Prev. Nutr. Food Sci. 2022;27(4):365-375
https://doi.org/10.3746/pnf.2022.27.4.365
ISSN 2287-8602

Effects of Riceberry Rice Bran Oil Supplementation on Oxidative Stress and Cardiovascular Risk Biomarkers in Older Adults with Prehypertension

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ABSTRACT: We investigated the changes in the oxidative stress and cardiovascular disease risk biomarkers, including the activity of the cardiac autonomic nervous system, in older adults with prehypertension following Riceberry rice bran oil supplementation. A total of 35 women aged 60 to 76 years with prehypertension were randomly allocated to two groups, one of which was supplemented with rice bran oil (n=18) and the other with Riceberry rice bran oil (n=17) at 1,000 mg daily for 8 weeks. Prior to and after the supplementation, oxidative stress and cardiovascular risk biomarkers (primary outcomes), heart rate variability, and blood pressure (secondary outcomes) were investigated. Results showed that plasma malondialdehyde, blood glutathione disulfide, and tumor necrosis factor-alpha levels were significantly decreased, and the ratio of reduced glutathione to glutathione disulfide significantly increased in both groups after supplementation (all $P<0.05$). No significant differences were observed between groups. Heart rate variability and blood pressure did not statistically significantly change subsequent to supplementation in either group and did not differ between groups. In conclusion, Riceberry rice bran oil supplementation for 8 weeks alleviates oxidative stress and inflammation in older adults with prehypertension to a similar extent as rice bran oil supplementation.

Keywords: antioxidants, autonomic nervous system, blood pressure, cardiovascular diseases, rice

INTRODUCTION

The incidence of prehypertension or high normal blood pressure (BP) has increased steadily worldwide. This incidence is accelerated by the aging population and is higher in females than in males (Hu et al., 2017). It is estimated that prehypertension affects approximately 25～50% of adults worldwide (Egan and Stevens-Fabry, 2015). Epidemiological data from the InterAsia study reported that 21% of adults in Thailand were affected by prehypertension (Yu et al., 2008). Prehypertension has been related to cardiovascular control dysfunction and sympathetic hyperactivity (Mancia and Grassi, 2014); moreover, it has been linked to a risk of hypertension that is approximately twice that of individuals with normal BP levels. Hypertension is an important risk factor for cardiovascular diseases (CVDs), chronic kidney disease, and even death (Qaiser et al., 2020; Lydia et al., 2021). Effective regulation of prehypertension has been reported to decrease CVDs, such as coronary heart disease, stroke, and myocardial infarction, by more than 10% (Han et al., 2019).

Clinical studies on the prevention of hypertension have recommended that prehypertension can be managed by medications such as angiotensin-converting enzyme inhibitors, calcium channel blockers, diuretics, and beta blockers as well as lifestyle changes, including a healthy and balanced diet and physical activity (Egan and Stevens-Fabry, 2015). At present, there is a growing interest in the use of dietary supplements derived from edible plant, including fruits, vegetables, and cereals, in the prevention and management of hypertension. The most common elements of foods consist of potassium, nitrates, vitamins C and E, carotenoids, and polyphenols (Ardiansyah et al.,

Received 25 July 2022; Revised 25 October 2022; Accepted 22 November 2022; Published online 31 December 2022

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2006; Whelton et al., 2018; Jun and Xiang, 2020).

Among these foods, rice has been reported to provide health benefits because it contains several nutrients and antioxidant compounds (Leardkamolkarn et al., 2011). Rice bran is known to be rich in phytochemicals, including phytosterols that are beneficial for health (Zarei et al., 2017). Moreover, γ-oryzanol, tocopherols, and tocotrienols, which are present in pigmented rice bran extract, are powerful antioxidants that have been shown to be effective in the treatment of disorders such as CVDs, diabetes mellitus, kidney stones, fatty liver, and cancers (Jariwalla, 2001; Ardiansyah et al., 2006; Somintara et al., 2016).

Riceberry is a Thai dark purple variety of rice (*Oryza sativa* L.) that is a crossbreed of Hom Nil rice (Thai black rice) and Khao Dawk Mali 105 (Thai jasmine rice or Thai fragrant rice). Riceberry rice bran comprises high levels of antioxidants such as phenols and anthocyanin, which have been reported to have strong anticancer, antioxidant, antidiabetic, and antihypertensive properties and reduce sympathetic overactivity (Thamnarathip et al., 2016; Bruno and Ghiadoni, 2018; Mattioli et al., 2020; Boy et al., 2021). In addition, both *in vitro* and *in vivo* studies have revealed that γ-oryzanol, tocopherols, and tocotrienols found in the bran extract and oil of pigmented rice have antioxidant and antiinflammatory properties, inhibit cholesterol oxidation and tumor growth, and lower blood lipids and BP (Kim et al., 2013; Yoon et al., 2014; Somintara et al., 2016).

Experimental studies on supplementation with rice bran have proved its advantageous effects on blood lipoproteins and cholesterols in healthy, hypercholesterolemic, and type 2 diabetes individuals (Rajnarayana et al., 2001; Most et al., 2005; Lai et al., 2012). However, there is inadequate evidence in humans to support the antihypertensive effect of Riceberry rice bran. Hence, we aimed to investigate the effects of Riceberry rice bran oil (RRBO) supplementation on oxidative stress and cardiovascular risk biomarkers as well as cardiac autonomic nervous system activity and BP in older adults with prehypertension. We hypothesized that oxidative stress and cardiovascular risk biomarkers, cardiac autonomic nervous system activity, and BP levels would be improved with RRBO supplementation.

MATERIALS AND METHODS

Study design and participants

This study was a randomized clinical trial with an open-label dietary approach and was conducted from February to August 2019. This study was registered in the Thai Clinical Trials Registry (https://www.thaiclinicaltrials.org; registration no. TCTR20190322002; date of registration: 22/03/2019). Older women with prehypertension who enrolled in the Burapha University Hospital or the Aging Society of the Saensuk Municipality, Chonburi Province, were included. The sample size for this study was calculated based on the difference between two means. Devarajan et al. (2016) reported that the mean systolic BP (SBP) in patients with hypertension was reduced by 15 mmHg 1 month after supplementation with sesame oil mixed with rice bran oil (RBO), with a standard deviation of 17 mmHg. With an alpha error of 0.05, a beta error of 0.20, and the power of the test of 0.80, the sample size for this study was 16 per group, for a total of 20 participants, including a plausible 20% dropout proportion.

Screening of participants

All participants were screened using health questionnaire forms, which included questions on the present and past ailments, drugs and dietary supplements used, and physical activity behavior. All participants underwent measurements of anthropometric parameters, such as height, body mass, and body mass index; fat distribution parameters, such as waist and hip circumferences and their ratios; and physiological parameters, such as BP and pulse rate.

Participants were included if they met the following criteria: aged 60～80 years old and had an SBP of 120～139 mmHg or a diastolic BP (DBP) of 80～89 mmHg according to the 2007 European Society of Hypertension/European Society of Cardiology guidelines (Mansia et al., 2007). The exclusion criteria were as follows: regular smoker or drinker; regular exerciser; possessing underlying illnesses such as CVDs, diabetes mellitus, obesity, renal diseases, or thyroid diseases that may affect cardiac autonomic nervous system function; having liver or renal diseases that may influence waste clearance; having a history of allergy to Riceberry rice or its processed product; or taking any dietary supplements 2 months before participating in the study. To confirm the participants' BP levels, all participants had their BP levels measured in the morning twice, separated by a week.

Prior to screening, all participants received verbal and written information about the study details and a consent form for participation. Therefore, the written informed consents were obtained from the participants. All documents in this study are in accordance with the ethical standards of the Human Ethics Committee of Burapha University (approval no. 15/2562; date of approval: 12/02/2019) and the 1964 Declaration of Helsinki and its later amendments.

Experimental protocol

One week after screening, the experiment was initiated in the morning. The eligible participants were randomly allocated into one of the two study groups (1:1) using

the online software True Random Number Service (random.org). Randomization and allocation were carried out by a research assistant; thus, until the final analyses were completed, the researchers were unaware of which supplements the participants received. Each participant received either 1,000 mg/d of RBO or RRBO, 500 mg×2 capsules, 30 min after breakfast daily for 8 weeks. The duration and dosage of supplementation were considered based on previous reports in patients with mild-to-moderate hypertension and type 2 diabetes (Lai et al., 2012; Devarajan et al., 2016) and the availability of the study supplements. The primary outcomes were changes in oxidative stress and cardiovascular risk biomarkers. The secondary outcomes were changes in heart rate variability (HRV) and BP variables.

All participants were requested to maintain their daily lifestyles during the study period, including dietary consumption and physical activity behaviors. They were also requested to inform any research assistant or researcher of any alterations in their medical treatment, including changes in medicine, supplements, diet, or physical activity, as well as any adverse effects of the supplements received. If the participants changed their medical treatment or underwent any serious adverse effects resulting from the supplements, they were withdrawn from the study.

Study supplements

The RBO supplement used for the experiment was RBO with rice bran and germ oil capsules obtained from Khao Dawk Mali 105 rice. It was commercially supplied by Herbal One Co., Ltd. (Sam Phran, Thailand). Each capsule contained 1.35 g/100 g of γ-oryzanol, 245.22 mg/100 g of γ-tocopherol, 34.04 mg/100 g of γ-tocotrienol, and 1.68 mg/mL of the antioxidant 2,2-diphenyl-1-picrylhydrazyl (DPPH). β-Carotene and lutein levels were too low to be detected. Similarly, the RRBO supplement used in this study was RRBO with rice bran and germ oil capsules, which were commercially supplied by Sunfood Corp., Co., Ltd. (Mueang Samut Prakan, Thailand). Each capsule comprised 1.4 g/100 g of γ-oryzanol, 24 mg/100 g of γ-tocopherol, 45 mg/100 g of γ-tocotrienol, and 0.32 mg/mL of the antioxidant DPPH as well as 2.3 mg/100 g of β-carotene and 1.5 mg/100 g of lutein. All analyses were performed using high-performance liquid chromatography (HPLC) by the Central Laboratory Co., Ltd. (Bangkok, Thailand) and the Manose Health and Beauty Research Center Co., Ltd. (Chiang Mai, Thailand).

Throughout the study, the supplements were stored at room temperature (23～24°C) with a relative humidity of 40～50%. Packages were encoded and supplied to participants monthly by a research assistant. A supplementary intake record was provided to the participants to record their supplementation details. The participants were asked to fill in this record daily and return it every 4 weeks. Besides, participants were also reminded to take their supplements via telephone calls made weekly. These methods helped us determine compliance (≥80% of the supplementation was considered to be compliant), ensure adherence to the study experiment as much as possible, and minimize study withdrawal.

Blood sampling

After 12 h of overnight fasting, 10 mL of the participants' blood was collected via venipuncture between 8:00 a.m. and 9:00 a.m. Furthermore, 4 mL of blood samples were collected in ethylenediaminetetraacetic acid tubes and immediately centrifuged at 3,000 rpm at room temperature for 10 min, and plasma and serum samples were separated from whole blood and kept at −80°C until oxidative stress and inflammatory biomarker tests were performed. Then, 6 mL of blood was collected in glucose and heparin tubes and sent for analysis of cardiovascular risk biomarkers on the sampling day.

Oxidative stress and inflammatory biomarker assays

Blood glutathione (GSH) in its reduced form, glutathione disulfide (GSSG), and total GSH concentrations were measured as described previously by Nakmareong et al. (2012). The GSH/GSSG ratio was then calculated. Serum vitamin E levels were measured using HPLC (N Health Laboratory, National Healthcare Systems Co., Ltd., Bangkok, Thailand). Plasma malondialdehyde (MDA) levels, a biomarker of lipid peroxidation, were measured using the thiobarbituric acid reactive substance assay, as described previously by Kukongviriyapan et al. (2015). Plasma tumor necrosis factor-alpha (TNF-α) concentrations were measured using Human TNF-α enzyme-linked immunosorbent assay kits (ab181421, Abcam, Cambridge, UK) as per the manufacturer's instructions.

Cardiovascular risk biomarker assays

Fasting blood glucose (FBG) concentration and lipid profiles were measured by the Medical Laboratory Unit, Burapha University Hospital, Burapha University. FBG, serum triglyceride (TG), and serum total cholesterol (TC) concentrations were measured using enzymatic methods. Serum high-density lipoprotein cholesterol (HDL-C) concentrations were measured by the accelerator selective detergent method. These assays were completed using a standard automated laboratory machine (Architect c8000, Abbott, Lake Bluff, IL, USA). Serum low-density lipoprotein cholesterol (LDL-C) concentration was calculated based on the TC, HDL-C, and TG concentrations. The atherosclerogenic index, an indicator of CVD risk, was calculated based on the TC and HDL-C values using the following equation:

$$\text{Atherosclerogenic index} = \frac{\text{TC} - \text{HDL-C}}{\text{HDL-C}}$$

Cardiac autonomic nervous system activity and BP assessments

To assess the activity of the autonomic nervous system, HRV analysis was performed. BP and HRV assessments were conducted with the participant in a supine position after resting for 10 min. BP was assessed twice, 1 min apart, using an automatic digital BP monitor (Microlife BP 3AQ1, Microlife AG Swiss Corp., Widnau, Switzerland), and the mean of the two readings was reported. The pulse pressure, mean arterial pressure, and rate-pressure product was calculated using the SBP, DBP, and pulse rate values.

Lead II electrocardiography (PowerLab 4/30, ADInstruments, Bella Vista, NSW, Australia) was employed to record the short-term HRV for 10 min, and the HRV module of the LabChart® Pro software (ADInstruments) was used to analyze the HRV data. To analyze the HRV data, the time and frequency domains were interpreted. The time domain encompassed the values of the standard deviation of the normal beat-to-normal beat intervals (SDNN) and the root mean square of successive R-R interval differences (RMSSD), and the frequency domain comprised the values of total power, very-low, low, and high-frequency powers (direct current potential～0.04, 0.04～0.15, and 0.15～0.4 Hz, respectively) and low-/high-frequency ratio.

Anthropometric and body composition measurements

Participant height was measured using a stadiometer (Health-o-Meter ProSeries, Pelstar Inc., New York, NY, USA). Body mass, body mass index, and body composition were measured using a body composition analyzer (InBody270, InBody Co., Ltd., Daejeon, Korea) based on bioelectrical impedance analysis. Fat distribution was measured from waist and hip circumferences and their ratios. All measurements were conducted with the participant in the standing position and wearing minimal clothing, as described previously by Vierra et al. (2022).

Statistical analysis

Data were presented as mean and standard deviation. All statistical analyses were performed using IBM SPSS Statistics software (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test and visual histogram assessment were employed to determine the data distribution. The independent *t*-test was used to compare differences in variables between the groups at baseline. The two-way repeated-measures analysis of variance and paired *t*-test were used to compare differences in variables between the groups after the supplementation and in each group before and after the supplementation, respectively. A *P*-value of less than 0.05 was considered significant.

RESULTS

From an initial pool of 40 participants, 2 participants in the RBO group (10%) and 3 in the RRBO group (15%) were withdrawn from the study, as they could not sustain the daily supplementation of more than 80% for 8 weeks. Hence, 35 participants (87.5%)－18 participants in the RBO group (90%) and 17 participants in the RRBO group (85%)－completed the study, and their data were analyzed (Fig. 1).

Physical and physiological characteristics

Age, height, body mass, body mass index, percent body fat, fat mass, percent fat-free mass, fat-free mass, fat-free mass index, percent body water, water mass, protein mass, mineral mass, visceral fat level, basal metabolic rate, waist circumference, hip circumference, or waist/hip

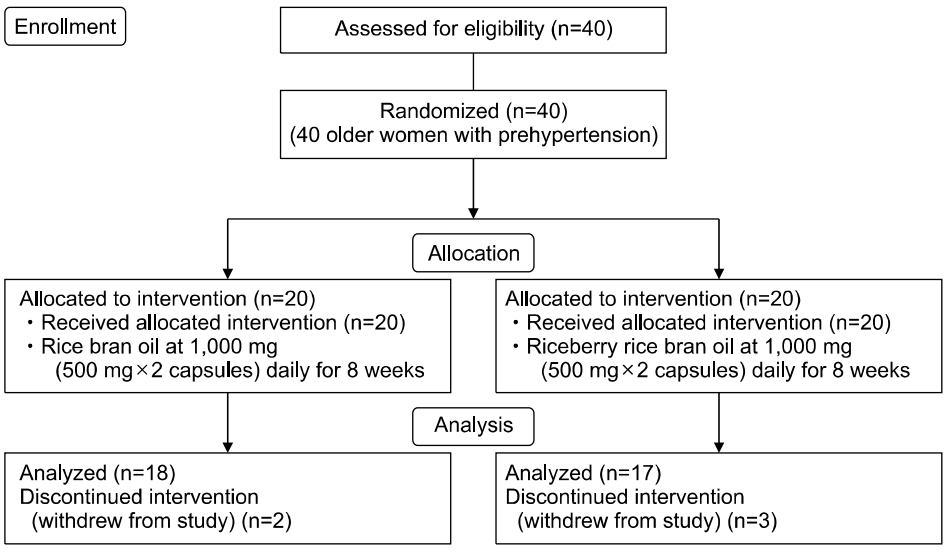

Fig. 1. Flow diagram of the study.

Table 1. Physical and physiological characteristics of participants before and after the supplementation

	Rice bran oil group (n=18)			Riceberry rice bran oil group (n=17)			*P*-value
	Before	After	Change (%)	Before	After	Change (%)	
Age (yr)	66.00±4.41	66.00±4.41	–	66.53±4.76	66.53±4.76	–	0.621
Height (m)	1.56±0.08	1.57±0.08	–	1.53±0.06	1.53±0.06	–	0.155
Body mass (kg)	57.98±11.64	57.71±11.44	−0.27 (−0.41)	56.79±6.57	55.95±6.18*	−0.84 (−1.40)	0.158
Body mass index (kg/m^2)	23.68±3.66	23.52±3.48	−0.16 (−0.57)	24.43±2.79	24.00±2.38*	−0.43 (−1.57)	0.495
Body fat (%)	34.61±7.73	34.15±7.40	−0.46 (−0.39)	34.67±7.76	34.05±7.91	−0.62 (−1.17)	0.866
Fat mass (kg)	20.63±7.47	20.47±7.58	−0.16 (−0.08)	19.59±5.93	19.58±5.71	−0.01 (−0.49)	0.955
Fat-free mass (%)	65.38±7.76	65.87±7.37	0.49 (0.86)	65.33±7.75	65.79±7.94	0.46 (0.08)	0.563
Fat-free mass (kg)	37.07±4.90	37.52±4.81	0.45 (1.31)	36.26±3.26	36.81±3.37	0.55 (1.54)	0.907
Fat-free mass index	0.65±0.08	0.66±0.07	0.01 (1.80)	0.64±0.08	0.66±0.08	0.02 (3.07)	0.779
Body water (%)	47.96±5.55	48.32±5.31	0.36 (0.84)	48.09±5.88	48.10±5.71	0.01 (0.11)	0.507
Water mass (kg)	27.20±3.61	27.53±3.57	0.33 (1.29)	26.69±2.39	27.08±2.50	0.39 (1.45)	0.926
Protein mass (kg)	7.19±0.98	7.29±0.94	0.10 (1.55)	7.07±0.63	7.17±0.65	0.10 (1.45)	0.680
Mineral mass (kg)	2.66±0.33	2.68±0.31	0.02 (0.57)	2.50±0.26	2.55±0.25	0.05 (2.29)	0.639
Visceral fat level	8.22±2.62	8.00±2.66	−0.22 (−2.63)	7.94±2.16	7.71±2.05	−0.23 (2.99)	0.905
Waist circumference (cm)	83.43±9.27	79.33±8.69	−4.10 (−0.27)	80.13±6.94	78.00±6.56	−2.13 (−2.12)	0.325
Hip circumference (cm)	99.07±8.43	97.94±9.03	−1.13 (−1.88)	96.69±5.19	95.43±6.89	−1.26 (−0.65)	0.104
Waist/hip ratio	0.89±0.05	0.89±0.06	0.00 (−0.10)	0.89±0.06	0.88±0.05	−0.01 (−0.61)	0.344
Basal metabolic rate (kcal/d)	1,170.83±105.72	1,180.17±103.86	9.34 (0.83)	1,153.29±70.44	1,164.94±72.91	11.65 (−1.02)	0.877

Data are presented as mean±SD.
*P<0.05, significantly different from before supplementation (paired t-test).

ratio were not significantly different between the RBO and RRBO groups before supplementation. Within-group analysis showed that body mass (P=0.024) and body mass index (P=0.042) significantly decreased in the RRBO group after supplementation. No significant differences were noted between groups (Table 1).

Oxidative stress biomarkers

Before supplementation, baseline GSH, GSSG, total GSH, vitamin E, and MDA concentrations and the GSH/GSSG ratio did not differ between the RBO and RRBO groups. Following the 8-week supplementation, GSSG and MDA concentrations decreased significantly in both the RBO (P<0.001 and P=0.009) and RRBO (P<0.001 and P=0.001) groups. In addition, the GSH/GSSG ratio increased significantly in both groups (both P<0.001). There were no significant differences between the groups after supplementation (Table 2 and Fig. 2～5).

Cardiovascular risk biomarkers

There were no significant differences in baseline FBG, TG, LDL-C, HDL-C, TC, or TNF-α concentrations; TC/HDL-C ratio; or the atherosclerogenic index between the RBO and RRBO groups before supplementation. Comparison of these values pre- and post-supplementation indicated that the TNF-α concentration decreased significantly in both the RBO (P=0.003) and RRBO (P=0.002) groups after supplementation. No significant differences were found between groups (Table 3 and Fig. 6).

Cardiac autonomic nervous system activity

No significant differences were observed at baseline in resting HRV variables, including values of SDNN, RMSSD, total power, very-low-frequency power, low-frequency power, low frequency in normalized unit power, high-frequency power, high frequency in normalized unit power, and the low-/high-frequency ratio between the RBO and RRBO groups before supplementation. After supplementation, the HRV variables were not statistically

Table 2. Antioxidant biomarkers of participants before and after the supplementation

	Rice bran oil group (n=18)			Riceberry rice bran oil group (n=17)			*P*-value
	Before	After	%Change	Before	After	%Change	
Total glutathione (μmol/L)	3,148.70±818.86	3,276.49±757.64	6.19	3,182.34±754.62	3,385.18±1,031.33	6.85	0.710
Vitamin E (mg/L)	13.56±2.61	13.91±2.90	4.66	13.04±3.58	13.13±3.22	2.06	0.579
Vitamin E (μmol/L)	31.47±6.05	32.29±6.74	4.61	30.27±8.32	30.48±7.48	2.06	0.584

Data are presented as mean±SD.

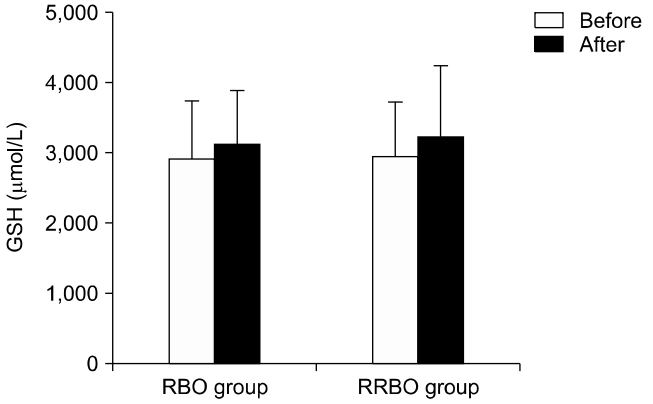

Fig. 2. Glutathione (GSH) in the rice bran oil (RBO) and Riceberry rice bran oil (RRBO) groups before and after supplementation. Data are presented as mean±SD.

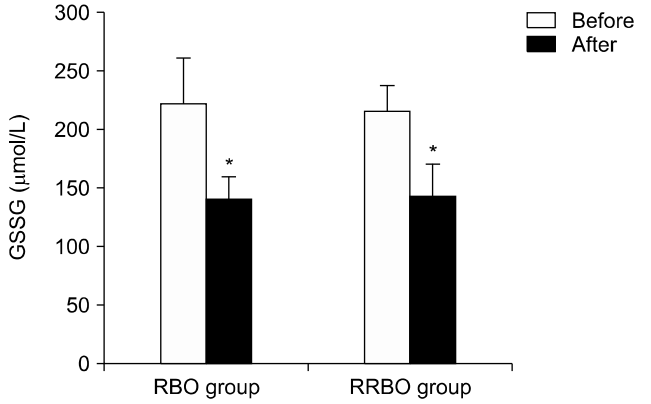

Fig. 3. Glutathione disulfide (GSSG) in the rice bran oil (RBO) and Riceberry rice bran oil (RRBO) groups before and after supplementation. Data are presented as mean±SD. *Statistically significant $P<0.05$.

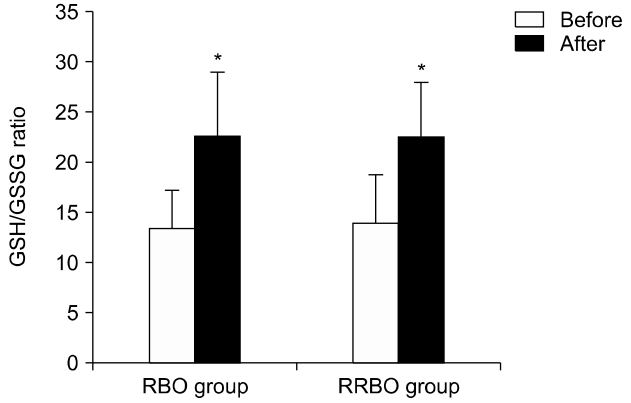

Fig. 4. Glutathione (GSH)/glutathione disulfide (GSSG) ratio in the rice bran oil (RBO) and Riceberry rice bran oil (RRBO) groups before and after supplementation. Data are presented as mean±SD. *Statistically significant $P<0.05$.

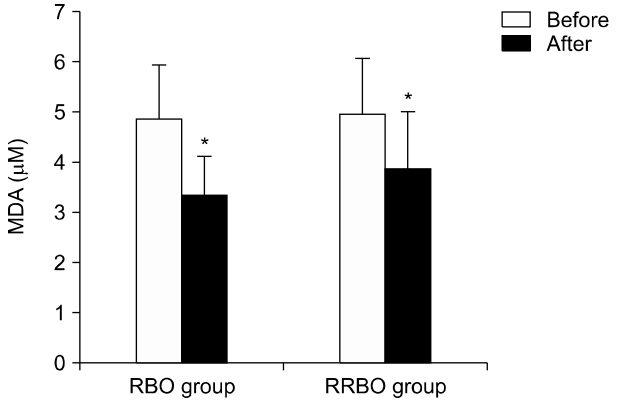

Fig. 5. Malondialdehyde (MDA) in the rice bran oil (RBO) and Riceberry rice bran oil (RRBO) groups before and after supplementation. Data are presented as mean±SD. *Statistically significant $P<0.05$.

Table 3. Cardiovascular risk biomarkers of participants before and after the supplementation

	Rice bran oil group (n=18)			Riceberry rice bran oil group (n=17)			*P*-value
	Before	After	Change (%)	Before	After	Change (%)	
Fasting blood glucose (mg/dL)	90.67±9.27	89.18±5.46	−1.49 (−0.49)	91.82±10.43	89.44±7.19	−2.38 (−1.77)	0.915
Triglyceride (mg/dL)	129.44±54.16	126.33±54.77	−3.11 (−4.84)	126.25±60.72	123.00±67.29	−3.25 (−4.20)	0.807
LDL-C (mg/dL)	139.67±27.96	135.83±26.62	−3.84 (−2.31)	155.81±33.99	142.65±39.74	−13.16 (−5.47)	0.699
HDL-C (mg/dL)	54.11±13.57	55.72±14.27	1.61 (3.59)	49.18±8.10	51.56±9.69	2.38 (6.00)	0.753
TC (mg/dL)	221.22±30.68	215.28±31.52	−5.94 (−2.60)	231.31±40.60	215.35±45.61	−15.96 (−4.53)	0.602
TC/HDL-C ratio	4.29±1.09	4.05±0.99	−0.24 (−4.75)	4.84±1.08	4.41±1.14	−0.43 (−7.65)	0.950
Atherosclerogenic index	3.29±1.09	3.05±0.99	−0.24 (−6.26)	3.84±1.08	3.41±1.14	−0.43 (−9.46)	0.950

Data are presented as mean±SD.
LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol.

significantly different in either the RBO or the RRBO group. Besides, no significant differences were detected between the groups (Table 4).

BP

Before supplementation, resting HR and BP variables, including SBP, DBP, pulse pressure, mean arterial pressure, and rate-pressure product at baseline, did not differ between the RBO and RRBO groups. Neither HR nor BP variables were significantly altered after supplementation in either the RBO or the RRBO group. There were also no significant differences between the two groups (Table 5).

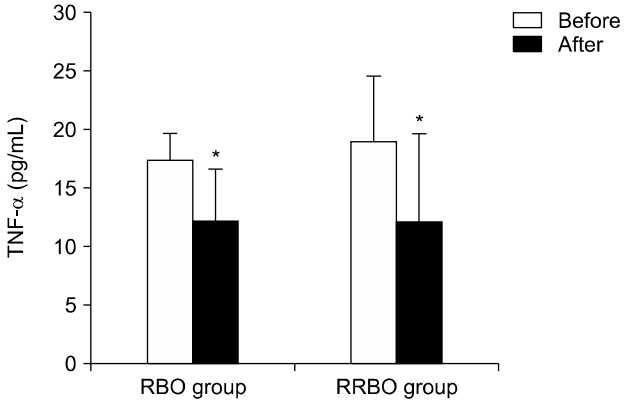

Fig. 6. Tumor necrosis factor-alpha (TNF-α) in the rice bran oil (RBO) and Riceberry rice bran oil (RRBO) groups before and after supplementation. Data are presented as mean±SD. *Statistically significant $P<0.05$.

DISCUSSION

The hypothesis underlying this study was that oxidative stress and CVD-risk biomarkers, cardiac autonomic nervous system activity, and BP variables would be improved by RRBO supplementation. As per the findings of this study, plasma MDA, blood GSSG, and TNF-α concentrations significantly decreased, while the GSH/GSSG ratio increased significantly in participant groups supplemented with either RBO or RRBO, with no significant difference between the groups. HRV and BP variables did not change after either form of supplementation, and no differences were found between the groups.

Supplementation with rice bran and its active components, such as oryzanols, tocopherols, tocotrienols, phytosterols, and nucleotides, has been shown in animal experiments to be effective against chronic diseases such as hypertension, dyslipidemia, diabetes mellitus, metabolic syndrome, obesity, and inflammation (Ardiansyah et al., 2009; Palou et al., 2015; Wang et al., 2015; Alauddin et al., 2016; Duansak et al., 2022; Munkong et al., 2022).

We compared the major elements detected in the supplements in this study. RBO and RRBO capsules contained equivalent concentrations of γ-oryzanol and γ-tocotrienol, but RRBO had a lower concentration of antioxidants and a markedly lower concentration of γ-tocopherol. However, it also contained β-carotene and lutein, which were not found in the RBO capsule. Based on the constituent analyses and findings of comparable effects on oxidative stress and inflammatory biomarkers after RBO and RRBO supplementation, we speculate that in

Table 4. Heart rate variability of participants before and after the supplementation

	Rice bran oil group (n=18)			Riceberry rice bran oil group (n=17)			*P*-value
	Before	After	%Change	Before	After	%Change	
SDNN (ms)	47.00±19.47	58.03±28.15	36.07	51.33±17.75	59.44±18.94	26.53	0.934
RMSSD (ms)	43.39±18.66	51.82±39.05	26.22	49.72±29.75	57.19±32.77	29.38	0.836
Total power (ms^2)	2,335.91±1,930.37	3,327.41±3,963.33	92.35	2,470.09±1,935.94	3,229.05±2,129.86	74.21	0.330
VLF power (ms^2)	855.55±590.30	1,187.05±923.29	89.26	963.97±539.46	1,326.06±925.34	272.39	0.703
LF power (ms^2)	693.77±1,305.95	555.42±600.71	−312.33	440.64±385.91	403.58±504.72	−58.22	0.506
LF power (nu)	35.02±9.77	32.55±11.55	−4.64	34.55±19.53	30.18±16.90	−3.45	0.611
HF power (ms^2)	707.98±692.24	1,038.82±1,568.50	102.94	994.60±959.90	1,385.90±2,948.92	111.53	0.737
HF power (nu)	46.26±10.13	49.12±12.50	10.39	50.07±15.59	51.56±14.21	11.65	0.706
LF/HF ratio	0.79±0.28	0.74±0.41	−2.84	0.69±0.53	0.69±0.52	−23.09	0.882

Data are presented as mean±SD.
SDNN, standard deviation of the normal beat-to-normal beat intervals; RMSSD, root mean square of successive R-R interval differences; VLF, very low frequency; nu, normalized unit; HF, high frequency.

Table 5. Heart rate and blood pressure of participants before and after the supplementation

	Rice bran oil group (n=18)			Riceberry rice bran oil group (n=17)			*P*-value
	Before	After	Change (%)	Before	After	Change (%)	
HR (beat/min)	68.57±10.31	67.70±8.74	−0.87 (−1.62)	64.07±7.73	63.52±6.74	−0.55 (−0.48)	0.313
SBP (mmHg)	124.13±10.41	121.17±14.26	−2.96 (−2.51)	127.18±14.80	123.37±11.80	−3.81 (−2.36)	0.998
DBP (mmHg)	75.04±6.58	74.26±8.81	−0.78 (−0.95)	74.35±9.24	72.47±11.64	−1.88 (−2.57)	0.634
PP (mmHg)	49.09±7.88	46.91±10.56	−2.18 (−4.78)	52.82±14.56	50.90±13.14	−1.92 (−0.99)	0.644
MAP (mmHg)	91.40±7.15	89.90±9.73	−1.50 (−1.67)	91.96±9.10	89.44±9.92	−2.52 (−2.57)	0.678
RPP (mmHgbpm)	8,361.45±1,119.17	8,126.91±1,610.05	−234.54 (−3.42)	8,180.26±1,245.12	7,806.76±1,098.38	−373.50 (−3.53)	0.615

Data are presented as mean±SD.
HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure; RPP, rate-pressure product.

addition to γ-oryzanol and γ-tocotrienol, γ-tocopherol and antioxidants, which are two major active ingredients found in RBO capsules, are important in the reaction against oxidative stress and inflammation. Other essential components of RRBO are β-carotene and lutein, which are not present in RBO capsules. Accordingly, our discussion focuses on these components. However, other detected components are discussed.

γ-Tocopherol is the major form of vitamin E. Vitamin E, which is present at higher levels in RBO than in RRBO capsules, has been shown to have several valuable biological properties, including antioxidative, antiinflammatory, wound healing, antiobesity, antihyperglycemic, antihypertensive, and antihypercholesterolemic activities (Wong et al., 2017; Yang et al., 2020). Xu et al. (2001) reported that γ-tocopherol and γ-tocotrienol from rice bran exhibit significant antioxidant activities an animal model. Furthermore, γ-oryzanol is an antioxidant that has been shown to reduce plasma MDA levels (Minatel et al., 2016). In this study, plasma MDA levels were reduced after RBO or RRBO supplementation. In alloxan-induced diabetic mice, γ-tocopherol supplementation for 2 weeks reduced inflammation and increased the levels of antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase (Shin et al., 2017). A series of experiments by Winklhofer-Roob et al. (2003), including healthy subjects and patients, found that large doses of vitamin E supplementation significantly improved *ex vivo* LDL oxidizability, total plasma peroxide concentrations, and urinary 8-oxo-7,8-dihydro-2'-deoxyguanosine excretion in healthy volunteers. In addition, a single oral dose of vitamin E supplementation significantly reduced iron-induced acute oxidative stress in patients undergoing chronic hemodialysis. Furthermore, long-term vitamin E supplementation also reduced *ex vivo* LDL oxidizability, *in vivo* lipid peroxidation, and lung inflammation in patients with cystic fibrosis.

Although γ-tocopherol and antioxidants were found at higher levels in RBO than in RRBO capsules, decreases in plasma MDA, blood GSSG, and TNF-α levels as well as an increase in the GSH/GSSG ratio were comparable between the RBO and RRBO groups. Hence, other biological active ingredients in RRBO, such as β-carotene and lutein, may be important in combating oxidative stress and inflammation. A study on streptozotocin-induced diabetic rats revealed that RRBO supplementation for 12 weeks significantly reduced MDA levels and restored antioxidant capacity as well as the levels of antioxidants such as superoxide dismutase, catalase, glutathione peroxidase, and coenzyme Q10 (Posuwan et al., 2013).

β-Carotene and lutein are carotenoids found in human blood. They are known to help in quenching free radicals and thus protect the body, especially the eye, from oxidative stress, apoptosis, mitochondrial dysfunction, and inflammation (Johra et al., 2020). Epidemiological studies have observed a negative correlation between dietary carotenoids or blood carotenoid levels and cancer or CVDs, such as hypertension and coronary heart disease (Kritchevsky, 1999; Zornoff et al., 2006; Yanagisawa et al., 2009). A study on hypertensive rats by Sung et al. (2013) revealed that lutein treatment for 3 weeks significantly decreased MDA and BP levels, including SBP, DBP, and mean arterial pressure, and increased GSH levels and nitric oxide synthase activity. In patients with early atherosclerosis, lutein supplementation for 3 months decreased the levels of interleukin-6 and monocyte chemoattractant protein-1 as well as serum LDL-C and TG levels (Xu et al., 2013). Lutein supplementation for 12 weeks also decreased CVD-risk biomarkers by reducing MDA and C-reactive protein levels in healthy nonsmokers (Wang et al., 2013).

A previous study on mice with atherosclerosis by Han et al. (2015) found that lutein supplementation for 24 weeks significantly reduced body weight, abdominal and total adipose tissue, and oxidative stress and improved fat metabolism, as indicated by decreased TC, TG, and LDL-C levels. Our findings were consistent with those of Han et al. (2015) in that we found significant decreases in the body mass and body mass index in participants supplemented with RRBO, of which lutein is an active ingredient. The improvement in these variables may be partly described as follows: (1) lutein reversed the downregulated protein expression of aortic heme oxygenase-1 and increased the mRNA and protein expression of aortic nicotinamide-adenine dinucleotide phosphate oxidase; or (2) lutein increased the mRNA and protein expression levels of hepatic peroxisome proliferator-activated receptor-α, carnitine palmitoyltransferase 1A, acyl CoA oxidase 1, LDL receptors, and scavenger receptor class B type I. However, we did not observe statistically significant improvements in the levels of glucose and lipids as well as the atherosclerogenic index in this study, suggesting that the supplementation effects are dose- and time-dependent.

Considering the participants' nutrient intake from supplementation, each capsule of RBO and RRBO is composed of only fat that yields energy, mainly oleic and linoleic acids (Phannasorn et al., 2021), which are monounsaturated omega-9 fatty acids and polyunsaturated omega-6 fatty acids, respectively. Explicitly, participants had received energy from 1,000 mg of RBO or RRBO at approximately 9 kcal/d. This energy was included in the daily energy intake from meals but was not examined in this study. Nevertheless, we did not observe negative alterations in the study variables, such as body composition, blood lipids, and BP, in participants in both groups. Conversely, we observed significant decreases in the body mass and body mass index of the participants supple-

mented with RRBO, as mentioned above.

β-Carotene functions as provitamin A and acts as a cytoprotective antioxidant by scavenging lipid radicals and quenching a singlet oxygen (Grune et al., 2010). Supplementation with low doses of β-carotene exerted beneficial effects on cardiomyoblasts by decreasing inflammation by suppressing nuclear factor-kappa B and increasing nuclear factor erythroid 2-related factor 2 levels, stimulating autophagy, and suppressing apoptosis (Lesmana et al., 2020). A report by Zhou et al. (2018) suggested that β-carotene supplementation reduced oxidative stress by controlling reactive oxygen species, MDA, nitric oxide, and superoxide dismutase as well as restoring the levels of nuclear factors erythroid 2-related factor 2 and heme oxygenase-1. Moreover, β-carotene administration reduced the production of proinflammatory cytokines such as TNF-α, interleukin-1β, interleukin-18, and cyclooxygenase-2.

In this study, neither HRV nor BP variables were statistically significantly improved in either the RBO or RRBO groups, although previous studies have reported that supplementation with rice bran and its antioxidant compounds phenols and anthocyanin enhanced HRV by reducing sympathetic activity, restoring sympathovagal balance, and alleviating vagal nerve inflammation (Bruno and Ghiadoni, 2018; Behl et al., 2021; Senaphan et al., 2021). Senaphan et al. (2021), in their study on rats fed a high-fat and high-fructose diet, demonstrated that rice bran hydrolysates restored HRV by reducing the low frequency/high frequency ratio and improved blood lipids, insulin sensitivity, hemodynamic variables, cardiac oxidative stress, and cardiac structural changes. Typically, in addition to the cardiac autonomic nervous system, BP control is associated with several influencing factors, including baroreflex sensitivity, endothelial function, and the renin-angiotensin system (Asemu et al., 2021). Hence, it is necessary to improve those factors for the reduction in BP. Moreover, although no changes in antihypertensive medications or related substances had been reported by our participants, other lifestyle behaviors that were not observed such as cigarette smoking, alcohol drinking, and mental stress could affect BP outcomes (Menanga et al., 2016). Furthermore, the participants were requested to maintain their physical activities and dietary intake during the entire study period. We did not restrict their lifestyles because it was impractical, particularly their intake of sodium- or potassium-containing foods, which could directly affect their BP (Zanchetti, 2015).

Although SBP and DBP levels in the RBO group were slightly lower by 2.96 mmHg (−2.38%) for SBP and 0.78 mmHg (−1.04%) for DBP, 61% and 56% of participants, respectively, had declined levels of SBP and DBP. Besides, reductions in the levels of SBP and DBP were greater in the RRBO group: 3.81 mmHg (−3%) for SBP and 1.88 mmHg (−2.53%) for DBP. The proportion of participants in this group who had lower SBP (65%) and DBP (59%), however, was comparable to that of the RBO group. There is a large body of evidence establishing that chronic oxidative stress and inflammation play important roles in augmenting BP levels (Griendling et al., 2021); thus, a significant decrease in oxidative stress and inflammatory biomarkers may help protect our participants with prehypertension from the adverse effects of elevated BP and may thus prevent or delay the development of hypertension (Krzemińska et al., 2022) and other disorders associated with oxidative stress and inflammation, including CVDs, neurological disease, atherosclerosis, obesity, diabetes mellitus, and cancers (Liguori et al., 2018).

This study has several limitations. First, we did not include a control group that received a placebo or inactive ingredients for comparison with the RBO and RRBO groups. Although we can investigate the changes in outcomes in each group by comparing the values before and after supplementation, the lack of a control group may make it difficult to detect any variations that could arise when there are no active elements to avoid possible bias. Second, although we calculated the sample size, this study had a relatively small number of participants in each group. Besides, this may also affect the statistical significance. Third, we did not investigate participants' nutrition information. The study participants were requested to record their physical activities and dietary intake throughout the study. An investigation of nutritional information would help clarify more factors that could affect the results. Finally, the analysis of the study supplements' components did not include other essential elements, including phenols, anthocyanins, phytosterols, or linoleic acid, which may limit an unequivocal discussion.

This study showed that RRBO supplementation for 8 weeks could have similar health benefits as RBO supplementation in older adults with prehypertension by reducing oxidative stress and inflammation. Future studies may extend supplementation periods or examine individuals with hypertension, especially in terms of its benefits in lowering BP levels. In addition, cardiovascular function should also be investigated to elucidate the mechanism of changes in BP.

FUNDING

This work was supported by the Burapha University, through the National Research Council of Thailand (grant no. 39/2562) and the Exercise and Nutrition Innovation and Sciences Research Unit, Burapha University, through the Burapha University Research and Development Fund.

AUTHOR DISCLOSURE STATEMENT

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Concept and design: PP. Analysis and interpretation: PP, OB. Data collection: PP, OB, JV. Writing the article: all authors. Critical revision of the article: PP, OB. Final approval of the article: all authors. Statistical analysis: PP. Obtained funding: PP, JP. Overall responsibility: PP.

REFERENCES

Alauddin M, Shirakawa H, Koseki T, Kijima N, Ardiansyah, Budijanto S, et al. Fermented rice bran supplementation mitigates metabolic syndrome in stroke-prone spontaneously hypertensive rats. BMC Complement Altern Med. 2016. 16:442. https://doi.org/10.1186/s12906-016-1427-z

Ardiansyah, Shirakawa H, Koseki T, Ohinata K, Hashizume K, Komai M. Rice bran fractions improve blood pressure, lipid profile, and glucose metabolism in stroke-prone spontaneously hypertensive rats. J Agric Food Chem. 2006. 54:1914-1920.

Ardiansyah, Shirakawa H, Shimeno T, Koseki T, Shiono Y, Murayama T, et al. Adenosine, an identified active component from the driselase-treated fraction of rice bran, is effective at improving metabolic syndrome in stroke-prone spontaneously hypertensive rats. J Agric Food Chem. 2009. 57:2558-2564.

Asemu MM, Yalew AW, Kabeta ND, Mekonnen D. Prevalence and risk factors of hypertension among adults: A community based study in Addis Ababa, Ethiopia. PLoS One. 2021. 16:e0248934. https://doi.org/10.1371/journal.pone.0248934

Behl T, Kumar S, Sehgal A, Singh S, Kumari S, Brisc MC, et al. Rice bran, an off-shoot to newer therapeutics in neurological disorders. Biomed Pharmacother. 2021. 140:111796. https://doi.org/10.1016/j.biopha.2021.111796

Boy FR, Casquete R, Martínez A, Córdoba MG, Ruíz-Moyano S, Benito MJ. Antioxidant, antihypertensive and antimicrobial properties of phenolic compounds obtained from native plants by different extraction methods. Int J Environ Res Public Health. 2021. 18:2475. https://doi.org/10.3390/ijerph18052475

Bruno RM, Ghiadoni L. Polyphenols, antioxidants and the sympathetic nervous system. Curr Pharm Des. 2018. 24:130-139.

Devarajan S, Singh R, Chatterjee B, Zhang B, Ali A. A blend of sesame oil and rice bran oil lowers blood pressure and improves the lipid profile in mild-to-moderate hypertensive patients. J Clin Lipidol. 2016. 10:339-349.

Duansak N, Schmid-Schönbein GW, Srisawat U. Anti-obesity effect of rice bran extract on high-fat diet-induced obese mice. Prev Nutr Food Sci. 2022. 27:172-179.

Egan BM, Stevens-Fabry S. Prehypertension—prevalence, health risks, and management strategies. Nat Rev Cardiol. 2015. 12:289-300.

Griendling KK, Camargo LL, Rios FJ, Alves-Lopes R, Montezano AC, Touyz RM. Oxidative stress and hypertension. Circ Res. 2021. 128:993-1020.

Grune T, Lietz G, Palou A, Ross AC, Stahl W, Tang G, et al. Beta-carotene is an important vitamin A source for humans. J Nutr. 2010. 140:2268S-2285S.

Han H, Cui W, Wang L, Xiong Y, Liu L, Sun X, et al. Lutein prevents high fat diet-induced atherosclerosis in ApoE-deficient mice by inhibiting NADPH oxidase and increasing PPAR expression. Lipids. 2015. 50:261-273.

Han M, Li Q, Liu L, Zhang D, Ren Y, Zhao Y, et al. Prehypertension and risk of cardiovascular diseases: a meta-analysis of 47 cohort studies. J Hypertens. 2019. 37:2325-2332.

Hu L, Huang X, You C, Li J, Hong K, Li P, et al. Prevalence and risk factors of prehypertension and hypertension in Southern China. PLoS One. 2017. 12:e0170238. https://doi.org/10.1371/journal.pone.0170238

Jariwalla RJ. Rice-bran products: phytonutrients with potential applications in preventive and clinical medicine. Drugs Exp Clin Res. 2001. 27:17-26.

Johra FT, Bepari AK, Bristy AT, Reza HM. A mechanistic review of β-carotene, lutein, and zeaxanthin in eye health and disease. Antioxidants. 2020. 9:1046. https://doi.org/10.3390/antiox9111046

Jun M, Xiang Y. The management of prehypertension in young adults. Saudi Med J. 2020. 41:223-231.

Kim HW, Kim JB, Shanmugavelan P, Kim SN, Cho YS, Kim HR, et al. Evaluation of γ-oryzanol content and composition from the grains of pigmented rice-germplasms by LC-DAD-ESI/MS. BMC Res Notes. 2013. 6:149. https://doi.org/10.1186/1756-0500-6-149

Kritchevsky SB. β-Carotene, carotenoids and the prevention of coronary heart disease. J Nutr. 1999. 129:5-8.

Krzemińska J, Wronka M, Młynarska E, Franczyk B, Rysz J. Arterial hypertension-oxidative stress and inflammation. Antioxidants. 2022. 11:172. https://doi.org/10.3390/antiox11010172

Kukongviriyapan U, Kukongviriyapan V, Pannangpetch P, Donpunha W, Sripui J, Sae-Eaw A, et al. Mamao pomace extract alleviates hypertension and oxidative stress in nitric oxide deficient rats. Nutrients. 2015. 7:6179-6194.

Lai MH, Chen YT, Chen YY, Chang JH, Cheng HH. Effects of rice bran oil on the blood lipids profiles and insulin resistance in type 2 diabetes patients. J Clin Biochem Nutr. 2012. 51:15-18.

Leardkamolkarn V, Thongthep W, Suttiarporn P, Kongkachuichai R, Wongpornchai S, Wanavijitr A. Chemopreventive properties of the bran extracted from a newly-developed Thai rice: The *Riceberry*. Food Chem. 2011. 125:978-985. https://doi.org/10.1016/j.foodchem.2010.09.093

Lesmana R, Felia Yusuf I, Goenawan H, Achadiyani A, Khairani AF, Nur Fatimah S, et al. Low dose of β-carotene regulates inflammation, reduces caspase signaling, and correlates with autophagy activation in cardiomyoblast cell lines. Med Sci Monit Basic Res. 2020. 26:e928648. https://doi.org/10.12659/MSMBR.928648

Liguori I, Russo G, Curcio F, Bulli G, Aran L, Della-Morte D, et al. Oxidative stress, aging, and diseases. Clin Interv Aging. 2018. 13:757-772.

Lydia A, Setiati S, Soejono CH, Istanti R, Marsigit J, Azwar MK. Prevalence of prehypertension and its risk factors in midlife and late life: Indonesian family life survey 2014-2015. BMC Public Health. 2021. 21:493. https://doi.org/10.1186/s12889-021-10544-y

Mancia G, Grassi G. The autonomic nervous system and hypertension. Circ Res. 2014. 114:1804-1814.

Mansia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, et al.; European Society of Hypertension; European Society of Cardiology. 2007 ESH-ESC Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Blood Press. 2007. 16:135-232.

Mattioli R, Francioso A, Mosca L, Silva P. Anthocyanins: a comprehensive review of their chemical properties and health effects on cardiovascular and neurodegenerative diseases. Molecules.

2020. 25:3809. https://doi.org/10.3390/molecules25173809
Menanga A, Edie S, Nkoke C, Boombhi J, Musa AJ, Mfeukeu LK, et al. Factors associated with blood pressure control amongst adults with hypertension in Yaounde, Cameroon: a cross-sectional study. Cardiovasc Diagn Ther. 2016. 6:439-445.
Minatel IO, Francisqueti FV, Corrêa CR, Lima GP. Antioxidant activity of γ-oryzanol: a complex network of interactions. Int J Mol Sci. 2016. 17:1107. https://doi.org/10.3390/ijms17081107
Most MM, Tulley R, Morales S, Lefevre M. Rice bran oil, not fiber, lowers cholesterol in humans. Am J Clin Nutr. 2005. 81:64-68.
Munkong N, Thim-Uam A, Pengnet S, Hansakul P, Somparn N, Naowaboot J, et al. Effects of red rice bran extract on high-fat diet-induced obesity and insulin resistance in mice. Prev Nutr Food Sci. 2022. 27:180-187.
Nakmareong S, Kukongviriyapan U, Pakdeechote P, Kukongviriyapan V, Kongyingyoes B, Donpunha W, et al. Tetrahydrocurcumin alleviates hypertension, aortic stiffening and oxidative stress in rats with nitric oxide deficiency. Hypertens Res. 2012. 35:418-425.
Palou M, Sánchez J, García-Carrizo F, Palou A, Picó C. Pectin supplementation in rats mitigates age-related impairment in insulin and leptin sensitivity independently of reducing food intake. Mol Nutr Food Res. 2015. 59:2022-2033.
Phannasorn W, Chariyakornkul A, Sookwong P, Wongpoomchai R. Comparative studies on the hepatoprotective effect of white and coloured rice bran oil against acetaminophen-induced oxidative stress in mice through antioxidant- and xenobiotic-metabolizing systems. Oxid Med Cell Longev. 2021. 2021: 5510230. https://doi.org/10.1155/2021/5510230
Posuwan J, Prangthip P, Leardkamolkarn V, Yamborisut U, Surasiang R, Charoensiri R, et al. Long-term supplementation of high pigmented rice bran oil (*Oryza sativa* L.) on amelioration of oxidative stress and histological changes in streptozotocin-induced diabetic rats fed a high fat diet; Riceberry bran oil. Food Chem. 2013. 138:501-508.
Qaiser S, Daud MNM, Ibrahim MY, Gan SH, Rahman MS, Sani MHM, et al. Prevalence and risk factors of prehypertension in university students in Sabah, Borneo Island of East Malaysia. Medicine. 2020. 99:e20287. https://doi.org/10.1097/MD.0000000000020287
Rajnarayana K, Prabhakar MC, Krishna DR. Influence of rice bran oil on serum lipid peroxides and lipids in human subjects. Indian J Physiol Pharmacol. 2001. 45:442-444.
Senaphan K, Kukongviriyapan U, Suwannachot P, Thiratanaboon G, Sangartit W, Thawornchinsombut S, et al. Protective effects of rice bran hydrolysates on heart rate variability, cardiac oxidative stress, and cardiac remodeling in high fat and high fructose diet-fed rats. Asian Pac J Trop Biomed. 2021. 11:183-193.
Shin J, Yang SJ, Lim Y. Gamma-tocopherol supplementation ameliorated hyper-inflammatory response during the early cutaneous wound healing in alloxan-induced diabetic mice. Exp Biol Med. 2017. 242:505-515.
Somintara S, Leardkamolkarn V, Suttiarporn P, Mahatheeranont S. Anti-tumor and immune enhancing activities of rice bran gramisterol on acute myelogenous leukemia. PLoS One. 2016. 11:e0146869. https://doi.org/10.1371/journal.pone.0146869
Sung JH, Jo YS, Kim SJ, Ryu JS, Kim MC, Ko HJ, et al. Effect of lutein on L-NAME-induced hypertensive rats. Korean J Physiol Pharmacol. 2013. 17:339-345.
Thamnarathip P, Jangchud K, Jangchud A, Vardhanabhuti B. Functional properties of protein hydrolysates from Riceberry rice bran. Int J Food Sci Technol. 2016. 51:1110-1119.
Vierra J, Boonla O, Prasertsri P. Effects of sleep deprivation and 4-7-8 breathing control on heart rate variability, blood pressure, blood glucose, and endothelial function in healthy young adults. Physiol Rep. 2022. 10:e15389. https://doi.org/10.14814/phy2.15389
Wang MX, Jiao JH, Li ZY, Liu RR, Shi Q, Ma L. Lutein supplementation reduces plasma lipid peroxidation and C-reactive protein in healthy nonsmokers. Atherosclerosis. 2013. 227:380-385.
Wang O, Liu J, Cheng Q, Guo X, Wang Y, Zhao L, et al. Effects of ferulic acid and γ-oryzanol on high-fat and high-fructose diet-induced metabolic syndrome in rats. PLoS One. 2015. 10: e0118135. https://doi.org/10.1371/journal.pone.0118135
Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018. 71:e127-e248.
Winklhofer-Roob BM, Rock E, Ribalta J, Shmerling DH, Roob JM. Effects of vitamin E and carotenoid status on oxidative stress in health and disease. Evidence obtained from human intervention studies. Mol Aspects Med. 2003. 24:391-402.
Wong SK, Chin KY, Suhaimi FH, Ahmad F, Ima-Nirwana S. Vitamin E as a potential interventional treatment for metabolic syndrome: evidence from animal and human studies. Front Pharmacol. 2017. 8:444. https://doi.org/10.3389/fphar.2017.00444
Xu XR, Zou ZY, Xiao X, Huang YM, Wang X, Lin XM. Effects of lutein supplement on serum inflammatory cytokines, ApoE and lipid profiles in early atherosclerosis population. J Atheroscler Thromb. 2013. 20:170-177.
Xu Z, Hua N, Godber JS. Antioxidant activity of tocopherols, tocotrienols, and gamma-oryzanol components from rice bran against cholesterol oxidation accelerated by 2,2'-azobis(2-methylpropionamidine) dihydrochloride. J Agric Food Chem. 2001. 49:2077-2081.
Yanagisawa A, Suzuki K, Kimura A, Ito Y, Hamajima N, Inoue T. Possible protective effect of serum beta-carotene levels on the association between interleukin-1B C-31T polymorphism and hypertension in a Japanese population. Clin Nutr. 2009. 28: 198-202.
Yang CS, Luo P, Zeng Z, Wang H, Malafa M, Suh N. Vitamin E and cancer prevention: Studies with different forms of tocopherols and tocotrienols. Mol Carcinog. 2020. 59:365-389.
Yoon SW, Pyo YG, Lee J, Lee JS, Kim BH, Kim IH. Concentrations of tocols and γ-oryzanol compounds in rice bran oil obtained by fractional extraction with supercritical carbon dioxide. J Oleo Sci. 2014. 63:47-53.
Yu D, Huang J, Hu D, Chen J, Cao J, Li J, et al. Prevalence and risk factors of prehypertension among Chinese adults. J Cardiovasc Pharmacol. 2008. 52:363-368.
Zanchetti A. Factors influencing blood pressure levels. J Hypertens. 2015. 33:1497-1498.
Zarei I, Brown DG, Nealon NJ, Ryan EP. Rice bran metabolome contains amino acids, vitamins & cofactors, and phytochemicals with medicinal and nutritional properties. Rice. 2017. 10:24. https://doi.org/10.1186/s12284-017-0157-2
Zhou L, Ouyang L, Lin S, Chen S, Liu Y, Zhou W, et al. Protective role of β-carotene against oxidative stress and neuroinflammation in a rat model of spinal cord injury. Int Immunopharmacol. 2018. 61:92-99.
Zornoff LA, Matsubara BB, Matsubara LS, Azevedo PS, Minicucci MF, Campana AO, et al. Beta-carotene supplementation results in adverse ventricular remodeling after acute myocardial infarction. Nutrition. 2006. 22:146-151.