021). Increasing one's immunity is one of the best ways to prevent transmission of the SARS-CoV-2 virus. This can be done by consuming immunostimulants made from natural ingredients that will improve the health. Most Indonesians have the knowledge to make home remedies for ailments out of natural ingredients. The process of passing on such local knowledge about traditional medicine from generation to generation is carried out orally. With the development of times, the process of inheriting knowledge related to traditional medicine is feared to experience erosion (Rosita et al, 2015). The science that can be used to obtain local knowledge on how to process natural ingredients into a nutritious medicine is ethnopharmacy. Ethnopharmacy comes from the word ethno which means tribe or group, and pharmacy i.e. a study of drugs or medicine. Ethnopharmacy is the study of how to treat and use drugs by certain tribes, the scope of which includes medicine and treatment using natural ingredients (Ningsih, 2016).

Ethnopharmacy includes the study of ethnobiology, ethnopharmaceutical, ethnopharmacology, and ethnomedicine. The use of traditional medicine in the era of the COVID-19 pandemic may be beneficial as a way of prevention by boosting the immune system and building one's endurance. However, the proper processing methods for plants that can be used as traditional medicine have not been understood to date. A tribe known for its unique culture and medical system that has survived to this day is the Osing tribe. The Osing tribe is evenly distributed in some districts, namely Giri, Sempu, Licin, Kalipuro, Glagah, Kabat, Rogojampi, Blimbingsari, Singojuruh, Songgon, Cluring, Banyuwangi Kota, Genteng, and Srono. Benelan Lor village and Badean village are located at Kabat district and Blimbingsari district respectively, while Aliyan and Pengatigan village is in Rogojampi district (Dhamayanti & Eka, 2019). Therefore, it is necessary to conduct an ethnopharmaceutical study in the village so that knowledge of traditional medicine is maintained, medicinal plants are documented, and knowledge about the use of medicinal plants in the Osing tribe, especially those having the potential for COVID-19 therapy is obtained.

2. Materials and Methods

The techniques used were snowball sampling and purposive sampling. Data collection was obtained through semi-structured interviews using open questions. The questionnaire used in this study is a research questionnaire and a triangulation questionnaire. The plants used in this study

were obtained and determined at Balai Konservasi Tumbuhan Kebun Raya Purwodadi, the Indonesian Institute of Science. The research was conducted on informants who meet the inclusion and exclusion criteria. The inclusion criteria in this study were people who are willing to become informants, informants who have knowledge of the Osing tribe's medicine, the original descendants of the Osing tribe, having experience in using medicinal plants for at least 5 years, using traditional plants as traditional medicine for the Osing tribe, and are trusted as traditional tribal healers. While the exclusion criteria in this study were informants who had studied the treatment of other tribes and people who migrated to other tribes. Data analysis was carried out in several stages, namely:

1. Plant identification
2. Analysis of the Use Value (UV)

$$UV = \frac{\Sigma Ui}{n}$$

UV $\quad$ = use value of each plant species;
Ui $\quad$ = number of informants who know and/ or use plants for types of diseases;
n $\quad$ = total informants who use plants

3. Informant Consensus Factor (ICF) Analysis

$$ICF = \frac{n_{ur} - n_t}{n_{ur} - 1}$$

ICF $\quad$ = value consensus factor informant;
n_{ur} $\quad$ = the number of plants used according to the informants in each disease category;
n_t $\quad$ = the number of plants in each disease category

4. Analysis of Fidelity Level (FL)

$$FL = \frac{N_P}{n} x100$$

Np $\quad$ = number of informants who claim specific uses for certain plants;
n $\quad$ = the number of informants who use the plant.

5. The plant potency literature study obtained from ethnopharmaceutical studies for COVID-19 therapy is based on journal searches from Pubmed, Google Scholar, and Researchgate. The range of journal publication years used were those from 2005 to 2020.

3. Results and Discussions

Based on the ethnopharmacy study at the Osing tribe's research, there are 30 types of diseases treated using traditional medicine. These types of diseases are categorised as infectious diseases caused by microorganisms; circulatory system; bones, muscles and joints; respiratory system; digestive system; nervous system; neoplasia; endocrine glands, metabolism and nutrition; and ear disorders. There are 66 species of plants found, which are believed to be the traditional medicinal ingredients of the Osing tribe. From this study, it is found that 75 traditional recipes made by traditional healers of the Osing tribe are boiled, pounded, brewed with water, kneaded, used immediately, grated, or steamed.

The people of Osing tribe use these traditional medicines by drinking it twice or thrice a day. To determine the types of plants that are considered essential and have the potential for bioactivity testing, the UV, ICF, and FL values were calculated. A plant is deemed to be crucial and has the potential for further investigation if it has a high UV value (close to 1 or more than 1) (Gazzaneo et al., 2005). Based on the results of UV calculations, the plants that are often used are turmeric, ginger, *kencur, suruh, gigen-gigen, manting* and *anggrek merpati*. Plant data are presented in

Table 1. Several species that are important for the treatment of certain diseases are obtained from the FL calculation. Plants that have a high FL value are considered potential for bioactivity testing and used as an alternative treatment for certain diseases. FL values are calculated based on high UV and ICF values to get the percentage of benefits from certain plants that are used as alternative treatments for certain diseases (Table 2). Based on the high UV, ICF and FL values, several plants were selected and considered to have great potential in treating certain diseases. A review of the literature of some of these plants was carried out regarding the plant activity as immunomodulators.

Table 1: Plants considered being important and often used by the Osing tribe, Benelan Lor Village, Badean Village, Pengatigan Village, Aliyan Village, and Kepundungan Village, Banyuwangi Regency

Plant	UV Value
Turmeric	3,8
Temulawak	2,4
Kencur	2
Suruh	1,2
Gigen-gigen	1
Manting	1
Anggrek merpati	0,8
Pace	0,8

The identification was carried out based on several disease categories that the patient informants often suffer from. These results are based on the calculation of the ICF value, if a disease has a high ICF value (close to a value of 1), meaning that many informants use plants to treat certain disease categories and there is an exchange of information between informants (Gazzaneo et al., 2005). From these data it is known that the highest ICF values are circulatory system diseases; microorganism infection; neoplasia; digestive system; bones, muscles and joints; and the respiratory system (Table 3).

Table 2: Plants that are considered important for treating certain disease categories

Plant		Disease categorization	FL (%)
Local Name	Scientific name		
Kencur	*Kaempferia galanga* L.	For the circulation system	62.50
Gigen-gigen	*Centella asiatica* L. Urb	For the circulation system	60.00
Suruh	*Piper betle* L.	For microorganism infection	57.14
Anggrek merpati	*Dendrobium crumenatum*	For the bones, muscles and joints	50.00
Manting	*Syzygium polyanthum* (Wight) Walp.	For the bones, muscles and joints	50.00
Temulawak	*Curcuma xanthorrhiza* Roxb.	For the circulation system	50.00
Pace	*Morinda citrifolia* L.	For the digestive system	40.00
Turmeric	*Curcuma domestica* Val.	For the circulation system	35.29

Table 3: Informant Consensus Factor (ICF) based on disease categories treated by informants

Disease Category	ICF Value
Circulatory system	0.425
Microorganism infection	0.400
Neoplasia	0.333
Digestive system	0.277
Bones, muscles and joints	0.238
Respiratory system	0.143

The plant used to treat circulatory diseases is *kencur*. Based on UV results, there are several plants that are believed to have properties as ingredients that are often used and are widely used to treat various diseases, including *temulawak,* ginger, turmeric, *suruh, gigen-gigen, manting, anggrek merpati*, and *pace*. Of the eight plants, based on literature studies in several journals, there are three plants that have immunomodulatory activity specially as imunostimulants i.e *temulawak*, turmeric, and *gigen-gigen*.

In this pandemic era, the role of immunomodulators is very important for our health. Immunomodulators help the body to optimize the function of the immune system, which is the main system that plays a role in the body's defense where most people are prone to immune system disorders. Low immunity in humans will make it easy to be exposed to diseases or viruses, one of which is that they will be easily exposed to COVID-19 (Izazi & Kusuma, 2020). There are various ways that can be used to increase the immune system, one of which is through the use of medicines made from natural ingredients such as *temulawak*, turmeric, and *gigen-gigen* (Djajakusumah, 2010).

Temulawak (*Curcuma xanthorriza*) and turmeric (*Curcuma domestica*) is often used as an ingredient in herbal medicine. The main bioactive compounds are curcumin compounds. Regarding the handling of COVID- 19, the use of curcumin either alone or in combination as an immunomodulator could increase the body's endurance (Prayudi, 2020, p.6). This can be seen through the UV value obtained and proven by the study of related literature. The results of clinical trials of curcumin can increase the body's immune system by acting as an immunomodulator. Curcumin and several active ingredients have been studied as potential antiviral candidates for SARS-CoV-2. Curcumin is able to bind to the SARS-CoV-2 protein receptor, by binding to the protease domain (6Lu7) and glycoprotein spikes (Postharvest, 2020). This bond has the potential to inhibit COVID-19 activities. Curcumin is able to block the host cell receptors for the entry of the virus so that viral infection can be prevented. Curcumin is known to inhibit the release of inflammation-causing body compounds or pro-inflammatory cytokines such as interleukin-1, interleukin-6 and tumor necrosis factor-α. Curcumin also has the effect of inhibiting the virus growth process, either directly by physically damaging the virus or by suppressing cellular signaling pathways that are important in the viral replication process (Prayudi, 2020, p. 7).

Gigen-gigen is also believed to have activity as an immunomodulator. Primary metabolites such as polysaccharides, mannose, glucans, xylose and fructose and secondary metabolites such as flavonoids, anthocyanins, alkaloids and terpenoids affect the immune system, the effect of these metabolites on the immune response through modulation of the activity of dendritic cells, T and B lymphocytes, as well as immune mediators such as interleukins, interferon (IFN), and tumor

necroting factor (TNF) (Trapika & Sholikhah, 2012). The ethanol extract on *gigen-gigen* could increase the immune system as indicated by the IgG level increase of mice blood serum induced by the BCG vaccine (Griana, 2019).

The benefits of using some of these plants are to build immune stimulation and inflammation modulation effects to manage the immune system. HCoV is generally a group of 30,000 single-stranded positive-sense RNA viruses. Two protein groups that characterize HCoV are structural proteins and non-structural proteins such as RNA polymerase (RdRp) (nsp12) (Sunarmi, 2014). Coronaviruses such as SARS and MERS have the ability to evade immune detection and suppress immune responses. During viral infection, the host factor elicits an immune response to the virus (Oladele et al., 2020). Initiation of adaptive immune responses against SARS-related coronavirus begins with the activation of respiratory dendritic cells (rDCs) after engulfing the viral antigen. Furthermore, rDCs migrate to the draining (mediastinal and cervical) lymph nodes (DLN) and present processed antigens to naïve T cells. T cells then become activated, proliferate and migrate to the site of infection (lung) (Aziz et al., 2020). Lymphopenia occurs due to lymphocyte drainage to the site of infection. In that case, it increases neutrophils/ lymphocytes (Channappanavar et al., 2014). T cells, especially CD4 + and CD8 + play a significant antiviral role to combat pathogens and increase the risk of developing autoimmunity/inflammation. CD4 + T cells increase the production of virus-specific antibodies by activating T-cell dependent B cells. However, CD8 + T cells are cytotoxic and kill virus-infected cells. Cytotoxic CD8+ T cells account for about 80% of total infiltrative inflammatory cells in the pulmonary interstitial in SARS-CoV infected patients and play a vital role in elimination of infected cells (Thevarajan et al., 2020). Cytokines, IL-17 recruit monocytes and neutrophils to sites of infection that exhibit inflammation and activate the downstream cascade of other cytokines and chemokines, including IL-1, IL-6, IL-8, IL-21, TNF-β, and MCP-1 (Vellingiri et al., 2020). Apoptosis of T cells is induced by BH3-like regions located in the C-terminal cytosolic domain of the SARS-CoV protein mediated by Bcl-xL (Maloir et al., 2017). Experimental evidence shows that the response of T cells to S protein and other structural proteins (including M and N proteins) is durable, persistent and provides evidence for designing new drugs and vaccines for SARS-CoV-2 (Le Bert et al., 2020).

Structural proteins are capable to induce a dominant, effective, and long-term response of memory cells to viruses. However, previous studies also reported the important role of CD8+ and CD4+ T cells in clearing SARS-CoV (Gao et al., 2010). The ACE2 protein that (Le Bert et al., 2020)binds to the human immunoglobulin G Fc (ACE2-Fc) domain of SARS-CoV-2 patients may have the benefit of traditional neutralizing antibodies that can be used as a treatment for infection. Ultimately, there will be a need for clinical trials to describe certain side effects of ACE2-Fc treatment (Sunarmi, 2014). Therefore, ACE2-Fc may play an important role in the treatment of SARS-CoV-2, if ACE2-Fc function is inhibited (Sunarmi, 2014). This immunological study shows how important it is to understand the basics of the immune response in these viruses, so that these immune cells can be induced to further attack the virus with increased specificity. Treatment that is mediated by local plants/herbs is thought to be able to strengthen the immune system to eliminate viral pathogens (Aziz et al., 2020).

4. Conclusions

Based on UV calculations in ethnopharmacy study, there are several plants that are considered important and are potentially effective; they are *temulawak,* turmeric*, kencur, suruh, gigen- gigen, manting, anggrek merpati,* and *pace*. Three of those eight plants, *temulawak,* turmeric, and *gigen-*

gigen may have potential immunomodulatory activities. Further research is needed to investigate the potential immunomodulatory effects of these plants against the SARS-CoV-2 viral infection.

References

Aziz, I. R., Armita, D., Hajrah, H., & Makmur, K. (2020). Indonesian Local Plant Regulatory Genes: Covid-19 Immunomodulator. *Technoscience: Media Information Science and Technology*, *14*(2), 234–242. https://doi.org/10.24252/teknosains.v14i2.15901

Channappanavar, R., Fett, C., Zhao, J., Meyerholz, D. K., & Perlman, S. (2014). Virus-Specific Memory CD8 T Cells Provide Substantial Protection from Lethal Severe Acute Respiratory Syndrome Coronavirus Infection. *Journal of Virology*, *88*(19), 11034–11044. https://doi.org/10.1128/jvi.01505-14

Dhamayanti, A. E., & Eka, A. (2019). *Ethnopharmaceutical Study on Medicinal Plants for the Osing Tribe in Benelan Lor Village, Badean Village, Pengatigan Village, Aliyan Village, and Kepundungan Village, Banyuwangi Regency*. Retrieved from http://repository.unej.ac.id/handle/123456789/90099

Djajakusumah, T.S. (2010). *The Role of Immunomodulator In The Treatment Of Sexuelly Transmitted Infections. PKB. New Perspective of Sexually Transmitted Infection Problems*. Surabaya. p. 144-163.

Gao, T., Yao, H., Song, J., Liu, C., Zhu, Y., Ma, X., … Chen, S. (2010). Identification of medicinal plants in the family Fabaceae using a potential DNA barcode ITS2. *Journal of Ethnopharmacology*, *130*(1), 116–121. https://doi.org/10.1016/j.jep.2010.04.026

Gazzaneo, L. R. S., Paiva de Lucena, R. F., & de Albuquerque, U. P. (2005). Knowledge and use of medicinal plants by local specialists in an region of Atlantic Forest in the state of Pernambuco (Northeastern Brazil). *Journal of Ethnobiology and Ethnomedicine*, *1*, 1–8. https://doi.org/10.1186/1746-4269-1-9

Griana, T. P. (2019). Potential Effect of Pegagan (*Centella asiatica* (L .) Urban) and Widuri (*Calotropis gigantea* (L .)) as Immunomodulator. *Journal of Food and Pharmaceutical Science*, *7*(2), 55–72.

KPC-PEN. (2021). Data Sebaran Situasi Virus COVID-19 di Indonesia. Retrieved from https://covid19.go.id/

Izazi, F., & Kusuma P, A. (2020). Results of Respondents Public Knowledge of the Processing Method of Temulawak (*Curcuma xanthorrhiza*) and Kencur (*Kaemferia galanga*) as Increased Immunity During COVID-19 Using the Proximity of the Leximancer Program Concept Respondent Results of C. *Journal of Pharmacy and Science*, *5*(2), 93–97.

Lucy, J., Florencia, L., Stefani, D., & Agustina Ika Susanti, D. (2017). Efek [The Effect Of Curcumin (Curcuma Xanthorrihiza) Dosage On Body Weight And Immune Response Of Mice Balb/c]. *Jurnal Sanis Dan Teknologi*, *1*(1), 32–50.

Maloir, Q., Ghysen, K., Von Frenckell, C., Louis, R., & Guiot, J. (2017). Acute respiratory distress indicative of antisynthetase syndrome. *Revue Medicale de Liege*, *73*(7–8), 370–375.

Ningsih, I. Y. (2016). Ethnopharmaceutical Study on the Use of Medicinal Plants by the Tengger Tribe in Lumajang and Malang Districts, East Java. *Pharmachy*, *13*(1), 10-20.

Oladele, J. O., Ajayi, E. I., Oyeleke, O. M., Oladele, O. T., Olowookere, B. D., Adeniyi, B. M., … Oladiji, A. T. (2020). A systematic review on COVID-19 pandemic with special emphasis on curative potentials of Nigeria based medicinal plants. *Heliyon*, *6*(9), 1–17. https://doi.org/10.1016/j.heliyon.2020.e04897

Postharvest, P. B. (2020). *Potential Food Ingredients for Anti Virus and Immune Booster. Potential Food Ingredients for Anti Virus and Immune Booster*. Retrieved from www.pascapanen.litbang.pertanian.go.id

Prayudi S. (2020). *Buku Saku: Bahan pangan potensial untuk anti virus dan imun booster* (Christina W., Sri Widowati, Setyadjit, Sri Yuliani, Sri Usmiati, Ed.) (1st Edition). Balai Besar Penelitian dan Pengembangan Pascapanen Pertanian. (p. 6–8).

Smd, R., Rostiana, O., & Hernani, E. R. P.. (2015). Excavation of Ethnomedical Science and Technology at Mount Gede Pangrango. *Herbal and Medicinal Plants Research Bulletin*, *18*(1), 13–28. https://doi.org/10.21082/bullittro.v18n1.2007.

Sunarmi, S. (2014). Preserving Biodiversity Through Learning Outside The Classroom And Challenging Assignments. *Journal of Biology Education, State University of Malang*, *6*(1), 117974. 38-49

Thevarajan, I., Nguyen, T. H. O., Koutsakos, M., Druce, J., Caly, L., van de Sandt, C. E., … Kedzierska, K. (2020). Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19. *In Nature Medicine*, *26*, pp. 453–455). https://doi.org/10.1038/s41591-020-0819-2

Trapika, I. S. C., & Sholikhah, E. N. (2012). *Effect of Pegagan Leave (Centella Asiatica [L]. Urban) Ethanol Extract on IFN- γ Secretion on the Spleen of Balb / C Mice that Infected with Listeria Monocytogenes*. In International Conference: Research and Application on Traditional Complementary and Alternative Medicine in Health Care (TCAM) (pp. 96–101).

Vellingiri, B., Jayaramayya, K., Iyer, M., Narayanasamy, A., Govindasamy, V., Giridharan, B., … Subramaniam, M. D. (2020). *COVID-19: A promising cure for the global panic. Science of the Total Environment*, 725, 138277. https://doi.org/10.1016/j.scitotenv.2020.138277