The Potential Roles of Jamu for COVID-19: A Learn from the Traditional Chinese Medicine

Dwi Hartanti, Binar Asrining Dhiani, Shintia Lintang Charisma, Retno Wahyuningrum*
Faculty of Pharmacy, Universitas Muhammadiyah Purwokerto, Indonesia

ABSTRACT

As the pandemic of the coronavirus disease 2019 (COVID-19) continues while there is no drug and vaccine available, every effort to discover one should be considered. This review aimed to discuss the potential use of jamu, the Indonesian traditional herbal medicine, to deal with COVID-19 by following those of more-established traditional Chinese medicine (TCM). The online literature search using the PubMed database, as well as the circulars from the Indonesian Ministry of Health, were carried out to collect data up to June 07, 2020. The use of TCM for the treatment and prevention of COVID-19 has been officiated in the Chinese National Clinical Guideline on COVID-19 Associated Pneumonia, with shen-fu-tang + su-he-xiang pill and xiang-sha-liu-junzi-tang as the most frequently suggested formulae to treat severe and recovery stages of COVID-19, respectively. In Indonesia, the highly promoted product for the prevention of this disease is likely the adaptation of a TCM formula, while the use of some other formulae, which mainly containing Zingiberaceae, is suggested by the Government for the said purpose. The rationalization of the use of medicinal plants and suggested polyherbal formulae, based on their available pharmacological activity and the bioactive compounds, is also discussed in this review. The use of jamu for COVID-19, however, needs to be carefully considered for the limited scientific data available to support it.

Keywords: COVID-19; jamu; traditional Chinese medicine; herbal medicine

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was announced as a global pandemic in February 2020. The cases exceeded 6.5 million cases and take toll death almost 400,000 people worldwide within four months, with the number of the total cases in America and Europe five times higher than those in Asia (WHO, 2020). Up to this day, there is no drug or vaccine available for COVID-19 therapy despite a massive effort from scientists around the world to discover them (Sanders et al., 2020). Repurposed drugs such as hydroxychloroquine, which initially seen as a prospective COVID-19 drug, have been proven to have no clinical benefit in the latest report, even though such a report has been claimed to be a flaw and resulted in an article retraction. The latest report on a double-blind, randomized, placebo-controlled trial of Remdesivir, a protide nucleotide analogs, resulted in shorter time recovery in hospitalized COVID-19 patients (Beigel et al., 2020). Hence, there is no clear evidence yet for any drug or vaccine that is beneficial for COVID-19 treatment. These traditional medicine systems have been part of Asian people’s life to treat any kind of illness. TCM has been proven to provide beneficial prevention for viral infection diseases, including influenza, pandemic SARS, and H1N1 (Luo et al., 2020). Recently, a case report mentioned the recovery of a highly-suspected COVID-19 patient who consumed qing-fei-pai-du formula (Ren et al., 2020). In the Chinese National Clinical Guideline on COVID-19 Associated Pneumonia, several formulae of TCM are suggested to treat each different disease stages (Chan et al., 2020). Jamu, the Indonesian traditional herbal medicine, is supposed to have similar potentials as those of TCM. However, the report on jamu for COVID-19 treatment is lacking up to this review is written.

In this review, the use of TCM, Ayurvedha, and jamu for COVID-19 cases are discussed. We will focus on the composition analysis on the most frequently suggested formulae in the Chinese Guideline and elaborate on their benefits claim. The information of the TCM formulae is then used for analyzing a registered jamu formula that is highly promoted and claimed for COVID-19 treatment in Indonesia, i.e., Herbavid-19. We also list the medicinal plants and herbal medicine formulae mentioned in the circulars from the Indonesian Ministry of Health. Lastly, we explore the consideration that
needs to be applied for *jamu* usage for COVID-19, as well as the rationalization of the use of the suggested medicinal plants and polyherbal formulae. The data presented in this review were mainly retrieved from the online database PubMed (https://pubmed.ncbi.nlm.nih.gov/). The name of plants mentioned in this article is written according to the accepted name in The Plant List (http://www.theplantlist.org/).

**TCM AND COVID-19**

TCM is included in the sixth edition of the Chinese COVID-19 Guideline since the 2nd edition to the final 7th one (Chan et al., 2020). Further, 23 provinces in China have adapted this Guideline and issued TCM program in the provincial Guideline on COVID-19 prevention, while 26 provinces officially established the integrative TCM, which combined TCM with the conventional treatment for the COVID-19 patient (Luo et al., 2020; Yang Yang et al., 2020). More than 85% of the total confirmed COVID-19 patients were reported to have been treated with TCM. The treatment with integrative Chinese–Western medicine was given to all COVID-19 cases in Shanghai, while the first recovered patient in Beijing was also treated with this combination medication (Chan et al., 2020).

In the Chinese Guidelines, TCM is used for the treatment of mild, moderate, severe, and recovery stages of COVID-19, which utilized 23, 11, 31, and 21 herbal formulae, respectively. Among those 75 formulae, there are 17 most frequently recommended herbal formulae in different guidelines. The most popular herbal formulae are including shen-fu-tang + su-he-xiang pill and xiang-sha-liu-junzi-tang (Ang et al., 2020). A slight difference in the herbal compositions of those formulae in each Guideline is evidenced, with the basic herbal compositions is listed in Table 1. The exhaustive evaluation of the available data on the Chinese medicines for COVID-19, both traditional and modern, showed that the benefits of treatment are mediated by its capability for strengthening the body resistance and diminishing viral pathogenic factors (Zhou et al., 2020).

### Table 1. Plant constituents of the most popular herbal formulae for the treatment of COVID-19 (Ang et al., 2020)

| Herbal formulae                                      | Indicated for          | The basic herbal composition                                                                 |
|-----------------------------------------------------|------------------------|---------------------------------------------------------------------------------------------|
| Shen-fu-tang + su-he-xiang pill                     | Severe stage           | *Panas ginseng* C.A.Mey. roots, *Aconitum carmichaelii* Debeaux roots, *Acorus calamus* L. rhizomes, *Curcuma longa* L. rhizomes, *Coriandrum officinale* Siebold & Zucc. pips, *Schisandra chinensis* (Turcz.) Baill. fruits, *Zingiber officinale* Roscoe rhizomes, and *Glycyrrhiza glabra* L. rhizomes and roots + *Liquidambar orientalis* Mill. oleoresins |
| Xiang-sha-liu-junzi-tang                            | Recovery stage         | *Codonopsis pilosula* (Franch.) Nannf. roots, preserved *Astragalus propinquus* Schischkin roots in honey, *Atractylodes macrocephala* Koidz. rhizomes, *Wolfiporia extensa* (Peck) Ginns sclerotia, *Glycyrrhiza glabra* rhizomes, and roots |

Another prominent traditional medicine system included in the national Guideline of COVID-19 is Ayurveda, which is believed to improve the immunity system mediated by psychoneuroimmune mechanisms and the meaning response (Golechha, 2020; Rajkumar, 2020). One of the formulae championed for this purpose is *chyawanprash*, which is traditionally used for its immunomodulatory, antioxidant, and hepatoprotective activities as well as respiratory system rejuvenation effect (Sharma et al., 2019). The medicinal plants that are recommended in the guidelines are includes *Allium sativum* L., *Cinnamomum verum* J.Presl, *Cuminum cyminum* L., *Curcuma longa* L., *Ocimum tenuiflorum* L., *Withania somnifera* (L.) Dunal, and *Zingiber officinale* Roscoe. All of these recommended medicinal plants exhibited the immunomodulatory properties in the form of single plant preparation (Sheoran et al., 2017; Subhrayjoti & Shalini, 2020; Tabarsa et al., 2020).
| Plant name               | Plant part | The main bioactive compounds                                      | The underlying pharmacological activity                                                                                                                                                                                                 |
|-------------------------|------------|------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Curcuma longa           | Rhizomes   | Curcumin and a polysaccharide as immunomodulators (Salehi et al., 2019; G. G. L. Yue et al., 2010) | Curcumin nanoparticles significantly stimulated primary humoral immune response and secondary humoral antibody titers in mice (Afolayan et al., 2018). Curcumin modulated the immune responses and might play a dominant role in the treatment of inflammation and metabolic diseases (Srivastava et al., 2011). Prolonged curcumin-injections was safe for functions of natural killer cells and antioxidative functions of macrophages as well as enhanced the mitogen and antigen-induced proliferation potential of T-cell (Varalakshmi et al., 2008). A polysaccharide stimulated in-vitro peripheral blood mononuclear cells (PBMCs) proliferation and cytokine production (G. G. L. Yue et al., 2010). |
| Curcuma zanthorrhiza    | Rhizomes   | Curcumin as immunomodulator                                      | The methanolic extract showed significant inhibitory activity on CD18/11a expression (Harun et al., 2015).                                                                                                                                                                                                 |
| Zingiber officinale var Rubrum | Rhizomes   | 6-gingerol, 6-shogaol, and 8-shogaol as antioxidants (Ghasemzadeh et al., 2016) | The oleoresin microcapsules showed antioxidant activity (Jayanudin et al., 2019).                                                                                                                                                                                                                  |
| Psidium guajava         | Leaves     | Quercetin and other polyphenols as immunostimulant; quercetin, gallic acid, ferulic acid, and caffeic acid as antioxidant (Gutiérrez et al., 2008; Laily et al., 2015) | The water and ethanolic extracts exerted in-vitro immunostimulatory activity in the lymphocyte proliferation assay (Laily et al., 2015). The crude ethanolic extract, its fractions, and some isolated compounds exhibited immunomodulatory effects in the head kidney leukocytes of striped catfish (Nhu et al., 2020). |
| Phyllanthus niruri      | Aerial parts | Phyllanthin, hypophyllanthin, niranthin, phyltetralin, astragalin, quercetin, corilagin, catechin, geraniin, gallic acid, and ellagic acid as immunomodulator (Jantan et al., 2019) | The aqueous extract was capable of dose-dependently inducing proliferation of PBMCs, increasing the release of nitric oxide, and enhancing phagocytic activity of macrophages isolated from tuberculosis patients (Putri et al., 2018). The aqueous extract exerted anti-inflammatory and antinoceceptive activities in rats carrageenan- and histamine-induced rats and acetic acid-induced mice, respectively (Adedapo & Ofuegbe, 2015). |
### Table 2. continued

| Plant name                  | Plant part | The main bioactive compounds                                                                 | The underlying pharmacological activity                                                                                                                                                                                                 |
|-----------------------------|------------|---------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| **Andrographis paniculata** | Aerial     | Andrographolide and other related diterpene lactones as immunomodulator; \(5\)-hydroxy-7,8-dimethoxyflavone, \(5\)-hydroxy-7,8-dimethoxyflavanone, \(\beta\)-sitosterol, stigmasterol, ergosterol peroxide, \(1\,4\)-deoxy-\(1\,5\)-dideohydroandrographolide, and \(19\)-O-acetyl-\(11\,12\)-didehydroandrographolide as antiinflammatory (Chao et al., 2010; Hossain et al., 2014). | The aqueous extract stimulated the proliferation of PBMCs and increasing the production of TNF-\(\alpha\) and IFN-\(\gamma\), as well as modulated the number of regulatory T cells in the carcinogen-induced esophageal cancerous rats (G. G.-L. Yue et al., 2019). The isolated anti-inflammatory compounds showed transcriptional inhibitory activity of NF-kappaB, as well as secretory reduction of TNF-alpha, IL-6, macrophage inflammatory protein-2 (MIP-2), and nitric oxide (NO) in LPS/IFN-gamma, stimulated RAW 264.7 macrophages (Chao et al., 2010). |
| **Moringa oleifera**        | Leaves     | Niaziminin B as immunomodulator; kaempferol-3-glucoside and chlorogenic acid as analgesic (Agarwal & Ambwani, 2018; Martinez-González et al., 2017) | The methanolic extract increased the count of white blood cells, lymphocyte, and neutrophil in cyclophosphamide-immunocompromised rats (Nlumbi et al., 2015). The hexane and ethanolic extracts showed antinociceptive, antiinflammatory, and antiarthritis induced by formalin, carrageenan, and collagen in rats, respectively (Martinez-González et al., 2017). |
| **Allium sativum**          | Bulbs      | Diallyl monosulfide, diallyl disulfide, diallyl trisulfide, diallyl tetrasulfide, diallyl pentasulfide, and diallyl hexasulfide as immunomodulators (Oosthuizen et al., 2017) | The mixture of diallyl polysulfides decreased interleukin-12 (IL12) levels in PBMCs (Oosthuizen et al., 2017). |

*E-ISSN 2477-0612*
**JAMU AND COVID-19**

In contrast, the use of *jamu* is not recognized in the Guideline of COVID-19 Patients (Indonesian Society of Respiriology, 2020). Despite a lack of scientific proof, several medicinal plants and herbal medicines have been championed and highly consumed by Indonesian in the hope that they will be protected from contracting the virus. Among those herbal medicines, Herbavid-19® was the highly promoted *jamu* for the COVID-19 medication. It consists of *Arctium lappa* L. fruits, *Coix lacryma-jobi* L. kernels, *Curcuma zanthorrhiza* Roxb. rhizomes, *Forsythia suspensa* (Thunb.) Vahl. fruits, *Glycyrrhiza glabra* L. roots, *Imperata cylindrica* (L.) Raeusch. rhizomes, *Lonicera japonica* Thunb. flowers, *Lophatherum gracile* Brongn. leaves, *Mentha arvensis* L. leaves, *Pogostemon cablin* (Blanco) Benth. leaves, and *Nepeta tenuifolia* Benth. Leaves. Herbavid-19® was registered with the claims of helping to maintain the immune system and relieve the symptoms associated with cough, fever, and sore throat (Indonesian NADFC, 2020b). Although Herbavid-19® is registered as traditional medicine made in Indonesia, its formula resemble the classical TCM yin-qiao formula, which mainly consists of the primary plant materials of *Lonicera japonica* and *Forsythia suspensa*. Yin-qiao is traditionally used for the prevention and treatment of respiratory tract infection and has been proven to improve the function of the upper respiratory mucosal immune system of mice with bacteria- and virus-stimulated upper respiratory mucosal dysfunction (Liu et al., 2015). Yin-qiao-san is another modification of yin-qiao included in the Chinese COVID-19 Guideline, which is mostly used in combination for the treatment of mild and moderate stages of COVID-19. For mild cases, yin-qiao-san is particularly indicated for expelling phlegm, relieving cough, and restoring normal lung function in feverish patients (Ang et al., 2020; Xu & Zhang, 2020). Previously, yin-qiao-san, in combination with ma-xing-shi-gan, has clinically proven to reduce the time of fever resolution in patients with mild infection of H1N1 virus (Wang et al., 2011). However, yin-qiao-san is not included in the Chinese Guideline or evaluated in any on-going clinical trials of TCM for the treatment of COVID-19 (Yang Yang et al., 2020).

The Indonesian Government has suggested the use of some medicinal plants as immunostimulatory agents to deal with COVID-19 based on the available safety and efficacy data. These medicinal plants are *Curcuma longa*, *Curcuma zanthorrhiza*, *Zingiber officinale* Roscoe var *Rubrum*, *Psidium guajava* L., *Phyllanthus niruri* L., and *Andrographis paniculata* (Burm.f.) Nees (Indonesian NADFC, 2020d). The use of *Moringa oleifera* Lam. and *Allium sativum* for their immunomodulatory activity and capability of relieving the symptoms of COVID-19 i.e., cough and sore throat, are also proposed by the Government. There are some herbal formulae intended for the same purpose as well (see Table 3), in which palm sugar (processed from exudates of *Cocos nucifera* L. or *Arenga pinnata* (Wurmb) Merr.) is commonly added to enhance the taste of the concoction (Ministry of Health of the Republic of Indonesia, 2020).

Recently, the Government published ‘Informatorium Obat Modern Asli Indonesia (OMAI) di Masa Pandemi COVID-19’. The OMAI term refers to standardized herbal medicine and fitofarmaka products, which according to the regulation of the Head of National Agency of Drug and Food Control no HK.00.05.4.2411, are those with standardized active constituents and have shown efficacy in preclinical or clinical studies. In total, there are 15 standardized herbal medicine and ten phytopharmaceutical products available for dealing with COVID-19 symptoms or improving the immune system included in the informative (Indonesian NADFC, 2020c). Furthermore, there are two immunomodulatory products registered as traditional medicines that are being clinically evaluated in patients with COVID-19 in June 2020. The first product is prepared from Cordyceps militaris (L.) Fr. sclerotia, while the second one is the polyherbal formula consist of Zingiber officinale var Rubrum rhizomes, Phyllanthus niruri aerial parts, and Blumea balsamifera (L.) DC. leaves (Indonesian NADFC, 2020a; Uly, 2020).

**CONSIDERATION OF JAMU USES FOR COVID-19**

The COVID-19 pandemic brings opportunities and challenges for researchers to discover effective treatments, including those originated from herbal medicines. Exploration of the active compounds from the natural product is a strategy that should not be missed, but the rush on claiming the efficacy without sufficient scientific evidence must be avoided. In Indonesia, herbal medicines are grouped into three categories, i.e., *jamu*, standardized herbal medicine, and fitofarmaka. The efficacy claim of *jamu* is based on the empirical data although the biological activity of commonly used plants in *jamu* has been scientifically investigated (Elfahmi et al., 2014). Indonesian Government encourages the use of the potential domestic resources for handling COVID-19. However, there is no herbal medicine that is registered for the prevention and treatment of COVID-19 in Indonesia. The claim of the efficacy of the products available for dealing with COVID-19 is more on the function of maintaining and increasing the human immune system. The widely used of herbal products, especially the products which claim formaintaining the human immune system and is associated with COVID-19 prevention or treatment, needs to be carefully considered and well
Table 3. Rationalization of the use of the suggested herbal formulae for dealing with COVID-19 symptoms and maintaining the immune system

| Formula name: Plant constituents | The main bioactive compounds | The underlying pharmacological activity | Traditional uses |
|---------------------------------|-----------------------------|----------------------------------------|------------------|
| **Formula 1: Cinnamomum verum** barks, *Citrus aurantifolia* (Christm.) Swingle fruits, and *Zingiber officinale* var. Rubrum rhizomes | Trans-cinnamaldehyde and its analogs of *Cinnamomum verum* as immunomodulators; 6-gingerol, 6-shogaol, and 8-shogaol of *Zingiber officinale* var. Rubrum as antioxidants (Qadir et al., 2018) | The inhibition of CD18/11a expression of leukocytes and enhancement phagocytosis of leukocytes by *Citrus aurantifolia*, amelioration of collagen type-II induced arthritis in mice by *Cinnamomum verum*, and antioxidant activity of *Zingiber officinale* var Rubrum (Harun et al., 2015; Qadir et al., 2018) | The variation of the *wedhang jahe*, traditionally used for warming the body, improving the appetite, aiding digestion, and helping with rheumatic pain (Beers, 2001) |
| **Formula 2: Alpinia galanga** (L.) Wild rhizomes, *Citrus aurantifolia* fruits, and *Curcuma longa* rhizomes | Curcumin and a polysaccharide as immunomodulators | The modulation of the phagocytes innate immune response by *Alpinia galanga*, immunomodulatory activity of *Citrus aurantifolia* and *Curcuma longa* (Jantan et al., 2011) | The modification of the classical *jamu kunyit asam* formula, traditionally used as a general tonic for maintaining overall health (Andrie et al., 2014) |
| **Formula 3: Curcuma zanthorrhiza** rhizomes, *Phyllanthus niruri* aerial parts, and *Zingiber officinale* var. Rubrum rhizomes | Phyllanthin and the related phenolic compounds of *Phyllanthus niruri* as immunomodulators; 6-gingerol, 6-shogaol, and 8-shogaol of *Zingiber officinale* var. Rubrum as antioxidants | The immunomodulatory, anti-inflammatory, and antinociceptive activities of *Phyllanthus niruri* and *Curcuma zanthorrhiza*, the antioxidant activity of *Zingiber officinale* var. Rubrum (Adedapo & Ofuegbe, 2015; Putri et al., 2018) | The variation of the classical *jamu temulawak*, traditionally used for hepatoprotection (Tampubolon et al., 2014) |
| **Formula 4: Kaempferia galanga** L. rhizomes, *Oryza sativa* L starches, and *Pandanus amaryllifolius* Roxb., leaves | Polysaccharides of *Oryza sativa* as immunomodulator, essential oil of *Pandanus amaryllifolius* as relaxant (Pradopo et al., 2017; L. C. Yang et al., 2015) | The inhibition of CD18/11a expression of leukocytes and enhancement phagocytosis of leukocytes by *Kaempferia galanga*, enhancement of macrophage phagocytosis and cytokine inductions by *Oryza sativa*, and reduction in blood pressure and pulse rate effects of *Pandanus amaryllifolius* (Harun et al., 2015; Pradopo et al., 2017; L. C. Yang et al., 2015) | The variation of the classical *jamu beras kencur* formula, traditionally used for a general tonic and invigorating, relieving tiredness, improving blood circulation and appetite (Beers, 2001) |
communicated to the public. Nevertheless, scientific studies to prove the efficacy of popular products need to be conducted.

There are four aspects need to be considered in the use of jamu to deal with COVID-19. First, the safety of the product should be guaranteed. Although jamu is used for a long time, there is no such evidence that the use of COVID-19 treatment is safe. The use of herbal medicines for therapeutic purposes on COVID-19 focused on the symptoms relieving as it is generally showed the best benefits in the chronic, ongoing post-infection symptoms rather than its acute stage (Wardle, 2020). While most of the herbal medicines exhibit immunomodulatory properties, cytokine storms which is caused by the hyper-stimulation of the immune system, is characterized as the most dangerous and potentially life-threatening event related to COVID-19 (Coperchini et al., 2020; Wardle, 2020). Second, the evidence of the safety and efficacy of herbal medicines should be obtained based on the clinical trials. As of March 2020, there are 14 clinical trials of TCM for the treatment of COVID-19 (Yang et al., 2020). In June 2020, there are two clinical trials of Indonesian herbal products for the same purpose in Jakarta. However, until to date, there is no result of those studies being published. Before the clinical trial of the herbal products is conducted, pre-clinical data must show the promising results on its safety and efficacy for further development steps. The efficacy data obtained from both in-vitro and in-vivo studies can be used as the rationale for the further clinical trial of selected plants or polyherbal formulae for prevention and alleviating the symptoms of COVID-19. The main bioactive compounds and the underlying pharmacological activities of the suggested medicinal plants and polyherbal formulae associated with COVID-19 are listed in Table 2 and 3, respectively.

Third, the molecular mechanism underlined the pharmacological effects of herbal medicine in COVID-19 treatment is still unclear. So far, the available data are obtained from the in-silico experiments, e.g., screening of classical TCM used for treating viral respiratory infection demonstrated that the active compounds exerted its activities through regulation of viral infection, immune and inflammation reactions, as well as hypoxia responses. In addition, hesperidin, a flavonoid commonly found in Citrus sp. peels, which is popularly championed to be natural prevention of COVID-19 in Indonesia, was reported to bind strongly to human angiotensin-converting enzyme-2 (hACE-2) and RNA dependent RNA polymerase (RdRp) as SARS-CoV-2 infection potential targets (Joshi et al., 2020; Zhang et al., 2020). Lastly, the potential danger of the delay in medical treatment due to jamu consumption should be recognized. Since herbal medicines are sold as over the counter product and can be accessed without a doctor’s prescription, their use as self-treatment of COVID-19 by patients who experience symptoms is highly possible (Yichang Yang, 2020). Jamu, and other herbal medicines, in general, should not be used in an emergency condition, including in the acute phase of viral infection. Delay in getting the right treatment in COVID-19 cases prolong the recovery process. In fact, in some cases, this delay can be fatal if the virus continues to replicate quickly in the patient’s body.

It is crucial to communicate the safe practice of jamu uses to the public. The products registered by the National Agency of Drug and Food Control are, at least, guaranteed to be safe to use, and hence should be the first criteria to be considered before consumption. Furthermore, the packaging, label, and expired date of a given product should be checked before it is used. In case jamu is self-prepared from raw material in the household setting, the selection and identification of the raw materials, the washing process, boiling process, the equipment used and also the overall sanitation and hygiene aspects need to be considered as they affect both its efficacy and safety (Ministry of Health of the Republic of Indonesia, 2020).

CONCLUSION

Unlike the prominent position of TCM for the treatment and prevention of COVID-19 in China, the use of jamu in Indonesia still has to take a long and steepy way to be used for this purpose. Further studies on the efficacy and safety of jamu products for COVID-19 in humans and also its molecular mechanisms are needed. Additionally, the safe use of both registered and suggested homemade jamu products should be well communicated to the public.

REFERENCES

Adedapo, A. A., & Ofuegbe, S. O. (2015). Anti-inflammatory and antinoceptive activities of the aqueous leaf extract of Phyllanthus amarus Schum (Euphorbiaceae) in some laboratory animals. Journal of Basic and Clinical Physiology and Pharmacology, 26(1), 89–94. https://doi.org/10.1515/jbcpp-2013-0126.

Afolayan, F. I. D., Erinwusia, B., & Oyeyemi, O. T. (2018). Immunomodulatory activity of curcumin-entrapped poly d,l-lactic-co-glycolic acid nanoparticles in mice. Integrative Medicine Research, 7(2), 168–175. https://doi.org/10.1016/j.imr.2018.02.004

Agarwal, M., & Ambwani, S. (2018). Exploring the immunomodulatory potential of niaziminin B found in Moringa oleifera Lam. in chicken through in silico
modeling and molecular docking studies. *Bulletin of Environment, Pharmacology and Life Sciences*, 7(11), 32–36.

Andrie, M., Taurina, W., & Ayunda, R. (2014). Uji aktivitas jamu gendong Kunyit asam (Curcuma domestica Val.; Tamarindus indica L.) sebagai antidiabetes pada tikus yang diinduksi Streptozotocin. *Traditional Medicine Journal*, 19(2), 95–102. https://doi.org/10.22146/tradmedj.8147.

Ang, L., Lee, H. W., Choi, J. Y., Zhang, J., & Lee, M. S. (2020). Herbal medicine and pattern identification for treating COVID-19: A rapid review of guidelines. *Integrative Medicine Research*, 9(2), article ID 100407. https://doi.org/10.1016/j.imr.2020.100407.

Beers, S.-J. (2001). *Jamu: The ancient Indonesian art of herbal healing*. Tuttle Publishing.

Beigel, J. H., Tomashek, K. M., Dodd, L. E., Mehta, A. K., Zingman, B. S., Kalil, A. C., Hoehmann, E., Chu, H. Y., Luetkemeyer, A., Kline, S., De-Castilla, D. L., Finberg, R. W., Dierberg, K., Tapson, V., Hsieh, L., Patterson, T. F., Sweeney, D. A., Short, W. R., … Lane, H. C. (2020). Remdesivir for the treatment of Covid-19 - preliminary report. *The New England Journal of Medicine*, 1–12. https://doi.org/10.1056/NEJMoa2007764.

Beigel, J. H., Tomashek, K. M., Dodd, L. E., Mehta, A. K., Zingman, B. S., Kalil, A. C., Hoehmann, E., Chu, H. Y., Luetkemeyer, A., Kline, S., De-Castilla, D. L., Finberg, R. W., Dierberg, K., Tapson, V., Hsieh, L., Patterson, T. F., Sweeney, D. A., Short, W. R., … Lane, H. C. (2020). Remdesivir for the treatment of Covid-19 - preliminary report. *The New England Journal of Medicine*, 1–12. https://doi.org/10.1056/NEJMoa2007764.

Chao, W.-W., Kuo, Y.-H., & Lin, B.-F. (2010). Anti-inflammatory activity of new compounds from Andrographis paniculata by NF-KB transactivation inhibition. *Journal of Agricultural and Food Chemistry*, 58(4), 2505–2512. https://doi.org/10.1021/jf903629j.

Chen, F., Chan, K. H., Jiang, Y., Kao, R. Y. T., Lu, H. T., Fan, K. W., Cheng, V. C. C., Tsui, W. H. W., Hung, I. F. N., Lee, T. S. W., Guan, Y., Peiris, J. S. M., & Yuen, K. Y. (2004). In vitro susceptibility of 10 clinical isolates of SARS coronavirus to selected antiviral compounds. *Journal of Clinical Virology*, 31(1), 69–75. https://doi.org/10.1016/j.jciv.2004.03.003.

Chen, L. G., Jan, Y. S., Tsai, P. W., Norimoto, H., Michihara, S., Murayama, C., & Wang, C. C. (2016). Anti-inflammatory and antinociceptive constituents of Atractylodes japonica Koidzumi. *Journal of Agricultural and Food Chemistry*, 64(11), 2254–2262. https://doi.org/10.1021/acs.jafc.5b05841.

Coperchini, F., Chiovato, L., Croce, L., Magri, F., & Roton, M. (2020). The cytokine storm in COVID-19: An overview of the involvement of the chemokine/chemokine-receptor system. *Cytokine & Growth Factor Reviews*, In press, corrected proof. https://doi.org/10.1016/j.cytogfr.2020.05.003.

El famhi, Herman J. Woerdenbag, & Kayser, O. (2014). Jamu: Indonesian traditional herbal medicine towards rational phytopharmacological use. *Journal of Herbal Medicine*, 4(2), 51–73. https://doi.org/http://dx.doi.org/10.1016/j.hermed.2014.01.002.

Ghasemzadeh, A., Jaafar, H. Z. E., & Rahmat, A. (2016). Variation of the phytochemical constituents and antioxidant activities of Zingiber officinale Var. Rubrum Theilade associated with different drying methods and polyphenol oxidase activity. *Molecules*, 21(6), article 780. https://doi.org/10.3390/molecules21060780.

Golechha, M. (2020). Time to realise the true potential of Ayurveda against COVID-19. *Brain, Behavior, and Immunity*, In press, corrected proof. https://doi.org/10.1016/j.bbi.2020.05.003.

Gutiérrez, R. M. P., Mitchell, S., & Solis, R. V. (2008). Psidium guajava: A review of its traditional uses, phytochemistry and pharmacology. *Journal of Ethnopharmacology*, 117(1), 1–27. https://doi.org/10.1016/j.jep.2008.01.025.

Harun, N. H., Septama, A. W., & Jantan, I. (2015). Immunomodulatory effects of selected Malaysian plants on the CD18/11a expression and phagocytosis activities of leukocytes. *Asian Pacific Journal of Tropical Biomedicine*, 5(1), 48–53. https://doi.org/10.1016/S2221-1691(15)30170-2.

Hossain, M. S., Urbi, Z., Sule, A., & Rahman, K. M. H. (2014). Andrographis paniculata (Burm. f.) Wall. ex Nees: A review of ethnobotany, phytochemistry, and pharmacology. *The Scientific World Journal*, 2014, 274905. https://doi.org/10.1155/2014/274905.

Indonesian NADFC. (2020a). *Cek Produk BPOM: H2 Health & Happiness Cordyceps militaris*. http://cekbpom.pom.go.id/index.php/home/produk/189uprd8mo53g16lgmvdx922/all/row/10/page/1/order/4/DESC/search/0/TR162397831.

Indonesian NADFC. (2020b). *Cek Produk BPOM: Herbavid-19*. http://cekbpom.pom.go.id/index.php/home/produk/sk63uosoguna8ro0vckk4quc31/all/
row/10/page/1/order/4/DESC/search/1/Herbadvig.

Indonesian NADFC. (2020c). Informatorium obat modern asli Indonesia (OMAI) di masa pandemi COVID-19 (1st ed.). Badan Pengawas Obat dan Makanan.

Indonesian NADFC. (2020d). Pedoman Penggunaan Herbal dan Suplemen Kesehatan dalam Menghadapi COVID-19 di Indonesia (1st ed.). National Agency of Drug and Food Control of Republic of Indonesia. https://online.flipbuilder.com/aeqr/texx/mobile/index.html.

Indonesian Society of Respirology. (2020). Protokol Tatalaksana COVID-19 (1st ed.). PDPI - PERKI - PAPDI - PERDATIN - IDAI.

Jantan, I., Haque, M. A., Ilangkovan, M., & Arshad, L. (2019). An insight into the modulatory effects and mechanisms of action of Phyllanthus species and their bioactive metabolites on the immune system. *Frontiers in Pharmacology*, 10, article 878. https://doi.org/10.3389/fphar.2019.00878.

Jantan, I., Harun, N. H., Septama, A. W., Murad, S., & Mesaik, M. A. (2011). Inhibition of chemiluminescence and chemotactic activity of phagocytes in vitro by the extracts of selected medicinal plants. *Journal of Natural Medicines*, 65(2), 400–405. https://doi.org/10.1007/s11418-010-0492-8.

Jayanudin, Fahrurrozi, M., Wirawan, S. K., & Rochmadi. (2019). Antioxidant activity and controlled release analysis of red ginger oleoresin (Zingiber officinale var rubrum) encapsulated in chitosan cross-linked by glutaraldehyde saturated toluene. *Sustainable Chemistry and Pharmacy*, 12, article 100132. https://doi.org/10.1016/j.scp.2019.100132.

Jiao, J., Yang, Y., Wu, Z., Li, B., Zheng, Q., Wei, S., Wang, Y., & Yang, M. (2019). Screening cyclooxygenase-2 inhibitors from *Andrographis paniculata* to treat inflammation based on bio-affinity ultrafiltration coupled with UPLC-Q-TOF-MS. *Phytotherapy*, 137, article 104259. https://doi.org/10.1016/j.fitot.2019.104259.

Joshi, R. S., Jagdale, S. S., Bansode, S. B., Shankar, S. S., Tellis, M. B., Pandya, V. K., Chugh, A., Giri, A. P., & Kulkarni, M. J. (2020). Discovery of potential multi-target-directed ligands by targeting host-specific SARS-CoV-2 structurally conserved main protease. *Journal of Biomolecular Structure and Dynamics*, 5, 1–16. https://doi.org/10.1080/07391102.2020.1760137

Laily, N., Kusumaningtyas, R. W., Sukarti, I., & Rini, M. R. D. K. (2015). The potency of guava *Psidium guajava* (L.) leaves as a functional immunostimulatory ingredient. *Procedia Chemistry*, 14, 301–307. https://doi.org/10.1016/j.proche.2015.03.042.

Liang, S., Meng, X., Wang, Z., Liu, J., Kuang, H., & Wang, Q. (2018). Polysaccharide from *Ephedra sinica* Stapf inhibits inflammation expression by regulating factor-B1/Smad2 signaling. *International Journal of Biological Macromolecules*, 106, 947–954. https://doi.org/10.1016/j.ijbiomac.2017.08.096.

Liu, L.-S., Lei, N., Lin, Q., Wang, W.-L., Yan, H.-W., & Duan, X.-H. (2015). The effects and mechanism of yinqiao powder on upper respiratory tract infection. *International Journal of Biotechnology for Wellness Industries*, 4, 57–60.

Luo, H., Tang, Q. L., Shang, Y. X., Liang, S. B., Yang, M., Robinson, N., & Liu, J. F. (2020). Can Chinese medicine be used for prevention of corona virus disease 2019 (COVID-19)? A review of historical classics, research evidence and current prevention programs. *Chinese Journal of Integrative Medicine*, 17, 1–8. https://doi.org/10.1007/s11655-020-3192-6.

Martínez-González, C. L., Martínez, L., Martínez-Ortiz, E. J., González-Trujano, M. E., Déciga-Campos, M., Ventura-Martínez, R., & Díaz-Reval, I. (2017). *Moringa oleifera*, a species with potential analgesic and anti-inflammatory activities. *Biomedicine and Pharmacotherapy*, 87, 482–488. https://doi.org/10.1016/j.biopha.2016.12.107.

Minaiyan, M., Ghannadi, A., Asadi, M., Etemad, M., & Mahzouni, P. (2014). Anti-inflammatory effect of *Prunus armeniaca* L. (apricot) extracts ameliorates TNBS-induced ulcerative colitis in rats. *Research in Pharmaceutical Sciences*, 9(4), 225–231.

Ministry of Health Republic of Indonesia. Surat Edaran tentang Pemanfaatan Obat Tradisional untuk Pemeliharaan Kesehatan, Pencegahan Penyakit, dan Perawatan Kesehatan, HK.02.02/IV.2243/2020 (2020) (testimony of Indonesian MoH).

Nfembali, J., Bbosa, G. S., Sembajwe, L. F., Gakunga, J., & Kasolo, J. N. (2015). Immunomodulatory activity of methanolic leaf extract of *Moringa oleifera* in wistar albino rats. *Journal of Basic and Clinical Physiology and Pharmacology*, 26(6), 603–611. https://doi.org/10.1515/jbcpp-2014-0104

Nhut, T. Q., Dam, N. P., Hang, B. T. B., Bach, L. T., Huong, D. T. T., Hue, B. T. B., Scippo, M.-L., Phuong, N. T., Quetin-Leclercq, J., & Kestemont, P. (2020). Immunomodulatory potential of extracts, fractions
and pure compounds from Phyllanthus amarus and Psidium guajava on striped catfish (Pangasianodon hypophthalmus) head kidney leukocytes. *Fish and Shellfish Immunology*, 104, 289–303. https://doi.org/10.1016/j.fsi.2020.05.051.

Oosthuizen, C., Arbach, M., Meyer, D., Hamilton, C., & Lall, N. (2017). Diallyl polysulfides from Allium sativum as immunomodulators, hepatoprotectors, and antimycobacterial agents. *Journal of Medicinal Food*, 20(17), 685–690. https://doi.org/10.1089/jmf.2016.0137

Pradopo, S., Sinaredi, B. R., & Januarisca, B. V. (2017). Pandan leaves (Pandanus amaryllifolius) aromatherapy and relaxation music to reduce dental anxiety of pediatric patients. *Journal of International Dental and Medical Research*, 10(3), 933–937.

Putri, D. U., Rintiswati, N., Soesatyo, M. H., & Haryana, S. M. (2018). Immune modulation properties of herbal plant leaves: Phyllanthus niruri aqueous extract on immune cells of tuberculosis patient - in vitro study. *Natural Product Research*, 32(4), 463–467. https://doi.org/10.1080/14786419.2017.1311888.

Qadir, M. M. F., Bhatti, A., Ashraf, M. U., Sandhu, M. A., Anjum, S., & John, P. (2018). Immunomodulatory and therapeutic role of Cinnamomum verum extracts in collagen-induced arthritic BALB/c mice. *Immunopharmacology*, 26(1), 157–170. https://doi.org/10.1007/s10787-017-0349-9.

Rajkumar, R. P. (2020). Ayurveda and COVID-19: Where psychoneuroimmunology and the meaning response meet. *Brain, Behavior, and Immunity*, In press, corrected proof. https://doi.org/10.1016/j.bbi.2020.04.056.

Ren, J. L., Zhang, A. H., & Wang, X. J. (2020). Traditional Chinese medicine for COVID-19 treatment. *Pharmacological Research*, 155, article 104743. https://doi.org/10.1016/j.phrs.2020.104743.

Salehi, B., Stojanović-Radić, Z., Matejić, J., Sharifi-Rad, M., Kumar, N. V. A., Martins, N., & Sharifi-Rad, J. (2019). The therapeutic potential of curcumin: A review of clinical trials. *European Journal of Medicinal Chemistry*, 163, 527–545. https://doi.org/10.1016/j.ejmech.2018.12.016.

Sanders, J. M., Monogue, M. L., & Jodlowski, T. Z. (2020). Pharmacologic treatments for coronavirus disease 2019 (COVID-19): A review. *JAMA*, 323(18), 1824–1836. https://doi.org/10.1001/jama.2020.6019.

Sharma, R., Martins, N., Kuca, K., Chaudhary, A., Kabra, A., Rao, M. M., & Prajapati, P. K. (2019). Chyawanprash: A traditional Indian bioactive health supplement. *Biomolecules*, 9(5), article 161. https://doi.org/10.3390/biom9050161.

Sheoran, N., Kumar, R., Kumar, A., Batra, K., Sihag, S., Maan, S., & Maan, N. S. (2017). Nutrigenomic evaluation of garlic (Allium sativum) and holy basil (Ocimum sanctum) leaf powder supplementation on growth performance and immune characteristics in broilers. *Veterinary World*, 10(1), 121–129. https://doi.org/10.14202/vetworld.2017.121-129.

Srivastava, R. M., Singh, S., Dubey, S. K., Misra, K., & Khar, A. (2011). Immunomodulatory and therapeutic activity of curcumin. *International Immunopharmacology*, 1(3), 331–341. https://doi.org/10.1016/j.intimp.2010.08.014.

Subhrayjoty, C., & Shalini. (2020). Immunomodulatory herbs of Ayurveda and COVID-19: A review article. *Journal of Ayurveda and Integrated Medical Sciences*, 5(2), 203–208.

Tabarsa, M., You, S. G., Yelithao, K., Palanisamy, S., Prabhu, N. M., & Nan, M. (2020). Isolation, structural elucidation and immuno-stimulatory properties of polysaccharides from Cuminum cyminum. *Carbohydrate Polymers*, 230, article 115636. https://doi.org/10.1016/j.carbpol.2019.115636.

Tampubolon, S. R., Ardana, I. B. K., & Sudira, I. W. (2014). Aktivitas alanin aminotransferase dan aspartat aminotransferase pada mencit yang diberikan jamu temulawak. *Indonesia Medicus Veterinus*, 3(3), 200–205.

Uly, Y. A. (2020, June 10). LIPI uji coba obat herbal ke 90 pasien COVID-19 di Wisma Atlet. *Kompas*. https://www.kompas.com/sains/read/2020/06/10/182943523/lipi-ujicoba-obat-herbal-ke-90-pasien-covid-19-diwisma-atlet?page=all.

Varalakshmi, C., Ali, A. M., Pardhasaradhi, B. V, Srivastava, R. M., Singh, S., & Khar, A. (2008). Immunomodulatory effects of curcumin: In-vivo. *International Immunopharmacology*, 8(5), 688–700. https://doi.org/10.1016/j.intimp.2008.01.008.

Wang, C., Pan, R., Wan, X., Tan, Y., Xu, L., Ho, C. S., & Ho, R. C. (2020). Immediate psychological responses and associated factors during the initial stage of the 2019 coronavirus disease (COVID-19) epidemic among the general population in China. *International Journal of Environmental Research and Public Health*, 17(5), article 1729. https://doi.org/10.3390/ijerph17051729.
Wardle, J. (2020). Traditional and complementary treatments do have a role to play in global health, but probably not in emerging pandemics. Advances in Integrative Medicine, 7, 1–2. https://doi.org/10.1016/j.aimed.2020.02.003.

WHO. (2020). Coronavirus disease (COVID-19) situation reports. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.

Xu, J., & Zhang, Y. (2020). Traditional Chinese medicine treatment of COVID-19. Complimentary Therapies in Clinical Practice, 39, article ID 101165. 10.1016/j.ctcp.2020.101165.

Yang, L. C., Hsieh, C. C., & Lin, W. C. (2015). Characterization and immunomodulatory activity of rice hull polysaccharides. Carbohydrate Polymers, 124, 150–156. https://doi.org/10.1016/j.carbpol.2015.02.025.

Yang, R., Wang, L. I., Yuan, B. C., & Liu, Y. (2015). The pharmacological activities of licorice. Planta Medica, 81(18), 1654–1669. https://doi.org/10.1055/s-0035-1557893.

Yang, W. K., Kim, S. H., Jung, I. C., & Park, Y. C. (2019). Effects of Scutellaria baicalensis extract on cigarette smoke-induced airway inflammation in a murine model of chronic obstructive pulmonary disease. Journal of Medicinal Food, 22(1), 87–96. https://doi.org/10.1089/jmf.2018.4200.

Yang, Yang, Islam, M. S., Wang, J., Li, Y., & Chen, X. (2020). Traditional Chinese medicine in the treatment of patients infected with 2019-new coronavirus (SARS-CoV-2): A review and perspective. International Journal of Biological Sciences, 16(10), 1708–1717. https://doi.org/10.7150/ijibs.45538.

Yang, Yichang. (2020). Use of herbal drugs to treat COVID-19 should be with caution. The Lancet, 395(10238), 1689–1690. https://doi.org/10.1016/S0140-6736(20)31143-0

Yue, G. G.-L., Li, L., Lee, J. K.-M., Kwok, H.-F., Wong, E. C.-W., Li, M., Fung, K.-P., Yu, J., Chan, A. W.-H., Chiu, P. W.-Y., & Lau, C. B.-S. (2019). Multiple modulatory activities of Andrographis paniculata on immune responses and xenograft growth in esophageal cancer preclinical models. Phytomedicine, 60, article 152886. https://doi.org/10.1016/j.phymed.2019.152886.

Zandifar, A., & Badrfam, R. (2020). Iranian mental health during the COVID-19 epidemic. Asian Journal of Psychiatry, 51, article 101990. https://doi.org/10.1016/j.ajp.2020.101990.

Zhang, D. H., Wu, K. L., Zhang, X., Deng, S. Q., & Peng, B. (2020). In silico screening of Chinese herbal medicines with the potential to directly inhibit 2019 novel coronavirus. Journal of Integrative Medicine, 18(2), 152–158. https://doi.org/10.1016/j.joim.2020.02.005.

Zhi, H. J., Zhu, H. Y., Zhang, Y. Y., Lu, Y., Li, H., & Chen, D. F. (2019). In vivo effect of quantified flavonoids-enriched extract of Scutellaria baicalensis root on acute lung injury induced by influenza A virus. Phytomedicine, 57, 105–116. https://doi.org/10.1016/j.phymed.2018.12.009.

Zhou, Z., Zhu, C. S., & Zhang, B. (2020). Study on medication regularity of traditional Chinese medicine in treatment of COVID-19 based on data mining. China Journal of Chinese Materia Medica, 45(6), 1248–1252. https://doi.org/10.19540/j.cnki.cjcm.20200220.502.