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Changes in body weight and leptin: intervention of gambir extract in obese model rats

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ABSTRAK

Latar Belakang: *Peningkatan prevalensi obesitas menjadi masalah kesehatan yang serius sehingga diperlukan terapi alternatif. Gambir mengandung katekin yang memiliki sifat antiobesitas yang dapat digunakan sebagai terapi alternatif.*
Tujuan: *Penelitian ini bertujuan untuk menganalisis pengaruh intervensi ekstrak gambir terhadap berat badan dan leptin pada tikus model obesitas.*
Metode: *Penelitian ini merupakan penelitian labolatorik dengan rancangan pre-post test. Subjek penelitian yaitu tikus wistar jantan dengan jumlah 36 ekor. Tikus dibagi menjadi 6 kelompok yaitu KN (tikus sehat), K- (tikus obesitas), KP (tikus obesitas diberi Orlistat 10,8 mg/200gBB/hari), P1 (tikus obesitas diberi ekstrak gambir 20 mg/200gBB/hari), P2 (tikus obesitas diberi ekstrak gambir 40 mg/200gBB/hari), dan P3 (tikus obesitas diberi ekstrak gambir 80 mg/200gBB/hari). Data penelitian dianalisis menggunakan software SPSS versi 23.0. Uji beda kelompok dilakukan dengan One-way ANOVA jika data berdistribusi normal dan Kruskall Wallis jika data tidak berdistribusi normal.*
Hasil: *Hasil penelitian menunjukkan terdapat perbedaan yang bermakna rerata berat badan (p=0,000) dan kadar leptin (p=0,001) antar kelompok tikus. Kelompok P3 memiliki rerata berat badan dan kadar leptin yang paling rendah, bahkan melampaui kelompok K+ dan mendekati kelompok KN.*
Kesimpulan: *Intervensi ekstrak gambir dosis 80mg/200gBB/hari pada tikus obesitas dapat menurunkan perolehan berat badan dan menurunkan kadar leptin*.

KATA KUNCI: *berat badan; gambir; katekin; leptin; obesitas*

ABSTRACT

Background: *The increasing prevalence of obesity is a serious health problem that requires alternative therapy. Gambir contains catechins with anti-obesity properties that can be used as an alternative therapy.*
Objectives: *This study aims to analyze the effect of gambier extract intervention on body weight and leptin in obese rat models.*
Methods: *This research was laboratory research with a pre-post-test design. The research subjects were male Wistar rats with a total of 36 rats. Rats were divided into 6 groups, namely KN (healthy rats), K- (obese rats), KP (obese rats given Orlistat 10.8 mg/200gBB/day), P1 (obese rats given gambir extract 20 mg/200gBW/day), P2 (obese rats given gambir extract 40 mg/200gBW/day), and P3 (obese rats given gambir extract 80 mg/200gBW/day). Research data were analyzed using SPSS software version 23.0. The different group tests were carried out using One-way ANOVA if the data were normally distributed and Kruskall Wallis if the data were not normally distributed.*
Results: *The results showed a significant difference in mean body weight (p=0.000) and leptin levels (p=0.001) between groups of rats. The P3 group had the lowest average body weight and leptin levels, surpassing the K+ group and approaching the KN group.*

Conclusions: *Gambir extract intervention at 80mg/200gBW/day in obese rats can decrease weight gain and reduce leptin levels.*

KEYWORDS: *body weight; catechin; gambir; leptin; obesity*

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INTRODUCTION

Obesity is a metabolic disorder characterized by increased adipose tissue mass due to a positive energy balance (1). Obesity is a serious public health problem with a Body Mass Index >30 kg/m^2 (2). According to the World Obesity Federation, as much as 38% of the world's population over five suffers from obesity and is expected to reach 51% in 2035. Obesity is estimated to affect nearly half of adults (49%) in America, 39% in Europe, and 11 % in Southeast Asia in 2035 (3). The prevalence of obesity in Indonesia in the age group over 18 years has increased by 7% from 2013 to 2018 (4). In 2025, 7.5 out of 10 Indonesians are expected to be obese, or 10% of male and 14,8% female of the population(5).

Obesity is a major public health problem in developed and developing countries(6). Individuals with overweight and obese nutritional status have death rates of 47.48 and 66.67 per 1000 people per year respectively (7). Recent studies found that overweight obesity contributed to 5.5% of total deaths (8). Obesity also contributes to cardiovascular disease, metabolic syndrome, type 2 diabetes mellitus, cancer, and various reproductive disorders (6).

Obesity is caused by an imbalance in incoming and outgoing energy (9). Energy imbalance will disrupt the energy homeostasis system (10). In the case of obesity, the energy homeostasis system is disrupted, which creates excess body weight (11). The brain regulates Body weight in response to external signals to control food intake (12). In the long term, this mechanism leads to the development of obesity (13).

Research shows a close relationship between leptin levels, adiposity, and body fat percentage (14). Leptin levels indicate how much energy is stored in fat and calorie intake (15). Excessive leptin will lose normal functions such as appetite suppression and weight loss. Leptin incompetence will lead to a lack of clinical use of leptin resulting in leptin resistance which is the beginning of the development of obesity (16).

Obesity can be prevented or controlled in various ways, such as food, exercise, and medication. However, anti-obesity drugs such as Orlistat and Sibutramine have been associated with various negative side effects, including high blood pressure, constipation, dry mouth, headaches, heart attacks, and trouble sleeping (6). In addition, pharmacological therapy in the long term requires a lot of money, so an alternative pharmacological therapy that is safe, effective, and cheaper is needed, namely the

use of phytochemical compounds (17). Gambir is one of the typical Indonesian plants that the community has widely used as a spice and medicine (18). Gambir extract is produced from the plant's dried leaves and young twigs and is used as an astringent in Asia (19). Gambir is beneficial in various health problems, such as anti-hyperlipidemia, antiaging, reducing plaque halitosis, and oxidative stress (20). Besides that, it can also be used as a mixture of medicinal and food ingredients (21).

Gambir contains various kinds of bioactive substances (18). The most abundant content in gambir is catechin (22). Gambir contains 97% catechins (23). Recent studies have shown that catechin bioactive compounds have antioxidant and anti-obesity properties (24,25). Intervention studies conducted in the obese group showed that the content of catechins in beverages significantly reduced individual weight in the intervention group by 8-10% (26). In addition, catechins can reduce leptin levels and directly reduce body weight through increased energy expenditure and fat oxidation (27).

Research on gambir extract as a treatment for obesity in reducing body weight and improving leptin has never been done in vivo. This study aims to determine the effect of gambir extract intervention on body weight and leptin in obese rat models.

MATERIALS AND METHODS

This type of research is a laboratory experiment with a pre-post test design for calculating body weight and a post-test for checking leptin levels. This research was conducted in the Center for Food and Nutrition Studies Laboratory, Gadjah Mada University. This research was conducted in April-May 2023. The sample for this study used male Wistar rats aged 8-12 weeks with a body weight of 150-200 grams.

The sample size of 36 rats was calculated using the Sample Size Calculation in Animal Studies formula. Rats were divided into 6 groups using simple random sampling. The rat group consisted of KN (healthy rats), K- (obese rats), KP (obese rats given Orlistat 10.8 mg/200gBW/day), P1 (obese rats given gambir extract 20 mg/200gBW/day), P2 (Obese rats given gambir extract 40 mg/200gBW/day), and P3 (obese rats given gambir extract 80 mg/200gBW/day).

The ingredients used are G-Fit brand gambir extract obtained from CV Uncaria Herbal Indonesia, standard feed, and High Fat High Fructose (HFHFr) feed. Leptin levels were measured using the ELISA method using the Rat Leptin ELISA Kit. Adaptation was carried out for 7 days while obesity induction and intervention were carried out for 4 weeks each. Obesity modeling was done by administering HFHFr. Rats are categorized as obese if the Lee index is >300 g/cm3. Data on body weight and leptin levels were then analyzed using SPSS For Windows version 23.0 software. The different group test was conducted using One-way ANOVA and Kruskal Wallis. This study was approved by the Research Ethics Commission of the Faculty of Medicine, Universitas Sebelas Maret with number 67/UNS.27.06.11/ KEP/EC/2023.

RESULTS AND DISCUSSION

Obesity induction was carried out after adaptation for 7 days. **Table 1** shows that

obesity has been achieved in the HFHFr-induced group for 4 weeks. The group with the highest average Lee index was group P2. The statistical test results showed a significant difference in the average Lee index between groups of rats after obesity induction.

Table 1. Different averages of the lee index after induction

Group	n	After induction mean ± SD (g/cm3)	p-value
KN	6	292.99 ± 1.79	0.001*
K-	6	349.63 ± 2.35	
K+	6	347.06 ± 1.782	
P1	6	347.24 ± 3.66	
P2	6	350.75 ± 1.67	
P3	6	347.68 ± 2.14	

Source: Primary Data

Description: KN (Healthy rats; K- (Obese rats); K+ (obese rats given Orlistat 10.8 mg/200gBB/day), P1 (obese rats given gambir extract 20 mg/200gBW/day), P2 (obese rats given gambir extract 40 mg/200gBW/day), and P3 (obese rats given gambir extract 80 mg/200gBW/day); n (total rats)

**) Significant p-value<0.05 with Kruskal Wallis test*

Table 2. Different averages of body weight before and after treatment

Group	n	Before treatment mean ± SD (g)	Before treatment mean ± SD (g)	Δ Body weight mean ± SD (g)
KN	6	214.00 ± 2.61	241.17 ± 3.97	27.17 ± 2.40
K-	6	260.50 ± 3.83	333.50 ± 4.23	73.00 ± 1.27
K+	6	259.50 ± 3.27	295.33 ± 2.50	35.83 ± 1.17
P1	6	261.50 ± 4.18	313.00 ± 4.86	51.50 ± 1.05
P2	6	261.50 ± 2.88	298.67 ± 3.93	37.17 ± 1.94
P3	6	260.17 ± 2.93	295.33 ± 3.14	35.17 ± 1.47
p-value		0.000[a*]	0.000[a*]	0.000[b*]

Source: Primary Data

Description : KN (Healthy rats; K- (Obese rats); K+ (obese rats given Orlistat 10.8 mg/200gBB/day), P1 (obese rats given gambir extract 20 mg/200gBW/day), P2 (obese rats given gambir extract 40 mg/200gBW/day), and P3 (obese rats given gambir extract 80 mg/200gBW/day); n (total rats); Δ body weight (The different of average body weight before and after Treatment).

[a]) *One-way* ANOVA

[b]) *Kruskal Wallis*

*) Significant p-value<0.05

The results showed that all rats fed the HFHFr diet for 4 weeks were obese. An indicator of successful obesity in rats is when the Lee index is >300 g/cm^3. (28). The P2 group had a higher Lee index because the initial body weight was already high. Lee's index was calculated by measuring body weight and naso-anal length. This study's results align with previous studies which explained that a high-fat diet intervention succeeded in inducing obesity in rats as measured by the Lee index(29).

Giving a high-fat diet to rats will increase body weight and produce a significant increase in adiposity compared to the normal diet group(30). The underlying mechanism is a positive energy balance that results in overweight and obesity. A high-fat diet increases hypo-thalamic gene expression in increasing calorie intake so that adiposity occurs as a physiological response of the body (31).

Body Weight

The body weight of the rats was weighed before and after being given the intervention. Gambir extract intervention in the treatment group was given after obesity was achieved. Based on Table 2 above, it is known that there is a significant difference in the average body weight between groups of rats after the gambir extract intervention with a significance value of 0.000. The P3 and K+ groups had the lowest average body weight compared to the obesity-induced treatment group, where there was a decreased weight gain. This study is in line with the previous study which stated that giving EGCG inhibited weight gain (32). Similar studies also show that the catechins in green tea prevented weight gain in rats on a high-fat diet(3335).

The treatment group with a dose of 80 mg/200gBW/day (P3) in this study experienced the greatest reduction in body weight gain compared to the other two doses. The results of this study are in line with previous research which conducted two repeated studies where the first study showed results that catechins did not reduce body weight. On the contrary, after increasing the dose in the second repeat study, the results showed significant weight loss(36). The weight loss effect resulting from catechins' intervention in tea depends on increasing the dose (32). The gambir extract that was intervened in this study contained catechins with a high amount of about 98%. Catechins have anti-obesogenic properties that inhibit digestion and increase energy expenditure and fat oxidation through thermogenesis-activated β-adrenoceptors from brown adipose tissue (26). Catechins as a source of natural alpha-glucosidase inhibitors slow down glucose absorption (37). Alpha-glucosidase inhibitors increase GLP-1 levels after eating. The incretin hormone GLP-1, a glucagon-like peptide, slows digestion, reduces feelings of hunger, and helps you feel fuller faster after eating(38).

This mechanism decreases the supply of calories, thereby reducing body weight. The catechins in green tea can synergistically affect energy expenditure, fat oxidation, and possibly fat absorption, so they have the potential for weight loss and maintenance(39). Another pathway known so far is activating AMPK by catechins, one of the polyphenols. Activated AMPK reduces gluconeogenesis

and fatty acid synthesis and increases catabolism, leading to weight loss(40).

Leptin

Leptin is a hormone whose level is directly proportional to adiposity. Leptin levels were measured after 4 weeks of intervention. **Table 3** shows that all treatment groups intervening with gambir extract had lower leptin levels than the K- group. The P3 group had the lowest average leptin levels compared to the obesity-induced treatment group. Based on the One-way ANOVA test showed that there was a significant difference in the average leptin levels between groups of rats with a significance value of 0.001.

This study's results align with several previous studies as shown in the following **Table 4**.

Table 3. Different averages of leptin levels after treatment

Group	n	After treatment mean ± SD (ng/mL)	p-value
KN	6	1.40 ± 0.11	0,000*
K-	6	12.07 ± 0.28	
K+	6	2.97 ± 0.15	
P1	6	7.02 ± 0.10	
P2	6	3.06 ± 0.37	
P3	6	1.90 ± 0.19	

Source: Primary Data

Description: KN (Healthy rats; K- (Obese rats); K+ (obese rats given Orlistat 10.8 mg/200gBB/day), P1 (obese rats given gambir extract 20 mg/200gBW/day), P2 (obese rats given gambir extract 40 mg/200gBW/day), and P3 (obese rats given gambir extract 80 mg/200gBW/day); n (total rats)

*) *Significant p-value<0.05 with One-way ANOVA*

Table 4. Relevant research

Title	Result	The study's distinction
The Anti-Obesity Potential of Green Tea: The Effect on Leptin and Adiponectin (27)	Epigallocatechin Gallate (EGCG) rich green tea consumption reduces leptin levels and directly reduces obesity.	The intervention used is gambir which is rich in catechins.
Anti-obesity and antidiabetic effects of Yerba Mate (Ilex paraguariensis) in C57BL/6 J mice fed a high-fat diet (41)	Polyphenol yerba mate herbal tea reduces leptin levels in mice fed a high-fat diet.	The intervention used is gambir, rich in catechins, and the subject is not specifically in obese rats.
Green Tea, Black Tea, and Oolong Tea Polyphenols Reduce Visceral Fat and Inflammation in Mice Fed High-Fat, High-Sucrose Obesogenic Diets (42)	Rats receiving an EGCG injection (85 mg/kg body weight) have lower serum leptin levels.	The intervention used is gambir which is rich in catechins.

Beneficial effects of tea catechins on diet -induced obesity: stimulation of lipid catabolism in the liver (43)	Tea catechin supple - mentation resulted in a considerable reduction in hyper leptinemia.	The intervention used is gambir which is rich in catechins; the subjects were rats, and the intervention was a month.

This study's results indicate that gambier rich in catechins can reduce serum leptin in rats. Other research states that consuming green tea containing catechins can reduce leptin levels and their effect on the hypothalamus, promoting weight loss (27). Leptin levels in the blood reflect energy stores and fat mass(44).

Obese individuals have high levels of circulating leptin which is then exacerbated by a high-fat diet(45). Leptin levels correlate with adiposity in that adipocytes secrete leptin into the bloodstream with fat mass(46). Catechins will decrease body fat mass which then triggers a decrease in adiposity (47). It will impact leptin secretion by adipose tissue, resulting in low leptin levels in the rats that were intervened with catechin-rich gambir extract.

CONCLUSION AND RECOMMENDATIONS

Gambir rich in catechins has the potential as an alternative therapy for obesity. Gambir significantly decreased body weight gain and reduced leptin levels. Gambir extract intervention at a dose of 80 mg/200 gBW/day for 4 weeks had an average body weight and leptin levels lower than the K+ group and even close to the KN group. The authors suggest assessing leptin levels before and after the intervention.

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