Pharmacokinetics of 10-gingerol and 6-shogaol in the plasma of healthy subjects treated with red ginger (*Zingiber officinale* var. Rubrum) suspension

JUTTI LEVITA[1], DINA MULYANA SYAFITRI[1,2], RINI DAUD SUPU[1,3], MUTAKIN MUTAKIN[4], SANDRA MEGANTARA[4], MAYA FEBRIANTI[5] and AJENG DIANTINI[2]

[1]Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Padjadjaran University, Jatinangor, West Java 45363; [2]Clinical Pharmacy, Riau Islands General Hospital, Tanjung Pinang, Riau Islands 29125; [3]School of Health Science (STIKES) Bina Mandiri Gorontalo, Gorontalo, North Sulawesi 96128; [4]Department of Pharmaceutical Analysis and Medicinal Chemistry, and [5]Department of Biological Pharmacy, Faculty of Pharmacy, Padjadjaran University, Jatinangor, West Java 45363, Indonesia

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Abstract. Red ginger (*Zingiber officinale* var. Rubrum) is among the most widely consumed medicinal herbs in Indonesia. Ginger rhizome contains phenol compounds including gingerol and shogaol. 10-gingerol has been reported to exhibit the greatest anti-inflammatory and anti-oxidant activities compared with those of other gingerols. Pharmacokinetic studies on ginger have been reported, but there is a lack of such study on red ginger. The present work studied the pharmacokinetics of 10-gingerol and 6-shogaol in the plasma of healthy subjects treated with a single dose of red ginger suspension. Healthy subjects (n=19) were given a single dose of red ginger suspension (2 g/15 ml), and blood samples were taken at baseline (0 min), 30, 60, 90, 120, and 180 min. Analysis of 10-gingerol and 6-shogaol was performed by dissolving 200 μl of the subjects' plasma in 800 μl acetonitrile. The mixture was vortexed and centrifuged at 20,440 x g for 15 min at room temperature. The supernatant was filtered using Millipore membrane (pore size 0.2 μm) and injected into an RP-C18 column for liquid chromatography-mass spectrometry. A mixture of 0.1% (v/v) formic acid in water and acetonitrile (38:62) was used as the mobile phase. The maximum plasma concentration (Cmax) and time to reach Cmax of 10-gingerol and 6-shogaol were 160.49 ng/ml (38 min) and 453.40 ng/ml (30 min), respectively. The elimination half-lives were 336 and 149 min for 10-gingerol and 6-shogaol, respectively. Thus, 10-gingerol and 6-shogaol were absorbed after per oral single dose of red ginger suspension and could be quantified in the plasma of the healthy subjects. Additionally, the red ginger analytes exhibited relatively slow elimination half-lives.

Correspondence to: Professor Jutti Levita, Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Padjadjaran University, Jl. Raya Bandung-Sumedang km 21, Jatinangor, West Java 45363, Indonesia
E-mail: jutti.levita@unpad.ac.id

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Introduction

Several studies have reported on the concentration of gingerols in fresh ginger (*Zingiber officinale* var. Roscoe) rhizomes, for instance, the methanol extract of *Z. officinale* var. Roscoe rhizome cultivated in Hawaii contained 6-, 8- and 10-gingerol at concentrations of 2,100, 288 and 533 μg/g, respectively (1); the methylene chloride extract of *Z. officinale* var. Roscoe rhizome cultivated in America yielded 880, 93 and 120 μg/g of 6-, 8- and 10-gingerol, respectively (2); and the fresh rhizome of *Z. officinale* var. Roscoe cultivated in Taiwan contained 806 μg/g of 6-gingerol (3). Furthermore, phytochemical screening of the chloroform extract of *Z. officinale* var. Roscoe rhizome cultivated in Pakistan has given positive results on the presence of alkaloid, phlobotannins, flavonoids, glycosides, saponins, tannin and terpenoids, while indicating the absence of steroids (4). Alkaloids, carbohydrates, glycosides, proteins, saponins, steroids, flavonoids and terpenoids has been identified in *Z. officinale* var. Roscoe, and phenolic compounds including gingerol and shogaol (5-7), while reducing sugars, tannins, oils and acid compounds were absent. Similarly, results of proximate analysis of the rhizome have indicated mostly carbohydrates (71.46%) and crude protein (8.83%) with a small crude fibre content of 0.92% (5).

A comparative study of *Z. officinale* var. Roscoe pulp and peel demonstrated that the hydro-alcoholic extract of the peel exhibited marked inhibition of the growth of colon cancer cells on MTT assay, while the pulp extract exhibited high anti-inflammatory and antioxidant activities, allegedly due to differing polyphenolic content and lipophilic composition (8). Data on the effects of *Z. officinale* var. Roscoe have been reviewed, and it has been concluded that the rhizome of this plant has potential as an anti-inflammatory and anti-oxidative

source, nonetheless further research has been suggested prior to confirming its efficacy (9). The medicinal properties of *Z. officinale* var. Roscoe may be due to the presence of gingerol, paradol and shogaols, among other compounds (10).

Gingerols are homologues of 1-(3-methoxy-4-hydroxy phenyl)-3-keto-5-hydroxyhexane, shogaols are dehydration products of the gingerols, and paradols are β-ketone hydroxyl deoxygenation products of gingerols (11). In previous studies *Z. officinale* var. Roscoe has exhibited anti-inflammatory activity (8,12-16). 10-gingerol (Fig. 1A) has been reported to exhibit the highest anti-inflammatory and anti-oxidant activities compared with those of other gingerols (17). Other studies on 6-gingerol have confirmed its inhibition of nitric oxide production in activated J774.1 mouse macrophages and prevention of peroxynitrite-induced oxidation and nitration reactions (18). This compound may also inhibit cyclooxygenase (COX)-2 expression by blocking the activation of p38 mitogen-activated protein kinase and nuclear factor-κB in phorbol ester-stimulated mouse skin (19). However, studies on the effects of red ginger (*Z. officinale* var. Rubrum) are limited.

Previous study by Fikri *et al* (20) concluded that the hot water extract of *Z. officinale* var. Rubrum rhizome inhibited the rate of prostaglandin production *in vitro*. Furthermore, a computational study of gingerol and shogaol against COX enzymes reported that 6-gingerol and 6-shogaol were preferential COX-2 inhibitors and therefore potential candidates for development into anti-inflammatory drugs (21). Pharmacokinetic studies of the dry extract of ginger rhizomes (at doses of 100 mg to 2 g) in the plasma of healthy American volunteers have been conducted (22,23). However, there is a lack of reports on red ginger. Thus, the present work studied the pharmacokinetics of 10-gingerol (Fig. 1A) and 6-shogaol (Fig. 1B) in the plasma of healthy Indonesian volunteers treated with a single dose (2 g) of red ginger suspension. The aims of this study were to: i) Determine if red ginger suspension is absorbed and biotransformed in humans; and ii) assess the human pharmacokinetics of 10-gingerol and 6-shogaol.

Materials and methods

Instruments. Instruments used in the study were a liquid chromatography-mass spectrometry (LC-MS) XEVO-QTOF MS (Waters-MassLynx 4.1 SCN719; PT Kromtekindo Utama, Jakarta, Indonesia) equipped with an RP-C18 column (2.1 x 100 mm), a UV-visible double beam spectrophotometer (Specord 200; Analitik Jena AG, Jena, Germany), a digital analytical balance [Ohaus Pioneer; Ohaus Instruments (Shanghai) Co., Ltd., Shanghai, China], an Eppendorf Centrifuge 5424 R, a vortex mixer (Cole-Parmer, Vernon Hills, IL, USA), a dipotassium ethylenediamine tetraacetic acid (K2EDTA) tube (BD Vacutainer; BD Biosciences, Franklin Lakes, NJ, USA) and chemical glasswares.

Chemicals and plant materials. 10-gingerol of standard 98% purity (Sigma-Aldrich; Merck KGaA, Darmstadt, Germany; CAS no. 23513-15-7) and 6-shogaol of standard 98% purity (Sigma-Aldrich; CAS no. 555-66-8) were purchased from Quartiz Indonesia (PT Indogen Intertama, Jakarta, Indonesia); methanol hypergrade for LC-MS (LiChrosolv®; CAS no. 67-56-1) and acetonitrile gradient grade for liquid chromatography (LiChrosolv® CAS no. 75-05-08) were purchased from the Central Laboratory of Padjadjaran University (Jatinangor, West Java, Indonesia); and 1 kg of fresh rhizome of *Z. officinale* var. Rubrum was purchased from the Research Institute for Spices and Medicinal Plants (Balittro) Manoko Lembang (Bandung, Indonesia). The fresh rhizome was taxonomically identified at the Laboratory of Plant Taxonomy, Department of Biology, Faculty of Mathematics and Natural Sciences, Padjadjaran University, and the voucher specimen (no. 415/HB/08/2017) was retained in our laboratory for future reference.

Preparation of red ginger (Zingiber officinale var. Rubrum) suspension. The 1 kg of fresh rhizome of *Z. officinale* var. Rubrum was thin-sliced (1-2 mm) and dried in a dehydrator at 50˚C for 4 h. The dried rhizome was ground and each portion per subject contained 2 g of the powder dissolved in 15 ml hot distilled water (70˚C).

Identification of 10-gingerol and 6-shogaol in Z. officinale var. Rubrum suspension. Identification of 10-gingerol and 6-shogaol in *Z. officinale* var. Rubrum suspension was performed by dissolving the suspension in 15 ml methanol hypergrade. The mixture was vortexed and centrifuged at 20,440 x g at room temperature for 15 min. The supernatant was scanned at 200-380 nm in a double beam UV spectrophotometer against the methanol hypergrade its maximum wavelength (λmax) was compared with those of 10-gingerol and 6-shogaol.

Preparation of 10-gingerol and 6-shogaol standard solutions. A total of 2.5 mg of each of the 10-gingerol and 6-shogaol standards was dissolved in 100 ml methanol hypergrade in a volumetric flask (25 μg/ml). The solutions were scanned at 200-380 nm in the double beam UV spectrophotometer against the methanol hypergrade to obtain the λmax's of 10-gingerol and 6-shogaol. Various concentrations were prepared by diluting the standard solution (Tables I and II) (24).

Optimization of LC-MS analytical conditions. The 10-gingerol and 6-shogaol standard solutions (2.5, 5.0, 10.0, 15.0, 20.0 and 25.0 ng/ml) were filtered using Millipore membranes (pore size 0.2 μm; EMD Millipore, Billerica, MA, USA) and injected into the LC-MS RP-C18 column. The optimized conditions of the LC-MS are presented in Table III.

Validation of analytical method

Selectivity. The selectivity of the method was investigated by comparing the chromatogram of extracted blank plasma (3 ml) obtained from six randomly selected participants described below, each spiked with 25.0 ng/ml 6-shogaol.

Linearity. Linearity of the standard curves was calculated using human plasma spiked with various concentrations (2.5, 5.0, 10.0, 15.0, 20.0 and 25.0 ng/ml) of 10-gingerol and 6-shogaol. The concentrations were plotted against the area under curves (AUCs) of the 10-gingerol and 6-shogaol chromatograms. The regression line (y=ax+b) and the coefficient of correlation (r) of the data were calculated.

Table I. Preparation of 10-gingerol standard solutions.

Blank plasma, μl	10-gingerol, μl	Acetonitrile, μl	Final concentration, ng/ml
200	-	800.0	Blank
200	2.5	797.5	2.5
200	5.0	795.0	5.0
200	10.0	790.0	10.0
200	15.0	785.0	15.0
200	20.0	780.0	20.0
200	25.0	775.0	25.0

Table II. Preparation of 6-shogaol standard solutions.

Blank plasma, μl	6-shogaol, μl	Acetonitrile, μl	Final concentration, ng/ml
200	-	800.0	Blank
200	2.5	797.5	2.5
200	5.0	795.0	5.0
200	10.0	790.0	10.0
200	15.0	785.0	15.0
200	20.0	780.0	20.0
200	25.0	775.0	25.0

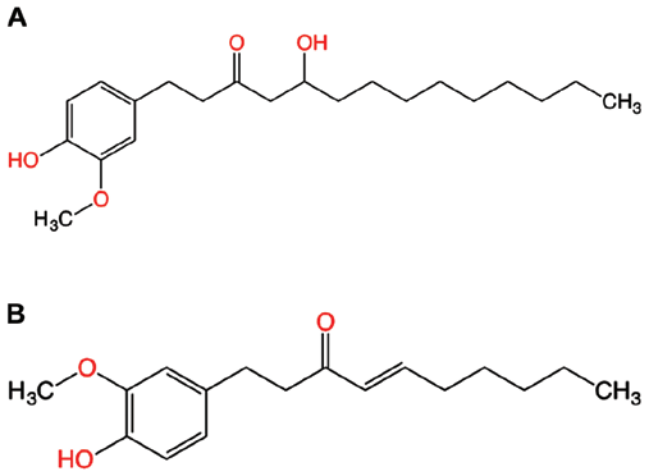

Figure 1. Chemical structure of (A) 10-gingerol and (B) 6-shogaol, downloaded from http://www.chemspider.com/Chemical-Structure.147055.html?rid=a2e8c30f-67ff-43bb-9b9d-b526a54aae92&page_num=0 for 10-gingerol and http://www.chemspider.com/Chemical-Structure.4445106.html?rid=aff2295b-35aa-43d5-807a-8b26311f4469 for 6-shogaol and redrawn using ChemDraw Professional 15.0.0.106 (PerkenElmer, Waltham, MA, USA; licensed to Padjadjaran University, West Java, Indonesia, no. 623018920).

Accuracy and precision. The accuracy and precision of the method were evaluated by analyzing 10-gingerol and 6-shogaol in three sets of quality control samples [lower concentration of quality control (LCQC)=2.5 ng/ml; medium concentration of quality control (MCQC)=15 ng/ml; and higher concentration of quality control (HCQC)=25 ng/ml each] within the same day. Each solution was injected into the column in three replicates. The percentage recovery and standard deviation (SD) were calculated to ascertain accuracy and precision of the analytical method, respectively.

Limit of detection (LOD) and limit of quantification (LOQ). The LOD and LOQ were calculated by using: LOD=(3xSD)/b; and LOQ=(10xSD)/b where b is the *y*-intercept of the linear regression curve (25).

Subjects and treatment. A total of 21 participants (8 females and 13 males) aged 21-30 years, with body mass indices (BMIs) of 18-25, non-smokers and/or alcohol drinkers, were solicited by advertisement from May to September 2017. All participants were confirmed to be healthy by physical examination at Padjadjaran Clinic, Padjadjaran University (Jatinangor, Indonesia; Table IV). Two of the participants (R14 and R20) had low BP (90/60). Initially both were included in the study, but one of them (R14) vomited during the treatment, and was excluded. One of the participants (R21) was menstruating on the day of preliminary health screening and was excluded. The remaining 19 subjects continued the study. All study procedures were administered at the Faculty of Pharmacy, Padjadjaran University following collection of signed written informed consent according to the principles of the Declaration of Helsinki. The subject protocols and treatment were approved by the Research Ethics Committee of Padjadjaran University (approval nos. 1211/UN6.C.10/PN/2017 for 10-gingerol and 924/UN6.C.10/PN/2017 for 6-shogaol). The subjects were asked to avoid all foods containing ginger within 7 days prior to the project and completed a food checklist to verify that they were not consuming any ginger-rich food or beverages. All subjects received the Sundanese standard meal (one portion of white rice equivalent to 240 cal, 100 g of fried chicken/tofu equivalent to 110-120 cal, hot tea equivalent to 70 cal, and a banana/orange 3 times/day at 24 h pre-study and for breakfast on the day of the study.

The red ginger suspension was administered the subsequent morning after the standard breakfast had been received. Each subject was given one portion of red ginger suspension (2 g in 15 ml of water) as a single oral dose, and 3 ml blood samples were taken from the subjects at baseline (0 min), 30, 60, 90, 120 and 180 min. The blood was put into the K2EDTA vacutainer tubes. Plasma was separated by centrifuging at 20,440 x g for 15 min at room temperature and kept at -20˚C until assayed.

Pharmacokinetics of 10-gingerol and 6-shogaol. Analysis of 10-gingerol and 6-shogaol was performed by dissolving 200 μl of the subjects' plasma in 800 μl acetonitrile. The mixture was vortexed and centrifuged at 20,440 x g for 15 min at room temperature. The supernatant was filtered using Millipore membrane (pore size 0.2 μm) and injected into the RP-C18 column embedded in the LC-MS XEVO-QTOFMS.

Results and Discussion

Identification of 10-gingerol and 6-shogaol in Z. officinale var. Rubrum suspension. Gingerol and/or shogaol were indi-

Table III. LC-MS optimum analytical conditions for 10-gingerol and 6-shogaol (N_2 gas temperature 350˚C; drying N_2 gas flow rate 10 l/min; nebulizer pressure 50 psi).

LC-MS parameter	Setting condition
Merk/Type	Waters Xevo QTof -MassLynx 4.1 SCN719
Column	BEH Shield RP18 Ø 1.7 μm; 2.1 x 100 mm
Mobile phase	Phase A: 0.1% (v/v) formic acid in water; phase B: acetonitrile
Time setting (ratio phase A:phase B)	0-6th min (38:62); 6-9th min (0:100); 9-15th min (38:62)
Flow rate; retention time	300 μl/min; 15 min
Mass spectrometer mode/ion detection	Electrospray ionization (ES+) ionization/multiple reaction monitoring mode

LC, liquid chromatography; MS, mass spectrometry.

Table IV. Preliminary health screening of the participants.

		Health status				
Subject code	Age, years	Height, cm	Weight, kg	Blood type	BP, mmHg	Result
R1	22	160	63	A	120/80	Healthy
R2	21	164	61	O	120/80	Healthy
R3	21	176	72	AB	110/70	Healthy
R4	22	164	64	B	110/70	Healthy
R5	22	175	63	O	120/80	Healthy
R6	22	165	55	A	110/80	Healthy
R7	22	172	56	A	110/70	Healthy
R8	22	165.5	66	O	120/80	Healthy
R9	22	164	55	O	100/60	Healthy
R10	25	169	60	B	120/80	Healthy
R11	26	168	65	O	120/80	Healthy
R12	30	161	58	A	100/70	Healthy
R13	22	164	54	A	100/70	Healthy
R14	23	157	65	O	90/60	Excluded[a]
R15	22	160.5	49	AB	100/70	Healthy
R16	22	155	48	AB	120/80	Healthy
R17	25	157	48	O	100/70	Healthy
R18	25	145	45	O	100/80	Healthy
R19	23	159	51	O	100/70	Healthy
R20	22	155	44	A	90/60	Healthy
R21	23	157	62	B	110/80	Excluded[b]

[a]Due to low blood pressure and vomiting upon administration of red ginger suspension; [b]due to menstruation at time of study.

cated to be present in the red ginger suspension by the λmax of red ginger suspension in methanol (λmax=286 nm) which was similar to those of 10-gingerol (λmax=284 nm) and 6-shogaol (λmax=282 nm; Fig. 2).

Ethanol can extract gingerols more effectively than water; moreover, hot water is reportedly more effective than cold water (26). Ghasemzadeh *et al* (27) when working on the optimization procedure for the extraction of 6-gingerol and 6-shogaol (focusing on temperature 50-80˚C and time 2-4 h) reported that increasing the extraction temperature (up to 76.9˚C) and time (3. h) induced the highest yield of 6-gingerol (2.74 mg/g dry weight) and 6-shogaol (1.59 mg/g dry weight) from *Z. officinale* var. Rubrum Theilade (27). The present work employed hot distilled water (70˚C) to extract 2 g of the red ginger (*Z. officinale* var. Rubrum) powder.

Validation of analytical method. The LC-MS analytical method was selective for both 6-shogaol (Fig. 3) and 10-gingerol (Fig. 4) as proven by the respective chromatogram peaks that were free of interference at the retention time of 6-shogaol (6.70 min) and 10-gingerol (8.26 min). The MS

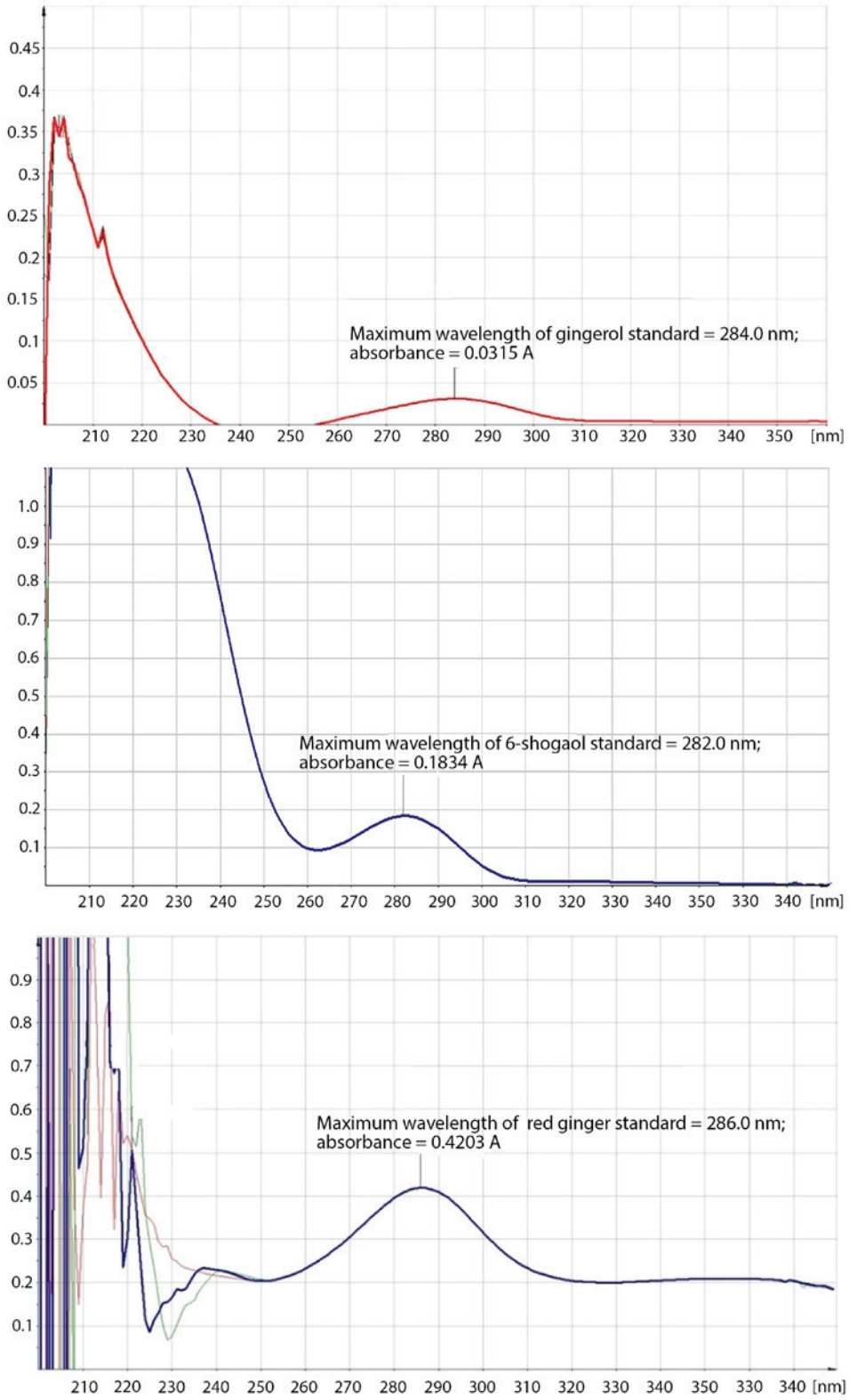

Figure 2. Ultraviolet spectra of 10-gingerol standard (λmax=284 nm; A=0.0315); 6-shogaol standard (λmax=282 nm; A=0.1834); red ginger suspension (λmax=286 nm; A=0.4203). λmax, maximum wavelength; A, absorbance.

spectrum confirmed and correlated the chromatogram peak with the mass-to-charge ratio (m/z). Our MS spectra indicated the base peak of 6-shogaol [M+1] (m/z=277.3869; MW 6-shogaol=276.376); and the base peak of 10-gingerol [M+1] (m/z=351.2959; MW 10-gingerol=350.4923).

Linearity of the standard curves was constructed using human plasma spiked with various concentrations (2.5, 5.0, 10.0, 15.0, 20.0 and 25.0 ng/ml) of 10-gingerol and 6-shogaol (Fig. 5). The LCQC (2.5 ng/ml), MCQC (15.0 ng/ml) and HCQC (25.0 ng/ml) of the ginger analytes were assayed

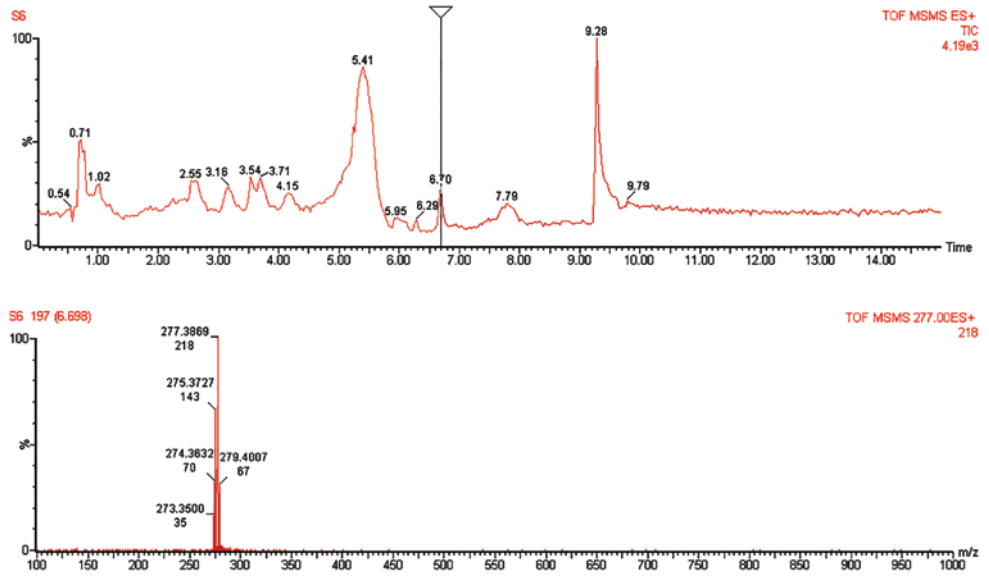

Figure 3. Representative chromatogram of human plasma spiked with 6-shogaol standard (retention time=6.70 min) (upper panel); and the mass spectrum of 6-shogaol [M+1] (m/z=277.3869; MW 6-shogaol=276.376) (lower panel).

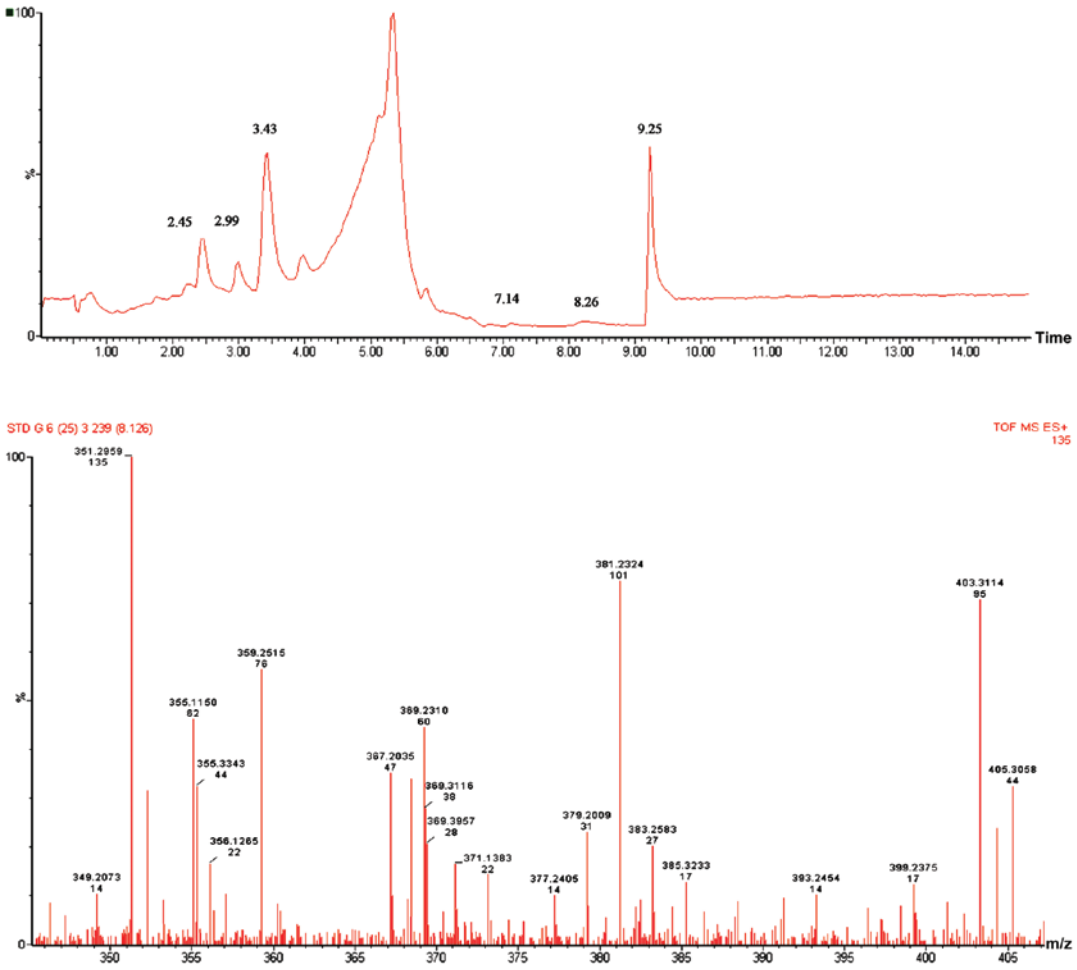

Figure 4. Representative chromatogram of human plasma spiked with 10-gingerol standard (retention time=8.26 min) (upper panel); and the mass spectrum of 10-gingerol [M+1] (m/z=351.2959; MW 10-gingerol=350.4923) (lower panel).

on an intra-day basis to determine the accuracy and precision of the method. The intra-day values for the SD ranged from 0.16-0.69 for 10-gingerol and 0.74-1.49 for 6-shogaol, whereas the recovery of the analytes was 100.64-104.44% for 10-gingerol and 103.40-104.22% for 6-shogaol. The data (plot of AUC of the chromatogram peak against the concentration

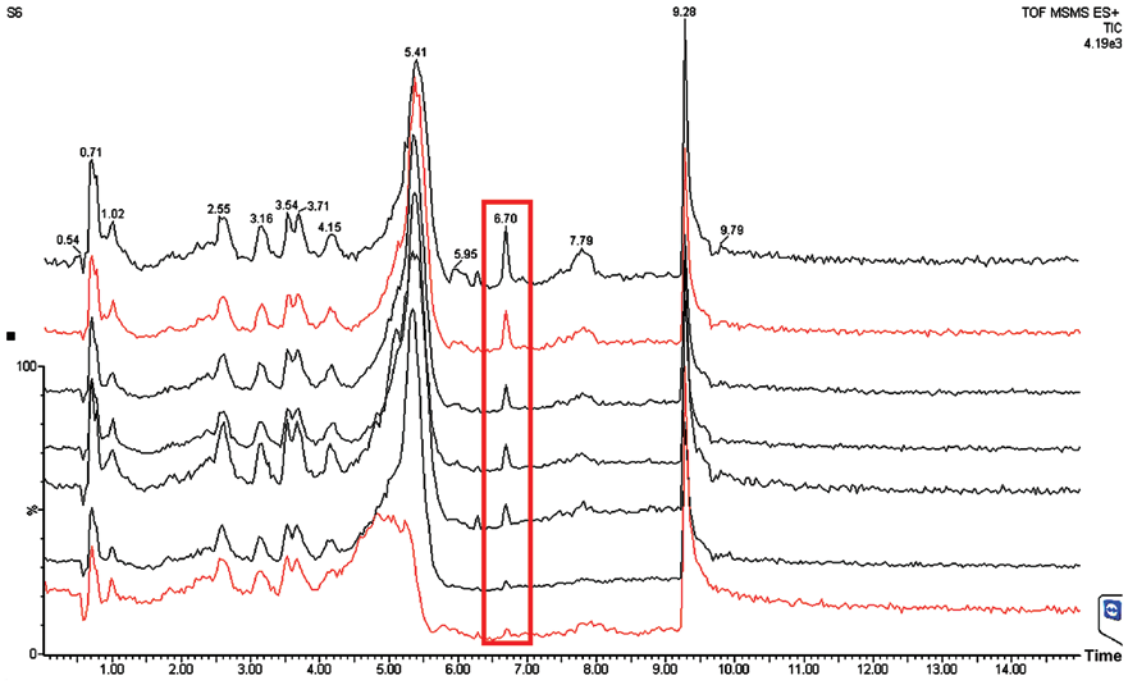

Figure 5. Chromatograms of human plasma spiked with various concentrations of 6-shogaol standard (retention time=6.70 min).

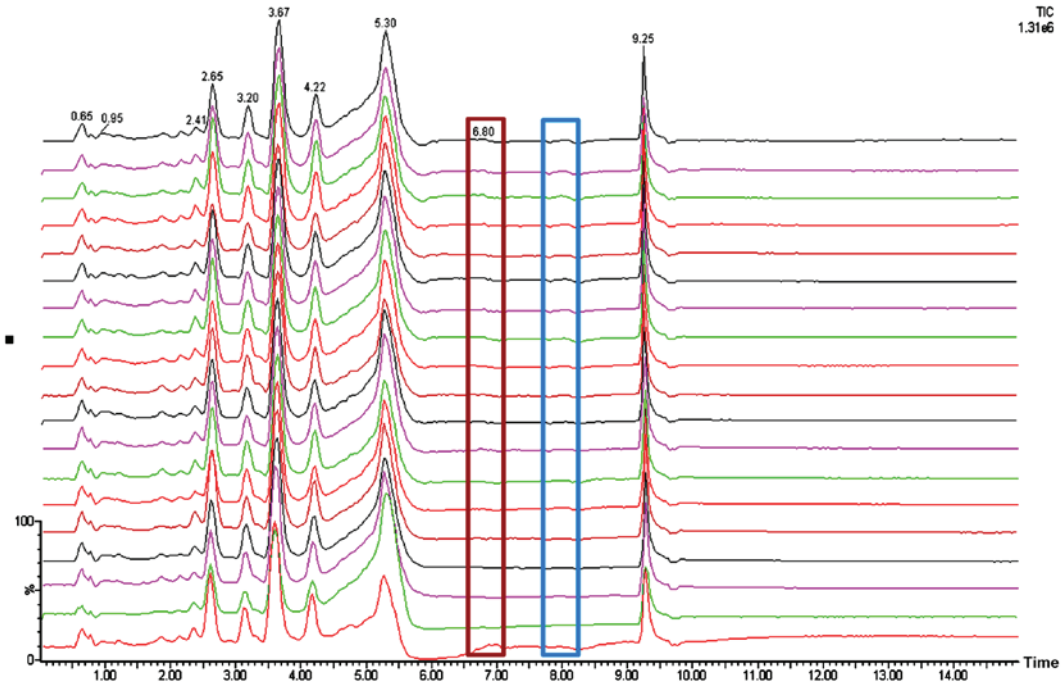

Figure 6. Chromatograms of 10-gingerol (blue rectangle; t_R=8.0 min) and 6-shogaol (red rectangle; t_R=6.80 min) in the plasma of 19 subjects after 30 min treatment with red ginger suspension. A mixture of 0.1% (v/v) formic acid in water and acetonitrile (38:62) was used asthe mobile phase. t_R, retention time.

of 10-gingerol/6-shogaol; not shown) correlated as indicated by r values >0.99 (Table V).

The LODs in human plasma for 10-gingerol and 6-shogaol were 1.31 and 1.51 ng/ml, respectively, and the LOQs were 4.36 and 5.03 ng/ml, respectively.

Characteristics of the subjects. All 19 subjects who completed the study were proven healthy by a physical examination upon enrollment (Table IV); however, 3-6 months prior to the start of the study, several subjects had suffered from gastritis (1/19; 5.26%), allergy (7/19; 3.68%; cold urticaria and/or seafood allergy), joint arthritis (1/19; 5.26%) and dengue hemorrhagic fever (1/19; 5.26%). The subjects also confirmed their weekly exercise as jogging and walking (7/19; 3.68%), football (2/19; 10.53%) and badminton (1/19; 5.26%).

Pharmacokinetics of 10-gingerol and 6-shogaol. 10-gingerol and 6-shogaol could be quantified in the plasma of healthy

Table V. Validation of the 10-gingerol and 6-shogaol analytical method.

Concentration of analyte, ng/ml	Mean concentration, ng/ml	Standard deviation	Recovery, %	Coefficient of correlation (r)	Slope
10-gingerol					
2.5	2.53	0.16	101.28		
15.0	15.67	0.57	104.44	0.9991	6.3195
25.0	26.16	0.69	100.64		
6-shogaol					
2.5	2.59	0.74	103.40		
15.0	15.63	1.49	104.22	0.9987	2.7070
25.0	26.04	0.78	104.14		

Table VI. Pharmacokinetic profile of 10-gingerol and 6-shogaol in the plasma of healthy subjects treated with a single dose of red ginger suspension.

Parameter (n=19)	10-gingerol	6-shogaol
AUC, ng/ml/min	948.750	268.140
Cmax, ng/ml	160.49	453.40
Tmax, min	38	30
T½ elimination, min	336	149

AUC, area under the curve; Cmax, maximum plasma concentration; Tmax, time to reach Cmax; T½, elimination half-life.

subjects treated with a single dose of red ginger suspension. They were eluted at 6.80 min (6-shogaol) and 8.0 min (10-gingerol; Fig. 6), compared with the pure compounds (for 6-shogaol, 6.70 min and for 10-gingerol, 8.26 min; Figs. 3 and 4), respectively. There was a slight difference of elution time between the standards (pure 6-shogaol and 10-gingerol compounds) and that of red ginger suspension due to different conditions; the standards were spiked *in vitro* into human plasma, while the red ginger suspension was administered orally and taken *ex vivo* from the subjects' blood. The pharmacokinetic profile of each of the red ginger compounds is presented in Table VI.

According to elimination half-lives (T½), 10-gingerol and 6-shogaol were eliminated from the plasma at 336 and 149 min, respectively (Table VI). The maximum plasma concentration (Cmax) of 10-gingerol (160.49 ng/ml) was lower than that of 6-shogaol (453.40 ng/ml; Table VI).

These findings were different to those of Zick *et al* (22) who studied the pharmacokinetic profile of 6-, 8- and 10-gingerol and 6-shogaol in dry extract of ginger at doses of 100 mg to 2 g in 27 healthy American participants (9 males, 22 females, mostly Caucasians). They identified that no free 6-, 8-, 10-gingerol or 6-shogaol was present, but 6-, 8- and 10-gingerol and 6-shogaol glucuronides were detected. Furthermore, in the plasma of healthy Caucasians, the concentration of 10-gingerol has been quantified higher than that of 6-shogaol (23).

The present study used a single dose (2 g) of red ginger (*Z. officinale* var. Rubrum) suspension, administered orally to 19 healthy Indonesian participants (13 males and 6 females). Both 10-gingerol and 6-shogaol could be detected and quantified. In the plasma of the healthy Indonesians, 10-gingerol was quantified to a lower level than 6-shogaol.

10-gingerol and 6-shogaol exhibited slower elimination in Indonesian subjects compared with that in Caucasians (T½ elimination <120 min). In the current study, no serious adverse effects were reported following ingestion of the red ginger suspension, though several female subjects complained of the potent pungent odor and spicy taste that caused stomach discomfort. These mild adverse effects were consistent with those reported by Zick *et al* (22) and in a previous review study by Chrubasik *et al* (28), who documented that the majority of the disadvantages were transient gastrointestinal reactions, such as gas and bloating.

In conclusion, 10-gingerol and 6-shogaol were absorbed after per oral single dose of red ginger suspension and could be quantified in the plasma of healthy Indonesian subjects. The Cmax of 10-gingerol (160.49 ng/ml) was lower than that of 6-shogaol (453.40 ng/ml). Notably, the two red ginger analytes exhibited relatively slow elimination half-lives. In the present trial, no serious adverse effects were reported following ingestion of the red ginger suspension, but several female subjects complained about the potent pungent odor and spicy taste that caused stomach discomfort. Overall, the present pharmacokinetic findings of 10-gingerol and 6-shogaol in Indonesian subjects confirmed that different ethnicities may contribute to different pharmacokinetic profiles. Identification of these differences may lead to personalized-medicine, and thus contribute in a clinical context, particularly in the discovery and development of anti-inflammatory drugs.

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Availability of data and materials

The datasets used and/or analyzed in the current work are available from the corresponding author on reasonable request.

Authors' contributions

JL and AD were principally responsible for conception and design of the study. JL, MM and AD participated in the acquisition of the reported data. DMS, RDS, SM and MF participated in the processing, analysis and interpretation of the reported data. JL and SM contributed to the writing and revising of the manuscript. All authors read and approved the final manuscript to be published.

Ethics approval and consent to participate

Written informed consent was obtained from all participants. Research Ethics Committee of Padjadjaran University (Bandung, Indonesia) approved the study procedures (approval nos. 1211/UN6.C.10/PN/2017 for 10-gingerol and 924/UN6.C.10/PN/2017 for 6-shogaol).

Patient consent for publication

Informed consent was obtained for publication of the participants' data.

Competing interests

The authors declare that they have no competing interests.

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