Original Article

The effect of red ginger bread consumption on the physiological parameters of healthy subjects

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ABSTRACT

A new variant of red gingerbread containing 6% of red ginger powder (named RGB), has been produced. The bread, preferred by 30 panelists, could be stored for approximately 9 days without showing deterioration or the growth of mold. This work aimed to study the effect of 14 days consumption of RGB on the body mass index (BMI), abdominal circumference, blood pressure, urinalysis parameters, and the lipid profile of healthy subjects. The healthy subjects (n=20) were treated with a piece of RGB daily for 14 consecutive days, and on day-15th their BMI, abdominal circumference, blood pressure, urinalysis parameters, and lipid profile were recorded. Before the study, a high-performance liquid chromatography (HPLC) analysis was conducted and revealed that 381.17 µg/mL of total flavonols (calculated as 10-gingerol) is contained in RGB. RGB demonstrated a medium strength of antioxidant activity (IC_{50} = 144.095 µg/mL) and could reduce the abdominal circumference (4.25%; p = 0.004) and blood pressure (systolic 9.42%; p = 0.000 and diastolic 9.09%; p = 0.000) of the subjects, but did not alter their BMI nor urinalysis parameters. Furthermore, the total cholesterol of the subjects was significantly decreased, whereas the high-density lipoprotein (HDL) value was increased. Nonetheless, no change in low-density lipoprotein (LDL) and triglyceride were detected. In conclusion, the RGB could be proposed as a healthy variant of bread.

Keywords: Bread, Cholesterol, Diastole, Gingerol, Systole, *Zingiber officinale* var. Rubrum

Introduction

Many efforts have been done to improve the taste and to add new variants of white bread. White bread is commonly enriched with spices or phenolic-abundant plant extracts, as reported previously, e. g. sweet potato flour [1], baobab fruit extract [2, 3], broccoli sprouts [4]. Most of those studies reported that plant enriched-breads had shown antioxidant activity [4-8] and stomach cancer chemoprevention [4]. Another study concluded that apple skin powder enriched muffins contained high dietary fiber and revealed antioxidant activity [9-11]. Enrichment of common ginger (*Zingiber officinale* var. Roscoe) powder [12], as well as red ginger (*Zingiber officinale* var. Rubrum) powder in bread [13], was also reported. A recent study reported that the addition of phenolic compounds in bread could improve the bread structure and antioxidant effect [14].

Studies in humans have also been reported. The addition of baobab fruit extract to white bread was proven could significantly reduce glycemic response in humans [2]. A pharmacokinetic study of red ginger suspension in adult humans has also been reported [15]. However, no such investigation on the effect of red ginger-supplemented bread in healthy subjects was found.

Phytochemical screening of the dried rhizome and the water extract of red ginger revealed the presence of flavonoid, quinone, and monoterpenoid/sesquiterpenoid [16], which led us to select this particular plant for our bread. Previously, we reported that red ginger supplemented-bread exhibited longer

Access this article online	
Website: www.japer.in	**E-ISSN:** 2249-3379

How to cite this article: Sulastri T, Sunyoto M, Reuben Suwitono M, Levita J. The effect of red ginger bread consumption on the physiological parameters of healthy subjects. J Adv Pharm Educ Res. 2022;12(3):28-35. https://doi.org/10.51847/mznq1HW7vK

storage time compared to the control bread [13]. This work was conducted to study the effect of 14 days of consumption of bread enriched with 6% of red ginger powder (RGB) **(Figure 1)** on the body mass index, blood pressure, urinalysis parameters, and lipid profile of healthy subjects. The flavonol content of RGB (calculated as 10-gingerol) and its antioxidant activity were also assayed.

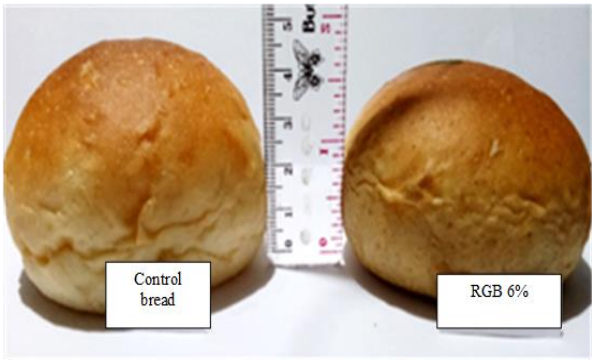

Figure 1. Control bread without the addition of red ginger powder (left) and bread enriched with 6% of red ginger powder (right).

Scientific hypothesis

We hypothesize that the addition of 6% of red ginger powder to the bread will add antioxidant properties to the bread due to the polyphenolic compounds (*e. g.* gingerol in the red ginger powder) content. We also expect the 6% red ginger enriched bread (RGB) to maintain the blood pressure and improves the lipid profile of the healthy subjects.

Material and Methods

Samples

Fresh red ginger rhizomes were purchased from the Research Institute for Spices and Medicinal Plants (Balittro) Manoko Lembang, Indonesia and were taxonomically identified at the Laboratory of Plant Taxonomy, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Indonesia.

Chemicals

1,1-diphenyl-2-picrylhydrazyl (DPPH) (TCI CAS No. 1898-66-4, purity >97.0%), quercetin hydrate (Sigma-Aldrich CAS No. 849061-97-8, purity ≥95%), [10]-gingerol (Sigma-Aldrich CAS No. 23513-15-7, purity ≥98%), ethanol 96% (EMSURE CAS Number 64-17-5), methanol HPLC grade (Merck CAS No. 67-56-1).

Subjects and study designs

The study was aimed to investigate the effect of 14 days consumption of RGB on the lipid profile of healthy subjects. The protocol has been approved by Universitas Padjadjaran Ethics Research Committee (https://kep.unpad.ac.id/ document No. 696/UN6.KEP/EC/2019) by following the principles of the Declaration of Helsinki. The minimum number of subjects was calculated by the following: $n = 2 (Z\alpha + Z [1-\beta])2 \times SD2/d2$ [17]. Written informed consent was obtained from the subjects after a comprehensive explanation of the procedure involved. Initially, twenty-four healthy young adults: 7 males and 17 females agreed to participate in this study, but 4 males failed to continue, and their data were excluded. The twenty subjects were confirmed as healthy by a local GP (and urinalysis strip test), aged 19 to 23 years (mean 19.60 + 1.095 years), with body mass index (BMI) 23.65 ± 5.97 kg/m2 (mean ± SD). The inclusion criteria were healthy young adult individuals (18–25 years) with no cardiovascular medication, no diagnosed allergy, and having BMI between 20 and 30 kg/m2, no smoking and alcohol drinking habit, no history of hypertension, and dyslipidemia in the family.

Instruments

Ultra-violet spectrophotometer (Rigor Ultra-3000, http://hyperions.co/products/uv-vis/ultra-3000-series/), digital analytical balance (ME analytical balance, Mettler Toledo), liquid chromatography (Agilent 1220 Infinity LC, Agilent Technologies), reversed-phase liquid chromatography column (Agilent Zorbax SB C-18) 4.6 ID x 250 mm, particle size 10 µm, slicer (Ellane VC 60 MP machine (dimension 50x27x48cm3, weight 24 kg, 550 watts, 300 rpm, capacity 125kg/hour), grinding machine (Vitamax MPS 1394), baking oven ((Mahyih MY-339), Lipid Pro Analyzer, and chemical glassware.

Laboratory methods

Antioxidant activity was measured based on the method of Garcia and co-workers [18]. LC analysis was performed according to the laboratory standard.

Preparation of red ginger powder

Fresh red ginger rhizomes were washed under tap water, peeled off their skin, thin-sliced using a slicer machine, and sundried in a bamboo container for approximately 6 hours. The dried red ginger slices were powdered using a grinding machine and sifted using a 200-mesh sieve. The yield of the powder was 11% w/w.

Preparation of red gingerbread containing 3%, 4.5%, and 6% red ginger powder (RGB)

Materials used for preparing the RGB (1000 g) were local margarine (130 g), butter (50 g), sugar (200 g), sodium bicarbonate (3 tsp), eggs (4), *Saccharomyces cerevisiae* solid yeast (50 g), salt (1/2 tsp), sweet condensed milk (40 g), the freshly prepared red ginger powder (3%, 4.5%, and 6%. 3% is equal to 30 g, 4.5% is equal to 45 g, 6% is equal to 60 g), wheat flour (*quantum sufficit*), and water (200 mL).

Water, sugar, wheat flour, condensed milk, eggs, sodium bicarbonate, and solid yeast were mixed and developed for 20 minutes to make the dough. The red ginger powder, margarine,

butter, and salt were poured, stirred until homogenous, and was allowed to sit for 10 minutes at room temperature. The dough was folded and divided into @50 g, developed for 45 minutes at 37 °C to allow the second fermentation to occur, and all bread was baked for 10 minutes at 190 °C (upper flame)- 200 °C (lower flame). The bread was then allowed to cool at room temperature, and each bread was packed into a single sealed plastic pouch. The control bread was prepared by using similar materials and procedures but without the addition of the red ginger powder.

Antioxidant activity assay using diphenyl-picrylhydrazyl (DPPH) method

Antioxidant activity was measured based on the method of Garcia and co-workers [18] with a few modifications. A sample of 2.0 mL (50 µg/mL) was added with 3.0 mL of DPPH (40 µg/mL). The mixture was allowed to stand for 30 minutes at room temperature. The absorbance of the mixture was then measured using a spectrophotometer (Rigol U3000) at 515 nm against a blank.

Determination of 10-gingerol in the RGB extract

The peak wavelength of standard 10-gingerol in ethanol was confirmed by using an ultraviolet spectrophotometer at 286 nm. The RGB extract was prepared as follows: 50 g of RGB was soaked with 150 mL 96% ethanol for 3x24 hours and filtered. RGB extract 60,000 ppm solution was prepared by dissolving 300 mg of extract into 5 mL ethanol. Analysis of 10-gingerol in the RGB was performed by injecting 100 µL of the RGB extract into the 20 uL sample loop of the LC system utilizing the RP-C18 column. A mixture of water-methanol (30:70) was used as the mobile phase. The level of 10-gingerol in the RGB was calculated by employing the linear regression of the 10-gingerol standard curve.

The effect of RGB on the BMI, abdominal circumference, blood pressure, urinalysis parameters, and the lipid profile of healthy subjects

The study was performed at the research center and dormitory of the Indonesian Adventist University (West Java, Indonesia) and was completed within 2 weeks. The participants (n=20) were measured for their BMI (kg/m2), abdominal circumference (cm), blood pressure (mmHg), urine analysis parameters: leucocyte (Leu/µL), protein (mg/dL), nitrite (mg/dL), urobilinogen (mg/dL), pH, ketones (mg/dL), blood (Rbc/µL), SG-scientific gravity, glucose (mg/dL), and bilirubin (mg/dl). Moreover, their lipid profile: total cholesterol (mg/dL), triglyceride (mg/dL), HDL or high-density lipoprotein (mg/dL), and LDL or low-density lipoprotein (mg/dL), was also determined by a capillary puncture on the third finger of the right hand before the RGB intervention (day-0th). On the test days (day-1st to the day-14th) the participants were conditioned with standard dormitory meals for breakfast with the addition of one piece of RGB (after breakfast) given daily. On day-15th, the bodyweight, abdominal circumference, blood pressure, and lipid profile of the subjects were again recorded.

Statistical analysis

The IC_{50} was calculated by employing GraphPad Prism free trial software downloaded from https://www.graphpad.com/. The test used to determine the normality distribution of the antioxidant data was ANOVA, followed by the Duncan test. The normality test used to analyze the anthropometric data of the subjects were the Kolmogorov-Smirnov test and T-paired test. The normality test used to analyze the urinalysis data, blood pressure, and the lipid profile of the subjects was the Kolmogorov-Smirnov test and Wilcoxon signed-ranks test.

Results and Discussion

Antioxidant activity (DPPH method)

The antioxidant activity of the red ginger enriched bread proved that bread enriched with 6% red ginger powder possesses the strongest radical scavenging activity (IC_{50} = 144.095 µg/mL) compared to the other varieties of bread. An increase in the concentration of red ginger powder added to the bread is positively correlated with the antioxidant activity **(Figure 2)**.

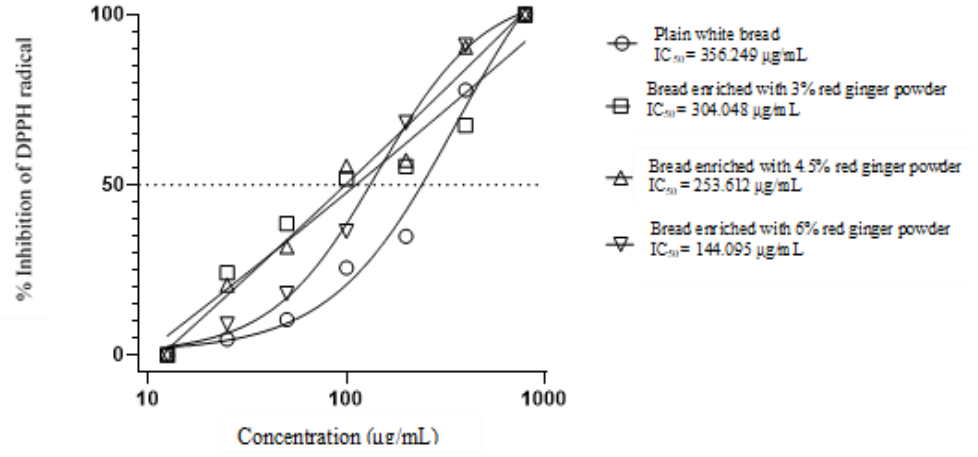

Figure 2. IC_{50} curves of bread enriched with red ginger powder

This work continued our previous study in discovering a new variant of healthy bread. Red ginger enriched bread containing 6% red ginger powder (named RGB), has been produced. The bread, preferred by 30 panelists, has been proven could be stored for approximately 9 days without showing deterioration or the growth of mold [13]. The antioxidant activity of the red ginger enriched-breads proved that bread enriched with 6% red ginger powder possesses the strongest radical scavenging activity (IC_{50} = 144.095 µg/mL) compared to the other varieties of bread **(Figure 2)**. It was predicted that flavonols containing in red ginger powder had solely contributed to this radical scavenging activity.

Flavonols, e. g. kaempferol, gingerol, shogaol, quercetin, etc., are flavonoids with a carboxyl (-C=O) group and a hydroxyl (-OH) in position 3 of the C ring [19, 20]. These secondary metabolites are present abundantly in plants. A food diet with flavonols was found to be associated with an increase in health benefits, due to its antioxidant potential [21-24].

Determination of 10-gingerol in the RGB extract

To ensure that the method is appropriate for the determination of 10-gingerol in the RGB, a validation procedure was applied and resulted that the analytical method is accurate (% recovery = is 103.58) and high precision (RSD = 1.1424%). The LOD is 6.03 µg/mL and LOQ = 20.11 µg/mL.

The LC chromatogram of the 10-gingerol standard in the validated system indicated that this compound was eluted at 40.307 minutes **(Figure 3)**. A similar LC condition for RGB extract showed that 10-gingerol was positively contained in the bread, as proved by the presence of a small peak at 43.198 minutes **(Figure 4)**. The difference in the retention time indicated that the baking process (10 minutes at 190 °C) might have converted the 10-gingerol in RGB to its dehydrated form.

Gingerol is a thermolabile flavonol compound due to its β-hydroxy keto group in the structure. This compound undergoes dehydration to form shogaol [25, 26]. However, a previous study reported that the low-temperature drying process of ginger rhizome (up to 60 °C) did not significantly affect the content of 6-gingerol [27].

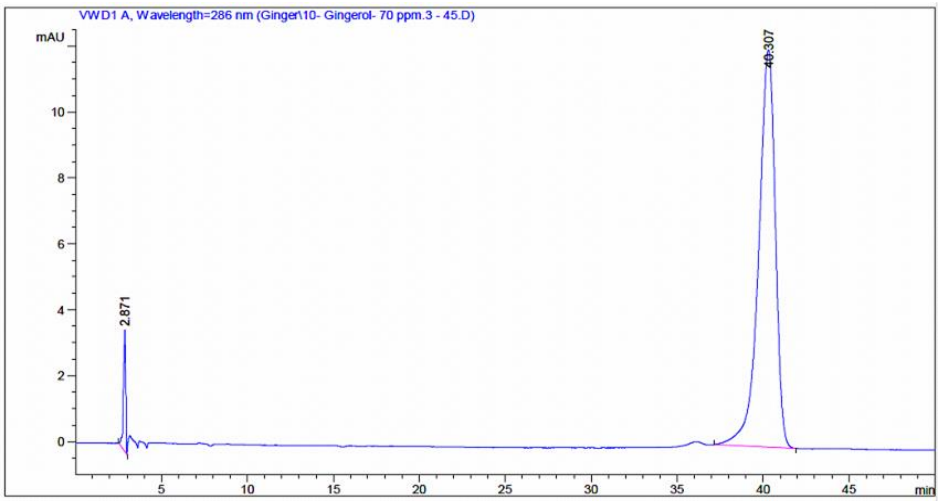

Figure 3. LC chromatogram of 10-gingerol standard (tR = 40.3 min)

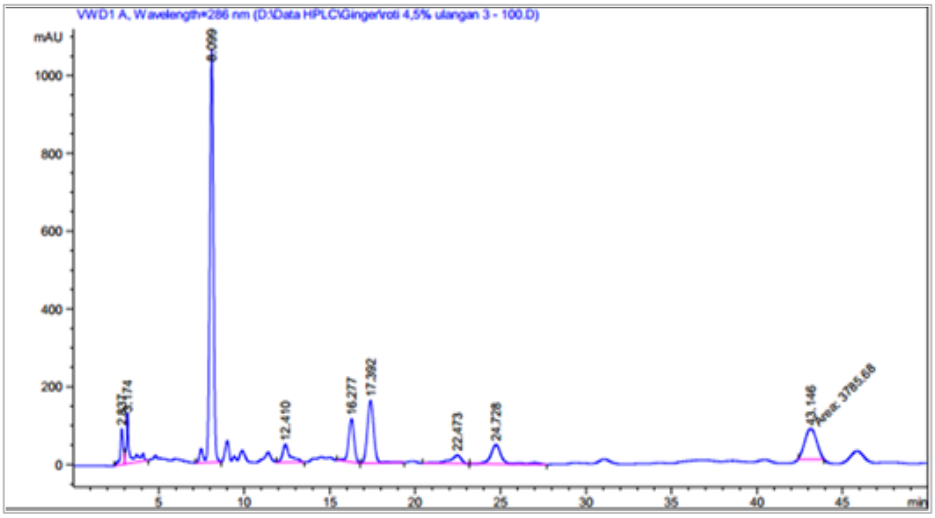

Figure 4. LC chromatogram of 10-gingerol in RGB extract (tR = 43.146 min)

By employing the linear regression equation of the 10-gingerol standard curve (y= 11.79x -35.33), the concentration of the flavonol compounds in RGB extract, calculated as 10-gingerol, is 381.17 µg/mL or 0.038% w/v.

The effect of RGB on the BMI, abdominal circumference, and blood pressure of healthy subjects

The consumption of RGB for 14 days significantly lowered both the systolic and diastolic blood pressure as well as the abdominal circumference of the subjects **(Table 1)**.

Table 1. The effect of RGB on the BMI, abdominal circumference, and blood pressure of the subjects (n=20). * denotes significant difference ($p < 0.005$)

Parameter		Mean	t/Z	*p*-value
BMI (kg/m^2)	Pre	23.6490	0.773	0.449
	Post	23.5780		
Abdominal circumference (cm)	Pre	77.4450	3.297	0.004*
	Post	74.1475		
Systolic (mmHg)	Pre	116.75	5.482	0.000*
	Post	105.75		
Diastolic (mmHg)	Pre	82.50	6.097	0.000*
	Post	75.00		

Ginger, which contains calcium, magnesium, potassium, and phosphorus, has been proven to possess a role in the regulation of blood pressure. A quasi-experimental design on 80 outpatients with hypertension at Menoufia University Hospital in Egypt treated with ginger for a month indicated a significant decrease in blood pressure of the patients treated with ginger compared to the control group [28]. Furthermore, it was reported in a systematic and meta-analysis review article that ginger supplementation (dose of > 3 g/day; duration > 8 weeks) had reduced the blood pressure of subjects with the age < 50 years [29].

The effect of RGB on the urinalysis parameters (leucocyte, protein, nitrite, urobilinogen, pH, ketones, red blood cells, SG-scientific gravity, glucose, and bilirubin) and the lipid profile (total cholesterol, triglyceride, HDL, and LDL of the subjects is presented in **Tables 2 and 3**. The intervention with RGB did not alter all urinalysis parameters. A decrease in leucocyte level and pH and a slight increase of gravity and ketone in the urine of the subjects were observed, although the values are not significant **(Table 2)**. Nevertheless, the 14-day daily consumption of RGB after breakfast could significantly decrease the total cholesterol ($p = 0.032$) and increase the HDL level ($p = 0.000$) in the blood of the subjects **(Table 3)**. RGB has been proven to contain flavonol compounds **(Figure 4)**, which contribute to its pharmacological activity.

Table 2. The effect of RGB on the urinalysis parameters of the subjects (n=20)

Parameter		Mean	t/Z	*p*-value
Leukocyte (Leu/µL)	Pre	6.2500	-1.000	0.317
	Post	3.5000		
Nitrite (mg/dL)	Pre	0.0000	-1.000	1.000
	Post	0.0000		
Urobilinogen (mg/dL)	Pre	0.2000	0.000	1.000
	Post	0.2000		
Protein (mg/dL)	Pre	0.0000	0.000	1.000
	Post	0.0000		
pH	Pre	5.2000	-3.378	0.705
	Post	5.1500		
Erythrocyte (Rbc/µL)	Pre	0.0000	0.000	1.000
	Post	0.0000		
SG	Pre	1.0035	-2.650	0.008
	Post	1.0090		
Ketone (mg/dL)	Pre	0.0000	0.000	0.317
	Post	0.2500		
Bilirubin (mg/dL)	Pre	0.0000	0.000	1.000
	Post	0.0000		
Glucose (mg/dL)	Pre	0.0000	0.000	1.000
	Post	0.0000		

Table 3. The effect of RGB on the lipid profile of the subjects (n=20)

Parameter		Mean	t/Z	p-value
Total cholesterol (mg/dL)	Pre	132.90	2.314	0.032*
	Post	122.00		
LDL (mg/dL)	Pre	74.60	0.304	0.765
	Post	73.20		
HDL (mg/dL)	Pre	33.70	-5.970	0.000*
	Post	41.95		
Triglyceride (mg/dL)	Pre	106.75	0.966	0.346
	Post	98.35		

* denotes significant difference ($p < 0.005$)

It was reported that ginger had exerted reasonable anti-inflammatory, antioxidant, antiplatelet, antihypertensive, and hypolipidemic effects in *in vitro* and animal studies [30]. The ginger extract could also remarkably reduce the abnormalities of heart structure in diabetic rats and improved the serum apo, leptin, cathepsin G, and homocysteine levels [31]. A very recently published article reported that treatment by ginger extract could reduce fibrosis of diabetic rat's myocardial which was predicted through regulation of the expression of genes involved in the SMAD/TGF-β pathway [32].

Furthermore, a study on more than one thousand subjects in Finland, aged 42-60, free of prior coronary heart disease or stroke, treated with dietary flavonoids, proved that high intakes of flavonoids may be correlated with decreased risk of ischaemic stroke and possibly with reduced cardiovascular disease mortality [33]. A meta-analysis study about intervention trials for patients suffering from cardiovascular disease demonstrated that there was a negative correlation between flavonol intake and coronary heart disease and stroke [34]. Moreover, resveratrol and flavonols have been proven to possess vasorelaxant and antioxidant activity which improve cardiovascular function [35]. Interestingly, a prospective cohort study (n=56048 participants) reported that a moderate habitual intake of flavonoids (approximately 500 mg/day) is inversely associated with all-cause, cardiovascular- and cancer-related mortality [36]. Furthermore, a systematic review reported that there were twenty-two phase II and one phase III clinical trials that used flavonoids as a single agent or combined with other therapeutics against hematopoietic/lymphoid or solid cancer. Among those, flavopiridol is the most frequently used [37].

However, reports about red ginger (*Zingiber officinale* var. Rubrum) are still limited or none.

Conclusion

The new variant of bread containing 6% red ginger powder (named RGB) could be proposed and developed as a healthy bread. RGB indicates a medium strength of antioxidant activity and significantly reduces the abdominal circumference and blood pressure of healthy subjects. This bread also improves the lipid profile of the subjects. However, further studies in larger subjects are still needed.

Acknowledgments: This work was funded by (1) Universitas Padjadjaran Academic-Leadership Grant 2019 and (2) the Indonesian Adventist University (UNAI). We would like to thank (1) the Rector of Universitas Padjadjaran; (2) the Dean of Postgraduate School Universitas Padjadjaran; and (3) the Dean of Faculty of Mathematics and Natural Sciences of the Indonesian Adventist University (UNAI), for their supports and facilitation to this work.

Conflict of interest: None

Financial support: None

Ethics statement: The protocol study in humans has been approved by Universitas Padjadjaran Ethics Research Committee (https://kep.unpad.ac.id/ document No. 696/UN6.KEP/EC/2019) by following the principles of the Declaration of Helsinki.

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