

### Effect of Intervention with Rice Bran Oil-Emulsion Beverage on Metabolic Syndrome Markers in Men

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#### Abstract

The objective of this study was to analyze the effect of intervention with rice bran oil-emulsion beverage on serum triglycerides, HDL-c, and blood pressure in men with metabolic syndrome aged 35-60 years. This study used a double-blind randomized controlled trial design. The subjects were assigned into two groups, i.e. 19 people in the intervention group who were given rice bran oil-emulsion beverage equivalent to 28.80 mg oryzanol/glass, two glasses a day for four weeks; and 17 people in the control group who were given placebo beverage in the same quantity. The results showed that trend increase in serum HDL-c and decrease blood pressure of the intervention group after intervention, although they were not significantly different from the control group (p>0.05). Intervention using rice bran oil-emulsion had the potential of preventing the development of metabolic syndrome.

Keywords: hypertension; lipid profile; metabolic syndrome; rice bran.

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#### 1. Introduction

Incidence of diseases and causes of death in Indonesia nowadays have shifted, in which non-communicable disease (NCD) trend increases more rapidly but the incidence of infectious disease is still quite high. Types of NCDs with high prevalence are hypertension, coronary heart disease (CHD), type 2 diabetes mellitus, and cancer [1,2]. Progression of these diseases is in line with the development of obesity and metabolic syndrome. Metabolic syndrome is part of a number of risk factors that causes myocardial infarction and diabetes mellitus. Its global prevalence is quite high, i.e. 20-25% of the adult population. Meanwhile, its prevalence in the US and Chinese population are 22.90% and 23.20%, respectively [3-5]. The prevalence reaches 10-30% in Asia and 28.4% in Indonesia [6,7]. Metabolic syndrome is multidimensional risk factor for cardiovascular disease. It has several criteria, one of which is defined by International Diabetes Federation (IDF). The criteria for metabolic syndrome according to IDF consensus in 2006 are having central obesity defined by certain ethnic specific values of waist circumference, was added with two of four other clinical signs. The physical symptom of metabolic syndrome is obesity or overweight characterized by increased waist circumference or body mass index (BMI). The biochemical symptoms are characterized by increased level of triglycerides (TG) and blood glucose, decreased serum high-density lipoprotein cholesterol (HDL-c) levels and increased blood pressure. The combination of various metabolic or clinical disorders can be ascertained to be far more instrumental in causing cardiovascular disease than any of the stand-alone disorders [8,9]. HDL-c has anti -oxidative molecules which has the potential to inhibit lipid oxidation. HDL-c levels may be decreased due to oxidative stress. Its ability to remove cholesterol from peripheral tissues is evidently suppressed by oxidative stress such as excessive intake of fat and carbohydrates, obesity, and increased chronic low-grade inflammation characterized by an increase in tumor necrosis factor alpha (TNF- $\alpha$ ) levels. Therefore, the quantity and quality of HDL-c need to be maintained in order not to decrease. Failure to do so will result in the increased incidence of cardiovascular disease [10-12]. Many functional foodstuffs found nowadays contain bioactive components that are useful for improving body function, thereby protecting us from diseases. Several studies have shown that bioactive components of fruits and vegetables contain dietary fibers and are high in antioxidants compound; thus, beneficial to health. One of these bioactive components contained in the functional foodstuffs is oryzanol. Oryzanol is a bioactive component in rice bran oil (RBO) which has antioxidant properties. It has been proven scientifically to maintain health and improve lipid profiles, as well as blood glucose in obese people [13-16]. This study aimed to analyze the effect of intervention RBO emulsion on TG levels, HDL-c levels and blood pressure.

#### 2. Materials and Methods

#### 2.1. Materials

The materials used in this study were RBO, sugar ester, carboxymethylcellulose (CMC), sucralose, salt, flavoring and water. Emulsion beverage was made by mixing the RBO with sugar ester, CMC and water; then homogenized at a speed of 1000 rpm for 15 minutes.

The emulsions obtained were diluted with water and then the sucralose and salt were added. The flavoring was added in the final stage and the products were put into the labeled packages. These emulsion beverages contained active ingredients equivalent to 28.80 mg oryzanol/glass.

#### 2.2. Methods

#### 2.2.1. Design, location and time of study

This was a double-blind randomized controlled trial. The selected subjects should met the inclusion criteria and were willing to sign informed consent. The subjects were gathered at the first meeting to be given an explanation of this study's benefits. This study was conducted in Mintohardjo Navy Hospital in Central Jakarta, from August 2014 to July 2015. It passed the ethical review conducted by Ethics Committee of Faculty of Medicine, University of Indonesia Number: 870/UN2.F1/ETIK/2014.

#### 2.2.2. Research subjects

The target population were obese men, aged  $\geq 35$  years, working in Mintohardjo Navy Hospital in Jakarta and Cilangkap Navy Public Health Office in West Java. The subjects met the criteria for metabolic syndrome defined by IDF in 2006, as follows: obese men aged 35-60 years; waist circumference > 90 cm; had two other clinical signs that matched with the criteria (TG > 150 mg/dL, HDL-c < 40 mg/dL, fasting blood glucose levels  $\geq 100$  mg/dL, systolic blood pressure  $\geq 130$  mmHg and diastolic  $\geq 85$  mmHg). Subjects who used diabetes, heart disease, and antihypertensive medications were excluded. Minimum number of subjects was calculated by using a minimum sample size formula for estimating mean differences between groups. Minimum number of subjects in each group based on the values of TG and HDL-c levels in the previous studies were 16 and 3 people, respectively. Therefore, we chose the larger minimum sample size (16 people). To anticipate the possibility of drop-out, 5 people were added to each group. Therefore, the total subjects for each group became 21 people. Randomization was performed at the beginning of study to determine the treatment to be received. The subjects in the intervention group received placebo beverages twice a day. At the end of study, only the data from 19 people in the intervention group and 17 people in the control group complited so that could be analyzed.

#### 2.2.3. Biochemical analysis

Venous blood sampling was performed after the subjects did a 10-hour fasting. Venous blood samples (5 ml) were collected by medical personnel at the beginning and end of the intervention. Serum lipid profiles were then analyzed by DSI kits Number 60111321 and 60111509, while the blood glucose was analyzed by DSI kit Number 60108392. The results were interpreted by using UV-Vis spectrophotometer. Blood pressure was measured by using a mercury sphygmomanometer, at the beginning and end of the intervention.

#### 2.2.4. Statistical analysis

We performed bivariate analysis on the data of biochemical analyses (pre- and post- intervention) and presented the results in tabular form. The next analysis was independent sample t-test to analyze the data of biochemical analyses between the intervention and control groups. The results were considered as significantly different if p-value < 0.05.

### 3. Results and Discussion

#### 3.1. Subjects' biochemical characteristics by group

Diastolic

Variable	Control (n=17)	Intervention (n=19)
TG (mg/dL)	$246.59 \pm 112.19$	$191.00 \pm 97.21$
HDL-c (mg/dL)	$33.59 \pm 7.77$	$33.47 \pm 6.54$
Blood glucose	$92.29 \pm 25.36$	$94.26\pm36.09$
Blood pressure		
Systolic	$129.41 \pm 17.48$	$126.32 \pm 14.98$

 $85.00\pm9.35$ 

 $86.58 \pm 8.98$ 

Table 1: Subjects' biochemical characteristics by group

Our results showed that subjects' serum TG and HDL-c levels in the control group were higher than the ones in the intervention group. Serum glucose levels in the control group were lower than the intervention group. Systolic blood pressure in the control group was higher than the intervention group, while diastolic blood pressure in the intervention group was higher than the control group. These results were not statistically significant (p>0.05).

Metabolic syndrome accompanied with visceral obesity are closely related to insulin resistance. It may lead to hypertension, high levels of serum TG, low levels of serum HDL-c and hyperglycemia; which is in turn associated with cardiovascular disease. The diseases caused by these conditions (i.e. type 2 diabetes mellitus and CHD) occur with the increasing BMI and visceral fat [3,17].

# 3.2. The Effect of intervention with RBO-emulsion beverage on serum triglyceride levels in men with metabolic syndrome

Subject's group	Serum triglycerides (mg/dL)		
	Before intervention	After intervention	Difference
Control group	$246.59\pm7.77$	$214.18 \pm 150.93$	$-32.41 \pm 131.59^{a}$
Intervention group	$191.00\pm97.21$	$206.42\pm127.03$	15.42 81.03 <sup>a</sup>

Table 2: Effect of intervention with RBO-emulsion on serum triglycerides

<sup>a</sup> Figures followed by the same letters in the different row showed no significant difference between groups (p>0.05)

Table 2 showed a decline in mean serum TG levels in the control group and an increase in the mean serum levels in the intervention group. However, the magnitude of change in serum TG levels in both groups was not significant. In this research consumption of subjects are the same as before intervention. They Serum TG level in the intervention group did not decrease after the intervention, while the serum level in the control group decreased but was still above the normal values. It was due to the fat intake that was still within the limit of requirement values; thus, the active ingredient contained in rice bran was not able to work to decrease serum TG levels.

Our results were not in line with the previous studies and several other researches indicating that rice bran intervention, either in the form of powder or oil-emulsion beverage, was able to decrease serum TG levels in the blood, either in animals or humans [18,19].

Another study showed that vitamin E (tocopherol and tocotrienol) contained in RBO was only effective in decreasing low-density lipoprotein (LDL) and total cholesterol by inhibiting the enzyme activity of  $\beta$ -hydroxy- $\beta$ -methylglutaryl coenzyme A (HMG-CoA). Therefore, the fat was not synthesized by the body and cardiovascular disease could be prevented [18].

Our findings were in line with the previous study related to RBO intervention, which indicated that the use of RBO-emulsion beverage on obese people could decrease serum LDL and total cholesterol levels. However, serum glucose and TG levels remained unchanged after the intervention [20].

Another study on the intervention using rice bran porridge in elementary school students indicated that there was a significant increase in serum TG levels in the intervention group (p=0.014). Mean while, there was a decrease in the serum TG levels in the control group although not significant (p=0.012) [21].

## 3.3. The Effect of intervention with RBO-emulsion beverage on serum HDL-c levels in men with metabolic syndrome

Subject's group	Serum HDL-c levels (mg/dL)		
	Before intervention	After intervention	Difference
Control group	$33.59 \pm 7.77$	$35.82\pm8.31$	$2.24\pm4.86^a$
Intervention group	$33.47 \pm 6.54$	$34.53 \pm 9.31$	$1.05\pm4.96^{\rm a}$

Table 3: Effect of intervention with RBO-emulsion on HDL-c

<sup>a</sup> Figures followed by the same letters in the different row showed no significant difference between groups (p>0.05)

Mean serum HDL-c levels in the control group before and after the intervention were higher than the intervention group. There was an increase in serum HDL-c levels in both groups but not significant.

This study showed that there was an increase in serum HDL-c levels after intervention. Several other studies indicated an increase in serum HDL-c levels after rice bran intervention. It was due to the bioactive components in rice bran ( $\gamma$  oryzanol and ferulic acid) that had potent antioxidant activities. In addition, monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs) contained in RBO could increase serum HDL-c levels in the blood [17,22].

Besides the reasons above, the increase in serum HDL-c levels might also be caused by the frequency and type of exercise performed by the subjects during this study. The subjects performed the exercise at least twice a week and they did various kinds of sport.

This exercise contributed to the increased serum HDL-c levels among people with metabolic syndrome. As we have already known, HDL-c level can also be improved by doing physical activities. It is not only affected by dietary intake [23].

3.4. The Effect of intervention with RBO-emulsion beverage on systolic blood pressure in men with metabolic syndrome

Subject's group	Systolic blood pressure (mmHg)		
	Before intervention	After intervention	Difference
Control group	$129.41 \pm 17.48$	$126.47 \pm 10.57$	$-2.94 \pm 0.40^{a}$
Intervention group	$126.32\pm14.98$	$121.58\pm12.14$	$-4.74\pm0.13^{\rm a}$

Table 4: Mean values of systolic blood pressure by subject's group

<sup>a</sup> Figures followed by the same letters in the different row showed no significant difference between groups (p>0.05)

Mean systolic blood pressure in the control group before and after the intervention were higher than the intervention group. The values were almost normal but not significant.

According to the IDF criteria in 2006, men with metabolic syndrome are defined as having hypertension if the systolic blood pressure  $\geq$  130 mmHg and diastolic blood pressure  $\geq$  85 mmHg.

Increased blood pressure may occur through three main points, i.e. autonomic nervous system (ANS) disorders, insulin resistance, and abnormal structure and function of the blood vessels. Those three things can influence one another [24].

3.5. The Effect of intervention using RBO-emulsion beverage on diastolic blood pressure in men with metabolic syndrome

Subject's group	Diastolic blood pressure (mmHg)		
	Before intervention	After intervention	Difference
Control group	$85.00 \pm 9.35$	$85.88 \pm 7.95$	$0.00\pm0.70^{a}$
Intervention group	$86.58 \pm 8.98$	$82.11 \pm 9.76$	$-4.47 \pm 0.13^{a}$

#### Table 5: Mean values of diastolic blood pressure by subject's group

<sup>a</sup> Figures followed by the same letters in the different row showed no significant difference between groups (p>0.05)

The mean diastolic blood pressure in the control group before the intervention was lower than the intervention group. After the intervention, the mean in the control group was higher than the one in the intervention group. The mean in the intervention group decreased toward normal value but it was not significant.

This study showed a decline in systolic and diastolic blood pressure. It might be due to antioxidant, MUFA and PUFA contents in rice bran, in which each of these active ingredients was effective in lowering blood pressure if it is contained in foodstuffs [24].

This study has strength and limitation. The strength of our study lies in the ability of RBO-emulsion which evidently has a tendency to increase HDL-c levels and decrease blood pressure after being analyzed. It can be assumed that intervention using RBO-emulsion beverage in men with metabolic syndrome may prevent the development of cardiovascular disease. This study's limitation lies in the small sample size, due to the difficulty of finding the subjects with the specified criteria.

#### 4. Conclusion and Recommendation

Intervention using RBO emulsion tends to improve serum HDL-c levels and decrease systolic and diastolic blood pressure. There were no changes in serum TG levels.

It is recommended to use functional foodstuffs (e.g. rice bran beverage) and do regular physical activities, so that the development of metabolic syndrome can be diminished.

#### References

- [1] Departemen Kesehatan Republik Indonesia. *Riset Kesehatan Dasar 2007.* Jakarta: Departemen Kesehatan Republik Indonesia, 2008.
- [2] Kementerian Kesehatan Republik Indonesia. *Riset Kesehatan Dasar 2013*. Jakarta: Kementerian Kesehatan Republik Indonesia, 2013.
- [3] International Diabetes Federation. The IDF Consensus Worldwide Definition of the Metabolic Syndrome.

Belgium: International Diabetes Federation, 2006, pp. 2-24.

- [4] H.B. Sánchez, M.O. Harhay, M.M. Harhay and S. McElligott. "Prevalence and trends of metabolic syndrome in the adult U.S. Population, 1999–2010". *Journal of the American College of Cardiology*, vol. 62(8), pp. 697-703, Aug. 2013.
- [5] G. Li, M. de Courten, S. Jiao and Y. Wang. "Prevalence and characteristics of the metabolic syndrome among adults in Beijing, China". *Asia Pacific Journal of Clinical Nutrition*, vol. 19(1), pp. 98-102, 2010.
- [6] P. Nestel, R. Lyu, L.P. Low, W.H.H. Sheu, Nitiyanant W, I. Saito, et al. "Metabolic syndrome: recent prevalence in East and Southeast Asian populations". *Asia Pacific Journal of Clinical Nutrition*, vol. 16(2), pp. 362-367, 2007.
- [7] P. Soewondo, D. Purnamasari, S. Waspaji and S. Soegondo. "Prevalence of metabolic syndrome using NCEP/ATP III criteria in Jakarta, Indonesia: the Jakarta primary non-communicable disease risk factors surveillance 2006". ACTA Medica Indonesiana, vol. 42(4), pp. 199-203, Oct. 2010.
- [8] A. Marjani. "A review on the role of triglyceride in metabolic syndrome". *Asian Journal of Pharmaceutical and Clinical Research*, vol. 8(3), pp. 1-3, Jan. 2015.
- [9] G.G. Schwartz, S.G. Olsson, M. Szarek and W.J. Sasiela. "Relation of characteristics of metabolic syndrome to short-term prognosis and effects of intensive statin therapy after acute coronary syndrome: An analysis of the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) trial". *Diabetes Care*, vol. 28(10), pp. 2508-2513, Oct. 2005.
- [10] S. Furukawa, T. Fujita, M. Shimabukuro, M. Iwaki, Y. Yamada, Y. Nakajima, et al. "Increased oxidative stress in obesity and its impact on metabolic syndrome". *Journal of Clinical Investigation*, vol. 114(12), pp. 1752-1761, Dec. 2004.
- [11] A.T. Effendi, Hardinsyah, Y.H. Effendi, M. Dewi and N.M. Nurdin. Nutrigenomik, Resistensi Insulin, Sindrom Metabolik, Prediabetes. Bogor: IPB Press, 2013, pp. 1-11.
- [12] R.R. Erusan, N. Devarajan, M. Ganesan and M. Raghunathan. "Correlation between obesity and inflammation in cardiovascular diseases-evaluation of leptin and inflammatory cytokines". *Open Journal* of Endocrine and Metabolic Disease, vol. 2(2), pp. 7-15, May 2012.
- [13] M. Bullo, P. Casas-Agustench, P. Amigo-Correig, J. Aranceta and J. Salas-Salvado. "Inflammation, obesity and comorbidities: the role of diet". *Public Health Nutrition*, vol. 10(10A), pp. 1164–117, Oct. 2007.
- [14] E. Damayanthi, L. Kustiyah, M. Khalid and H. Farizal. "Aktivitas antioksidan bekatul lebih tinggi daripada jus tomat dan penurun aktivitas antioksidan serum setelah intervensi minuman kaya antioksidan,

Jurnal Gizi dan Pangan, vol. 5(3), pp. 205–210, Nov. 2010.

- [15] D. Giugliano, A. Ceriello and K. Esposito. "The effects of diet on inflammation emphasis on the metabolic syndrome". *Journal of the American College of Cardiology*, vol. 48(4), pp. 677-685, Aug. 2006.
- [16] E.P. Ryan. "Bioactive food components and health properties of rice bran". Journal of the American Veterinary Medical Association, vol. 238(5), pp. 593-600, Mar. 2011.
- [17] S.M. Grundy, JHB Brewer, J.I. Cleeman, J.S.C. Smith, C. Lenfant, et al. "Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition". *Arteriosclerosis, Thrombosis, and Vascular Biology*, vol. 24(2), pp. 433-438, Feb. 2004.
- [18] C.W. Chen and H.H. Cheng. "A rice bran oil diet increases LDL-receptor and MG-CoA reductase mRNA expressions and insulin sensitivity in rats with streptozotocin/nicotinamide-induced type 2 diabetes". *Journal of Nutrition*, vol. 136(6), pp. 1472–1476, Jun. 2006.
- [19] T.A. Wilson, R.J. Nicolosi, B. Woolfrey and D. Kritchevsky. "Rice bran oil and oryzanol reduce plasma lipid and lipoprotein cholesterol concentrations and aortic cholesterol ester accumulation to a greater extent than ferulic acid in hypercholesterolemic hamsters". *The Journal of Nutritional Biochemistry*, vol. 18(2), pp. 105-112, Feb. 2007.
- [20] E. Damayanthi and C.M. Dwiriani. "Pengkajian minuman bekatul, minyak bekatul dan tomat untuk kesehatan lipid dan kadar glukosa serta status imun pada orang dewasa gemuk". Research Article, Department of Community Nutrition-Bogor Agricultural University, Bogor, 2012, pp. 1-10.
- [21] A.A. Akbar, S. Sirajuddin and B. Bahar. "Pengaruh pemberian bubur bekatul instan terhadap kadar profil lipid anak sekolah dasar obesitas di Makassar". *E-Journal Program Pascasarjana Universitas Hasanuddin*, pp. 1-11, 2014.
- [22] A. Moongngarm, N. Daomukda and S. Khumpika. "Chemical compositions, phytochemicals, and antioxidant capacity of rice bran, rice bran layer, and rice germ". *Elsevier*, vol. 2, pp. 73-79, 2012.
- [23] K. Mahan and S. Escott-Stump. Krause's Food Nutrition and Therapy. 12<sup>th</sup> edition. Philadelphia: Saunders Elsevier, 2008.
- [24] S. Haris and T. Tambunan. "Hipertensi pada sindrom metabolik". Sari Pediatri, vol. 11(4): 257-263, 2009.