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Review Article

Traditional medicinal herbs for healthiness and fitness during the Covid-19 pandemic in Indonesia: literature review

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ABSTRACT

The spread of Coronavirus Disease-19 (Covid-19) has made the Indonesian people optimize their efforts to maintain health and fitness. One of the efforts is traditional medicinal herbs, especially traditional Indonesian medicine or 'jamu', used empirically to increase immunity. The literature review aimed to describe the formula of traditional medicinal herbs in Indonesia to maintain health and fitness during the Covid-19 pandemic. The literature review searched articles on Pubmed, ScienceDirect, and Google Scholar. The selected articles were the last ten years' articles. The keyword was 'Covid-19 and herbs and immunostimulant or immunomodulator and Indonesia'. The article was published the last ten (10) years, in English or Indonesian, and discusses traditional medicinal herbs for maintaining health and fitness during the Covid-19 pandemic in Indonesia. The selection was made by reading the title, abstract, and full article to analyze the quality of the research. Data extraction was carried out to describe the formula's name, simplicia of the ingredients, pharmacological activity, and secondary metabolites. The literature review found five (5) articles that met the inclusion and exclusion criteria with thirteen (13) formulas. The formula was jamu, and the formula was from traditional Chinese medicine and Ayurveda. Each formula contained simplicia that support each other's properties for health and fitness maintenance. The simplicity was used as an immunomodulator, reducing the symptoms of Covid-19 and overcoming the comorbid factors that accompany the Covid-19 disease. The government's efforts to increase the independent actions of healthy life in Indonesia can be supported by traditional herbs.

Keywords: Covid-19, Ingredients, Traditional, Health, Fitness

Introduction

The spread of the infectious Coronavirus Disease-19 (Covid-19), which began in 2019, affected economic stability and education in Indonesia, including the economic recession, the high mortality rate of health workers, and the emergence of distance learning. The first case of Covid-19 infection in Indonesia was reported in March 2020 [1] . Covid-19 had been increasing in the past two years until the Indonesian government issued a vaccine policy to prevent Covid-19 starting in January 2021 [2].

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Drug classification of Covid-19 consists of antiviral, antimalarial, antidiabetic, glucocorticoid, antibiotic, antiparasitic, anti-tuberculosis, antiasthma, antithrombotic, anticoagulant, phosphoinositide 3-kinase (PI3K) inhibitory agent, anticancer agent, human ACE2 agent, recombinant human deoxyribonuclease (rhDNase) enzyme, immunotherapy and convalescent plasma therapy (CPT). Adjuvant therapy using supplements, nutraceuticals, and herbal medicines is also needed to relieve symptoms and improve the healing process in patients with Covid-19 [3, 4].

The use of medicinal plants in traditional medicinal herbs (called "Jamu" in Indonesia) has increased during the Covid-19 pandemic in Indonesia. Some medicinal herbs or "Jamu" have been used to maintain health and fitness, especially as immunomodulators, although only limited to empirical evidence [5]. The problem of immunity is closely related to health-related quality of life (HRQoL), empowerment of patient/community, and satisfaction with health care [6]. The differences in countries and beliefs lead to the differences in HRQoL because it's related

to health knowledge and socioeconomic health [7]. The use of traditional medicinal herbs to maintain health and fitness and improve the immune system is expected to increase community empowerment in preserving health and ultimately improve socioeconomic and HRQoL in the face of the Covid-19 pandemic.

The guidelines set by the Indian Council of Medical Research (ICMR) and the World Health Organization (WHO) suggested that herbal remedies, herbs, spices, and nutrients can help manage Covid-19 by boosting immunity in patients. The role of herbs as immunomodulators is like a double-edged knife. On the one hand, it can function as an immunosuppressant needed by a positive covid-19. But the other hand, the immunostimulant activity of herbal medicines is required to increase immunity which helps prevent Covid-19. Therefore therapy with herbal medicine/ Herbal medicine must be used wisely in terms of the species of plant that were used in the formula, secondary metabolites, and the dosage [8].

This literature review was expected to provide an overview of the use of traditional medicinal herbs to maintain health and fitness during the Covid-19 pandemic in Indonesia. This literature review was carried out using the keyword immunomodulator because most traditional medicinal herbs used are immunomodulators. However, the results of this literature review might have also been able to describe other pharmacological activities of herbs that are useful for alleviating the symptoms of other diseases similar to the symptoms of Covid-19. This literature review aimed to describe the formula, plant species, secondary metabolites, and their pharmacological activities either as immunomodulators or other pharmacological activities.

Materials and Methods

This research was descriptive. It described the formula, plant species, secondary metabolites, and their pharmacological activities that support the efficacy of herbs to maintain health and fitness during the Covid-19 pandemic in Indonesia. Article searches were carried out in the Pubmed database, Science Direct, and Google Scholar with the keyword strategy "Covid-19 and herbs and immunostimulant or immunomodulator and Indonesia". The database will be searched for articles from the publication of the last ten (10) years.

The inclusion criteria of the article were articles from scientific journals with publications in the last ten (10) years, in English or Indonesian, that discuss traditional medicinal herbs or jamu that are often used in Indonesia to maintain health and fitness during the Covid-19 pandemic. The exclusion criteria for the article were articles that were not open access and discussed the efforts of other countries in the use of traditional medicinal herbs during the Covid-19 pandemic, even though the plant species described are similar to plant species in Indonesia.

Articles were selected from the database by searching the title and abstract and screened based on the inclusion and exclusion criteria. The selected papers were assessed for quality research. It tested the quality for narrative review using SANRA. The quality of the pre-post study was analyzed using the tool from the NIH on the web: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools, The quality of qualitative research was analyzed with tools that can be accessed from https://www.researchconnections.org/childcare/datamethods /downloads/QualitativeResAssessTool. pdf page. No tools for accessing research quality are found for in-vivo methods, so research access tools quantitative data accessed from the https://www.researchconnections.org/childcare/datamethods / downloads/quantitativeresearch.pdf page was used. The quality of the article was poor if the results showed a score of 0-4. The data were extracted from the articles to describe the name of the traditional medicinal herbs, simplicia or plant species, secondary metabolites, and pharmacological activities.

Results and Discussion

Article screening results

In total, five (5) articles met the inclusion and exclusion criteria. The flow of article screening is depicted in **Figure 1**. Two (2) articles were narrative reviews [9, 10], one (1) article was a pre-post study [11], one (1) article was in vivo study [12], and one (1) article was a qualitative study [13]. The good quality of all articles can be judged from the article quality assessment results that showed a value of more than four (>4). A more detailed explanation of the characteristics of the article and the assessment of the quality of the article can be seen in **Table 1**.

Table 1. Characteristics and results of the quality assessment of the included articles

Article	Research Method	Article quality assessment result
Fidrianny *et al*. [9]	Narrative review	7
Hartanti *et al*. [10]	Narrative review	10
Hamid *et al*. [11]	Pre-post study	9
Ikawati *et al*. [12]	In vivo study	8
Jannah *et al*. [13]	Qualitative study	10

The name of the formula and its herbal constituent

Table 2 explains that the five articles describe thirteen (13) kinds of traditional medicinal herbs used to maintain health and fitness during the Covid-19 pandemic in Indonesia. One (1) formula had been developed by pharmaceutical industries in Indonesia (PT. Soho Indonesia). The herb was used to relieve symptoms of respiratory disease [12]. One (1) formula was registered under Herbavid-19 [10]. Two (2) formulas were traditional Chinese medicine (TCM), namely Shen Shen-fu-tang + Su-he-Xiang pills and Xiang-Sha-Liu-junzi-tang. Both of these formulas were popular for the treatment of Covid-19. Shen Shen-fu-tang + Su-he-Xiang pills are indicated for the severe stage of Covid-19, while Xiang-sha-Liu-junzi-tang is used for the Covid-19 recovery stage [10].

One (1) formula came from ayurvedic [10]. Four (4) formula have been used empirically to maintain health and fitness in Indonesia (kunyit asam, temulawak, beras kecur and wedang jahe) [10]. Two (2) formulas are derived as antiasthma and concentration enhancers from Moringa leave. These formulas were only tested in vivo [9]. One (1) formula is probiotic [11], and one (1) recipe is a modified formula of turmeric, ginger, brown sugar, and oranges [13].

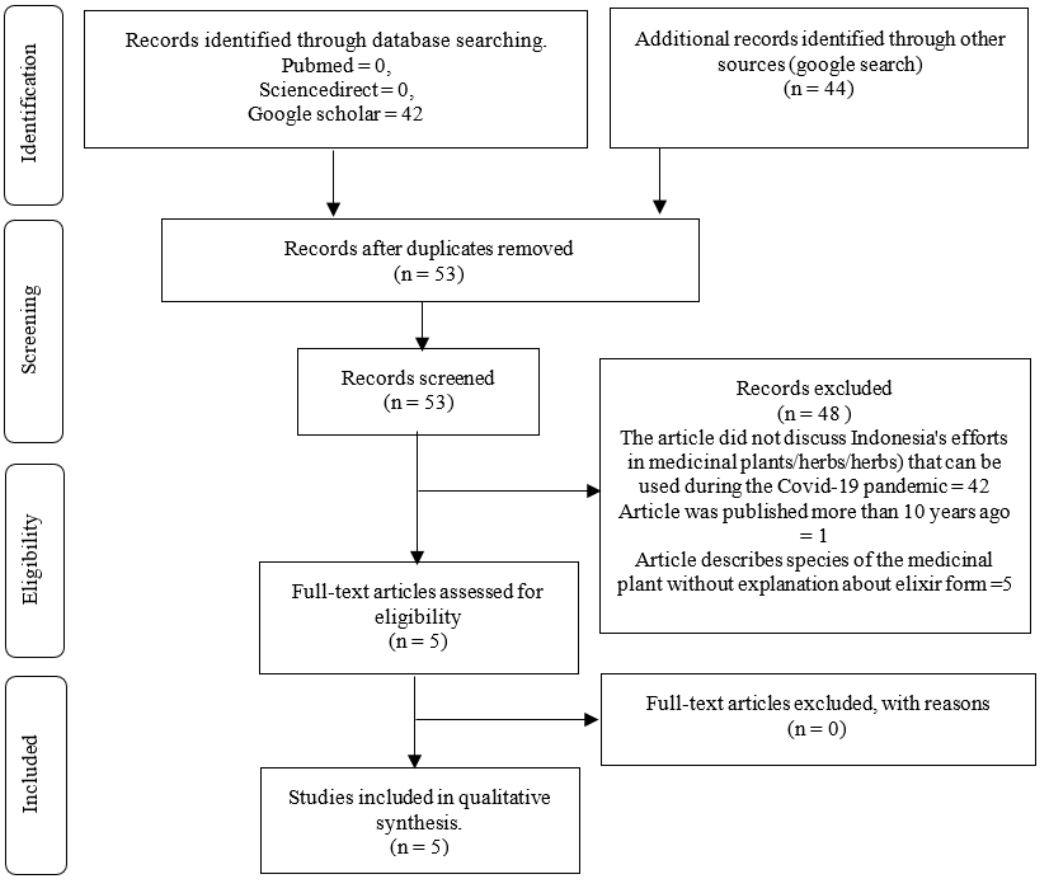

Figure 1. The article selection process in the literature review

Anti-asthma herb from Moringa oleifera Lam seeds

Fidrianny *et al*. stated that *Moringa oleifera* Lam seeds in animals experimental as an antiasthma were used at a dose of 250 mg/kg BW and 500 mg/kg BW. The use of these herbs had shown an improvement in respiratory function and a decrease in the severity of asthma symptoms. The safety of the formula was rated as good. Methanol extract of *Moringa oleifera* Lam seeds had a bronchodilator effect by blocking the release of inflammatory mediators into local lung tissue and inhibiting inflammatory mediators such as histamine [9].

Secondary metabolites or phytochemical compounds *of Moringa oleifera* Lam seeds are Pterygospermin, B-sitosterol-3-O-β-D-glucopyranoside, and 4-(α-L-rhamnosyloxy) benzyl isothiocyanate. The phytochemical constituents of *Moringa oleifera* Lam leaves are Benzyl isothiocyanate, Niazimicin, Glucosinolates, and Glucomoringin. The description above explained that the phytochemical constituents are primarily found in the leaves compared to the seeds; therefore, studies to evaluate the anti-asthmatic effects of the leaves had been encouraged using dexamethasone as a positive control. The results showed that the leaves had a significant impact on mast cell degranulation, anti-inflammatory, and bronchospasm [9].

Cookies concentration enhancer of Moringa oleifera Lam leaves

Moringa oleifera Lam cookies consumed 5-10 g for two weeks could improve the concentration ability in adolescent boys aged 13-15 years. *Moringa oleifera* Lam seed extract had a mechanism as a modulator of cholinergic activity through the signaling pathways of Akt, CREB, and ERK1/2. *Moringa oleifera* Lam seed extract can be used as a potent neuropharmacological drug to fight amnesia. This extract had been shown to protect scopolamine-induced mice from memory and learning dysfunction. *Moringa oleifera* Lam Leaves extract exerted a partial memory-enhancing effect by increasing cholinergic function and reducing oxidative stress. However, suppressing monoamine oxidase (MAO) and regional blood flow increased dopaminergic function [9].

Table 2. Herbs Formula for Maintaining Health and Fitness during the Covid-19 Pandemic in Indonesia

Article	Herbs Formula	Herbs Composition
Fidrianny *et al*. [9]	Formula for Anti-asthma Cookies Concentration Enhancer	*Moringa oleifera* Lam Seeds *Moringa oleifera* Lam Leaves
Hartanti *et al*. [10]	Herbavid-19	*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.) Rausch. rhizomes, *Lonicera japonica* Thunb. Flowers, *Lophatherum gracile* Brongn. Leaves, *Mentha arvensis* L. leaves, *Pogostemon cablin* (Blanco) Benth. Leaves, and *Nepeta tenuifolia* Benth. Leaves
	Kunyit Asam	*Alpinia galanga* (L.) Willd rhizomes., *Citrus aurantifolia* fruits,and *Curcuma longa* rhizomes
	Temulawak	*Curcuma zanthorrhiza* rhizomes, *Phyllanthus niruri* aerial parts, and *Zingiber offinale* var. R*ubrum* rhizomes
	Beras kencur	*Kaempferia galanga* L. rhizomes, *Oryza sativa* L starches, and *Pandanus amaryllifolius* Roxb. leaves
	Wedang Jahe	*Cinnamomum Verum* barks, *Citrus aurantifolia* (Christm.) Swingle fruits, and *Zingiber Officinale* var. *Rubrum* rhizomes
	Shen Shen-fu-tang + *Su-he-xiang* pils	*Panax ginseng* C.A.Mey. roots, *Aconitum carmichaelii* Debeaux roots, *Acorus calamus* L. rhizomes, *Curcuma longa* L. rhizomes, *Cornus offinalis* Siebold & Zucc. pulps, *Schisandra chinensis* (Turcz.) Baill. fruits, *Zingiber offinale* Roscoe rhizomes, and *Glycyrrhiza glabra* L. rhizomes and roots + *Liquidambar orientalis* Mill. oleoresins
	Xiang-Sha-Liu-junzi-tang	*Codonopsis pilosula* (Franch.) Nanny. Roots, preserved *Astragalus propinquus* Schischkin roots in honey, *Atractylodes macrocephala* Koidz. rhizomes, *Wolfioria extensa* (Peck) Ginns sclerotia, *Glycyrrhiza glabra* rhizomes, and root
	Cyawanprash	*Allium sativum* L., *Cinnamomum Verum* J.Presl, *Cuminum cyminum* L., *Curcuma longa* L., *Ocimum tenuiflrum* L., *Withania somnifera* (L.) Dunal, and *Zingiber offinale* Roscoe.
Hamid *et al*. [11]	Coconut Water Probiotics	*The water of Cocos nucifera* L
Ikawati *et al*. [12]	Relieve respiratory disease symptoms	*Curcuma xanthorrhiza* rhizome, *Vitex trifolia* leaves, *Zingiber Officinale* Rhizome, *Citrus* fruit, and *Echinacea purpurea* herb
Jannah *et al*. [13]	Modified formula from turmeric-ginger-red sugar-orange	*Curcuma longa* L Rizomes; *Zingiber offinale* var Rubrum Rhizomes; *Citrus aurantifolia* (Christm.) Swingle Fruits

Coconut water probiotics

Coconut water is rich in sugar, protein, and fat. It is suitable for supporting the growth of lactic acid bacteria (LAB) *Lactobacillus casei* strain Shirota. Coconut water is developed as a fermentation medium. Coconut water contains simple carbohydrates (glucose and fructose) and minerals (calcium and phosphorus). Simple carbohydrates can fermentable sugars and be a carbon source for microorganisms—the minerals act as natural sources of electrolytes [11].

The use of probiotics made from fermented coconut water stated that the manufacture of coconut water probiotics using lactic acid bacteria (LAB) *Lactobacillus casei* strain Shirota is expected to meet the needs of live probiotics and electrolyte sources. In an in vivo study using puppies as experimental animals, viral pathogenesis infection can cause severe lymphopenia conditions due to a decrease in CD4 cells that can cause death, and probiotics can reduce this event with their physiological and immunological effects such as regulating T (NK) cell activity, preventing viral infection and increase interferon-γ (IFN-γ) levels [11].

Herbavid19®

Herbavid is an herb containing *Arctium lappa* L fruit, *Coix lacryma-jobi* L kernel, *Curcuma zanthorrihiza* Roxb Rizhomes, *Forsythia suspensa* (Thunb.) Vahl fruit, *Glycyrrhiza glabra* L root, *Imperata cylindrical Rizhomes* (L) Raseusch, *Lonicera japonica* flower, *Lophatherum gracile* Brongn, *Mentha arvensis* L leaves, *Pogostemon cablin* (Blanco) Benth leaves, and *Nepeta tenuifolia* leaves. The herb was registered with claims to help maintain the immune system and relieve cough, fever, hoarseness, or an itchy throat. The Herbalvid19 formula is a reformulation of the TCM formula called yin-Qiao. The primary plants in yin-qao are *Lonicera japonica* and *Forsythia susp*ensa. This formula has been traditionally used to prevent and treat respiratory tract infections. It can improve the function of the upper respiratory mucosal immune system in experimental mice with upper respiratory mucosal dysfunction due to disease of bacteria and viruses [10].

Kunyit asam

Kunyit is *Curcuma longa* Rhizomes. Asam is Tamarind and is often replaced with *Citrus aurantifolia* fruit. The combination of *Alpinia galanga* (L) Wild Rhizomes, *Citrus aurantifolia* Fruit, and *Curcuma longa* Rizhomes can be use as an immunomodulator. The active substances to support the activity are polysaccharides and curcumin. *Alpinia galanga* can modulate the phagocytosis of the

innate immune response. This herb is traditionally used to maintain a healthy body [10].

Temulawak

The combination of *Curcuma zanthorrhiza* Rhizomes, *Phyllanthus niruri* Herb, and *Zingiber Officinale* var. Rubrum rhizomes also showed immunomodulatory activity. Temulawak is the local name of *Curcuma zanthorrhiza*. Phyllanthus and phenolic components of *Phyllanthus niruri* can be used as immunomodulators, anti-inflammatory and antinociceptive. In addition, 6-gingerol, 6-shogaol, and 8-school from *Zingiber officinale* var. Rubrum is active as an antioxidant that strengthens the immunomodulatory effect of *Phyllanthus niruri*. The addition of *Curcuma zanthorrhiza* rhizomes from temulawak can function as a hepatoprotection [10].

Beras kencur

Beras is *Oryza sativa* while kencur is the local name of *Kaempferia galanga* L. This herb contains *Kaempferia galanga* L. Rhizomes, *Oryza sativa* starch, and *Pandanus amaryllifolius* Roxb leaves. Polysaccharides in *Oryza sativa* can be used as immunomodulators. Essential oils from *Pandanus amaryllifolius* can be used as relaxants. *Kaempferia galanga* has the pharmacological activity of inhibiting the expression of CD18/11a from leukocytes and increasing phagocytosis of leukocytes. *Oryza sativa* can increase macrophage phagocytosis and cytokine induction. *Pandanus amayllifolius* can lower blood pressure and pulse. The combination of these ingredients is traditionally used as a general and refreshing tonic, relieves fatigue, and increases blood circulation and appetite [10].

Wedang Jahe

The combination of *Cinnamomum verum* bark, *Citrus aurantifolia* (Christm.) Swingle fruit and *Zingiber officinale* var Rubrum Rhizomes in *Wedang Jahe* are traditionally used to warm the body, increase appetite, protect digestion and reduce rheumatic pain. Jahe is the local name for ginger. Trans-cinnamaldehyde and its analogs of *Cinnamomum Verum* are active as an immunomodulator. 6-gingerol, 6-shogaol, and 8-shogaol from *Zingiber offinale* var. Rubrum is an antioxidant. The pharmacological activity of *Citrus aurantifolia* was shown by inhibiting the expression of CD18/11a leukocytes and increasing leukocyte phagocytosis. The improvement of type-II collagen-induced arthritis of *Cinnamomum Verum* had been tested in vivo using experimental animals. *Zingiber offinale* var Rubrum also active as corigen saporis and odoris [10].

Shen Shen-fu-tang + Su-he-Xiang pills

The pills' ingredients are *Panax ginseng* C.A.Mey root, *Aconitum carmichaelii* Debeaux root, *Acorus calamus* L Rhizomes, *Curcuma longa* L Rhizomes, powder of *Cornus Officinalis* Siebold & Zucc sawdust, *Schisandra Chinensis* (Turcz.) Baill., *Zingiber offinale* Roscoe Rhizomes and. root of *Glycyrrhiza glabra* L. and oleoresin from *Liquidambar orientalis* Mill. The herb was used in early-stage therapy of Covid-19. The herb is used because of its ability to build body resistance against viral pathogens [10].

Xiang-sha-Liu-junzi-tang

Xiang-Sha-Liu-junzi-tang contains *Codonopsis pilosula* (Franch.) Nanny root, *Astragalus propinquus* Schischkin root in honey, *Atractylodes macrocephala* Koidz rhizomes, Skelorotia of *Wolfioria extensa* (Peck) Ginns, and *Glycyrrhizomes glabra* roots and rhizomes. This herb was used in the recovery stage of Covid-19. This herb is used for its ability to build the body's resistance to viral pathogens. *Glycyrrhiza glabra* is rich in glycyrrhizin, showing antiviral activity against clinically isolated SARS coronavirus. It's also known as an anti-inflammatory and immunomodulator so that it functions significantly in the treatment of COVID-19 [10].

Chyawanprash

Chyawanprash is traditionally used as an immunomodulator, antioxidant, hepatoprotective, and rejuvenation of the respiratory system. The composition of the plants consisted of *Allium sativum* L., *Cinnamomum Verum* J.Presl, *Cuminum cyminum* L., *Curcuma longa* L., *Ocimum tenuiflrum* L., *Withania somnifera* (L.) Dunal, and *Zingiber offinale* Roscoe. These plants are also recommended as immunomodulators in single plant dosage forms [10].

Relieve respiratory disease symptoms

Ikawati *et al*. examined a formula developed by PT Soho Indonesia. It stated the combination of *Curcuma xanthorrhiza* rhizome, *Vitex trifolia* leaves, *Zingiber Officinale* Rhizome, Citrus fruit, and *Echinacea purpurea* herb in one formula provided a synergistic effect on alleviating respiratory symptoms. These symptoms can decrease when the immune system increases. The immunomodulatory activity of this herb had been investigated by macrophage phagocytosis activity, lymphocyte proliferation activity, and antibody titer measurement (non-specific immunomodulatory effect). The dosage for use for experimental animals is 245 mg/kg BW up to 980 mg/kg BW [12].

Echinacea has long been used conventionally to treat various infections and wounds. This plant displays many immune-modulating activities, consisting of the stimulation of immune functions, such as the phagocytic activity of macrophages and suppression of the pro-inflammatory response of epithelial cells to viruses and bacteria. *Citrus aurantifolia* contains flavonoids, and flavanone glycosides, consisting of hesperidin, naringin, and naringenin that are productive as immunomodulators and antioxidants. Hesperidin has been studied and exhibits anti-asthmatic activity by inhibiting the production of asthma-associated cytokines. Naringin has antitussive activity in a guinea pig model with allergic cough induced by cigarette smoke exposure.

Vitex trifolia leaves (legundi) relieve symptoms of respiratory diseases such as flu and upper respiratory tract infections. The leaves contain vitexicarpin, which is helpful as a tracheospasmolytic and anti-allergic. The immunomodulatory

activity was caused by lymphocyte proliferation. Its phytochemical compounds display stimulatory activity on macrophage phagocytosis. The immunostimulant activity of the active compound was seen in the oxyburst phagocytosis assay using human polymorphonuclear cells. Research stated that the combination of Vitex trifolia leaves and Curcuma xanthorrhiza rhizome extract provided tracheospasmolytic effects and anti-allergic activity [12].

Zingiber Officinale rhizome (ginger) is an antitussive and anti-inflammatory agent. Ginger is also active as an immunostimulant by increasing the function of macrophages and contributing to the phagocytic activity of macrophages. Several phytochemical components of ginger, such as (6)-gingerol, (8)-gingerol, and (10)-gingerol, were also reported to inhibit lymphocyte proliferation with slightly different potencies [12].

Modified formula from turmeric-ginger-red sugar-orange

Herbal medicine can use for warming and refreshing the body. The preparation is effortless, just by boiling the ingredients. Lime juice (*Citrus aurantifolia* (Christm.) Swingle) is given for fresh taste. The immunomodulatory activity of *Citrus aurantifolia* (Christm.) Swingle inhibits CD18/11a expression from leukocytes and increases leukocyte phagocytosis. This fruit has also been used traditionally to clear phlegm in the respiratory tract. Curcuminoids in *Curcuma longa* L have been widely known to have immunomodulatory activity by increasing the effect on the main functions of T cells, natural killer (NK) cells, macrophages, and total splenocytes in vivo. *Zingiber officinale* can increase the number of lymphocytes, increase the toxicity of cancer killer cells (natural killers), synthesize specific antibodies, and stimulate the activity of macrophages [13].

Indonesia is rich in biodiversity. The herbal treatment was developed by the community increasingly. The herbal treatment is an effort to live healthy independently. Therefore, the Indonesian government encourages the development of medicinal plants in multi-sectoral areas, including the health, agriculture, forestry, and other informal sectors [14]. One of the efforts to develop medicinal plants during the Covid-19 pandemic is utilizing the family medicine garden (Taman Obat Keluarga (TOGA)). The program is organized by the community in Traditional Health Independent Care. The purpose of traditional health self-care is to increase the community's ability to carry out health maintenance and overcome minor health problems by using TOGA. The principal traditional use of medicinal plants is to revitalize the body and make the body work optimally—the body's ability to adapt to the environment increases. The use of medicinal plants for COVID-19, has three main activities, namely immunomodulators, reducing Covid-19 symptoms, and overcoming comorbid factors that accompany Covid-19 disease [15].

The literature review showed that the thirteen (13) herbs had been used empirically. Two (2) ingredients are derived from Moringa leaves as antiasthma and concentration enhancers. These ingredients were only tested in vivo [9]. It's called using empirically based. The use of empirical-based in traditional medicine has two forms, namely modern form, and fresh form. The modern form must have a distribution permit from the National Agency of Drug and Food Control (Badan Pengawas Obat dan Makanan (BPOM)) with good packaging conditions and good physical form. In contrast, the fresh form must contain the correct type of plant, composition, dosage, sound processing, and proper consuming method [15].

The examples of the fresh form in the literature review are coconut water probiotics [11], *kunyit Asam, temulawak, beras kencur, wedang jahe* [10], and modified formulas of turmeric, ginger, brown sugar, and oranges [13]. Respiratory symptom relief herbs [12], Shen Shen-fu-tang + Su-he-Xiang pills, Xiang-Sha-Liu-junzi-tang, Cyawanprash, Herbavid-19 [10], antiasthma herbs, concentration enhancer cookies [9] is a modern form, so it requires a suitable composition and dosage.

Moringa oleifera Lam has been used widely in Indonesia. Its properties are very diverse, ranging from anticancer, antidiabetic, antihypertensive, overcoming malnutrition, and increasing endurance. *Moringa oleifera* Lam can be used to treat comorbidities that accompany Covid-19. The antibacterial and antifungal activity of *Moringa oleifera* Lam is due to the Pterygospermin in the seeds. Another activity that supports the use of *Moringa oleifera* Lam is anti-inflammatory activity. This activity is supported by Benzyl isothiocyanate in the leaves and moriginine and morphine in the roots [9].

The use of fermented coconut water in probiotic form is an immunomodulator [11]. Besides being used as a probiotic, virgin coconut oil (VCO) can also use coconut, obtained from enzymes and centrifugation without involving the heating process of the coconut flesh. VCO contains a lot of medium-chain saturated fatty acids, namely lauric acid, caprylic acid, myristic acid, and palmitic acid, which are easily digested by the body into energy [16].

Hartanti *et al*. described three formulas with *Glycyrrhiza glabra*. Glicirizin can function as an immunomodulator, anti-inflammatory, and SARS-antiviral [10]. These results were reinforced by Silveira *et al*. who succeeded in defining 39 plants or herbal medicines that can be used for Covid-19 patients. The benefit/risk assessment of the herbal medication was found to be positive in 5 cases (*Hedera helix, Sambucus nigra, Glycyrrhiza glabra, Althaea Officinalis,* and *Commiphora molmol*), promising in 12 cases (*Echinacea angustifolia, Andrographis paniculata, Allium sativum, Echinacea purpurea*, *Magnolia Officinalis, Justicia pectoralis,* volatile oil of *Eucalyptus globulus, Zingiber officinale, Pelargonium sidoides, Pimpinella anisum, Salix sp, Mikania glomerata*), and the remainder was unknown [17].

Kunyit asam is a traditional herb that has been preserved for generations. The main ingredient is *Curcuma longa* rhizomes and other herbs that can provide the pH, such as tamarind or citrus fruits so that it serves to stabilize the yellow color of curcumin of *Curcuma longa* rhizomes. *Curcuma longa* rhizomes contains curcumin and polysaccharides as immunomodulators. Genes that play a role in curcumin bioactivation are the CURS1, CURS2, and CURS3 genes. The gene's activity is to catalyze curcumin synthesis by condensing feruloyl-CoA with diketide-CoA in the

biosynthesis of curcuminoids [18]. Ebenezer *et al*. in their systematic review stated that curcumin is one of twenty compounds that have potential as anti-SARS-Cov agents at concentrations between 3.3 and 10 mmol/L. Curcumin has the highest 3CL protease inhibitory activity with an IC50 value of 40 microliter/L [19].

Systematica review by Anunciação *et al*. regarding the effectiveness of curcumin as an anticancer was stated that the anticancer activity of curcumin was caused by its anti-inflammatory, antioxidant effects, reduction of prostate-specific antigen (PSA) levels and a reduction in the degree of dermatitis in patients receiving radiotherapy. Six articles were included in the review with four hundred and fifty (450) individuals consisting of two hundred and fifty-nine (259) in the intervention group and one hundred and ninety-one (191) in the control group. The effectiveness of curcumin as an anti-inflammatory, antioxidant, PSA-lowering agent and in dermatitis has been well proven with limited side effects and good tolerance. The use of curcumin in the treatment of cancer is only as a co-adjuvant therapy. Research on the bioavailability of curcumin that explains the relationship between curcumin dose and its activity in neoplastic cells is still very much needed to produce more consolidated scientific evidence with more precise safety data. The research can increase the effectiveness of cancer therapy and improve the quality of life of patients [20].

Alpinia galanga (L.) Will contain a terpene, phenolic, and alkaloid components. The most extensive secondary metabolites are galangal diterpene A, galangal diterpene B, 1,8-cineole, and α-pinene [21]. *Alpinia galanga* (L.) Will acts as an immunomodulator by modulating the innate immune response of phagocytes [10]. *Citrus aurantifolia* contains flavonoids that are efficacious as immunomodulators [12]. Another activity of *Citrus aurantifolia* is as a phlegm thinner [13]. The immunomodulatory activity of *Citrus aurantifolia* is activated by inhibiting the expression of CD18/11a from leukocytes and increasing leukocyte phagocytosis [10].

Hartanti *et al*. described the temulawak can be productive as a hepatoprotector because of the comprehensive benefits of *Curcuma xanthorrhiza* Roxb in the formula [10]. This herb is widely used to treat indigestion, jaundice, and vaginal discharge increases endurance and maintains health. Another advantage of temulawak is to refresh the body, accelerate metabolism, healthy liver function, and improve appetite as an immunomodulator and hepatoprotector. The research reported that giving temulawak can increase the immune response in chickens provided the bird flu vaccine [16].

Nugraha *et al*. stated that *Curcuma zanthorrhiza* rhizomes contains curcuminoids (1% -2%), volatile oil (3% -12%), xanthorrhizol (44.5%), and camphora (1.39%). Curcumin, monodemethoxycurcumin, and bisdemethoxycurcumin belong to curcuminoids. Xanthorizol is an immunosuppressant that can treat Covid-19 because of its ability to inhibit pro-inflammatory cytokines. Patients with Covid-19 are susceptible to cytokine release syndrome (CRS). Thus, using xanthorrhizol might decrease the pro-inflammatory response in patients with Covid-19 with or without CRS. However, the use of xanthorrhizol needs to be done carefully because no research has been conducted on Covid-19. The use of xanthorrhizol may also worsen the condition of patients with Covid-19 because of the lack of research on this [22].

Flavonoids of *Phyllanthus niruri* L can be efficacious as immunomodulators [16, 18]. The gene that plays a role in flavonoid biosynthesis is psbA. This gene has a mechanism to regulate the antioxidant system [18]. Other active substances in *Phyllanthus niruri* L for immunomodulators are phyllanthin, geraniin, niranthin, quercetin, astragalin, phyltetralin, corilagin, catechin, hypophyllanthin, gallic acid, and ellagic acid [10]. The extract can be used as adjuvant therapy in acute and chronic infectious diseases like tuberculosis, hepatitis, upper respiratory tract infections, and herpes zoster [16]. *Phyllanthus niruri* L also has anti-inflammatory and antinociceptive activity because of the active substance of philantin and phenolic compounds. The aqueous extract induced dose-dependent proliferation of Peripheral Blood Mononuclear Cells (PBMC), increased nitric oxide release, and the phagocytic activity of macrophages isolated from tuberculosis patients. The aqueous extract also has antinociceptive and anti-inflammatory activity in acetic acid-induced and histamine and carrageenan-induced mice [10].

Zingiber offinale var Rubrum contains essential oils with active substances such as zingiberene, kamfena, lemonin, borneol, shogaol, cineol, phellandrene, zingiberol, gingerol and zingerone. This herb is used empirically to increase stamina. It is also supported by the primary metabolites found in ginger, namely calories, carbohydrates, protein, sodium, iron, potassium, magnesium, phosphorus, zinc, folate, vitamin C, vitamin B6, vitamin A, riboflavin, and niacin [16]. The oleoresin *Zingiber offinale* var Rubrum can be processed into an instant beverage to improve health [11]. The genes that play a role in regulating the active compounds' biosynthesis of *Zingiber Officinale* var Rubrum are CDPK and psBA. CDPK works on increasing calcium and immunogenicity, and the psBA gene plays a role in regulating antioxidant systems [18].

The in vivo study conducted by Elmeged *et al*. that used thirty-six (36) Sprague Dawley male albino rats (weight 150±l0g), stated that ginger had a robust impact in enhancing the immune of mice that were injected with carbon tetrachloride. This activity is caused by the presence of flavonoids in ginger The flavonoids contribute to the protecting capacity of the liver via the way of means of inhibiting cytochrome P-450 aromatase A [23].

Hartanti *et al*. described Herbavid-19 [10]. The main compound of the formula is burdock fruit (*Arctium lappa* L). Burdock contain fenilpropanoid (Arctigenin and Arctiin), and inulin. Inulin has the anticancer, immunomodulatory, antiinflamatory and hepatoprotective effects. Arctiin and arctigenin have antiviral effects and enhance the immune response against some influenza viruses. Arctigenin protects nerve cells from damage caused by ethyl alcohol and amyloid, inhibits the synthesis of -amyloid, reduces their damage during ischemia. Other properties of Arctigenin are radioprotective, diuretic, antitumor and anti-inflammatory effects [24].

Hartanti *et al*. described *beras kencur*. *Pandanus amaryllifolius* Roxb leaves in the formula are used as corigen odoris [10]. Amylum in *Oryza sativa* L uses as a suspending agent of kaempferol of *Kaempferia galanga* L. Polysaccharide of *Oryza sativa* L is also produced as an energy source. *Oryza sativa* L provides most of the daily calories in humans [25]. *Kaempferia galanga* L contains the psbA gene that plays a role in flavonoid biosynthesis. This gene functions in the regulation of the antioxidant system. Flavonoids occur naturally in this plant. It can produce various pigment and non-pigmented compounds and is involved in several biological processes and functions for human health, including immunomodulators. Flavonoid pigments are readily visible markers in molecular genetic experiments and gene expression regulation [18].

The mixture of *Cinnamomum Verum* barks, *Citrus aurantifolia* (Christm.) Swingle fruits, and *Zingiber Officinale* var. Rubrum rhizomes in wedang jahe can be used as body warmers, increase appetite, protect digestion and reduce rheumatism. Research conducted by Chandra and Pandey reported that in the antioxidant activity test using the 2,2 diphenyl-1-picrylhydrazyl test, water extract and ethanol extract of *Cinnamomum Verum* had almost the same capacity to inhibit free radicals (IC50=13.3 and 13.53 g/ml), but it found the activity to be lower than ascorbic acid (IC50=9.96). g/ml). Whereas in the assay of analgesic activity using tail immersion test and acetic acid-induced wriggling test method in Swiss albino rats that reared under standard laboratory conditions, aqueous extract of *Cinnamomum verrum* at a dose of 600 mg/kg body weight showed the maximum time required for response to thermal stimulation for 5.25±0.48 s and the maximum writhing inhibition percentage was 32.61%. In contrast, diclofenac responded at 7.25 ±0.25 s and 67.39% inhibition in the immersion tail and wriggling tests, respectively. The ethanol extract of *Cinnamomum verum* with a dose of 600 mg/kg body weight showed the maximum time required for response to thermal stimulation (6.75 ± 0.47 seconds) and the maximum % inhibition of wriggling (44.57%). The result indicated that the ethanol extract has higher antioxidant and analgesic activity than aqueous extract. It was allegedly because the potential for biological compounds that were successfully dissolved in the two solvents was different, so the antioxidant and analgesic activity of the ethanol extract was higher than that of the aqueous extract [26].

Shen Shen-fu-tang + Su-he-Xiang pills and Xiang-Sha-Liu-junzi-tang are formulas adapted from TCM. Laboratory trials further support evidence for the beneficial clinical effect of TCM. Glycyrrhizin, which is the active constituent of the roots and rhizomes of *Glycyrrhiza glabra* in TCM, can inhibit the replication of clinical isolates of the SARS virus. Another review reported that the combination of conventional drugs in TCM showed beneficial effects such as reducing mortality, relieving symptoms, and controlling fungal infections in patients with SARS. Still, this evidence was insufficient due to poor methodological quality [27].

SARS-CoV-2 uses the host ACE2 receptor for cellular entry. Therefore, TCM with ACE2 targeting capacity plays a vital role in preventing SARS-CoV-2 infection. Some secondary metabolites that play a role in ACE2 inhibition include emodin from the genus Rheum and Polygonum, baicalin *from Scutellaria baicalensis*, and nicotianamine from some foodstuffs (e.g., soybeans), scutellarin, luteolin from Veronicalina riifolia, and tetra-O-galloyl-β-D-glucose (TGG) from Galla Chinensis. They can significantly inhibit the SARS-CoV S-protein and ACE2 interaction, although these compounds' anti-SARS-CoV activity remains evaluated. In addition, inhibition of the 3a ion channel by emodin or kaempferol derivatives, namely juglanine, can prevent virus release from infected cells. Saikosaponin, quercetin, glycyrrhizin, and TSL-1 extracted from *Toona sinensis* Roem have potential anti-SARS-CoV effects by inhibiting cellular virus entry, as well as its adsorption and penetration [27].

Panax ginseng contains saponins ginsenosides or triterpene glycosides, amino acids, phenols, proteins, alkaloids, polypeptides, and vitamins B1 and B2. *Panax ginseng* has immunomodulatory activity by influencing the hypothalamic-pituitary-adrenal (HPA) action. In vitro experiments also revealed increasing natural killer (NK) cell activity and increased immune cell phagocytosis after exposure to ginsenoside [28]. Fuzi, or lateral root of *Aconitum carmichaelii* Debeaux, has been widely used in Chinese medicine for tumors, poor circulation, heart failure, and pain. However, the toxicity of raw Fuzi has always been a significant concern for both healers and patients. The use of *Aconitum sp*. must be under strict clinical and regulatory supervision. Detoxification is done by soaking in water, sautéing, boiling, steaming, and roasting to reduce Fuzi's toxicity. Combination of Fuzi with *Glycyrrhiza uralensis* Fisch. Root, *Panax ginseng* C.A. Mey., or *Zingiber officinale* Roscoe was carried out to reduce toxicity and increase the effectiveness of Fuzi [29].

Acorus calamus L has been used traditionally. Its pharmacological activities are antispasmodic, carminative, anthelmintic, aromatic, expectorant, anti-nausea, nervine, stimulant, anti-asthmatic, bronchitis, fever, colic, antiepileptic, antidiarrheal, dysentery and stomach tumors. The compound of *Acorus calamus* L is glycosides, flavonoids, saponins, tannins, polyphenols, and essential oils that consist of calamine, clamenol, calameon, asarone, and sesquiterpenes [30].

Cornus Officinalis Siebold & Zucc is also a constituent component of Shen Shen-fu-tang + Su-he-Xiang pills. This herb has been developed as a therapeutic agent for atrophic dermatitis through its ethanol extract's anti-allergic, antioxidant, and anti-inflammatory activities. Ethanol extract from *Cornus Officinalis* inhibited the release of β-hexosaminidase from RBL-2H3 cells sensitive to dinitrophenyl-immunoglobulin E (IgE-DNP) antibody after being simulated by dinitrophenyl-human serum albumin (DNP-HSA) with an IC50 value of 0.178 mg/ml. The antioxidant activity was analyzed using DPPH, iron reduction assay, and the arresting activity of 2,20-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) with EC50 of 1.82; 10.76; and 0.6 mg/mL. In addition, the extract significantly inhibited the production of lipopolysaccharide (LPS)-induced nitric oxide (NO) and the expression of iNOS mRNA, expression of iNOS proteins, and pro-inflammatory cytokines

(IL-1β, IL-6, and TNF-α) through attenuation of NF- B activation in RAW 264.7 cells. The extract significantly inhibited TNF-α-induced apoptosis in HaCaT cells without any cytotoxic effect ($p < 0.05$). Furthermore, 2-furancarboxaldehyde and loganin were identified by gas chromatography/mass spectrometry (GC-MS) and liquid chromatography by tandem mass spectrometry (LC-MS/MS) analysis, respectively, as the main compounds. Molecular docking analyses suggest that loganin, cornuside, and naringenin 7-O- -D-glucoside potentially interfere with IgE binding to the human high-affinity IgE receptor (FceRI) [31].

Schisandra chinensis has anticancer activity by the induction of cell cycle arrest and apoptosis and inhibition of invasion and metastasis in cancer cell lines and experimental animals. It also has antimicrobial and antidiabetic activity by improving pancreatic function, stimulating insulin secretion, and reducing diabetes complications. In addition, this simplicia prevents accumulation of lipid and differentiation of preadipocytes and potential as anti-obesity. Other activities include protection against photoaging of the skin, osteoarthritis, sarcopenia, aging, and mitochondrial dysfunction, and increasing physical endurance and cognitive/behavioral function, which can be attributed to its general antiaging potential. It is supported by its bioactive components consisting of lignans, triterpenes, essential oils, flavonoids, phenolic acids, and polysaccharides, where lignans are the main components responsible for its effectiveness of it [32].

The root of *Codonopsis pilosula* (Franch.) Nanny has been used traditionally to treat cardiovascular disease. An in vitro study using a mouse embryonic stem cell (ES) based model by Wang *et al*. showed that the aqueous extract of the simplicia improved cardiac function in myocardial infarction. The extract increased cardiogenic differentiation in rat ES cells in vitro. The experiment was continued with a rat model of myocardial infarction with left anterior descending artery (LAD) ligation. Cardiac function assessment was performed using echocardiography for 1, 3, and 6 weeks after LAD ligation. Echocardiographic results in LAD ligated mouse models revealed a significant increase in infarcted heart at least six (6) weeks after administration of the extract. It is determined by left ventricular fractional shortening (FS), fractional area contraction (FAC), and ejection fraction (EF). Thus, aqueous extract from the root of *Codonopsis pilosula* (Franch.) Nannf increased the cardiogenic differentiation of ES cells and improved the cardiac function of the infarcted heart [33].

Secondary metabolites of astragalus roots are saponins, polysaccharides, amino acids, flavonoids, organic acids, glycosides, and alkaloids. It is used as traditional medicine as an anti-inflammatory, immune booster, slowing or preventing tumor growth, maintaining the cardiovascular system, regulating and preventing diabetes and other diabetes-related diseases, antioxidant and antiaging, helping wound healing and minimizing scarring, reducing symptoms of chemotherapy, treat colds and flu and provide adjunctive therapy in chronic asthma. The root has a significant diuretic effect which can eliminate urinary protein in experimental nephritis. The experiment with animals proved that astragalus root overcomes anemia. It was also shown to regulate blood sugar levels, maintain respiration, and act antibacterial. Astragalus root can improve and regulate the immune system by promoting the interferon system and improving the body's resistance to disease. The effect of low-level inhibition by astragalus root on cell transformation by viral carriers has also been demonstrated. At the same time, astragalus root also has a protective effect in mice infected with the influenza virus. In degenerative diseases, the impact of astragalus root has been proven through pharmacological tests with its activity in increasing myocardial contractility, protecting the cardiovascular system, fighting arrhythmias, dilating coronary arteries and peripheral vessels, lowering blood pressure, and reducing the pressure platelet adhesion, and reducing thrombosis. Other activities are antihyperlipidemic, antiaging, anti-hypoxia, antiradiation, and lipotropic [34].

Atractylodes macrocephala Koidz. Rhizomes are found in Xiang-Sha-Liu-junzi-tang. The main compounds are sesquiterpenoids and alkynes. *A. macrocephala*, with its pinnately incised leaves, is characterized by the presence of rich atractylon and the absence or deficiency of atractylodin. Its proven pharmacological activity is to improve gastrointestinal function. *A. macrocephala* Koidz rhizomes in TCM are used to strengthen the spleen. In addition, it also works in the innate immune response because it participates in immune memory and phagocytosis. The comparison experience of immunomodulatory activity between *A. macrocephala* and *A. japonica* in extract showed that the immunomodulatory activity of *A. macrocephala* was lower than that of *A. japonica*, but this difference was not significant. The extract significantly induced the secretion of granulocyte-colony stimulating factor (G-CSF) from MCE301 cells in a concentration-dependent manner [35].

Wolfioria extensa (Peck) Ginns sclerotia in Xiang-Sha-Liu-junzi-tang is traditionally used as a sedative, stomachic, and diuretic. Polysaccharides and triterpenoids are metabolites contained in this simplicia. Both metabolites have pharmacological activities as antitumor, anti-inflammatory, and stimulating activities [36].

Hartanti *et al*. also described Cyawanprash from ayurvedic medicine [10]. Jindal *et al*. describe experimental studies and clinical trials of Cyawanprash. An experimental study has shown that this herb is effective to improve cognition and memory, protecting against acute kidney injury and photoaging. The antioxidant activity of Cyawanprash is higher than vitamin C by its ability to minimize the genotoxic effects caused by mutagenic agents that are contained in betel and has a renoprotective impact on smokers. Clinical trials reported that Cyawanprash was effectively added to anti-tuberculosis treatment during recovery. Clinical trials on school-age children who took Cyawanprash for approximately six months proved to have increased immunity, energy levels, physical fitness, strength, stamina, and quality of life. This herb showed significant anti-allergic adaptogenic properties at the level of immunoglobulin E (IgE) and IgG [37].

A longitudinal, single-arm study by Jindal *et al*. on 50 health workers aged 20-60 years, with negative Real-Time Polymerase Chain Reaction (RT-PCR) that took 12 grams of Cyawanprash orally two times a day for 30 days, showed that 2 out of 50

volunteers were positive for Covid-19. Chyawanprash showed a 98.91% protection rate against Covid-19. The infection rate in the hospital dropped significantly. Chyawanprash showed a potential prophylactic agent against infection by SARS-CoV-2 infection, which was safe when used in recommended daily doses. However, a randomized control trial method with a larger sample size is still needed to prove the effectiveness of the prophylaxis [37].

Cyawanprash contains *Allium sativum* L. Secondary metabolites as an immunomodulator in *Allium sativum* L are diallyl disulfide, diallyl monosulfide, diallyl hexasulfie, diallyl pentasulfide, diallyl tetrasulfide, and diallyl trisulfide [10]. Genes involved in flavonoid biosynthesis in Allium sativum L include SG6, MYB1, SG7, MYB29, SG4, MYB4, MYB5, and R2R3-MYB. Anthocyanin activation in Allium sativum L involves the SG6 and MYB genes. The production of flavonols involves the SG7 and MYB29 genes. The R2R3-MYB gene is involved in anthocyanin biosynthesis. SG4 gene, MYB4, and MYB5 are involved in phenylpropanoid suppression and flavonoid synthesis. The NFAMI gene is involved as a receptor for the immune system. The GCLC gene functions as a GSH (Reduced glutathione) encoding with antioxidant function, preventing damage to proteins, lipids, and nucleic acids [18].

Another simplicia in Cyawanprash is *Cinnamomum verum* J. Presl. Cinnamaldehyde and its analogs in it are productive as immunomodulators. In experiments with mice, *Cinnamomum Verum* J.Presl was able to improve type-II collagen-induced arthritis [10]. *Cuminum cyminum* L also has potential antioxidant, antibacterial, antifungal, anti-inflammatory, antidiabetic, insecticidal, and immunomodulatory. The parts of plants such as leaves, seeds, roots, and flowers have several chemical compounds. Its crucial chemical compound is the essential oil of cumin aldehyde [38].

Ocimum tenuiflorum fresh leaves contain essential oil with components such as eugenol, caryophyllene, elemente, and germacrene D. The activity is radioprotective, anthelmintic, antiaflatoxin, antibacterial, anticancer, antidepressant, antidiabetic, antifungal/anticandidal, antimetastatic. Other activities of *Ocimum tenuiflorum* are antimicrobial, antioxidant, antiprotozoal, antistress, antiviral, anxiety, cardiac protective, chemoprotective, cognitive enhancement, hepatosuppression, hyperlipidemia, immunomodulatory, noise stress release, restoration of kidney damage, and wound healing activity [39].

Withania somnifera is an antioxidant, adaptogen, anxiolytic, anti-inflammatory, antivenom, antiparkinsonian, memory enhancer, and antitumor. In addition, various studies have also proven its activity as an immunomodulator, hypolipidemic, antibacterial, and cardiovascular protection in terms of sexual behavior. This activity is supported by secondary metabolites consisting of alkaloids, steroid components, saponins, and acyl groups such as cytoindoside VII and VIII [40].

Ikawati *et al*. investigated a formula containing *Vitex trifolia* leaves, *Curcuma xanthorrhiza* rhizomes, *Echinacea purpurea* herb, Citrus fruit, and *Zingiber Officinale* rhizomes (12)]. The activity of this herb, which relieves symptoms of respiratory disease, that supported by the presence of *Vitex trifolia* leaves. *Vitex trifolia* leaves are often used by traditional medicine therapists in Indonesia as anti-asthmatic, anti-allergic, and anticancer. Compounds as efficacious as tracheospasmolytics in this leaf are flavonoids, namely viteksicarpine [41].

Echinacea purpurea (L.) Moench is most commonly used for immunostimulants. The most common phytochemicals in *E. purpurea* are lipoproteins, betaine, alkamides, saponins, polysaccharides, polyacetylenes, sesquiterpenes, phenolic compounds (echinacoside and other caffeic acid derivatives, and chicoric acid). The immunostimulant activity of this plant species depends on the part of the plant used. The roots have more alkamides, while the leaves are a rich source of flavonoids. Both parts of these herbs are often used in traditional medicine as immunostimulants [42].

Jannah *et al*. modified a formula from turmeric-ginger-red sugar-orange. *Curcuma longa* L Rhizomes is added by *Zingiber offinale* var Rubrum Rhizomes to give a unique taste. The taste is a combination of sour taste and fresh taste [13]. The description of the thirteen formulas above has made it clear that the purpose of using traditional medicinal herbs during the Covid-19 pandemic, significantly as an immunomodulator, reducing Covid-19 symptoms and overcoming comorbid factors that accompany Covid-19 disease, has been well achieved. The formula was also developed from Traditional Chinese Medicine (TCM) and Ayurveda. The utilization of traditional medicinal herbs can support efforts to live healthy independently.

The herbs in this review are just one way to improve health and fitness. Immunization efforts with vaccination are still needed. Sookaromdee *et al*. stated that vaccination is a more effective primary prevention methods for COVID-19 although vaccine supply is an issue that remains to be considered [43]. Thus, the use of herbs is an additional preventive measure against Covid-19.

Conclusion

Traditional medicinal herbs used to maintain health and fitness during the Covid-19 pandemic were the development of local herbs, TCM, and Ayurveda with pharmacological activities as immunomodulatory, reducing Covid-19 symptoms and overcoming comorbid factors accompany the Covid-19 disease. The utilization of traditional medicinal herbs can support government efforts to increase living healthily and independently.

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