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Standardization of Ginger and Javanese Turmeric Crude Drugs and Total Flavonoid and Phenolic Content Profiles of Their Combination

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ABSTRAK

A combination of ginger (*Zingiber officinale* Roscoe) and Javanese turmeric (*Curcuma zanthorrhiza* Roxb.) rhizomes is used by Baturraden, Central Java, people to treat an ailment called *masuk angin*. This study aimed to evaluate the quality profile of ginger and Javanese turmeric crude drugs and determine the total flavonoid content (TFC) and the total phenolic content (TPC) of combinations of both crude drugs in five different weight ratios. Standardization of crude drugs used parameters, methods, and standards of the compendial Indonesian Herbal Pharmacopeia (IHP). Ginger crude drugs met the standard in parameters of morphology, loss on drying, acid-insoluble ash, ethanol extractable, and water extractable, while morphology and values of loss on drying, acid-insoluble ash, ethanol extractable, water extractable, and volatile content of Javanese turmeric were within their respective specifications. The TFC of Javanese turmeric is lower than that of ginger, but the opposite trend was observed for TPC. The crude drug weight ratio significantly affected the TFC and TPC of the ginger and Javanese turmeric combination. The combination with the highest TFC and TPC was Formula IV (7.11±0.37 mg Quercetin equivalent (QE)/g) and Formula II (21.65±1.49 mg Gallic acid equivalent (GAE)/g), respectively. Our study suggested that ginger and Javanese turmeric crude drugs were not of good quality, and their mixture in weight ratio of 25-75 provided the highest TPC warrant for further bioactivity evaluations.

Keywords: Crude Drugs, Polyherbal Combination, Quality Profile, Total Flavonoid Content, Total Phenolic Content

1. INTRODUCTION

Zingiberaceae plants have been long used as a staple ingredient of *jamu* in Indonesia. For example, ginger (*Zingiber officinale* Roscoe) and Javanese turmeric (*Curcuma zanthorrhiza* Roxb.) have been proven to contain bioactive compounds supporting their extensive traditional uses (Widyowati and Agil, 2018). Ginger is used for the traditional treatment of asthma, colds, cough, diarrhea, osteoporosis, stomachache, rheumatism, and vomiting (Shahrajabian et al., 2019).

Flavonoids, phenolic compounds, terpenoids, and vanilloids are the metabolites of ginger, with volatile oils as the most characterized ones. Ginger has been reported to show analgesic, androgenic, anti-Alzheimer's disease, anticancer and antitumor, antidiabetic, anti-hypercholesterolemia, antihyperlipidemic, antihypertensive, anti-inflammatory, antimicrobial, antioxidant, immunomodulatory, insecticidal, and melanogenesis inhibitory activities (Hamad et al., 2023; Zhang et al., 2022).

Javanese turmeric is traditionally used for appetite boosting and treating arthritis, constipation, diarrhea, fevers in children, hemorrhoids, leukorrhea, liver-related problems, skin eruption, and stomach disorders. The main secondary metabolites of this plant are curcuminoids, terpenoids, and volatile oils with a dominant constituent of xanthorrhizol. Javanese turmeric extracts have been evaluated for various pharmacological activities, i.e., antibacterial, anticancer and antitumor,

antidiabetic, antifungal, anti-inflammatory, antioxidant, hepatoprotective, and insecticidal, with some producing promising results (Rahmat et al., 2021).

People in Baturraden, Central Java, used a combination of ginger and Javanese turmeric decoction to treat *masuk angin*, which is defined as an ailment generally characterized by light headache, malaise, mild fever, and muscle soreness. Baturraden people use both plant materials in the form of fresh rhizomes or crude drugs (Triratnawati, 2011; Utaminingrum et al., 2021). The quality of crude drugs available in the community may vary significantly with genetics, plant development, environment, harvest and post-harvest processing, and storage conditions as the factors.

The quality of crude drugs can be divided into three aspects, i.e., identity, purity, and quality. The quality of a given crude drug directly affects its safety and efficacy, which was closely correlated to purity and content, respectively (Al-Harrasi et al., 2022; Das et al., 2019). Hence, it is important to standardize the quality of ginger and Javanese turmeric crude drugs to ensure their safety and efficacy during use. In addition, crude drug standardization is mandatory for those intended as the raw materials for standardized herbal medicines (*obat herbal terstandar*) and phytomedicines (*fitofarmaka*).

Flavonoids and phenolic compounds are well-known for their potent antioxidant properties, related to their role in scavenging free radicals. They can be quantitatively enumerated with total flavonoid content (TFC) and total phenolic content (TPC) analysis. The higher TFC and TPC in a given crude drug generally generated higher antioxidant activities (Hartanti et al., 2023b).

Herbal formulation should have components with the main, intended, activity and components with supporting activities to show good efficacy (Afendi et al., 2016). In the case of ginger and Javanese turmeric combination, antioxidant is one of those supporting activities, while anti-*masuk angin* is the main activity. Hence, TPC and TFC can be used as a measure to predict the efficacy of the combination in the *masuk angin* treatment.

This study aimed to standardize ginger and Javanese turmeric crude drugs and evaluate the TFC and TPC profile of both crude drugs when used individually and in combination with three different weight ratios. The findings of this research will provide information on the weight ratio of the combination containing the highest flavonoid and phenolic compound contents potentially studied further for their *masuk angin*-related bioactivities.

2. METHODOLOGY

2.1 Materials

Ginger and Javanese turmeric crude drugs were purchased from *Wisata Kesehatan Jamu* (WKJ) Kalibakung, Tegal. Reagents (Aluminum chloride, Chloral hydrate, and Follin Ciocalteau), reference compounds (Gallic acid and Quercetin), and solvents (acetone, chloroform, deionized water, ethanol, methanol, and n-toluene) were from Millipore Sigma (US).

2.2 Standardization of crude drugs

The identity aspect was characterized by parameters of macroscopic and microscopic morphology. The purity aspect was evaluated by parameters of loss on drying, total ash, and acid-insoluble test. The content aspect was characterized by ethanol extractable, water extractable, and volatile compound content parameters. Methods for all parameter evaluations and standard values followed those in Indonesian Herbal Pharmacopeia (IHP) (Indonesian MoH, 2017).

2.3 Preparation of crude drug mixture

Ginger and Javanese turmeric crude drugs were separately pulverized into fine powders. Both powdered crude drugs were mixed in a specified weight ratio to obtain five formulations (Table 1).

Table 1. Formulations of ginger and Javanese turmeric crude drug mixture

Formulation	Proportion (%)	
	Ginger	Javanese turmeric
Formula I	0	100
Formula II	25	75
Formula III	50	50
Formula IV	75	25
Formula V	100	0

2.4 Extraction

The crude drug mixture of each formulation was extracted with water in a ratio of 1:20 over a water bath at 110°C for 30 min. The extract was obtained by filtration and was freshly used for the determination of total flavonoid content (TFC) and total phenolic content (TFC).

2.5 Determination of total flavonoid total

The water extract was properly diluted and reacted with an Aluminum chloride solution according to a previous report (Hamad and Hartanti, 2023). A calibration curve of Quercetin ($y = 0.0085x + 0.1897$, $R^2 = 0.9626$) was utilized to calculate the TFC of each formulation. It was

calculated from the relationship of the concentrations and absorbances of five-series Quercetin solutions.

2.6 Determination of total phenolic total

The water extract was properly diluted and reacted with Folin-Ciocalteau solution according to a previous report (Hamad and Hartanti, 2023). A calibration curve of Gallic acid ($y = 0.0076x + 0.1665$, $R^2 = 0.9697$) was utilized to calculate the TPC of each crude drug mixture. It was obtained from the relationship of the concentrations and absorbances of five-series Gallic acid solutions.

2.7 Data analysis

The normally distributed TFC and TPC were individually evaluated by one-way ANOVA and Duncan's test (n=3). The analysis was conducted by SPSS ver. 26, with significant effect and difference assigned at p-value <0.05.

3. RESULTS AND DISCUSSIONS

The morphological characteristics of both crude drugs were highly similar to the standard described in the IHP. The ginger rhizome is a slightly flattened plate, with an elongated oval shape, the outer layer is rough, and the inner layer is smooth with fibrous, protruding, short fractures. The outer layer is yellowish brown, the inner one is yellowish white, and fibers with a bluish hint, with a characteristic odor and spicy and pungent taste.

On the other hand, the Javanese turmeric rhizomes are round or slightly oblong slices, light-weight, hard, easily broken, wrinkled outer surface, yellow to brown, irregularly curved slice area, uneven, with dusty fracture marks. The inside is orange-yellow to bright orange-brown, with a distinctive aromatic odor and sharp and bitter taste. The color of Javanese turmeric rhizome widely varied from light yellow to brownish orange according to plant accession and correlated to the phytochemical profiles (Minarni et al., 2023).

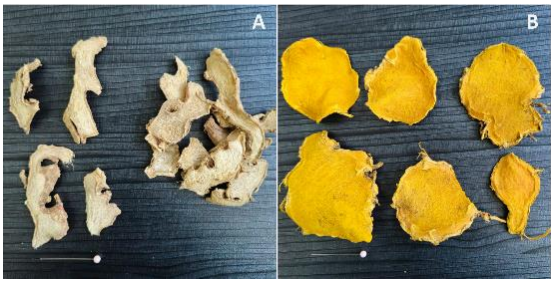

Figure 1. Macroscopic characteristics of ginger (A) and Javanese turmeric (B) crude drugs

About 80% of the diagnostic fragments of each crude drug were observed. The periderm of ginger and the parenchymal cortex of Javanese turmeric were not observed. Hence, the identity of the crude drugs was confirmed to be correct based on their macroscopical and microscopical morphology characters. Xylem and xylem elements are particularly important for powder microscopic ginger identification, with various distinctive forms, i.e. reticulate, scalariform, and helical. Big-sized oleoresin cell is also an important identity fragment of ginger (Gavrilova et al., 2022).

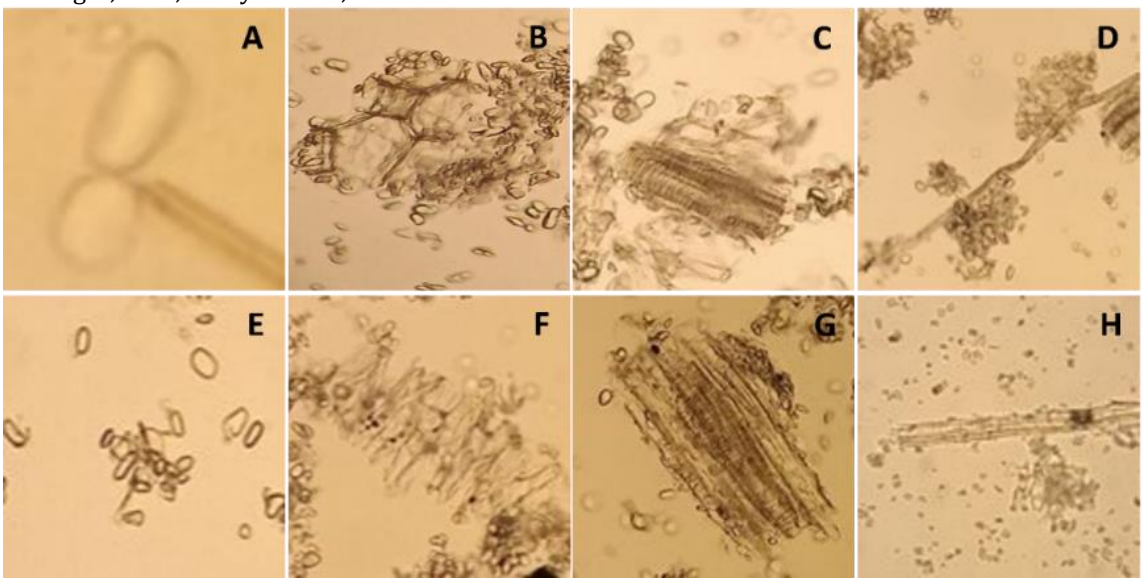

Figure 2. The diagnostic fragments of ginger (upper panel) and Javanese turmeric (lower panel) crude drugs, showing starch granules (A), cork in longitudinal view (B), xylem (C), fiber (D), starch granules (E), cork in tangential view (F), xylem (G), and sclerenchyma (H)

Table 2. The quality character profile of ginger and Javanese turmeric crude drugs

Parameters	Ginger		Javanese turmeric	
	Value	Standard	Value	Standard
Loss on drying (%)	9.4±0.1*	Not more than 10	8.6±0.3*	Not more than 10%
Total ash (%)	5.6±0.1	Not more than 4.2	5.7±0.3	Not more than 4.8
Acid-insoluble ash (%)	1.0±0.1*	Not more than 3.2	0.5±0.0*	Not more than 0.7
Ethanol extractable (%)	9.3±0.8*	Not less than 5.7	10.6±0.2*	Not less than 3.6
Water extractable (%)	17.2±2.1*	Not less than 15.8	16.4±0.9*	Not less than 9.1
Volatile content (%)	0.04±0.02	Not less than 0.80	1.80±0.10*	Not less than 1.20

*: The parameter is within the specified value

Ginger crude drugs met all requirements, except for total ash and volatile content. On the other hand, the values of loss on drying, acid-insoluble ash, ethanol extractable, water extractable, and volatile content of Javanese turmeric were within the specification. Hence, both crude drugs did not meet the standard for the total ash. Nevertheless, Javanese turmeric was of good quality in the content aspect.

Loss on drying and ash contents represented the purity aspect of a crude drug quality related to the microbial and heavy metal contamination risk, respectively. This aspect particularly modified the safety of the crude drug during use (Al-Harrasi et al., 2022). The loss on drying of ginger crude drugs in this study was comparable to those collected and dried in Enrekang, South Sulawesi, while that of Javanese turmeric was much lower than one from Ponorogo, East Java (Aziz et al., 2019; Syarifuddin et al., 2023).

Both crude drugs did not meet the standard for acid-insoluble ash. Medicinal plants might take siliceous and other earthly materials up during cultivation or post-harvest processing, which might end up with higher ash contents in crude drugs (Luo et al., 2020). As we bought crude drugs from WKJ Kalibakung, we don't know where the plant grown and how they were processed. Nevertheless, our result was lower than the total ash and acid-insoluble ash of Javanese turmeric crude drug originating from Malang, East Java (Cesarika and Syafah, 2018).

Ethanol extractable, water extractable, and volatile content represented content aspects of crude drug quality. This aspect is directly related to the compounds responsible for the bioactivity of a given crude drug during use. The ethanol and water extractable are particularly essential for crude drugs with unknown bioactive compounds, which indicated a quantitative measure of semi-to-nonpolar and polar compounds, respectively (Al-Harrasi et al., 2022).

The extractable matter of a given crude drug is widely varied according to post-harvest processing and extraction methods (Hamad and Hartanti, 2023; Yap et al., 2020). Similarly, volatile compound content also ranged depending on the seasonal, developmental, processing, and distillation method (Ajayi et al., 2016; Usai et al., 2016).

Table 3. Profile of TPC and TFC of ginger and Javanese turmeric crude drug mixtures

Formulation	TFC (mg QE/g)	TPC (mg GAE/g)
Formula I	1.10±0.02^{A}	21.65±1.49^{e}
Formula II	3.89±0.24^{B}	19.09±1.09^{d}
Formula III	5.47±0.13^{D}	12.50±0.38^{c}
Formula IV	4.32±0.04^{C}	8.55±0.20^{b}
Formula V	7.11±0.37^{E}	2.28±0.06^{a}

Different superscripted upper-case alphabets represented different TFCs, and lower-case ones represented different TPCs

Baturraden people utilize ginger and Javanese turmeric rhizome combinations in the form of decoction (Utaminingrum et al., 2021). Hence, in this study, the evaluation of TFC and TPC was subjected to the water extract of the combination of both crude drugs. Individually, ginger rhizomes contained higher levels of flavonoids but lower levels of phenolic compounds than Javanese turmeric in this study. Flavonoids have been detected in ginger rhizomes from Malang and Riyadh, Saudi Arabia (Alfuraydi et al., 2024; Lukiati et al., 2020).

Flavonoids, i.e., catechin, epicatechin, kaempferol, naringenin, quercetin, and rutin have been putatively detected in ginger rhizomes (Ghasemzadeh et al., 2010). On the other hand, the abundant phenolic compounds in Javanese turmeric rhizomes have also been reported from Bengkulu and Bogor, West Java (Minarni et al., 2023; Suryani et al., 2022). Curcuminoids are the main phenolic compounds of Javanese turmeric, with minor ones, i.e., 13-hydroxy-xanthorrhizol, 3-hydroxy-6-methyl acetophenone, dehydro-6-gingerdione, and vanillin have also been identified (Rahmat et al., 2021).

The weight ratio of ginger and Javanese turmeric crude drugs in the mixtures statistically affected their TFC (p=0.000) and TPC (p=0.000). The higher proportion of Javanese turmeric

generated formulation with a lower TFC. Hence, the ginger-only formulation (Formula V) showed the highest TFC. The opposite trend was observed in TPC, in which the Javanese turmeric-only formulation (Formula I) showed the highest TPC among other formulations.

Our results suggested that the mixture with the highest TFC and TPC were those containing 50-50 and 25-75 weight ratios of ginger and Javanese turmeric, respectively. The main bioactive compounds of ginger are gingerol and shogaol, while those of Javanese turmeric are curcuminoids and volatile oil (Indiarto et al., 2021; Rahmat et al., 2021). Curcuminoids, gingerol, and shogaol are phenolic compounds, and hence, TPC is more appropriate to be used as the marker to predict the efficacy of the combination of ginger and Javanese turmeric. From this point of view, a mixture with a higher TPC warrants further bioactivities evaluation should be Formula II.

The use of plant material combinations is preferable to those of single plants only. Polyherbal formulations might generate a synergistic interaction effect between their components, which eventually results in better efficacy or lower toxicity (Parasuraman et al., 2014; Yap et al., 2023). In addition, gingerol and shogaol from ginger with their spicy nature might improve the taste of the mixture, which would increase the acceptability and compliance during the use (Indiarto et al., 2021).

The different TPCs observed in a mixture with a different component weight ratio in this study were previously also reported in Indonesian and Malaysian polyherbal formulations (Hartanti et al., 2023a; Rahim et al., 2020). TFC of ginger and Javanese turmeric formulations was weakly correlated to their TPC ($r=0.210$, $p=0.759$). Hence, their phenolic compounds were likely not flavonoids. The phenolic compounds in ginger are gingerdiones, gingerol, gingerones, paradol, shogaol, and zingerol, while those of Javanese turmeric are curcuminoids and derivatives of vanillin and xanthorrhizol (Rahmat et al., 2021; Styawan et al., 2022).

4. CONCLUSIONS

Ginger crude drugs did not meet the standard for total ash and volatile content, while the total ash value of Javanese turmeric was not within the specification. The TPC of Javanese turmeric is higher than that of ginger. The crude drug mixture recommended for further evaluation of bioactivities is Formula II, with the weight ratio of both crude drugs 75-25.

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REFERENCES

Afendi, F.M., Rudi Heryanto, Darusman, L.K., Syahrir, N.H.A., Bakri, R., Qomariasih, N., 2016. Jamu informatics: A new perspective in jamu research. CICSJ Bull. 34, 47–52. https://doi.org/10.11546/cicsj.34.47

Ajayi, E.O., Sadimenko, A.P., Afolayan, A.J., 2016. GC–MS evaluation of Cymbopogon citratus (DC) Stapf oil obtained using modified hydrodistillation and microwave extraction methods, Food Chemistry. https://doi.org/10.1016/j.foodchem.2016.04.071

Al-Harrasi, A., Bhatia, S., Kaushik, D., Behl, T., Chigurupati, S., 2022. Standardization and quality control of crude drugs, in: Al-Harrasi, A., Bhatia, S., Kaushik, D., Behl, T., Chigurupati, S. (Eds.), Recent Advances in Natural Products Science. CRC Press, Boca Raton, pp. 210–234.

Alfuraydi, A.A., Aziz, I.M., Almajhdi, F.N., 2024. Assessment of antioxidant, anticancer, and antibacterial activities of the rhizome of ginger (Zingiber officinale). J. King Saud Univ. – Sci. 6, 103112. https://doi.org/10.1016/j.jksus.2024.103112

Aziz, Y.S., Ardyanto, M., Ikhza, M., 2019. Standarisasi parameter non spesifik simplisia rimpang kunyit (Curcuma domestica) dan temulawak (Curcuma xanthorrhiza Roxb.) di Kabupaten Ponorogo. J. Delima Harapan 6, 89–94.

Cesarika, E., Syafah, L., 2018. Pengaruh metode pengeringan rimpang temulawak, temugiring dan kunyit terhadap parameter non spesifik. Akademi Farmasi Putera Indonesia Malang.

Das, C., Bose, A., Mallick, S., Das, D., 2019. Development of standardization parameters of crude drugs used in Ayurvedic Balarista formulation. Orient. Pharm. Exp. Med. 19, 455–467. https://doi.org/10.1007/s13596-019-00386-w

Gavrilova, A., Gavrilov, G., Trifonova, D., 2022.

Contribution to the microscopic identification of Zingiberis rhizoma. Pharmacia 69, 93–97. https://doi.org/10.3897/pharmacia.69.e78304

Ghasemzadeh, A., Jaafar, H.Z.E., Rahmat, A., 2010. Identification and concentration of some flavonoid components in Malaysian young ginger (Zingiber officinale Roscoe) varieties by a high performance liquid chromatography method. Molecules 15, 6231–6243. https://doi.org/10.3390/molecules15096231

Hamad, A., Djaliasrin, A.D., Hartanti, D., 2023. Galangal and ginger essential oils exerted microbial growth inhibitory activity and preservation potential on tofu. Food Res. 7, 27–34. https://doi.org/10.26656/fr.2017.7(S1).7

Hamad, A., Hartanti, D., 2023. Effects of extraction time on total phenolic and flavonoid contents and antioxidant activities of a polyherbal drink. IOP Conf. Ser. Earth Environ. Sci. 1200, 012047. https://doi.org/10.1088/1755-1315/1200/1/012047

Hartanti, D., Chatsumpun, N., Kitphati, W., Peungvicha, P., Supharattanasitthi, W., 2023a. The standardized Jamu pahitan, an Indonesian antidiabetic formulation, stimulating the glucose uptake and insulin secretion in the in-vitro models. Heliyon 9, e14018. https://doi.org/10.1016/j.heliyon.2023.e14018

Hartanti, D., Chatsumpun, N., Sa-ngiamsuntorn, K., Supharattanasitthi, W., Kitphati, W., Peungvicha, P., 2023b. The physicochemical properties, antioxidant and antidiabetic activities, and hepatic safety profile of an Indonesian antidiabetic polyherbal formulation. Indones. J. Pharm. 34, 65–78. https://doi.org/10.22146/ijp.3243

Indiarto, R., Subroto, E., Angeline, Selly, 2021. Ginger rhizomes (Zingiber officinale) functionality in food and health perspective: A review. Food Res. 5, 497–505. https://doi.org/10.26656/fr.2017.5(1).361

Indonesian MoH, 2017. Indonesia Herbal Pharmacopeia, 2nd ed. Minister of Health, Jakarta.

Lukiati, B., Sulisetijono, Nugrahaningsih, Masita, R., 2020. Determination of total phenol and flavonoid levels and antioxidant activity of methanolic and ethanolic extract Zingiber officinale Rosc var. Rubrum rhizome. AIP Conf. Proc. 2231, 040003. https://doi.org/10.1063/5.0002657

Luo, L., Wang, B., Jiang, J., Fitzgerald, M., Huang, Q., Yu, Z., Li, H., Zhang, J., Wei, J., Yang, C., Zhang, H., Dong, L., Chen, S., 2020. Heavy metal contaminations in herbal medicines: Determination, comprehensive risk assessments, and solutions. Front. Pharmacol. 11, 595335. https://doi.org/10.3389/fphar.2020.595335

Minarni, M., Asyhar, R., Juliana, D., Yudha, Y.S., Nurcholis, W., 2023. Analysis of rhizome color and phytochemical content of 10 accessions of Curcuma zanthorrhiza Roxb. in Jambi, Indonesia. Biodiversitas 24, 149–155. https://doi.org/10.13057/biodiv/d240119

Parasuraman, S., Thing, G.S., Dhanaraj, S.A., 2014. Polyherbal formulation: Concept of ayurveda. Pharmacogn. Rev. 8, 73–80. https://doi.org/10.4103/0973-7847.134229

Rahim, N.F.A., Muhammad, N., Abdullah, N., Talip, B.A., Poh, K.H., 2020. The interaction effect and optimal formulation of selected polyherbal extracts towards antioxidant activity. Food Res. 4, 2042–2048. https://doi.org/10.26656/fr.2017.4(6).281

Rahmat, E., Lee, J., Kang, Y., 2021. Javanese turmeric (Curcuma xanthorrhiza Roxb.): Ethnobotany, phytochemistry, biotechnology, and pharmacological activities. Evidence-Based Complement. Altern. Med. 2021, 9960813. https://doi.org/10.1155/2021/9960813

Shahrajabian, M.H., Sun, W., Cheng, Q., 2019. Clinical aspects and health benefits of ginger (Zingiber officinale) in both traditional Chinese medicine and modern industry. Acta Agric. Scand. Sect. B — Soil Plant Sci. 69, 546–556. https://doi.org/10.1080/09064710.2019.1606930

Styawan, A.A., Susidarti, R.A., Purwanto, Windarsih, A., Rahmawati, N., Sholikhah, I.K.M., Rohman, A., 2022. Review on ginger (Zingiber officinale Roscoe):

Phytochemical composition, biological activities and authentication analysis. Food Res. 6, 443–454. https://doi.org/10.26656/fr.2017.6(4).500

Suryani, Anshory, A.C. Al, Marlin, Artika, I.M., Ambarsari, L., Nurcholis, W., 2022. Variability total phenolic content and antioxidant activity of Curcuma zanthorrhiza and C. aeruginosa cultivated in three different locations in West Java, Indonesia. Biodiversitas 23, 1998–2003. https://doi.org/10.13057/biodiv/d230434

Syarifuddin, I., Taebe, B., Noer, S.F., 2023. Standarisasi parameter non spesifik simplisia ekstrak etanol rimpang jahe merah (Zingiber officinale roscoe var. rubrum). FARBAL J. Farm. dan Bahan Alam 11, 78–84.

Triratnawati, A., 2011. Masuk Angin dalam Konteks Kosmologi Jawa. Humaniora 23, 326–335. https://doi.org/10.22146/jh.1033

Usai, M., Atzei, A.D., Marchetti, M., 2016. A comparative study on essential oil intraspecific and seasonal variations: Melissa romana Mill. and Melissa officinalis L. from Sardinia. Chem. Biodivers. 13, 1076–1087. https://doi.org/10.1002/cbdv.201500507

Utaminingrum, W., Nofrianti, Hartanti, D., 2021. Ethnopharmacological study of the polyherbal formula in Baturraden, Indonesia. Suranaree J. Sci. Technol. 28, 070024(1–8).

Widyowati, R., Agil, M., 2018. Chemical constituents and bioactivities of several Indonesian plants typically used in jamu. Chem. Pharm. Bull. 66, 506–518. https://doi.org/10.1248/cpb.c17-00983

Yap, J.Y., Hii, C.L., Ong, S.P., Lim, K.H., Abas, F., Pin, K.Y., 2020. Effects of drying on total polyphenols content and antioxidant properties of Carica papaya leaves. J. Sci. Food Agric. 100, 2932–2937. https://doi.org/10.1002/jsfa.10320

Yap, V.L., Tan, L.F., Rajagopal, M., Wiart, C., Selvaraja, M., Leong, M.Y., Tan, P.L., 2023. Evaluation of phytochemicals and antioxidant potential of a new polyherbal formulation TC-16: Additive, synergistic or antagonistic? BMC Complement. Med. Ther. 23, 93. https://doi.org/10.1186/s12906-023-03921-0

Zhang, S., Kou, X., Zhao, H., Mak, K.-K., Balijepalli, M.K., Pichika, M.R., 2022. Zingiber officinale var. rubrum: Red ginger's medicinal uses. Molecules 27, 775. https://doi.org/10.3390/molecules27030775