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Study of Jamu as Indonesian Herbal Medicine for Covid-19 Treatment

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ABSTRACT
The spread of the Severe Acute Respiratory Syndrome (SARS-CoV-2) virus has caused the COVID-19 pandemic for more than a year. Daily cases in Indonesia keep increasing following the high mortality rate, entitling it as the epicentre country of Asia. The government advises patients with mild symptoms to take self-isolation at home. Due to its rich cultures and beliefs in Indonesia, patients on independent isolation tend to take treatment on their own accord, such as using traditional herbal medicine renowned as jamu. This article is aimed to review the use of various types of concoctions in jamu taken as the prevention and additional therapy for COVID-19 patients. The review may advantage for COVID-19 treatment discovery through indigenous compound and medical care in societies. In writing this article, the author collected information from related articles in online sources such as Google Scholar, Pubmed, Science Direct, as well as circulars from the Indonesian Ministry of Health and treatment guidelines from the Food and Drug Supervisory Agency. Polyherbal formulations that have been widely recommended for COVID-19 treatment are 9 jamu formulas within *Zingiber officiale* for the highest herbal compound used and followed by other 21 herbal plants such as *Curcuma zanthorrhiza*, *Cinnomomun verum*, *Citrus aurantifolia* fruit, *Cymbapogon sitratus*, *Curcuma longa*, *Alpinea galangal*, etc. Five of all founded jamu identified for antivirus agent as well as mostly applied in immune booster tradisionally. Moreover, all of jamu formulas has antioxidant activities and antiinflamatory effect that would be promising for COVID-19 treatment, especially for Jamu Pahitan and Wedang Secang could be the candidates for COVID-19 therapy through increasing immunity and reducing risk factors for each symptom. No antagonistic interactions were found in the herbal concoctions, while several synergistic interactions that increase the pharmacological activity. This study would contribute a remarkable literacy since the use of jamu in preventing and treating COVID-19 as a new disease requires careful consideration due to the limited scientific data and clinical evidence to support its use.

Keywords: *COVID-19, Herbal, Polyherbal, Active Compound Interaction, Pharmacological Activity*

1. INTRODUCTION

Coronavirus Disease (COVID-19) was first discovered as a virus causing pneumonia in Wuhan, China. As a disease occurred from the new variant of the coronaviridae virus family, it is known to have gen's sequence similarities with Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), 88% and 50% respectively [1]. Since the infection phase may occur without symptoms, it is hard to detect the virus particle; hence COVID-19 has a faster and broader range of infection and dispersion [2]. On January 30, WHO determined COVID-19 as a Public Health Emergency of International Concern (PHEIC). Afterward, on February 11, 2020, the International Committee on Taxonomy of Viruses officially named this new coronavirus as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [3].

In Indonesia, the COVID-19 case was first found on March 2, 2020, in Depok, West Java. Cases of positive infection keep on increasing over time until the virus spread across all provinces in Indonesia. Further, there was a second wave of infection when the Delta variant or B1617.2 as the variant of concert entered Indonesia on May 2021. On August 4, 2021, it was confirmed that the positive cases had reached 3,532,567 people with a daily discovery of 35,867 people and an additional daily death of 1,747 cases [4]. The daily addition of cases and daily death rate are quite high, leading to Indonesia's entitlement as the epicentre of COVID-19 in Asia.

COVID-19 treatment therapy is still under continuous research to find the most effective cure and vaccine. This is a necessary effort in mitigating and controlling the COVID-19. The research usually uses evidence-based approach and multifactorial possibilities, namely through the clinical severity study, transmission and infection rate, as well as the efficacy of medication used in the therapy [5].

So far, some general antivirus medications such as remdesivir, favipiravir, and lopinavir-ritonavir, as well as antimalaria medication such as chloroquine and hydroxychloroquine have been used [6]. However, hydroxychloroquine is the first medication that has evidently been considered to have no clinical benefits in a prospective manner, since it does not significantly reduce the possibility of virus incubation period and death rate [7]. The latest report related to the effectiveness of remdesivir showed that it had reduced the duration of recovery from an average of 15 days to 10 days among the hospitalized in-patient adults. Besides, remdesivir reduces almost half of the mortality rate among the cured patients. [8] Unfortunately, the supply of this therapeutically medication in the various region keeps on decreasing and experience scarcity.

Other alternatives in curing the COVID-19 patients may be taken through convalescent plasma (CP) therapy. However, this type of medication may only be more effective for COVID-19 patients in an initial phase, where the virus has not yet cause severe damages to the lungs [9]. Various vaccines have been discovered through many types of virus sources, yet the continuing development of the variant of virus has incited debate regarding the efficacy and effectiveness of the respective vaccines, particularly in stopping the transmission or mitigating the virus infection.

In facing the COVID-19, China is the pioneer, where the case was first discovered, and thus, it becomes the first epicentre in the world. It has been simultaneously using medical guidelines merged from traditional Chinese medicine (TCM) and modern medication. The Chinese government stated that 91.50% of the total case occurred, or as much as 74,187 cases of COVID-19, was cured with the mentioned combination, and it produced promising results in all phases of infections. The result obtained refers to the management of the significant symptoms, namely in reducing symptoms, drop in body temperature, average in-patient duration in hospitals, an increase of recovery rate, a decrease of mortality rate in moderate symptoms, and may be used to mitigate the disease. Furthermore, when combined with modern biomedical, herbal cures may help relieve hypoxaemia and chronic obstructive pulmonary disease (COPD) [10].

Coronavirus is known to cause variety of symptoms in each patient with different severity and mortality rate according to the strength of their antibodies and comorbidities. The infection character of this virus makes it difficult for virus and infection control. Medication and control management of COVID-19 need to focus on early diagnosis, isolation, supportive treatment, as well as infection mitigation and control [11]. Hence, aside from medication effort, mitigation and countermeasures of several mild and moderate symptoms through the increase of immune system are also necessary to conduct. WHO has been encouraging innovation worldwide to use traditional medications as the new therapy development to find potential in curing and mitigating of COVID-19. Several compounds discovered as potentially holding up the coronavirus and boosting the immune system

are quercetin, myricetin, psoralidin, caffeic acid, tryptanthrin, lycorine scutellarein, silvestrol, saikosaponin, isobavachalone, and griffithsin [12]. Herbs are contributing in decreasing morbidity and mortality through their immunomodulatory function, it also suppresses the inflammation process; thus, it is capable of preventing worsening symptoms, increasing immunity, and protect body organs. [13]

Indonesia has been using herbal medicines in society for generations. The Herbs and Jamu Research (Ristoja) in 2017 alone has found 6,193 types of jamu formulas for 74 complaints or diseases from 505 out of 1,128 ethnics, in 11 provinces in Indonesia, outside of Java, Sumatera, and Bali. [14]. During this COVID-19 pandemic, the Ministry of Health also encourages people to use herbal medication, mainly through increasing immunity for mitigation purposes. The Foods and Drugs Monitoring Agency has also issued a Herbal Medication Pocket Book During COVID-19 as the guidelines to use herbs, specifically jamu. There are three types of home remedies classified based on the standardization of the materials and empirical tests in Indonesia, namely jamu, Standardized Herbal Medication (SHM), and Phytopharmaceuticals. Home remedies may also be found in the form of concoctions, either in powder or liquid. [15]

As Indonesian herbs, there has been no research concerning the material standardization or clinical tests made against jamu as empirical verification. Jamu has been used much by Indonesian society as cultural heritage due to its efficacy and utilization for generations. [16]. Jamu formula often consist of medicinal plants processed in traditional way or consisted of several kinds of herbs or poly-herbs simultaneously processed to produce several types of active compounds. It is necessary to pay attention to the poly-herbs management to still achieve the therapy efficacy without any interaction of active compounds that may lead to fatal side-effects. [17]

Therefore, this article review is aimed to collect researches related to Indonesian jamu formula used as therapeutic medication and mitigation against the COVID-19. The collection of information regarding jamu formula is also based on the publication of jamu's use during the COVID-19 pandemic among the society. The data obtained shall be used to find each active compounds from either mono-herbs or poly-herbs content within the concoctions, to then compare the effectivity between the two. Besides, the interaction among the active compounds in the poly-herbs shall be delivered as a comprehensive literacy in the use of jamu for the COVID-19 treatment and the interest of further study.

2. METHODS

This review was performed using the search terms "jamu for COVID-19" that found 312 articles in Google Scholar, 3 articles in Science Direct, and manually searched the references of select articles for additional relevant articles such as phytopharmaceuticals of herbs and antiviral prediction for SARS-CoV-2. Herbs component of jamu founded as COVID-19 treatment in society have compared to FORTI (Formularium of Traditional Indonesian Medicines) from the Ministry of Health as a reference for herbal medicines that are safe for consumption as well as an electronic book of Herbal Use Guidelines issued by BPOM. Moreover, the particular herbal component was checked for herbal-herbal interactions through https://www.drugs.com/condition/herbal-supplementation.html page and related articles. Additional articles are obtained by tracking citations from selected publications or directly accessing the journal's website. The literature search included all available and published reports for the period 2011 to 2021. Relevant articles were collected and reviewed.

3. RESULT

Indonesian jamu content of polyherbal that are widely used by society to treat and prevent COVID-19 are presented in Table 1. We found 9 jamu formulas with various herbal components. It is known that there are 22 types of herbal plants used and presented in Diagram 1 with 5 main bioactivities, such as immunomodulatory, antioxidants, anti-inflammatory, antiviral, and antibacterial.

The mostly used plant was *Zingiber officiale* (18%), followed by *Curcuma zanthorrhiza* (9%) and *Cinnomomun verum*, *Citrus aurantifolia* fruit, *Cymbapogon sitratus*, *Curcuma longa*, and *Alpinia alanga* that occupied at 6%. In traditional applied 9 kinds of jamu are used for increasing the immune system generally. Other benefits are known to be very diverse, such as relieving rheumatic pain, improving digestion and treating diarrhoea, improving blood circulation, increasing appetite, treating fever and colds, treating sore throat, asthma, or lung disease, and treating malaria.

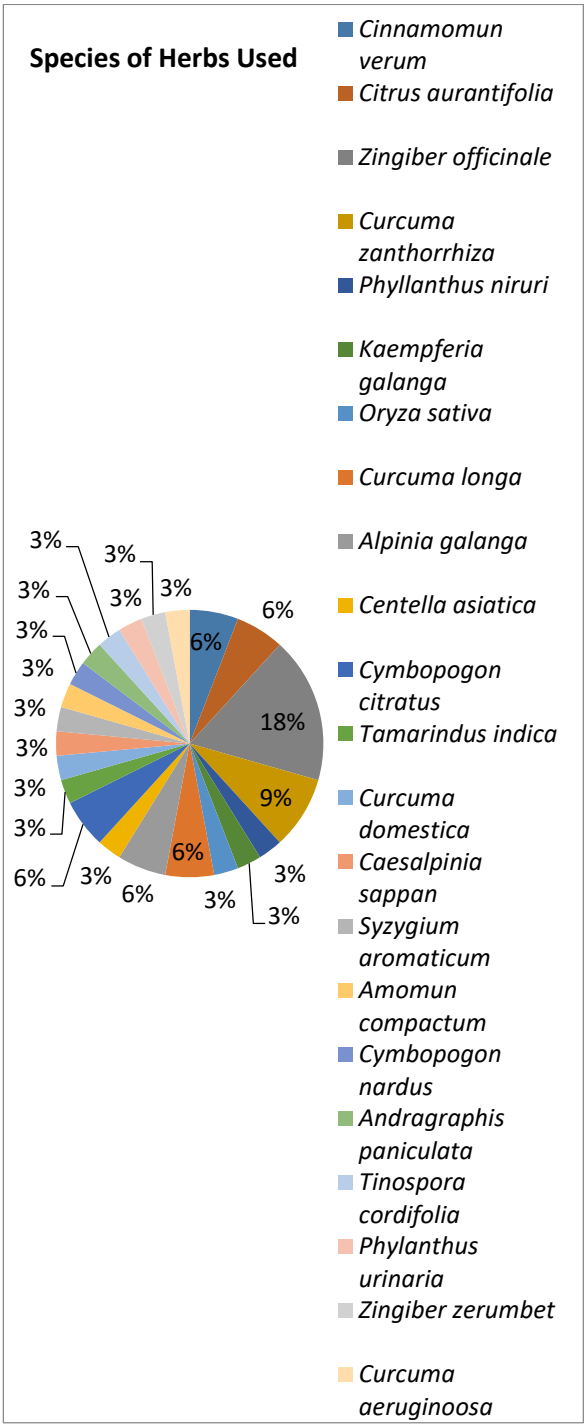

Diagram 1. Herbal Plant in Jamu Utilizing Founded

4. DISCUSION

4.1. Pharmacological Potential of Jamu for COVID-19

The thousands of Indonesian ethnic that separated throughout all region has different traditions and indigenous beliefs, including in the medical tradition. Jamu is a traditional Indonesian medicine that proved an effectivity from generation to generation. As the going spread of COVID-19 today, the Indonesian government has provided to encourage and direct public societies for traditional Indonesian medicine usage through the policy of the Ministry of Health and the Food and Drug Administration in handling COVID-19. However, the clinical research publications of herbs have not been completely found in evaluating an effective treatment of COVID-19 patients, but rather the function of maintaining and enhancing the body's immune system. This activity of the immune system is related with stimulator agents contained in herbs as a stimulator or modulator of various aspects of immunity in the body's system, both adaptive and innate [16]. Therefore, bioactive and pharmacological studies on herbs that are widely used and recommended during this pandemic need to be reviewed to determine the potential for the body's immune system. Furthermore, the active substances that have antiviral activity can be potential candidates for the treatment of COVID-19 involved the in silico analysis to predict objectively.

The results of the literature review found 9 herbal formulas that can be used and are often recommended for the treatment and prevention of COVID-19 in Indonesia, consisting of 22 different types of herbal plants. This result is very small when compared to the result of RISTOJA 2017 from the provinces of Kalimantan, Sulawesi, Nusa Tenggara, and Papua which found as many as 15,671 herbs for health and 1,183 healers / traditional remedies of them. From these ingredients, 11,218 information on types of medicinal plants were obtained; 9,516 were identified, consisting of 1,144 species and 187 genera, while 1,285 plants could not be identified. From all the medicinal plants obtained, various types of ingredients were found consisting of 2-5 types of constituent herbal ingredients [14]. Nevertheless, the composition of the herbs found was by the electronic book Guidelines for the Use of Herbs and Health Supplements in Facing COVID-19 in Indonesia issued by the Food and Drug Supervisory Agency and FORTI (Formulation of Traditional Indonesian Medicines) published in the Decree of the Minister of Health number (HK .01.07/MENKES/187/2017). Both publications are the basis for using herbal medicinal ingredients that have been recognized for their safety and health efficacy by the Indonesian government [16], [43], [44].

Table 1. Herbal formulas that are used for COVID-19 therapy and body immune booster

Herbs Formulation	Bioactive Compound	Pharmacologies Avtivities	Traditional Used
Wedang Jahe: *Cinnamomum verum*, *Citrus aurantifolia* (Christm.) fruit Swingle, and *Zingiber officinale* var. *Rubrum*	Trans-cinnamaldehyde as immunomodulatory from *C. verum* 6-gingerol,6-shogaol, and 8-shogaol as antioxidant from *Z. officinale*	*C. verum*: strong antioxidant (DPPH 71.12 ± 0.77%) [18]. *C. aurantifolia* fruit inhibit the expression of leukocyte CD18/11a which causes cell adhesion defects and increased leukocyte of phagocytosis [19]. *Z. officinale*, DPPH (IC50 0.64 g/ml), [6]-gingerol (50mg/kg) reduced pain relief in experimental rats by 50% as an effective analgesic and anti-inflammatory effect [20].	*Wedang Jahe* has used traditionally to keep body warm, increase appetite, improve digestion system, and help relieve rheumatic pain [21].
Jamu Temulawak-Meniran: *Curcuma xanthorrhiza*, *Phyllanthus niruri*, and *Zingiber officinale* var. *Rubrum*	Xanthorrhizol as antiinflamantory and antioxidant *C. xanthorrhiza* *P. niruri* as imunomodulatory from combination of 12 compounds tannin and flavonoid *Z. officinale*, 6-gingerol,6-shogaol, and 8-shogaol as antioxidant	*C. xanthorrhiza* in vitro decreased COX-2, iNOS, TNF-α and IL-6 levels; in vivo neutralized the effect of TPA-induced ODC, COX-2 and iNOS activation in mouse skin, and prevented IkBα degradation; blocked neurogenic and inflammatory pain responses in a formalin-induced pain test in mice [20]. *P. niruri* as immunomodulatory agent inhibit cellular and humoral immune responses in Balb/C mice; inhibits the release of ROS and NO, inhibits fMLP-induced neutrophil migration; inhibits the release of pro-inflammatory cytokines; and inhibits MyD88-dependent signaling pathways (NF-κB and MAPK)[22]	Jamu Temulawak-Meniran is often used traditionally for digestive disorders, jaundice, vaginal discharge, increasing immune and health [23].
Jamu Beras Kencur*:* *Kaempferia galanga* (L.), Saripati *Oryza sativa* (L.), and *Zingiber officinale* var. *Rubrum*	*K. galangal* contain ethyl-p-methoxycinnamate and curcuminoids as antiinflamantory and antioxidant Polysaccharides from Oryza sativa as immunomodulatory, γ-oryzanol as antiinflamantory and antioxidant *Z. officinale*, 6-gingerol,6-shogaol, and 8-shogaol as antioxidant	Ethyl-p-methoxycinnamate has protective effect since savage ROS and inhibits IL-1, and TNF-alpha[24] -oryzanol as anti-inflammatory prevent IL-6, TNF-α, and NF-κB [23].	Jamu Beras Kencur traditionally applied as a general tonic, relieves fatigue, raises blood circulation, and appetite[21]
Wedang Kunyit: *Curcuma longa*, *Alpinia galanga*, *Citrus aurantifolia*	Curcumin as antioxidant, antivirus, and antiinflamantory on *C. longa* Polysacaride from *A. galanga* has activity in imonomudolatory effect [25], phydroxycinnamaldehyde as antiinflamantory.	*C. longa* extract showed an increasing macrophage activity, reducing TNF-, IL-1β, IL-6, and MCP-1 production in microglial cells, and inhibiting the inflammatory response [26]. Curcumin has antiviral activity against different viruses such as influenza virus, respiratory syncytial virus (RSV), Herpes simplex 1 (HSV-1) papillomavirus (HPV), and Human norovirus (HuNoV)[27]. The effect of phydroxycinnamaldehyde has been shown to decrease chondrocyte degeneration in osteoarthritis patients [28].	Wedang Kunyit in traditionally medicine practice has been used for the treatment of strep throat, gout, rheumatism, hepatoprotective, and boosting the

			immune system [23].
Teh Pegagan: *Centella asiatica, Zingiber officinale, Curcuma xanthorrhiza*	Asiaticoside as immunomodulator in *C. asiatica* and several polyphenolic compounds with anti-inflammatory and antioxidant activity 6-gingerol,6-shogaol, and 8-shogaol as antioxidant from *Z. officinale* Xanthorizol as anti-inflammatory and antibacterial	Leaf extract of *C. asiatica* increased activity of lymphocyte proliferation in mice on the hepatitis-induced Balb/c pathway [29].	*C. asiatica* in Teh Pegagan is traditionally used for the treatment fever, and dementia [29]
Jamu Empon-Empon: *Zingiber officinale* var *Rubrum, Curcuma longa, Curcuma xanthorrhiza, Cymbopogon citratus*	6-gingerol,6-shogaol, and 8-shogaol as antioxidant from *Z. officinale* Curcumin as antioxidant, antivirus, and antiinflamantory pada *C. longa* *Xanthorizol* as antiinflamantory and antibacterial Minyak atsiri and polifenol *C. citratus* memiliki aktivitas antioxidant	Adding the boiled water from *C. citratus* fruit can significantly increase the TAS value (total antioxidant status) in both serum and liver samples of mice induced by diabetes [30].	Jamu Empon-empon has widely used to treat inflammation, bacterial infections, and enhance the body's immune system [31].
Jamu Kunyit Asam: *Tamarindus indica, Curcuma longa*	*T. indica* possess phenol, glicoside, mallic acid,tartaric acid that haave an antioxidant and antiinflamantory activity Curcumin as antioxidant, antivirus, and antiinflamantory in *C. longa*	The flesh of T. indica fruit has found in reducing NO levels and inhibiting pancreatic damage in streptozotocin-induced rats; the results of oral tests on mice also showed analgesic activity and increased recovery in mice induced [32].	Jamu Kunyit Asam is traditional treatment for getting rid of fever, curing constipation, asthma, diabetes, reducing nausea in pregnancy, slimming, and treatment of lung disease [33].
Jamu Pahitan: Daun *Andrographis paniculata, Tinospora cordifolia, Phyllanthus urinaria, Cymbopogon citratus,* Batang *Alstonia Scholaris, Curcuma xanthorrhiza, Zingiber zerumbet, Alpinia galanga, Curcuma aeruginosa*	*A. paniculata* leaves possessed many bioactive andrographolide as imunostimulator and anti-infektion; neoandrographolide proved anti-inflammantory activity; and 14-deoxyandrographolide as imunomodulator; *P. urinaria* leaves have 9 kind of flavonoids and 17 kind of tannin that affected in widely bioactive such as antioxidant , anti-inflamasi, and antivirus [34]; Alkaloids and triterpen from *A. scholaris* leaves as immunomodulatory, antiinflamantory, and antioxidant [35]; *Z. zerumbet* as antioxidant and anti-inflamantory from zerumbone and *α*-humulene [36]	The methanolic extract of *A. paniculata* inhibited 65% NO production by macrophages and significantly inhibited the formation of leg edema in induced rats for continually five days applied (50 mg/day) [26]. Andrographolide inhibits the production of oxygen radicals in neutrophils, inhibits macrophage migration, NF-B activity and TNF- and IL-12 production via the protein kinase C pathway, extracellular signaling-regulated kinase1/2 (ERK1/2) or the PI3K/Akt signaling pathway [37]. *P. urinaria* leaves have been shown to inhibit dengue virus, enteroviruses, hepatitis B virus (HCV) and human immunodeficiency virus (HIV); Antioxidant testing on A. scholaris showed the results of DPPH (63%), FRAP (74.88%), H_2O_2 (72.28%) and ROS (67.66%)[38]; Zingiber zerumbet extract can inhibit the action of cyclooxygenase,	Jamu Pahitan is traditional herbal medicine widely used for beauty treatment, malaria medicine, fever medicine, epilepsy, and asthma[38]

		lipoxygenase, myeloperoxidase and nitric oxide synthase enzymes that play a role in the inflammatory process [37].	
Wedang Secang: *Caesalpinia sappan, Syzygium aromaticum, Cinnamomum verum, Amomum compactum, Zingiber officinale Rosc., Cymbopogon nardus (L.) Rendl*	*C. sappan* has brazilin as a strong antioxidant, protosappanin, and chalcone as an anti-inflammatory and immunomodulator. *S. aromaticum* depends a lot of polyphenols, one of which is eugnol that Has antioxidant, anti-inflammatory, immunomodulatory and antiviral activity. Cineole as antibacterial in *A. compactum* [39].	The aqueous extract of *C. sappan* can extend the allograft survival time in murine skin induced by immune tolerance [40]. *S. aromaticum* exerts an anti-inflammatory and immunomodulatory activity from eugenol by suppressing the action of lipopolysaccharide (LPS) and the nuclear factor-κB (NF-κB) pathway. High antioxidant activity has been tested by various in vitro methods: DPPH, ROS, FRAP, ABTS, and ORAC. Clove extract has an important role in treating memory deficit due to oxidative stress effect which was demonstrated in scopolamine-induced rats. Eugeniin which isolated from extracts of *S. aromaticum* has been known to be antiviral for strains of herpes virus and Hepatitis-C virus by inhibiting viral DNA polymerase enzymes, as well as herpes simplex virus type 1 (HSV-1) and influenza-A virus when combined with acyclovir. [41].	Wedang Secang traditionally used to warm the body, treat colds, treat flatulence and diarrhea, treat sore throat, treat rheumatism and increase stamina[42].

Five of the 9 ingredients obtained, namely Wedang Kunyit, Empon-Empon, Kunyit Asam, Jamu Pahitan, and Wedang Secang have antiviral activity that has been clinically proven against enteroviruses, herpes, HIV, Influenza-A, respiratory syncytial virus (RSV), and Human norovirus (HuNoV) so that it can be a potential treatment agent for COVID-19 [13], [21], [45]. Meanwhile, herbs with immunomodulatory, antioxidant, and anti-inflammatory activities have the potential to prevent COVID-19 and reduce clinical symptoms of COVID-19. Anti-inflammatory agentt is an important mediator in the treatment of COVID-19 due to its application in one of the andgerous threats from SARS-CoV-2 infection is hemophagocytic syndrome (HPS) also called hemophagocytic lymphohistiocytosis [6] and also, macrophage activation syndrome (MAS), a subtype of HPS in which it develops like an autoimmune disease.

This syndrome shows hyperinflammatory symptoms that have been found in the lungs based on hispathological findings. This syndrome occurs due to an attack carried out by the body's immunity resulting in an extreme increase in pro-inflammatory cytokines. This syndrome can be observed through IL-1β, IL-2, IL-6, IL-7, G-CSF1, IP-10, MCP-1α, MIP-1α, TNF-, and sIL2R. The binding of SARS-CoV-19 to the Toll-Like Receptor (TLR) will be followed by the release of pro-IL-1b which is cleaved by caspase-1 which will induce the inflammation and IL-1b mediator activation of pneumonia. Clinical observations showed that the health of some patients deteriorated 6 - 8 days after infection. According to the disease tolerance theory, the most severe cases of COVID-19 could be due in part to an uncontrolled immune response to SARS-CoV-2 infection. This reduction in the inflammatory immune response could be considered a potential therapeutic target against severe COVID-19. Consequently, the suggestion of treat severe COVID-19 with immunomodulatory therapies such as those carried out in HPS is likely to be beneficial for overcoming hyperinflammation and ultimately ameliorating severe clinical syndromes [9]. The anti-inflammatory prevent IL-1b and IL-6 as modulating pro-inflammatory cytokines where there is a storm of pro-inflammatory cytokines in the alveoli.

In RISTOJA's discovery, there were 391 herbal formulas for immunomodulatory that were dominated by turmeric (*Curcuma longa*), betel leaves (*Piper betle* L.), ginger (*Zingiber officinale*). Accordance on our founded of the herbals compound consist by the composition of *Zingiber officinale* as well as the most widely used plant species in the treatment and prevention of COVID-19, followed by *Curcuma zanthorrhiza* and *Curcuma longa*. The types of herbs found showed compatibility with herbal plants recommended by BPOM for the treatment of COVID-19, such as ginger, curcuma, turmeric, meniran, and bitter. There are other medicinal plants recommended by BPOM but not found in this herbal review, namely the fruit and leaves of guava (*Psidium guava L.*). As for the exploration of Indonesian herbal medicines through RISTOJA, the most common ingredients found were herbs for pre/post-partum care which had 321 types of ingredients, followed by open wound herbs (315), malaria ingredients (288), diarrhoea ingredients (255) and hot/hot ingredients. fever (251), ingredients for cancer/tumour (223), tuberculosis (106), and HIV/AIDS (22) [14]. Unfortunately, there is no complete report regarding the composition of the ingredients used. Some herbs in certain ethnic groups must be used with certain rituals or prayers.

Another study conducted by the Ministry of Health to determine the preference for herbal medicine use among Indonesian people in 2010 and 2013 showed that there were 59.12% of the Indonesian population who had consumed herbal medicine (age > 15 years), both men and women, in rural and urban areas with 95.60% of users feeling the benefits. The herbal dosage form that is most preferred by the public is the liquid form, followed by steeping/powder, decoction/chopped, and capsule/pill/tablet form. Basic Health Research Data (Riskesdas) 2013 shows that households that use traditional health services are 30.40%, of which 77.80% choose skills without tools and 49.00% potions [43].

4.2. Herbs – Herbs Interaction in Jamu

Jamu as herbal medicine consists of several medicinal plants within complex bioactive content. The multi-herbs combination would enhance the effectiveness of treatment, consisting of the main component as the primary element in the treatment goal, supporting compounds that help strengthen the effect, then complement or balance. However, not all combinations of medicinal plants can achieve treatment effectiveness some can interact with each other differently, including; (1) a positive synergistic effect indicates that the combined compound has a beneficial interaction, (2) a negative effect indicates that the combined compound eliminate the benefits, and (3) does not synergize indicating that the combined compound does not affect the results of the compound benefit [46].

In addition, certainly pharmacological actions of the active herbal constituents are also needed due to significantly increase as well as be able on more strengthened by other plants instead of its single used [47]. This is possible since the molecules in one herb are not necessarily compounds that are naturally contained but in the form of host-specific metabolites or molecular complexes formed after other herbs co-administration [10].

Table 2. The Interaction into Herbs of Jamu

No	Jamu	Compound Combination	Interaction	Affected Pharmacology
1	Jamu Wedang Jahe	*Z. officinale – C. verum*	Synergistic	+ decrease blood glucose
2	Jamu Temulawak-meniran	*C. zanthorrhiza – P. niruri*	Synergistic	+ antioxidant , + antivirus
3	Jamu Beras Kencur	*Z. officinale – K. galanga*	Synergistic	+ antibacterial
4	Weandg Kunyit	*No reported yet*		
5	Teh Pegagan	*No reported yet*		
6	Jamu Empon-empon	*Z. officinale – K. galanga*	Synergistic	+ decrease blood glucose and colesterol
7		*C. longa – Z. officinale*	Synergistic	+ antibacterial
8	Jamu Kunyit Asam	*T. indica – C longa*	Synergistic	+ antioxidant
9	Jamu Pahitan	*T. cordifolia - Z. officinale*	Synergistic	+ antiinflamantory
10	Wedang Secang	*C. sappan – Z. zerumbet*	Synergistic	+ cytotoxic
11		*Z. officinale – S. aromaticum*	Synergistic	+ antivirus
12		*S. aromaticum – C. verum*	Synergistic	+ antioxidant

Notes: (+) show the increasing of pharmacology activities

Jamu Temulawak-meniran consists of *C. zanthorrhiza* or curcuma, *Phyllanthus niruri* or meniran, and ginger. It was found that there was a synergistic reaction between curcuma and meniran on antioxidant activity. Based on the antioxidant activity of all formulas shown in [48], the highest antioxidant activity (lowest IC50 value) was found in a mixed formula of 50% curcuma extract and 50% meniran extract. The activity of the mixed formula (IC50 9.47) was higher than that of curcuma extract alone (IC50 151.6) and meniran extract alone (IC50 101.91), but not as good as the activity of catechins as a positive control. In addition, the antiviral activity of curcuma and meniran also increased with a concentration of each component of 500 ppm which was indicated by the PCR results on viral cDNA decreasing in Simian Retrovirus Serotype-2 (SRV-2) virus [49].

The components of the jamu *Beras Kencur* include *Kaempferia galanga* (L.), *Oryza sativa* (L.) or rice, and *Zingiber officinale* var. Rubrum or red ginger. The combination of red ginger with *K. galanga* shows a synergistic effect that can increase antibacterial activity against *Staphylococcus aureus* bacteria. The results [49] showed that a single extract of *Z. officinale* had a minimum inhibitory concentration (MIC) of 62.5 g/ml and a minimum bactericidal concentration (MBC) of 125 g/ml, a single extract of kencur had a MIC of 500 g/ml and an MBC of 1000 g. /ml. The results of the combination of *Z. officinale* extract and aromatic ginger extract which increased antibacterial activity, all concentrations of the combined extract showed no growth of *Streptococcus pyogenes* at the lowest concentration of 62.5 g/ml. These results indicated that the combination of *Z. officinale* and *K. galanga* extracts were more effective than single extracts. However, no reports have been found for a combined effect with *Oryza sativa.*

The following herbal formula is a mixture of *Curcuma longa* or turmeric, *Alpinia galanga* or galangal, and *Citrus aurantifolia* or lime. There were no reports related to their interaction. Using turmeric reported could not be allowed in conjunction with other herbal supplements that caused blood clotting, such as capsicum, cloves, garlic, ginger, ginkgo, or red clover. Moreover, combining with lower blood sugar causes, such as alpha-lipoic acid, chromium, or garlic does not permit. In the Wedang turmeric formula, there are no ingredients that will induce an antagonist reaction as well as it is safe to consume. While had piperine from pepper contain bioavailability of curcumin would increase [50].

Centella tea with a mixture of *Centella asiatica*, *Zingiber officinale* or ginger, and *Curcuma zanthorrhiza* or curcuma has not report synergies or antagonist's interaction publication yet. In order to do so, avoid taking *C. asiatica* with other herbal caused drowsiness, such as 5-HTP (5-hydroxytryptophan), jeringa, or valerian. *C. asiatica* has been reported to interfere with blood glucose levels when given concomitantly with hypoglycemic therapy. In addition, the saponoside fraction of plant extracts containing brahmic acid and the derivatives were found to affect infertility in human and rat sperm [51].

There are no compounds found in Centella tea ingredients that cause these negative interactions so they can be safely consumed.

Jamu empon-empon consist of *Zingiber officinale* var Rubrum or red ginger, Curcuma longa or turmeric, *Curcuma zanthorrhiza* or curcuma, *Cymbopogon citratus* or lemongrass. There are studies in ginger consumption published that cannot be combined with turmeric due to significantly lower blood sugar levels agent ($P<0.05$) and control lipid profiles in diabetic-dyslipidemic rats. However, the other report showed the synergistic therapy of both extracts was most significant ($P<0.05$) controlling all parameters of diabetic dyslipidemia (78.00±1.06mg/dL FPG, 62.00±0.58mg/dL TG, 66.50±0, 76mg/dL cholesterol, HDL 32.00±0.36mg/dL, LDL 22.43±0.64 mg/dL, and VLDL 12.40±0.12mg/dL). Additionall, reports of relief from liver cirrhosis after carbon tetrachloride-induced poisoning in rats, as ginger alone or either in combination with curcumin at 100 mg/kg ameliorated liver injury in animals. In addition, another report at 200,400 mg/kg strengthened the activity of antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase) while decreasing the activity of liver function enzymes (alanine transaminase, aspartate aminotransferase) in acetaminophen-induced liver [52]. Synergistic activity was also found in galangal and lemongrass through their increasing antibacterial activity compared to a single application. The profile of the combination of galangal oil and lemongrass oil (volume ratio 3:7, 1:1, and 7:3) was tested against four pathogenic microorganisms (Staphylococcus aureus 0.5% and 4%, v/v, against Pseudomonas aeruginosa 40% and > 40% v/v, against Streptococcus bovis 0.25% and 0.5%, v/v, and against Candida albicans 0.25% and 0.5%, v/v). Synergistic activity was best recorded for only one ratio (volume ratio 3:7). This investigation provides evidence of their interaction as an herbal combination within the minimum effective dose [53].

Jamu tamarind-turmeric is reported to have a very strong antioxidant synergism greater than the synthetic antioxidant BHT which resembles vitamin E which is widely used by the food industry as a preservative [54]. Jamu Pahitan that have the most herbal medicinal compositions are *Andrographis paniculata* or sambiloto leaves, *Tinospora cordifolia* or bratawali leaves, *Phyllanthus urinaria* or meniran leaves, Cymbopogon citratus or lemongrass, *Alstonia scholaris* or pulai stems, *Curcuma xanthorrhiza*, *Zingiber zerumbet* or lempuyang, *Alpinia aeruginosa* or temu hitam. Single or synergistic formulations of *Tinospora cordifolia* with *Zingiber officinale* have been traditionally used in rheumatoid arthritis the treatment. *Tinospora cordifolia* has been reported to influence the proliferation, differentiation, and mineralization of bone-like as the matrix by in vitro osteoblast model system that is referred a potential anti-osteoporosis agent. The alcoholic extract of *Tinospora cordifolia* has been shown to stimulate osteoblast growth, promote cell differentiation into osteoblastic lineages and also increase mineralization of bone-like matrix [55]. The combination between *Tinospora cordifolia* and *Andrograhis paniculata* considered increasing its hepatoprotective activity. It was observed that AHPL/AYTAB/0613 significantly reduced levels of serum glutamic-oxaloacetic transaminase, serum glutamic pyruvic transaminase, alkaline phosphatase, total bilirubin, and also significantly increase the total protein level which has been tested in paracetamol-induced rats [50].

Wedang Secang consists of *Caesalpinia sappan* or sappan, *Syzygium aromaticum* or clove, *Cinnamomum verum*, *Amomum compactum* or cardamom, *Zingiber officinale*, *Cymbopogon nardus* (L.) Rendl. Secang extract and lempuyang rhizome showed a cytotoxic effect on MCF-7 cells with IC50 values of 30 and 155 g/mL, respectively. 0.57-0.85. The combination of 15 g/mL cup with 8 and 24 g/mL lempuyang showed cell cycle inhibition in the G2/M phase. The combination of the two also enhanced the occurrence of apoptosis induction compared to the control and single treatment. The combination of ethanolic extract of secang wood and lempuyang rhizome produces a synergistic cytotoxic effect. Combined synergism occurs through inhibition of the cell cycle in the G2/M phase and induction of apoptosis [56]. Ginger and clove extracts have been tested for synergistic interactions as antivirals. Indeed, nevermore do detect an antiviral effect when host cells pretreated with the extracts. Clove and ginger extracts significantly decreased feline calicivirus (FCV) infectivity in virus pretreatment and in coinfection and post-infection treatment but not in cell pretreatment. Eugenol may not be the only antiviral compound in clove extract and extracts in combination with ginger may induce viral inactivation than eugenol alone [56]. The combination of clove and cinnamon extracts also showed a synergistic effect in increasing the cytotoxicity of Hep G2 cancer cells and increasing DPPH radical scavenging [56]. All the herbal-herbal interactions found has summarized in Table 2.

4.3. Jamu Aplication for COVID-19 Treatment

Considering aspects in the using herbal medicine for the treatment of COVID-19 published in [21]. First, the product must be sure of its safety. Although for a long time does jamu used no clinical evidence, especially for COVID-19 treatment. The use of jamu for therapeutic purposes in COVID-19 is focused on symptom reduction as they generally show the best benefit in ongoing chronic post-infection symptoms rather than the acute stage [57]. Second, the evidence of the herbal safety and efficacy should obtain based on clinical trials. In traditional medicine in Indonesia, herbal medicines that have been clinically tested are called Fitofarmaka. The herbs are herbs that have not been standardized or clinically tested. Indonesia through the Food and Drug Supervisory Agency has issued a guidebook for the Original Indonesian Modern Medicine Informatorium (OMAI) during the COVID-19 Pandemic, in which there are 15 Leveraged Herbal Medicines for 5 groups to relieve symptoms of COVID-19 and increase immunity, as well as 10 Phytopharmacal to maintain immunity [15]. Jamu as a traditional medicine used for generation to generation can be analysed for its feasibility through efficacy data obtained from in-vitro and in-vivo studies as a rationale for use in the prevention and reduction of COVID-19 symptoms.

Third, the molecular mechanisms that underlie the pharmacological effects of herbal medicine in the treatment of COVID-19 remain unclear. So far, the available data were obtained from in-silico analysis. In addition, hesperidin, a flavonoid found in Citrus sp. The fruit peel, which is popularly championed as natural prevention of COVID-19 in Indonesia, is reported to have strong binding to human angiotensin-converting enzyme-2 (hACE-2) and RNA-dependent RNA polymerase (RdRp) as potential targets for SARS-CoV-2 infection [58]. The potential danger of delay in treatment due to consumption of herbal medicine must be known because herbal medicines are sold as over-the-counter products and can be accessed without a doctor's prescription, their use as COVID-19 self-medication by patients who experience symptoms is very possible [59]. Jamu and other herbal medicines generally should not be used in emergency conditions, including in the acute phase of viral infection. Delays in getting proper treatment for COVID-19 cases lengthen the recovery process. In fact, in some cases, this delay would fatal if the virus continues to replicate rapidly in the patient's body.

There has been no publication of detailed reports regarding the clinical use of jamu for COVID-19 treatment patients in Indonesia yet, either alone or in combination with modern medicine. In contrast to treatment in China through the guidelines, Traditional Chinese Medicine (TCM) has been used in the treatment of COVID-19 patients. There are 23 provinces in China that have adopted guidelines for the use of TCM and issued programs on COVID-19 prevention, while 26 provinces have officially established integrative TCM that combines TCM with clinical treatment for COVID-19 patients [21]. More than 85% of the total confirmed COVID-19 patients are reported to have been treated with TCM. Treatment with integrative medicine was given to all COVID-19 cases in Shanghai, while the first patient who recovered in Beijing was also treated with this combination drug [15]. In the Chinese Guidelines, TCM is used for the treatment of mild, moderate, severe, and convalescent stages of COVID-19. As of January 2020, the total confirmed cases treated by TCM have reached 60,107. In 102 cases of mild symptoms that were treated with TCM, the time of onset of clinical symptoms was 2 days faster, body temperature recovery time was 1.7 days shorter, the average length of hospitalization was 2.2 days faster, and the rate of CT images increased by 22%. In addition, in the treatment of acute patients, the mean length of hospitalization and time to PCR to negative has been 2 days shorter [60].

The research results and predictions of the interaction of active compounds from herbal plants in the composition of herbal ingredients with the COVID-19 virus from the types of herbs found from information on herbal formulas for COVID-19 are presented in Table 3. Based on the in silico test, all herbs contain herbal plants that have the potential to be a candidate for COVID-19 drugs because they can bind to the target of drug action on SAR-CoV-2 (Mpro, Spike Protein, Spike glycoprotein, RdRp, and Nonstructural Polyprotein) or the target site of viral infection to humans (ACE2). The herbal medicine with the highest number of herbal plants found to be able to bind to the target of the SAR-CoV-2 drug is Jamu Pahitan, which has 6 types of herbal plants that have a high affinity for the target. Then, herbal medicine wedang secang has 3 types of plants that are capable of affinity. Antiviral activity in Jamu Wedang Secang is likely to work more effectively it is due to the synergistic effect between ginger and clove which can increase antiviral activity. However, there is no clinical evidence regarding the use of herbal medicine for COVID-19 patients.

Table 3. Prediction of Phytochemical Activity of Herbal Plants from Jamu

Herbal Plan	Bioactive Compound	Prediction of Bioactive – SAR-CoV-2	Ref
Cinnamomun verum	Bergamol	Docking was carried out on protein targets including the major protease SARS-CoV-2 (SARS-CoV-2 M^{pro}), SARS-CoV-2 endoribonucleoase (SARS-CoV-2 Nsp15/NendoU), SARS-CoV-2 ADP−ribose−1″ phosphatase (SARS-CoV-2 ADRP), SARS-CoV-2 RNA-dependent RNA polymerase (SARS-CoV-2 RdRp), SARS-CoV-2 spike protein binding domain (SARS-CoV-2 rS), and human angiotensin converting enzyme ($hACE_2$) to bergamol essential oil. The docking results showed the affinity of bergamol to each target protein in sequence: 98.0kJ/mol, 91.2kJ/mol, 105.9kJ/mol, 71.9kJ/mol, −63.6kJ/mol, and 83.6kJ/mol respectively. However, this docking score is considered too high or too low affinity when compared to the comparison molecule so it is not feasible. The presence of binding to the target protein indicates that cinnamon can still prevent COVID-19, not as a candidate that can be used as a drug.	[61]
Citrus aurantifolia	Naringin	Naringin pretreatment significantly inhibited the expression of HMGB1 protein and LPS-induced proinflammatory cytokines (COX-2, iNOS, IL-1β and IL-6) in in vitro expression assays. HMGB1 is a ubiquitous DNA-binding core protein and can be actively released by immune cells, such as macrophages and monocytes, following inflammatory stimuli. HMGB1 also acts as a pro-inflammatory cytokine and regulates cytokine storm, increasing cytokines such as TNF-, IL-6, IL-1β, and IL-8.	[62]
Zingiber officinale	6 – Gingerol	In the molecular docking test between gingerol and COVID-19 virus RNA binding protein (6W4B), N-Terminal RNA Binding Protein (6VSB), spike glycoprotein (6M3M) showed binding affinities of -11.4082 KJ/mol, -12.9523 KJ/mol and -12.8835 KJ/mol. Molecular interactions between the spike glycoprotein COVID-19 virus and Gingerol make the hydrogen bond interactions with Val42, Pro58, Ser60, Thr68 change form an unbond interaction with Arg40, Phe41, Val42, Phe57, Pro58, Lys59, Ser60, Ile66, Thr68, Ile92 residues from spike COVID-19 glycol protein.	[63]
Curcuma xanthorrhiza	Xanthorrhizol	Xanthorrhizol has anti-inflammatory activity by inhibiting inflammatory cytokines in adipose tissue and expression of tumor necrosis factor (TNF-α). This studies have shown that xanthorrhizol prevents changes in immune cells in adipose tissue so that it can downregulate inflammatory cytokine genes. Xanthorrhizol also has the activity of reducing the expression of the interleukin gene (IL-1β) in muscle. Another study showed that xanthorrhizol can reduce serum IL-6 levels and increase serum transformation growth factor (TGF-β) in SLE patients with hypovitamin D.	[63]
Phyllanthus niruri	Phyllanthin	The docking results for 6W41 and 5R7Y proteins showed a score of -84.20kCal/mold and -90.65kCal/mol which indicated the ability of the ligand inhibitor. Binding to 6W41 inhibited viral infiltration, while binding to 5R7Y was predicted to inhibit viral translation and replication.	[64]
Kaempferia galangal and *Alpinia galanga*	Galangin	Molecular docking was performed on the selected protein targets, namely RBD-S (PDB ID:6LXT), PD-ACE2 (PDB ID: 6VW1), and the SARS-CoV-2 protease (PDB ID: 6LU7). Galangin, phenylpropane from galangal was proven to bind three receptors with lower energy than the reference compound used: -12.96Kcal/mol, -7.89Kcal/mol, and -7.60Kcal/mol, respectively. These findings indicate that the two compounds have better binding interactions and can inhibit initial viral infection to host cells.	[65]
Curcuma longa	Curcumin	The anti-inflammatory mechanism of curcumin is by inhibiting the production and release of proinflammatory cytokines, such as IL-1, IL-6, IL-8, TNF-a. Curcumin also showed good binding affinity for nucleocapsids (ΔG = -8.75 kcal/mol, Ki=0.39μM), nsp10 (ΔG = -7.85kcal/mol, Ki = 1.77μM) which was comparable to ivermectin with nucleocapsids. (ΔG =-7.11 kcal/mol,Ki = 6.17 M) and nsp10 (ΔG =- 9.82 kcal/mol, Ki = 63.20nm), and remdesivir with nucleocapsid(ΔG = -6.30 kcal /mol, Ki = 23.94) and nsp10(ΔG = -6.54 kcal /mol, Ki = 16.02 M)	[66], [67]
Centella asiatica	Aciatic acid	Docking was carried out on the main protease SARS-CoV-2 (6LU7) with Centella asiatica. The results showed that the asiatic acid derivative AA9 had the best affinity for inhibiting the main protease SARS-CoV-2 with a binding free energy (∆G) value	[68]

		of -9.90 kcal/mol, compared to favipiravir which had a G value of -4. 58 kcal/mol. AA9 also interacts with the main protease of SARS-CoV-2 via hydrogen bonding with Gly143. This study demonstrated that asiatic acid and its derivatives have a higher binding affinity for the main protease SARS-CoV-2 compared to favipiravir.	
Cymbopogon citratus	Citronela and patchouli alkolhol	Inhibition of citronella essential oil from C. citratus against ACE2 showed an affinity value of -4.8kCal/mol and Patchuoli alcohol alcohol -6.9kCal/mol. Patchuoli alcohol scores were higher than the control so that C. citratus essential oil had potential antiviral activity through its active compound patchouli alcohol. Predictably, patchouli alcohol can inhibit Asn 667 and Ser 701 APN by hydrogen bonding.	[69]
Tamarindus indica	Tripsin (Tamarin Tripsin Inhibitor/ TTI)	Molecular docking studies have been carried out to model the binding interactions of various pro-inhibitors of 3CL and other proteases, such as TMPRSS2 (37,82-84). The pTTI-derived peptide also proved to be a strong candidate to block this protease because TTI is known to inhibit the serine protease co-operating with SARS-CoV-2 infection and characterize neutrophil activity in viral-induced lung injury. In addition, trypsin acid inhibitors (TTIs) exhibit several beneficial effects on the reduction of inflammatory markers (tumor necrosis factor [TNF-α], leptin) and biochemical parameters (fasting glycemia, triglycerides, and very low-density lipoprotein [VLDL]), in addition to to improve pancreatic functional and mucosal integrity in obesity models. Thus, TTI can contribute to combating two severe overlapping problems with high costs and complex social implications, obesity and COVID-19.	
Caesalpinia sappan	Brazilein	Molecular docking was performed on the selected protein targets, namely RBD-S (PDB ID:6LXT), PD-ACE2 (PDB ID: 6VW1), and the SARS-CoV-2 protease (PDB ID: 6LU7). Brasilien was shown to be able to bind to three receptors with lower energy than the reference compound used, namely -10.52 Kcal/mol, -7.56 Kcal/mol, and -7.43Kcal/mol, respectively.	[65]
Syzygium aromaticum	Eugnol	The results of the molecular docking test showed that the compound eugenol was very potential as an inhibitor of Mpro COVID-19 with the Angiotensin Converting Enzyme 2 (ACE2) receptor. Eugenol is also reported to have a good affinity of -6.3 kcal/mol to inhibit the COVID-19 protease.	[70]
Amomun compactum		*No publication yet*	-
Andragraphis paniculata	Andrograph olide	Docking analysis of the compound with the SARS-CoV-2 protease yielded a negative value for the free energy of the binding site -3.094357 KJ/mol, indicating a high affinity for the binding pocket. All binding conformations of the compound in the active binding pocket involve H-bond and salt bridge interactions. These compounds indeed bind proteases with 4 hydrogen bonds with 3 residues, namely Gly143, Cys145 and Glu166. Andrographolide successfully docked at the SARS-CoV-2 Mpro binding site. The computational approach also predicts this molecule to have good solubility, pharmacodynamic properties and target accuracy. This molecule also complies with Lipinski's rules, which makes it a promising compound for further biochemical and cell-based assays to explore its potential for use against COVID-19.	[71]
Tinospora cordifolia	Tinosporasi de	Docking between viral protein and Tinosporaside ligand resulted in affinity scores for Spike protein (-5.7kCal/mol), Main Protease (-7.9kCal/mol), and RNA dependent RNA polymerase virus (-6.6kCal/mol). in the prediction tool, Swiss-ADME, a cheminformatics platform was used to predict the pharmacokinetics and potential drug contingencies from phytoconstituents indicating that there would be no adverse pharmacokinetic-pharmacodynamic herb-drug interactions with concomitant drug therapies.	[72]
Phylanthus urinaria	Quercetin and quercitrin	In the molecular docking test, the compounds quercetin and quercitrin in meniran were able to bind to Mpro from SARS-CoV-2 (lowest binding energy for quercitrin -10.36 kcal/mol, -8.47 kcal/mol for quercetin). Mpro is an enzyme that plays an important role in viral replication, binding to this protein will make bioactive compounds an inhibitor and prevent viral replication.	[73]

5. SUGGESTIONS FOR FURTHER DEVELOPMENT

In future research, it is hoped that it will be able to analyze herbal-drug interactions so that the potential and threats to the use of herbs together with modern medicines can be identified. Multiherbal interactions also need to be analyzed simultaneously for all components of herbal medicine to determine the overall interaction. Prediction of the interaction of all polyherbals from herbal medicine to the target of COVID-19 virus treatment also needs to be done as a holistic analysis.

6. CONCLUSION

There are 9 types of herbs from 22 types of herbal plants that have been widely used by the community in COVID-19 therapy. These herbal ingredients are widely used to increase endurance and relieve symptoms caused by COVID-19. There were no negative or antagonistic interactions between the herbal ingredients in each herb, so it was safe to consume without losing the efficacy of each plant, but instead was able to increase the pharmacological activity of several compounds such as anti-inflammatory, antibacterial, antiviral, antioxidant, and hepatoprotective activities. The results of the in silico test on each component of the herbal medicine show that all types of herbal medicine contain herbal plants that have the potential to be COVID-19 drugs. Most of the inhibitory activity was found in Jamu Pahitan and Wedang Secang. In addition to being a candidate for COVID-19 treatment, all herbs can be used to prevent COVID-19 233w by increasing immunity and reducing risk factors for each symptom. However, no field evidence has been found regarding the use of herbal medicine as a single therapy or in combination with modern medicine for COVID-19 patients in Indonesia.

AUTHORS' CONTRIBUTIONS

All of authors have made substantial and intellectual contribution to the work article, and given approval for the final version of manuscript.

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