

ETHNOBOTANICAL STUDY OF MEDICINAL PLANT USAGE DURING COVID-19 PANDEMIC: A COMMUNITY-BASED SURVEY IN INDONESIA

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ABSTRACT

Before the availability of a vaccine, Indonesian population relied on traditional medicines to prevent COVID-19. Any species used by indigenous people could lead to further investigations in modern pharmacology, to preserve ancient knowledge, and to plan for plants' conservation. The study aimed to discover and record species, methods of preparation, route of administration, and motivation in using medicinal plants by the Indonesian population during the COVID-19 pandemic. Participants of survey were selected from the people who live in Java and Bali for responding to an online structured questionnaire. Relative Frequency of Citation (RFC) was employed in the quantitative analysis of the collected data. The pharmacological relevance of the five plants with the highest RFC was further reviewed. The results showed that respondents used 59 plants from 28 families. Five species with the highest RFC were *Curcuma longa* (0.707), *Zingiber officinale* (0.674), *Cymbopogon citratus* (0.269), *Kaempferia galanga* (0.174), and *Curcuma zanthorrhiza* (0.165). Most plants were prepared by boiling (77.97%) and administered orally as a single ingredient or mixed with other herbals. Respondents believed that the plants were beneficial as immune-booster (71.26%), maintain good health (24.85%) and stamina (12.28%), and prevent viral infection, including COVID-19 (5.39%). The most commonly used plants might be scientifically based to boost immunity. However, their usage against COVID-19 and the medicinal value of herbal mixtures should be further investigated.

Keywords: COVID-19, Ethnobotany, Indonesia, Medicinal plants

INTRODUCTION

Corona Virus Disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). It was found in China in December 2019 and spread to other countries, including Indonesia. The first two confirmed COVID-19 cases in Indonesia were reported on March 2, 2020, and the numbers keep rising since then (Djalante *et al.* 2020). Based on history, previous SARS-CoV coronavirus also caused an outbreak in China in 2003.

The genetic sequence analysis showed that SARS-CoV-2 was similar around 79% to SARS-CoV. Thus, most of the studies on its prevention and medication were adopted from the previous outbreak (Ghaffari *et al.* 2020).

The Indonesian Ministry of Health released health protocols to prevent and control COVID-19 (HK.01.07/MENKES/382/2020), which included the suggestion to wear masks, washing hands frequently, social distancing, and immunity enhancement through clean and healthy living behavior. During the SARS outbreak, natural medicine showed beneficial effects in preventing and treating patients, particularly in high-risk subjects (Boozari &

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Hosseinzadeh 2020; Y. Li *et al.* 2020). The usage of medicinal plants as a prophylaxis measure against COVID-19 was also recommended by Ayurveda and Traditional Chinese Medicine (Boozari & Hosseinzadeh 2020; Khanal *et al.* 2020; Vellingiri *et al.* 2020). Further, many studies have proven the antiviral, anti-inflammatory, and immunomodulatory properties of medicinal plants that are potentially helpful to combat viral diseases (Lin *et al.* 2014; Khanna *et al.* 2020).

Indonesia has abundant natural resources in plant species and the local people have used them as herbal remedies. Some of the ethnobotanical studies recorded the importance of Indonesian biodiversity as traditional medicines in different health conditions (Nahdi & Kurniawan 2019; Taek *et al.* 2019; Jadid *et al.* 2020). Those studies are significantly important to converse precious indigenous knowledge and publish them as academic literature. In the present study, we conducted an online survey to identify the use of medicinal plants by the Indonesian population during the COVID-19 pandemic. The comprehensive data from respondents on the species of medicinal plants, method of preparation and administration, as well as motivation to use, were documented. While antivirus and vaccines

are vital, the research on natural medicine regarding COVID-19 may be used as a reference to develop new drug candidates and as home-based remedies in the future that are inexpensive, commonly, and easily implemented in society. The study aimed to discover and to record species, methods of preparation, route of administration, and motivation in using medicinal plants by the Indonesian population during the COVID-19 pandemic.

MATERIALS AND METHODS

Study Area

A survey was conducted in Java and Bali Island (Figure 1), which consist of 7 provinces, namely Special Capital Region of Jakarta ($6^{\circ}12'S$, $106^{\circ}49'E$), Banten ($6^{\circ}30'S$ $106^{\circ}15'E$), West Java ($6^{\circ}45'S$ $107^{\circ}30'E$), Central Java ($7^{\circ}30'S$ $110^{\circ}00'E$), Special Region of Yogyakarta ($7^{\circ}47'S$ $110^{\circ}22'E$), East Java ($7^{\circ}16'S$ $112^{\circ}45'E$), and Bali ($8^{\circ}20'06''S$ $115^{\circ}05'17''E$). All the regions have diverse ethnicities such as Bantenese in Banten, Balinese in Bali, and Javanese in other regions. Respected to the ethnicity, each of the regions has its traditional language. However, natives speak Indonesian in their daily lives.

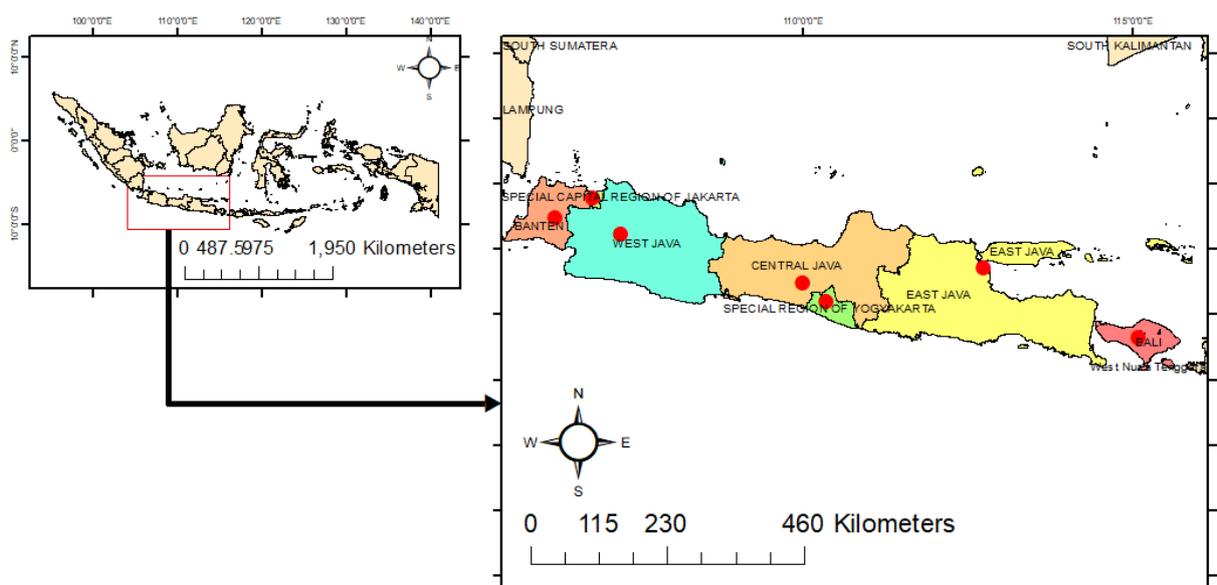


Figure 1 Study area of the ethnobotanical survey in 7 provinces in Indonesia

Data Collection

A cross-sectional study was undertaken using a self-administered and structured questionnaire. The questionnaire consisted of three parts that aimed to collect the respondents demographic characteristics, medicinal plants data, and respondents' motivation using the plants during the pandemic. The data collection was carried out by online survey from June to August 2020. The questionnaire was in Indonesian and examined by two experts in pharmacy and Bahasa Indonesia fields then piloted among 30 participants to ensure its validity before being used to collect data. A guide to estimate the minimum sample size of respondents required for this study based on the formula (Pourhoseingholi *et al.* 2013).

$$n = \frac{z^2 p(1-p)}{d^2}$$

Where:

Z = The statistic corresponding to level of confidence.

P = Expected prevalence of COVID-19.

d = Precision.

In this study, the respondents included indigenous people living in Java and Bali islands and consuming medicinal plants during the COVID-19 pandemic in Indonesia. The respondents' motivation to use the plants was also recorded. Any dubious data that could not be confirmed was excluded. The questionnaire and methodology for this study were approved by the Faculty of Medicine, Udayana University (Ethics approval number: 1195/UN14.2.2.VII.14/LT/2020).

Plant Identification

The scientific names of medicinal plants reported by respondents were determined using cross-references between their local names and database in Indonesian Herbal Pharmacopeia, Indonesian Herbal Formulary (PERMENKES NO.6/2016), and Indonesian Traditional Medicine Formulary (HK.01.07/MENKES/187/2017). Herbal specimens could not be collected due to the strict travel restrictions regulated by the Indonesian government during the COVID-19 pandemic in the study area. The scientific names of the reported

plants were checked with The Plant List website (accessed on January 8, 2021, <http://www.theplantlist.org>).

Data Analysis

The collected data were evaluated by using Microsoft Office Excel (2016) spreadsheets. Further, quantitative data analysis to show the local importance of each plant species was demonstrated by using the relative frequency of citation (RFC) (Aziz *et al.* 2017). with the formula below:

$$RFC = FC/N (0 < RFC < 1)$$

Where:

FC = Number of informants mentioning a particular species.

N = Total number of respondents

RESULTS AND DISCUSSION

Indonesia is an inhabitant of about 80% of the world's medicinal plants which local people use to prevent and cure many ailments (Elfahmi *et al.* 2014). In the current study, an online survey was conducted to collect data regarding medicinal plant usage by Indonesian during the COVID-19 pandemic. The respondents were limited to those who were native and living in 8 provinces in the two most densely populated islands in Indonesia (Java and Bali islands) (Table 1). Moreover, based on the Indonesian government's official website (www.covid19.go.id), most of the confirmed COVID-19 cases were located in both islands and the prevalence reached 82.2%. Based on the prevalence of COVID-19 and the statistic corresponding to the level of confidence is 1,96 with a precision of 5%, the minimum number of respondents for this study was 224 respondents. However, in this study, 344 respondents participated and this number exceeded the minimum sample.

As shown in Table 1, 82.04% (274) of respondents were female. This result is in line with several studies (Villena-Tejada *et al.* 2021; Brahmi *et al.* 2022; Odebunmi *et al.* 2022). Which indicated the domination of females in using medicinal plants. This predominance is probably related to several factors such as women being more familiar with medicinal plants because they

are also being used as cooking ingredients. Correspondingly, in most populations, women are believed to bear the responsibility for the family health needs causing them to be more informed about using medicinal plants than their male counterparts (Torres-Avilez *et al.* 2016). In the current study, most of the respondents came from the Province of Bali. A Hindu-most populated area in Indonesia (Statistics Indonesia 2010). The Balinese are well known for their local wisdom called Usada, a traditional medicine inspired by the Hindu holy book Ayurveda (Muderawan *et al.* 2020). Age is

another sociodemographic factor contributing to the use of medicinal plants. Several studies found that older age was the main user of traditional medicine (Rahayu *et al.* 2020). On the contrary, 67.37% (225) of respondents in this study were 20 to 40 years old. Indicating the younger age group was also interested in using medicinal plants during the pandemic of COVID-19. Similar survey studies conducted in Algeria and Morocco during the pandemic also showed similar results (Belmouhoub *et al.* 2021; Brahmi *et al.* 2022; Chebaibi *et al.* 2022).

Table 1 Demographic characteristics of respondents

Characteristic	Number of Respondents (n = 334)	Percentage (%)
Gender		
Male	60	17.96
Female	274	82.04
Province of Origin		
Special Capital Region of Jakarta	13	3.89
Banten	2	0.60
West Java	35	10.48
Central Java	8	2.40
East Java	24	7.19
Special Region of Yogyakarta	6	1.80
Bali	246	73.65
Age (years)		
< 20	35	10.48
20 – 40	225	67.37
> 40	74	22.16
Religion		
Islam	66	19.76
Hindu	247	73.95
Protestant	12	3.59
Catholic	8	2.40
Buddha	1	0.30

Table 2 Medicinal plants used by respondents during the COVID-19 pandemic in Indonesia

Family	Scientific Names	Local Names (Indonesia)	Common Names (English)	Part used	Method of Preparation ^a	RFC ^b	Motivation of use ^c	Reported from ^d
Acanthaceae	<i>Andrographis paniculata</i> (Burm.f.) Nees	<i>Sambiloto</i>	Green chiretta	Leaves	Boil	0.030	A, B, D, E	1, 5, 7
Amaryllidaceae	<i>Allium cepa</i> L.	<i>Bawang merah</i>	Shallot	Bulb	Boil, burning, eaten directly	0.006	B	6,7
	<i>Allium sativum</i> L.	<i>Bawang putih</i>	Garlic	Bulb	Eaten directly	0.063	A-E	3-7
Anacardiaceae	<i>Spondias pinnata</i> (L.f) Kurz.	<i>Cemcem</i>	Common hog-plum	Leaves	Cold infusion	0.006	B	7
Annonaceae	<i>Annona muricata</i> L.	<i>Sirsak</i>	Soursop	Leaves	Boil	0.015	A-D	3,7
Apiaceae	<i>Apium graveolens</i> L.	<i>Seledri</i>	Celery	Leaves	Boil	0.003	B	3
	<i>Centella asiatica</i> (L.) Urb.	<i>Pegagan</i>	Asiatic pennywort	Leaves	Boil, eaten directly	0.021	A,B,D,E	7
	<i>Coriandrum sativum</i> L.	<i>Ketumbar</i>	Coriander	Fruit	Boil	0.012	A,B,D,E	3, 5, 7
	<i>Foeniculum vulgare</i>	<i>Adas</i>	Fennel	Fruit	Boil	0.003	B	4

Family	Scientific Names	Local Names (Indonesia)	Common Names (English)	Part used	Method of Preparation ^a	RFC ^b	Motivation of use ^c	Reported from ^d
Arecaceae	Mill. <i>Cocos nucifera</i> L.	Kelapa	Coconut	Fruit (water & oil)	Eaten directly	0.009	B	7
Asteraceae	<i>Blumea balsamifera</i> (L.) DC.	Sembung	Buffalo-ear	Leaves	Boil	0.006	B,D	7
	<i>Gynura procumbens</i> (Lour.) Merr.	Sambung nyawa	Longevity spinach	Leaves	Boil	0.003	B	6
	<i>Pluchea indica</i> (L.) Less.	Beluntas	Indian camphorweed	Leaves	Boil	0.009	B	7
	<i>Sonchus arvensis</i> L.	Tempuyung	Perennial Sow-thistle	Leaves	Boil	0.003	B	7
Basellaceae	<i>Anredera cordifolia</i> (Ten.) Steenis	Binabong	Gulf madeiravine	Leaves	Boil	0.003	B	1
Caricaceae	<i>Carica papaya</i> L.	Pepaya	Papaya	Leaves	Boil	0.003	E	3
Fabaceae	<i>Caesalpinia sappan</i> L.	Secang	Brazilwood	Wood	Boil	0.027	A-E	3-7
	<i>Clitoria ternatea</i> L.	Bunga telang	Asian pigeonwings	Flower	Boil	0.009	A,D	5, 7
	<i>Erythrina variegata</i> L.	Dadap	Tiger's claw	Leaves	Boil	0.003	A,D	7
Lamiaceae	<i>Tamarindus indica</i> L.	Asam jawa	Tamarind	Fruit	Boil	0.060	A-E	1, 3-7
	<i>Mentha piperita</i> L.	Pipermin	Peppermint	Leaves	Hot infusion	0.009	A,B,D,E	2, 3, 7
	<i>Peronema canescens</i> Jack	Sungkai	False elder	Leaves	Boil	0.003	B	3
Lauraceae	<i>Cinnamomum burmanni</i> (Nees & T.Nees) Blume	Kayu manis	Batavia cinnamon	Bark, Leaves	Boil, burning, cold and hot infusion	0.114	A-E	1-7
Malvaceae	<i>Hibiscus sabdariffa</i> L.	Rosela	Roselle	Flower	Boil	0.003	B	7
Meliaceae	<i>Azadirachta indica</i> A.Juss	Mimba	Neem	Leaves	Eaten directly	0.003	B	7
Moraceae	<i>Artocarpus altilis</i> (Parkinson ex F.A.Zorn) Fosberg	Sukun	Breadfruit	Leaves	Boil	0.003	B	7
Moringaceae	<i>Moringa oleifera</i> Lam.	Kelor	Drumstick tree	Leaves	Boil, hot infusion	0.045	A-E	3-7
Myrtaceae	<i>Melaleuca cajuputi</i> Powell	Kayu putih	Cajuput	Oil	N/A	0.003	C	1,7
	<i>Syzygium aromaticum</i> (L.) Merr. & L.M.Perry	Cengkeh	Clove	Flower	Boil, hot infusion	0.048	A-E	2-7
	<i>Syzygium polyanthum</i> (Wight) Walp.	Salam	Indonesian bay leaf	Leaves	Boil	0.021	A-E	3, 5-7
Oleaceae	<i>Olea europaea</i> L.	Zaitun	Olive	Fruit (Oil)	Eaten directly	0.003	B	3
Pandanaceae	<i>Pandanus amaryllifolius</i> Roxb.	Pandan	Pandan	Leaves	Boil	0.003	A,D	2
Phyllanthaceae	<i>Sauropus androgynous</i> (L.) Merr.	Katuk	Sweet leaf	Leaves	Cold and hot infusion	0.021	A,B,D,E	7
	<i>Phyllanthus niruri</i> L.	Meniran	Gale of the wind	Leaves	Boil, hot infusion	0.009	A,B	5, 7
Piperaceae	<i>Piper betle</i> L.	Sirih	Betel	Leaves	Boil, eaten directly	0.072	A-E	1, 3
	<i>Piper crocatum</i> Ruiz & Pav.	Sirih merah	Celebes pepper	Leaves	Boil	0.072	B	7
	<i>Piper nigrum</i> L.	Lada	Black pepper	Seed	Boil	0.003	B	3
	<i>Piper retrofractum</i> Vahl	Cabai jawa	Javanese long pepper	Fruit	Boil	0.003	E	7
Poaceae	<i>Cymbopogon citratus</i> (DC.) Stapf.	Serai dapur	Lemongrass	Stem, Leaves	Boil, hot infusion	0.269	A-E	1-7
	<i>Oryza sativa</i> L.	Beras	Rice	Starch	Cold infusion	0.024	A,B,D,E	3-7
Ranunculaceae	<i>Nigella sativa</i> L.	Jintan hitam	Black seed	Seed	Boil	0.012	A,B,E	3, 5, 7
Rutaceae	<i>Citrus aurantiifolia</i> (Christm.) Swingle	Jeruk nipis	Egyptian lime	Fruit	Juiced, boil, hot and cold infusion	0.177	A-E	1-7
	<i>Citrus hystrix</i> DC.	Jeruk purut	Kaffir lime	Leaves, Fruit	Boil	0.006	B,E	6
	<i>Citrus limon</i> (L.) Osbeck	Lemon	Lemon	Fruit	Cold and hot infusion	0.108	A-E	1, 3-5, 7
	<i>Citrus reticulata</i>	Jeruk	Mandarin	Fruit	Eaten directly	0.021	A,B,E	4, 7

Table 3 Plants mixture used by respondents during the COVID-19 pandemic in Indonesia (continued)

Plants	Mixture No.*																														
	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	
<i>C. asiatica</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	
<i>C. sativum</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	
<i>F. vulgare</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	
<i>C. sappan</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	+	-	-	-	+	-	-	+	+	-	
<i>C. ternatea</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>T. indica</i>	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-	-	
<i>M. Piperita</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	
<i>P. canescens</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>C. burmanni</i>	-	-	-	-	-	-	+	-	+	+	-	-	-	+	-	-	-	-	-	+	-	-	+	+	-	+	+	-	+	-	
<i>A. altilis</i>	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>S. aromaticum</i>	-	-	-	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-	+	-	+	-	-	-	+	+	-	+	-	
<i>S. polyanthum</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	
<i>O. europea</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>P. amaryllifolius</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>S. androgynous</i>	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>P. niruri</i>	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>P. betle</i>	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	
<i>P. crocatum</i>	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>P. retrofractum</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	
<i>C. citratus</i>	-	-	-	-	+	+	-	-	-	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<i>C. aurantiifolia</i>	-	+	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	+	
<i>C. lemon</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	-	-	-	-	
<i>I. verum</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	
<i>A. Galanga</i>	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-	-	
<i>B. pandurate</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	
<i>C. longa</i>	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	
<i>C. zanthorrhiza</i>	-	-	-	-	-	-	-	+	-	-	+	-	+	-	+	-	+	-	-	+	+	+	+	+	+	+	+	+	+	+	
<i>C. zedoaria</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>A. compactum</i>	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	+	-	
<i>K. galangal</i>	+	+	+	+	-	+	-	+	+	-	-	-	-	-	-	-	-	-	-	+	+	+	+	-	-	-	-	+	+	+	
<i>K. rotunda</i>	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	+	
<i>Z. officinale</i>	+	+	+	+	+	+	+	+	+	-	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
<i>Z. officinal var. rubrum</i>	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Z. zerumbet</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	
Total plants mixed	4	4	4	4	4	4	4	4	4	4	4	4	5	5	5	5	5	5	5	6	6	6	6	6	6	7	7	7	8	9	10

Notes: + = plants available in mixtures. * All mixtures were prepared by boiling and administered orally

Table 4 Method of preparation for medicinal plants used during the COVID-19 pandemic in Indonesia

Category	Frequency	%*
Boil	46	77.97
Eaten directly	6	10.17
Cold Infusion	18	30.51
Hot Infusion	8	13.56
Burning	5	6.78

Notes: *some of the plants were prepared by more than one method. Thus, the total percentage may not add up to 100%.

Table 5 The motivation for medicinal plants used by respondents during the COVID-19 pandemic in Indonesia

Category	Frequency	%*
to boost the immune system	238	71.26
to keep healthy	83	24.85
to build stamina	41	12.28
other motives	41	12.28
to prevent virus infection, including COVID-19	18	5.39

Notes: *some respondents reported more than one reason for herbal use. Thus, the total percentage may not add up to 100%.

The present study revealed that respondents used 59 species of medicinal plants from 28 families (Table 2) both singly or in herbal mixtures (Table 3). Additionally, most of the plants were prepared by boiling and then consumed orally (Table 4). Indonesian traditional medicine in the form of polyherbal drinks has existed for generations so called *lolob* (in Bali) and *jamu* (in Java). Some of the reported plants in the present study that are also used in *lolob* formulation namely *S. pinnata*, *B. balsamifera*, *E. variegata*, *C. burmanni*, *C. asiatica*, *A. indica*, *P. amaryllifolius*, *P. niruri*, *S. androgynous*, *P. betle*, *C. aurantiifolia*, *C. zanthorrhiza*, *K. rotunda*, *Z. officinale*, and *Z. zerumbet* (Sujarwo *et al.* 2015). Similarly, other reported plants were commonly available in *jamu* formula such as *C. verum*, *C. aurantifolia*, *Z. officinale* var. *Rubrum*, *T. indica*, *A. galanga*, *C. longa*, *C. zanthorrhiza*, *P. niruri*, *K. galanga*, *O. sativa*, and *P. amaryllifolius* (Elfahmi *et al.* 2014; Hartanti *et al.* 2020). These plants were empirically used for various medicinal purposes (Elfahmi *et al.* 2014; Sujarwo *et al.* 2015). Further, the current study revealed that respondents consumed *Jamu Kunyit Asam* and *Jamu Beras Kencur* during the pandemic (Table 3, Mixture No. 5 and No. 9, respectively). The composition of herbal mixtures could be varied according to individual preferences and local recipes. For example, Mixture No.20, 29, 45, 52, and 59 in Table 3 showed the variation of *Jamu Kunyit Asam*. However, there was limited data related to the efficacy of the modified version of *jamu* formula. Further research should be conducted to support the use of those herbal mixtures in term of efficacy test.

Most respondents believed that the plants' consumption was beneficial during the pandemic because they could enhance immunity, maintain health and stamina, and prevent viral infection (Table 5). A study showed that the interest in and use of immune-related herbals worldwide increased during the COVID-19 pandemic (Hamulka *et al.* 2020). Other ethnopharmacological studies confirmed the usage of medicinal plants such as *A. cepa*, *A. sativum*, *C. asiatica*, *C. papaya*, *T. indica*, *C. burmanni*, and *C. longa* to boost immunity by traditional healers and society in various health conditions (Siew *et al.* 2014; Anywar *et al.* 2020; Oladele *et al.* 2020; Lin *et al.* 2021). Meanwhile,

review studies confirmed the benefit of natural immune enhancer intakes such as *A. panniculata*, *A. sativum*, *M. piperita*, *M. cajuputi* essential oil, *C. sinensis*, *N. sativa*, and *Z. officinale* to prevent COVID-19 and improve overall patient health (Boozari & Hosseinzadeh 2020; Sen *et al.* 2020; Silveira *et al.* 2020).

Some of the medicinal plants reported in the current study have been also recommended by the Indonesian Ministry of Health (HK.02.02/IV.2243/2020) to maintain well-being and prevent illness during the pandemic. In the official announcement, six herbal mixtures consisting of *Z. officinale* var. *rubrum*, *C. aurantiifolia*, *C. verum*, *C. longa*, *A. galanga*, *C. asiatica*, *C. zanthorrhiza*, *K. galanga*, *P. amaryllifolius*, *M. oleifera*, and *A. sativum*. The mixtures were recommended to boost the immune response and also have similar preparation and administration methods as reported in this study. Likewise, *C. longa*, *Z. officinale*, *C. verum*, and *P. nigrum* also have been recommended by the Indian Ministry of AYUSH (Ayurveda, Yoga, and Naturopathy, Unani, Siddha, and Homeopathy) to boost immunity as a prophylaxis measure against COVID-19 (Khanal *et al.* 2020).

The beneficial effect of medicinal plants as immune-enhancer against COVID-19 should be confirmed scientifically. In viral diseases, the infection could be fought by the host's immune response. When viruses infect the host cells, innate immunity blocks virus replication, promotes virus clearance, stimulates tissue repair, and activates a prolonged adaptive immunity (G. Li *et al.* 2020). Moreover, viral infection and inflammation of lung tissues are observed in COVID-19. Thus, the antiviral and inflammatory activities of medicinal plants are essential properties to combat COVID-19 (Khanal *et al.* 2020). On the other hand, it should be noticed that the immune system is complicated and highly regulated by numerous molecular and cellular events. Therefore, immunity enhancement may be either valuable or destructive to the organism, depending on the overall degree of modulation and the pathophysiological condition (Gertsch *et al.* 2011).

Based on the calculation of RFC, five plants had the highest scores: *C. longa*, *Z. officinale*, *C.*

citratius, *K. galanga*, and *C. xanthorrhiza*. Therefore, further literature review in the current study was highlighted for those plants. Turmeric (*C. longa*) contains curcumin, a polyphenol with various pharmacological actions. The compound showed immunomodulation activity through several mechanisms, especially by regulating inflammatory factors (Tasneem *et al.* 2019; Behl *et al.* 2021). Likewise, the polysaccharide extract from turmeric could enhance the immune system (Yue *et al.* 2010). A computational study regarding anti-SARS-CoV-2 showed that curcumin exhibited a high potency to block the virus's main protease (C19M^{pro}), which plays an important role in the viral replication process. Curcumin had lower binding energy to C19M^{pro} than other compounds from *P. nigrum*, *Z. officinale*, *N. sativa*, *S. aromaticum*, *A. sativum* and *A. cepa* (Ibrahim *et al.* 2020).

Ginger (*Z. officinale*) contains some compounds with anti-inflammatory and immunomodulatory activities such as 6-gingerol, 6-shogaol, zingerone, and 6-paradol (Choi *et al.* 2018). An alcohol extract was reported to induce phagocytosis by macrophages in mice while crude extract increased humoral and cell-mediated immune responses (Gautam *et al.* 2020). Meanwhile, another molecular docking evaluation showed the ability of zingiberene, 6-gingerol, zingerone, gingerenone-A, 6-shogaol, and 6-dehydrogingerdione to block C19M^{pro}. But their potencies were considerably low due to higher binding energies than N3 inhibitor as control (Garg *et al.* 2020).

An *in vivo* and *in vitro* study revealed the immunomodulatory effect of water extract and essential oil from lemongrass (*C. citratius*). The water extract with linalool oxide and epoxy-linalool as major compounds could prevent the production of IL-1 β but induce IL-6 production by macrophages. Meanwhile, its essential oils which contained neral and geranial could inhibit cytokine production *in vitro* (Sforcin *et al.* 2009). Moreover, geraniol, another compound in its essential oil, inhibited the S1 subunit in spike proteins of SARS-CoV-2 through a docking simulation (Wani *et al.* 2020).

The rhizome part of cutcherry (*K. galanga*) is rich in bioactive compounds such as ethyl-p-methoxycinnamate and diarylheptanoids with anti-inflammatory and immunomodulation activity (Jagadish *et al.* 2016; Yao *et al.* 2018). Its

polysaccharides isolate enhanced the immunoregulation capability of CD4⁺ T cells (Yang *et al.* 2018). Furthermore, a computational study exhibited the activity of its bioactive compounds (kaempferol, kaempferol glycosides, and acylated kaempferol glucoside derivatives) to block the 3a channel protein of SARS-CoV. Inhibition of this channel would inactivate virus production and allow the host to build up its immunity system (Schwarz *et al.* 2014). Another docking investigation indicated that kaempferol, due to its hydroxyl, ketone, and ether groups, was a stronger C19M^{pro} inhibitor than other tested natural compounds (Khaerunnisa *et al.* 2020).

The crude polysaccharide extract of Javanese turmeric (*C. xanthorrhiza*) could enhance the immune system by activating of NF-kappaB (Kim *et al.* 2007). Xanthorrhizol and *C. xanthorrhiza* extract significantly inhibited the production of inflammatory cytokines, such as tumor necrosis factor-alpha, interleukin-6 and -1 β , and C-reactive protein (Kim *et al.* 2014). Moreover, curcumin, demethoxycurcumin, and bisdemethoxycurcumin in *C. xanthorrhiza* (similar compounds also contained in *C. longa*) showed their potential as C19M^{pro} inhibitors (Khaerunnisa *et al.* 2020; Sumaryada & Pramudita 2020). However, another study revealed that their inhibition actions were lower than nelfinavir, a protease inhibitor used as a drug standard (Khaerunnisa *et al.* 2020). Meanwhile, another docking investigation on the similarity of active sites exposed that bisdemethoxycurcumin had a greater ability to inhibit the binding pocket of C19M^{pro} than N3 inhibitor, as the control ligand (Sumaryada & Pramudita 2020).

Other plants with lower RFC values (Table 2) such as *A. galanga* and *A. paniculata*, *Citrus sp.*, *C. sinensis*, *S. androgynous*, *F. vulgare*, *O. europea*, and *A. graveolens* also confirmed to have immunomodulatory properties and potential against COVID-19 (Elfahmi *et al.* 2014; Khaerunnisa *et al.* 2020; Utomo *et al.* 2020). Regarding COVID-19, most of the antiviral studies of medicinal plants and their compounds were based on computational methods and resulted in a preview of their potential against COVID-19. Though some of the reported medicinal plants showed low molecular potency in blocking target sites, it is necessary to

highlight that the immunomodulatory actions support their beneficial role during the COVID-19 pandemic. Further pre-clinical and clinical investigations are needed to warrant their efficacy as health-promoting agents against COVID-19. These ethnobotany research results may be necessary to anticipate another trans-boundary animal or plant diseases pandemic by studying their bioactive compound for pharmacopeia studies in more detail.

CONCLUSION

During the COVID-19 pandemic, there were 59 medicinal plants belonging to 28 families used by Indonesian. The plants were prepared mainly by boiling and administered orally. Based on the RFC value, the most important plants were *C. longa*, *Z. officinale*, *C. citratus*, *K. galanga*, and *C. zanthorrhiza*. Also, respondents believed that those plants could boost immunity, maintain health and stamina, and prevent COVID-19. In general, the medicinal plants reported in the current studies were confirmed by scientific literature to be beneficial as immune-booster during the COVID-19 pandemic. Meanwhile, their ability to block SARS-CoV-2 infection was mainly studied only through molecular docking evaluations. More research should be conducted to ensure their potency against SARS-CoV-2 and their efficacy when used as a single ingredient or in mixtures with other herbs. Also, actions should be taken to preserve the community's traditional knowledge of using medicinal plants.

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