**ORIGINAL ARTICLE**

# Potential of Rice Bran Extract to Decrease Body Weight, Triglyceride, and Malondialdehyde Levelsin Obese Rat

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## ABSTRACT

**Background:** Obesity is a consequence of fat accumulation in adipose tissue and it increases oxidative stress. Rice bran extract (RBE) is reported as functional food that has high antioxidant and anti-obesity effect.
**Aim:** To prove the effect of RBE to decrease body weight, triglyceride (TG), and malondialdehyde (MDA) in obese Sprague Dawley rats.
**Methods:** Randomized experimental pre-post-test with control group design. Obese rats were induced by high fat sucrose diet for 6 weeks and RBE used hexane solvent. Thirty rats were divided into 5 groups: healthy rats as negative control (K-); obese rats as positive control (K+); obese rats treated with 100 mg/kgBW RBE ($X_1$); obese rats treated with 150 mg/kgBW RBE ($X_2$); obese rats treated with 200 mg/kgBW RBE ($X_3$). Treatments were administrated for 3 weeks after obesity induction. Triglyceride and MDA level were assessed by GPO and TBARS method respectively. Statistical analysis usedpaired t-test and ANOVA.
**Results:** Rice bran extract with various dosage significantly decreased body weight, TG, and MDA level (p=0.00). Triglyceride level between $X_2$ and $X_3$ did not show a significant different (p=0.94). Beside that, MDA level of $X_2$ and $X_3$ were significantly different compared with K+ (p=0.00, and p=0.00).
**Conclusion:**Rice bran extract was able to decrease body weight. High dosage of RBE (150 mg/kgBW and 200 mg/kgBW) had the same ability to decrease TG and MDA level in obese rats.
**Keywords:** body weight*, malondialdehyde*, obesity, rice bran extract, triglyceride

## INTRODUCTION

Obesity with complication of diabetes mellitus and cardiovascular disorders is a major chronic disease that causes mortality in the worldwide.[1]In 2015, *World Health Organization* (WHO) stated that overweight and obese population of adults over 1980 and 2013 from 30% to 38% in women and 29% to 37% in men.[2]It is estimated that overweight and obesity cases are 38% and 20% in 2030.[3] These problems becomehealth challenge both in developed and developing countries.[2]

Obesity is associated with excess body weight in individualthat results in impaired motor function, risk of falling, and injury are very high due to disturbed balance control.[4] Obesity occurs because of the accumulation of excess fat in adipose tissue due to an imbalance energy intake and physical activity.[5] Excessing fat leads to increase free fatty acid and inhibits the process of lipogenesisthat resultsin increasingtriglyceride (TG) levels.[6]Triglycerideslevels are used as measurement index of the fat accumulation.[7] Obesity prevention is devoted to reduceTG levels in the body.[8]

Obesity can also trigger oxidative stress that results in production of reactive oxygen species (ROS) increased.[9] Increased ROS over cell antioxidant result in lipid peroxidation.[10] One of markersto determine lipid peroxidation is *malondialdehyde*(MDA). *Malondialdehyde*is a specific marker of oxidative damage in obesity.[11] Persons with obesity have increased ROS that are followed by increased MDA which is an effective factor in development of oxidation, cellular damage, and metabolic disease.[12]

Obesity prevention has been largely conducted such as management of dietary intake, increased physical activity, and consumption of anti-obesity drugs, but it still considered less promising in the management of obesity. Thesefindings make researchers to find appropriate strategy without drugs by consumption of functional food as therapeutic way to treat obesity.[13] One of functional foodswhich isreported as anti-obesity is rice bran.[14] Rice bran is secondary product of rice milling process with good source of nutrients.[1,15] Rice bran contains high antioxidants such as γ-oryzanol, vitamin E groups (tocopherols and tocotrienols), flavonoid,macronutrient contents like carbohydrate, fat, protein, and dietary fiber.[16,17] These antioxidant compounds are potentially protective as risk factors in obese adults.[18]

Many reports stated that rice bran extract has anti-obesity effect.[14] Clinical studies reported that rice bran antioxidants can improve lipid profiles in humans. Antioxidantsof vitamin E groups (*tocopherols* and *tocotrienols*) in rice bran act to prevent lipid peroxidation.[16]What distinguishes this study from previous studies is the independent variable which includes doses of rice bran extract with high doses doubled from previous studies, research materials originating from Indonesian local rice with IR 64 varieties, the length of time of rice bran extract treatment and site research.Therefore, this study is necessary to conduct. This study aimed to prove the effect of RBEto decreasebody weight, TG, and MDAin obeseSprague Dawley rats.

## MATERIAL AND METHODS

This research was an experimental study (true experimental laboratory) with a randomized pre-post test design with a control group design. This study used male Sprague-Dawley (SD) male rats. In this study, the subjects were divided in 5 groups: 2 control groups and 3

experiment groups. The treatment was an administration of rice bran extract for 21 days in obese rats given a High Fat Diet (HFSD) for 42 days. Thirty Sprague Dawley rats (white, male, weight 150-200 grams, age 8-10 weeks) were obtained from an animal-study farm in Sleman, Central Java, Indonesia. The rats caring were conducted in animal-study Laboratory, Faculty of Medicine, Diponegoro University, Indonesia. Rats were placed into individual cage with adequate lighting by 12 hours of dark and light cycle and then acclimatized. The temperature in the room was 28-32$^0$C. Animal's diet and drinks were conducted by ad libitum. Elementary mice were used in this study because there were many studies of obesity models with humans. This is what causes elementary mice to be obese and is characterized by a polygenic phenotype that reflects human obesity.[20,21,19,20]

**Extraction procedures:** IR-64 rice bran was obtained from rice milling factory in Demak Regency, Central Java, Indonesia. Fine rice bran passed 40 mesh's sieve. Oven temperature stability at 120$^0$C for 3 minutes and left at room temperature for 12 hours to inactivate lipase that caused rancid odor and to maintain bioactive components such as antioxidant activity in rice bran.[21] Rice bran was stored in freezer before used.[15]

The extraction of rice bran used maceration method. The solvent used hexane (boiling point 67-69$^0$C).[22,23,24]The filtering process used filter paper and concentrated with a rotary evaporator to obtain thick rice bran extract. The antioxidant activity was measured by *1,1-diphenyl-2-picrylhydrazyl* (DPPH) method with three replications and crude fiber content was measured by gravimetric method.

**Interventions:** The induction of obesity was conductedorally for 6 weeks used HFSD which was consisted of 15% pork oil, 5% quail egg yolk, and 45% sucrose from total dietary intake.[25] Rats were divided into 5 treatment groups namelyhealthy rats and normal diet as negative control (K-), obese rats as positive control (K+), obese rats with intervention 100 mg/kgBWof RBE ($X_1$), obese rats with intervention 150 mg/kgBWof RBE ($X_2$) and obese rats with intervention 200 mg/kgBW of RBE ($X_3$). Intervention for 21 dayswas conducted by feeding tube with 0.5% of additional*carboxymethyl cellulose* (CMC).

Body weight, food intake,and water intakeof rats were evaluated weekly. Foodintake of rats wasknown by measuring the foodd's leftoverevery day. Food intake of each individual in all groups was20 grams. In the pre and post test, rats were fasted for 8-12 hours and then blood sampling was done via *retro-orbital plexus* with combination of ketamine, xylazine, aquadest (2:1:1) as much 0.1 ml/200 g. At the end of the study, rats were sacrificed.

**Study Variables:** The independent variable in this study was rice bran extract. The dependent variables in this study were body weight, triglyceride levels, and MDA levels.Body weight of ratswere measured using *Omron*digital scale with a precision level of 0.1 gram. The levels of triglyceride serum were measured using *Dyasis*kit (Germany) with enzymatic method of *glycerol phosphate oxidaseparaamino antipryne* (GPO-PAP) at wavelength of 546 nm. *Malondialdehyde*plasma was measured by *BioAssay System* kit (China) with *thiobarbituric acidreactive substance* (TBARS) method using spectrophotometer at wavelength of 534 nm.

**Data collection and analysis:** Results were expressed as mean±SD. Normality of data was analyzed using *Shapiro-Wilk*due to sample size ≤ 50. The differences of each group were analyzedusing *paired t-test*. The differences between groupswere analyzed using *one-way* ANOVA and followed by *Bonferroni*or *Tamhane*post hoc test. Data were analyzed with significance value at p<0.05.

**Ethical clearance:** Ethics clearancewas obtained from Faculty of Medicine Diponegoro University and central public hospital Dr. Kariadi, Semarang, Indonesia with registered number 07/EC/H/FK-RSDK/II/2018.

## RESULTS

**Body weight:** The mean body weight of rat after RBE intervention with various dosages showed a significant decrease (p=0.00). The highest decrease in mean was shown in 200 mg/kgBWgroup. The meanchange in body weight among obese group and intervention groups of various dosage showed significant difference (p<0.05). Significant difference in mean of body weight changes were also shown in various dosage of RBE intervention groups (*p*<0.05). This proves that the greatest negative weight changes with increasing RBE dosagesand the best body weight changes was shown in intervention group of 200 mg/kgBW RBE (Table 1 and Table 2).

**Levels of triglyceride (TG):** The mean TG levels of rat after RBE intervention with various dosages showed a significant decrease (p<0.05). The highest decrease in TG level was shown in 200 mg/kgBW group. The meanschange of TG level among obese group and intervention group of RBE with various dosages showed significant difference (p<0.05). There was no significant difference in mean change of TG levelamong150 mg/kgBWgroup and 200 mg/kgBWgroup (p=0.94). These findings provedthat the decrease of TG level in obese rat with RBE dosage of 150 mg/kgBWwas as well as 200 mg/kgBW(Table 3 and Table 4).

**Levels of Malondialdehyde(MDA):** Mean of MDA level in ratafter RBE intervention with various dosages showed a significant decrease (p<0.05). The highest decrease in MDA levels was shown in 200 mg/kgBW group. The means change of MDA level among obese group (K+) and intervention group of RBE with dosage 150 mg/kgBW and 200 mg/kgBW showed significant difference (p=0.008 and p=0.640). There was no significant difference in mean change of MDA levelamong various dosages groups (p<0.05). These findings proved that RBE dosages of 100 mg/kgBW, 150 mg/kgBW and 200 mg/kgBWwere as well as to lower MDA level in obese rat. The protective effects of RBE on oxidative stress wereproven in this study. The changes in MDA level of healthy rat and obese rat showed that standard feeding in obese rat would have an impact on same changes in MDA levelin healthy rat. Significant differences in MDA changes in healthy rat compared with RBE intervention group at dosages of 150 mg/kgBW and 200 mg/kgBW further reinforced evidence that both of dosages resulted in lowering oxidative stress (Table 5, 6).

Table 1. Means of body weight changes before and after RBE intervention

| Groups | Body weight (g) | | Δ | $P^{+}$ | $P^{++}$ |
|---|---|---|---|---|---|
| | pre-intervention | post-intervention | | | |
| Healthy rats | 268.91 ± 0.91 | 274.46 ± 0.37 | 6.55±1.08 | 0.00* | 0.00* |
| Obese rats | 281.55 ± 1.27 | 305.28 ± 0.70 | 23.73±1.08 | 0.00* | |
| Obese rats + 100 mg/kgBW RBE | 281.15 ± 1.37 | 276.80 ± 0.76 | -4.35±1.98 | 0.00* | |
| Obese rats + 150 mg/kgBW RBE | 281.30 ± 1.16 | 271.75 ± 0.61 | -9.55±1.71 | 0.00* | |
| Obese rats + 200 mg/kgBW RBE | 281.23 ± 1.08 | 265.81 ± 0.18 | -15.41±1.03 | 0.00* | |

Values are mean±SD (n=6 rats/group). *; significant value at $p<0.05$, Δ; the changes between pre and post-intervention. $p^{+}$; *paired t-test*. $p^{++}$; *one-way* ANOVAfollowed by *Bonferroni*post-hoc test.

Table 2. Bonferroni post hoc test results for weight changebefore and after RBE intervention

| Groups | Weight (gram) Mean±SD | Values*p* | | | | |
|---|---|---|---|---|---|---|
| | | $K_-$ | $K_+$ | $X_1$ | $X_2$ | $X_3$ |
| $K_-$ | 6.55 ± 1.08 | - | 0.00* | 0.00* | 0.00* | 0.00* |
| $K_+$ | 23.73 ± 1.08 | | - | 0.00* | 0.00* | 0.00* |
| $X_1$ | -4.35 ± 1.98 | | | - | 0.00* | 0.00* |
| $X_2$ | -9.55 ± 1.71 | | | | - | 0.00* |
| $X_3$ | -15.41 ± 1.03 | | | | | - |

*; significant value at $p<0.05$

Table 3. Means of TG serum level changes before and after RBE intervention

| Groups | TG serum levels (mg/dl) | | Δ | $P^{+}$ | $P^{++}$ |
|---|---|---|---|---|---|
| | pre-intervention | post-intervention | | | |
| Healthy rats | 44.40 ± 3.68 | 54.37 ± 3.69 | 9.97±6.56 | 0.01* | 0.00* |
| Obese rats | 115.54 ± 2.31 | 131.69 ± 4.42 | 16.15±6.12 | 0.00* | |
| Obese rats + 100 mg/kgBW RBE | 115.28 ± 2.08 | 95.35 ± 12.71 | -19.92±12.17 | 0.01* | |
| Obese rats + 150 mg/kgBW RBE | 115.72 ± 2.44 | 85.29 ± 8.33 | -30.42±6.39 | 0.00* | |
| Obese rats + 200 mg/kgBW RBE | 115.41 ± 2.78 | 77.46 ± 0.86 | -37.95±3.37 | 0.00* | |

Values are mean±SD (n=6 rats/group). *; significant value at $p<0.05$, Δ; the changes between pre and post-intervention. $p^{+}$; *paired t-test*. $p^{++}$; *one-way* ANOVAfollowed by *Bonferroni*post-hoc test.

Table 4. Bonferroni post hoc test results for TG changebefore and after RBE intervention

| Groups | Triglyceride (mg/dl) Mean±SD | Values*p* | | | | |
|---|---|---|---|---|---|---|
| | | $K_-$ | $K_+$ | $X_1$ | $X_2$ | $X_3$ |
| $K_-$ | 9.97 ± 6.56 | - | 1.00 | 0.00* | 0.00* | 0.00* |
| $K_+$ | 16.15 ± 6.12 | | - | 0.00* | 0.00* | 0.00* |
| $X_1$ | -19.92 ± 12.17 | | | - | 0.22 | 0.00* |
| $X_2$ | -30.42 ± 6.39 | | | | - | 0.94 |
| $X_3$ | -37.95 ± 3.37 | | | | | - |

*; significant value at $p<0.05$

Tabel 5. Means of MDAplasma level changes before and after RBE intervention

| Groups | MDA plasma levels (nmol/ml) | | Δ | $P^{+}$ | $P^{++}$ |
|---|---|---|---|---|---|
| | pre-intervention | post-intervention | | | |
| Healthy rats | 1.69 ± 0.06 | 1.95 ± 0.10 | 0.25±0.15 | 0.00* | 0.00* |
| Obese rats | 3.85 ± 0.20 | 4.20 ± 0.09 | 0.34±0.27 | 0.02* | |
| Obese rats + 100 mg/kgBW RBE | 3.96 ± 0.16 | 2.35 ± 1.19 | -1.61±1.09 | 0.01* | |
| Obese rats + 150 mg/kgBW RBE | 3.94 ± 0.09 | 1.86 ± 0.94 | -2.07±0.89 | 0.00* | |
| Obese rats + 200 mg/kgBW RBE | 3.89 ± 0.17 | 1.05 ± 0.50 | -2.84±0.37 | 0.00* | |

Values are mean±SD (n=6 rats/group). *; significant value at $p<0.05$, Δ; the changes between pre and post-intervention. $p^{+}$; *paired t-test*. $p^{++}$; *one-way* ANOVAfollowed by *Tamhane*post-hoc test.

Table 6. Bonferroni post hoc test results for MDA changebefore and after RBE intervention

| Groups | MDA (nmol/ml) Mean±SD | Values*p* | | | | |
|---|---|---|---|---|---|---|
| | | $K_-$ | $K_+$ | $X_1$ | $X_2$ | $X_3$ |
| $K_-$ | 0.25 ± 0.15 | - | 1.00 | 0.07 | 0.01* | 0.00* |
| $K_+$ | 0.34 ± 0.27 | | - | 0.06 | 0.00* | 0.00* |
| $X_1$ | -1.61 ± 1.09 | | | - | 0.99 | 0.32 |
| $X_2$ | -2.07 ± 0.89 | | | | - | 0.64 |
| $X_3$ | -2.84 ± 0.37 | | | | | - |

*; significant value at $p<0.05$

## DISCUSSION

This study showed that RBE intervention with various dosages for 21 days was proven significantly to decrease body weight, serum TG level, and MDA plasma in obese rat ($p$<0.05), compared with obese group without RBE intervention that showed a significant increasein body weight, serum TG level, and MDA plasma level ($p$<0.05). In this study, high dosage of 200 mg/kgBWRBE showed that the greatest changesto decreasebody weight, serum TG level, and MDA plasma level in obese rat. The weight loss in this study was greatest followed by an increase in RBE dosage, whereas the dosages of 150 mg/kgBW and 200 mg/kgBW showed equally good effects to lower serum TG and MDA plasma level in obese rat.

The content of pork oil in HFSD feed contains high levels of unsaturated fat and calories so it can be absorbed easily by body and leads to higher body weight gain than normal feed.[26]Administration of high fat and sucrose diet for 2 weeks can increase body weight significantly and trigger obesity. Excessive consumption of sucrose can have the same effect as fructose on obesity.[27]Wang et al.[28] stated that administration of high fat diet in rat could increase body weight compared with rat fed low fat diet.

Groups with various dosages of RBE intervention can essentially prove weight loss after obesity induced. Groups with high dosage of 200 mg/kgBW had greater effect on weight loss than 100 mg/kgBW and 150 mg/kgBW group. This is associated with appetite decreased of intervention group because the fiber and antioxidant content in rice bran can suppress leptin by giving longer satiety.[29] A study proved that administration of RBE in animal-study can losebody weight. The content of triterpen alcohol and sterol in rice bran and oryzanol can decrease activity of fat metabolism resulting in fatty acids synthesis is low in the liver and weight reduction in obeseanimal-study.[30]

In obesity-induced rat, there is an increase in adipose tissue and peripheral insulin resistance associated with increased lipogenesis leading to elevated triglycerides in the liver.[31]Justo et al.[32] proved that the treatment of rice bran enzyme extract could reduce *hypertriglyceride* in obese rat according to given dosage. This is accompanied by a significant decrease in triglyceride level after administration of rice bran enzyme extract. The decrease of triglyceride level in obese rat with RBE intervention in line with the study results of Wang et al.[28] showed that rice bran enzyme extract can decrease triglyceride level in fat induced animal-study. Justo et al.[1] showed that rice bran supplementation may also have other beneficial effects because it is not only prevents metabolic and biochemical changes associated with obesity induction but also can prevent changes in adipocyte structure and pro-inflammatory in white adipose tissue.

The decrease of triglyceride level in obese ratwith RBE intervention was in line with the findings of rice bran extract content.Sterol that has antioxidant properties effectively improves lipid profiles. Sterol acts effectively to compete with cholesterol in combining the mixture of micelles in fat metabolism. The content of oryzanol in rice bran is reported to have beneficial effects on decreasing cholesterol level by weakening the Apo-B synthesis in humans.[32]

*Malondialdehyde*is the end product of lipid peroxidation caused by oxidative damage to lipids and serves as a marker of oxidative stress in patients with cardiovascular disease.[33] Obesity is often associated with increased oxidative stress and ROS due to excess nutrients resulting in oxidation reactions leading to the formation of free radicals.[9]

The protective effect of RBE on oxidative stress in this study was supported by the study of tocotrienols contained in rice bran extract that gave a protective effect on ROS in cardiometabolic animal-study.[34]Tocotrienol also serves as protection against vascular function including decreased lipid peroxidation.[16]Tocotrienolis considered to have stronger antioxidant properties compared with α-tocopherol because they have an unsaturated side chain allowing more efficient penetration into tissues that have a layer of saturated fat such as brain and liver. Experimental studies showed that tocotrienols have anexcellent effect on free radicals prevention than α-tocopherol in the fat distribution of cell membranes.The high activity of antioxidant tocotrienol can prevent the occurrence of hyperlipidemia.[35] In addition, oryzanol in rice bran can improve pancreatic β-cell dysfunction in animal-study induced by high-fat diet and prevents apoptosis both in vivo and in vitro.[29]

Limitations in this study was no measurement of antioxidant component content in RBE of IR 64 varieties used in obeserat study that can explain the protection mechanism from intervention to body weight, serum triglyceride, and MDA plasma level.There was also no measurement of total antioxidant capacity in rat's body that can influence the protective effect of RBE on oxidative stress. Measurement of leptin and adiponectin levels was not conducted in this study so it could not be explained the previous study.

## CONCLUSIONS

Based on the results, RBE intervention of various dosagesfor 21 days wasproven to decrease body weight, serum triglyceride, and MDA plasma level in obese rat. The dosage of 200 mg/kgBWhad greater potential to lower body weight, serum triglyceride, and MDA plasma level after RBE intervention. The dosage of 150 mg/kgBW and 200 mg/kgBWshowed as well as to lower serum triglyceride and plasma MDA level in obese rat. The antioxidant compounds in RBE had been shown to have anti-obesity effects in this study. Further study needs to conduct specific assessment on analysis of antioxidant compounds content in RBE that most influenced in the prevention of obesity.

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