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The physiological response of obese rat model with rambutan peel extract treatment

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ABSTRACT

Objective: To determine body weight gain, expression of Igf-1 and Igf-1 receptor on obese rat model treated with rambutan peel extract (RPE) as a physiological response.

Methods: Normal and obese rat feed with normal and high calorie diet around 12 weeks and continued to treat with ellagic acid, RPE 15, 30 and 60 mg/kg body weight respectively. Physiological responses observed were weight gain and expression of Igf-1 with its receptor. Body weight of rat was weighed once per week. Expression of Igf-1 and igf-1R observed with fluorescence immunohistochemistry. The intensity of Igf-1 and Igf-1R expression was analysis using FSX-BSW software.

Results: The lowest weight gain was obtained on obese rat model treated with RPE 30 mg/kg body weight. The expression of Igf-1 and Igf-1R were reduced on obese rat model treated with RPE compared with obese rat model of non treatment ($P<0.05$). The low expression of Igf-1 and Igf-1R was found on obese rat model treated with ellagic acid and RPE 30 mg/kg body weight.

Conclusions: The RPE was effecting to the physiological response on obese rat model. The RPE 30 mg/kg body weight inhibited body weight gain and decreased the expression of Igf-1 and Igf-1R of obese rat model.

1. Introduction

Obesity is increasing worldwide and rapidly becoming a health problem of epidemic proportions. The prevalence of overweight and obesity has increased sharply in both adults and children in two decade. It is predicted that worldwide prevalence of obesity showed a significant increase. Currently 1.6 billion adults worldwide are overweight and at least 400 million of them are obese. In 2015, an estimated of 2.3 billion adults will be overweight and 700 million of them will be obese[1].

This is believed to be related to the excessive consumption of food rich in calories related with worst eating habits such binge eating, night eating, high fructose corn syrup, alcohol abuse, smoking, *etc*. Good eating habits by healthy food and food rich in antioxidants may play a protective role against metabolic diseases. It is known that equilibrium between oxidants and antioxidants is crucial to the body. The advantage of antioxidant substances is one important factor to control individual healthy life that has a protective effect at level population[2].

Polyphenols are the most abundant antioxidants and their intake is 10 times higher than the intake of vitamin C and 100 times higher than that of vitamin E or carotenoids. Phenolic compounds act as capture electrons from reactive oxygen species and prevent elevation of its activity[3,4]. Furthermore, phenolic compounds such as flavonoid and tannin are particular that can capture metals like iron

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involved in free radical formation[5]. Indirectly, polyphenols can interfere with the cellular detoxification systems, such as superoxide dismutase, catalase or glutathione peroxides[2]. Rambutan (*Nephelium lappaceum*) is a tropical fruit, which is widely grown in Indonesia. Its production reached 811 993 tons per year[6]. On 1 g of rambutan fruit, as much as 0.4 g can be consumed while the rests are peels and seeds. Thus 487 195.8 tons of wastes are produced and not used even though rambutan peel contains compounds with strong antioxidant activity[7,8]. Recently our study found that the main phenolic compounds are tannins and flavonoids[9,10], which were identified as geraniin, coraligin, and ellagic acid (EA)[8]. This study focused on physiological response with parameter body weight gain, expression of Igf-1 and Igf-1 receptor on obese rat model treated with rambutan peel extract (RPE).

2. Materials and methods

2.1. Ethical consideration

The study was approved by ethical review committee of Brawijaya University Research Ethics Committee as a member of National Research Ethics Committee of Republic Indonesia.

2.2. Material preparations

This research was used 12-week old normal and obese male rat model. Obesity was determined by Lee Index[11]. The rambutan peel was extracted with ethanol and dried by rotary evaporator, then dissolved with corn oil and water. There were two prepared-control treatments, placebo as negative control and ellagic acid as positive control. The ellagic acid used in this study obtained from Sigma catalogue 14668.

RPE solution was prepared by weighed the 0.1 g RPE added 2 drops of corn oil stirred until homogeneous and sterile aquadest distillated water was added to the stock of RPE obtain of the concentration of 1%. Then RPE treatment dosage 15, 30 and 60 mg/kg body weight was devised by picking up 15, 30 and 60 mL of stock solution plus 85, 70 and 40 mL distilled water respectively. Standard volume of given was body weight of rat multiplying by % concentration.

2.3. Subject

The rats obtained from Wistar Laboratory, Bandung-Indonesia, were divided into six treatment groups: non-treatment (NT), placebo (P), EA 15 μg/kg body weight (relation water/corn oil), and three doses of RPE (15, 30, 60 mg/kg body weight). The animals were kept in standard rat cages at Biosains Laboratory. All normal rats were fed with normal diet whereas obese rats were fed with phokphan 551 as a high-calorie source of diet. The RPE treatment was given using oral administration method every two days for 12 weeks. The group of obese rats was continuously fed *ad libitum* with high calorie diet while the normal rats received standard diet without physical exercise. The rat body weight gain, food intake, and amount of feces were measured once per week. After 12 weeks, the rats were sacrificed based on standard protocol from university research ethics. Visceral fat was taken from the posterior caudal and 0.5 g visceral fat was fixed by 4% paraformaldehyde hereafter embedded with liquid paraffin. Paraffin blocks were sliced to get microanatomy slide. The histology slides were stained by Hematoxylin-Eosin to measure adipocyte. The expression of Igf-1 receptor and ligand was determined by immunofluorescence with specific antibody.

2.4. Measurement of weight gain

Body weight of rat was weighed with triple beam equipment once per week until 12 weeks. Food consumptions and feces production of rats at metabolic cages were measured on Week 1, 4, 10 and 12 respectively.

2.5. Immunofluorescence analysis

The expression of Igf-1 and Igf-1R observed by immunofluorescence double staining used standard protocol method of Bancroft and Gamble[12]. We used primary antibodies IgG mouse for Igf-1 and IgG rat to receptor (Lifespan Bioscience). The primary antibody was dissolved in 2% bovine serum albumin (1:1 500) then incubated at room temperature for 1 h. The secondary antibody used goat-anti-mouse IgG-FITC and goat-anti-rabbit IgG-Rhod (Santa Cruz Biotechnology) which was dissolved in 2% bovine serum albumin (1:2 000). The slides were incubated for 1 h at room temperature and washed with phosphate buffer solution three times for 10 min. Once dried, the immunofluorescence visualization could be performed. Result of immunofluorescence was visualized by Olympus FSX100 microscope and analyzed using FSX-BSW program to determine Igf-1 and Igf-1R expression in visceral adipocyte.