EFFECT OF MANGOSTEEN (*Garcinia mangostana* L.) PEEL EXTRACT ON WEIGHT LOSS AND ADIPOSE TISSUE MASS IN MICE

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**Abstract.** Mangosteen (*Garcinia mangostana* L.) peel contains some secondary metabolites, such as xanthones. The present study aimed to investigate the effect of extract from mangosteen peel on the potential weight loss and reducing adipose tissue mass in mice. Male mice fed an high-fat diet (HFD) for 8 weeks were supplemented with mangosteen peel extract (ME) (200 mg/kg/day) for an additional 6 weeks while mice fed a standard diet (SD) were used as normal controls. The results revealed that ME treatment decreased body weight and fat mass including visceral adipose tissue, epididymal white adipose tissue, subcutaneous adipose tissue. The results suggest that ME is effective in reducing weight and adipose tissue mass in HFD-fed mice.

**Keywords:** Mangosteen peel extract, weight loss, adipose tissue, mice.

1. **INTRODUCTION**

In the past, obesity was considered a problem only in high-income countries, but in the past few decades, it has emerged in both low- and middle-income countries with a high prevalence of obesity, and rates are increasing especially in urban areas. High body fat mass in obese people leads to serious medical complications, including hypertension, type 2 diabetes, steatosis, and some other types of cancer, reducing the quality of life and life expectancy of people.

Current obesity treatment involves many aspects such as lifestyle changes, bariatric surgery, or pharmaceutical therapy (Alamuddin et al., 2016). Among them, measures related to lifestyle changes such as dietary management by reducing total energy intake (Shinde et al., 2021) and exercise are considered fundamental for the prevention and treatment of obesity. However, this approach requires significant patient commitment and are difficult to apply widely due to high surgical risks and high treatment costs (Alamuddin et al., 2016). The use of weight-loss drugs also brings many serious side effects such as pulmonary arterial hypertension (aminorex), non-fatal cardiovascular events (sibutramine), cardiovascular toxicity, and valvular heart disease (Krentz et al., 2016). Therefore, the need to find more plant-based medicinal herbs to help safely and effectively treat overweight and obesity.

Mangosteen (*Garcinia mangostana* L.) belongs to the family Seclusive and is a species of tropical evergreen tree widely distributed throughout the tropics of Asia and Africa, especially in Southeast Asia such as Malaysia, Sri Lanka, Indonesia, Burma, Philippines, Thailand, and Vietnam. In Vietnam, mangosteen is a fruit tree that is grown a
lot in the Mekong Delta and the Southeast region, mainly in the provinces of Ben Tre, Vinh Long, Tra Vinh, and Binh Duong. In Southeast Asia, the rind of the mangosteen fruit is one of the traditional remedies for ailments such as colic, diarrhea, dysentery, wound infections, wounds, and chronic ulcers (Liu et al., 2015). Mangosteen peel is also known to be the richest plant of xanthone derivatives discovered to date. Of the more than 200 xanthone derivatives found in plants, sixty compounds are derived from mangosteen, mainly concentrated in the peel (Ee et al., 2016). Xanthones have many biological activities such as antibacterial activity (Salem Abuzaid et al., 2018), anti fungal activity, anti-inflammatory activity, antioxidant activity and especially anticancer activity (Akao et al., 2008; Ee et al., 2016). Therefore, the discovery of xanthone in mangosteen peel is considered one of the great discoveries of medicine.

This study was conducted to evaluate the effects of xanthone extract from mangosteen peel on the body weight and the growth certain types of white adipose tissue. From that result, evaluate the anti-obesity effect on experimental mice, creating a scientific basis to evaluate the anti-obesity effect of xanthone extract from mangosteen peel.

2. RESEARCH SUBJECTS AND METHODS

2.1. Experimental animals

Healthy male white mice (Mus musculus), with weight in the range of 35 - 40 grams (8 - 10 weeks old) were provided by the National Institute of Hygiene and Epidemiology. Mice were kept in cages and maintained at a temperature of 25 – 27 ºC and humidity ranged 40-60 %, under a 12 hour dark/light cycle.

2.2. Preparation of mangosteen peel extract

Mangosteen peel was dried in an incubator at 60 ºC and then ground into a fine powder. The powder was extracted in 80 % ethanol according to the solvent/material ratio of 100 ml/5 g. The mixture was placed in an ultrasonic bath at 60 ºC for 2 hours. After that, the mixture was kept in a refrigerator at 4-8 ºC, and the sediment was collected for study.

2.3. Acute oral toxicity test

The mice were randomly divided into 4 groups, each having 6 mice. Each group was administered a dose of 300, 2000, 5000, 6000 mg/kg, body weight with a volume of 0.5 ml/mice. Mice were observed for a period of 72 hours for signs of toxicity including behavioral (tremors, convulsions), morphological (skin, fur, eyes), and physiological (bodyweight variation) changes, including mortality and compared with respective controls. In addition, the animals were monitored daily for additional 7 days for delayed signs of toxicity and mortality. Finally, the median lethal dose (LD_{50}) was determined (OECD Test guideline, 2001).

2.4. Experimental design

The study was conducted at the Laboratory of Experimental Animals, Department of Human and Animal Physiology, Faculty of Biology, Hanoi National University of Education.
Mice were fed a high-fat diet for 8 weeks with 2 diets: (1) Standard diet: Food provided by the National Institute of Hygiene and Epidemiology; (2) High-fat diet: 45% standard diet and 55% boiled lard. According to AIN 76 standard, the nutritional composition of standard food includes carbohydrate 260 kcal/100 grams, protein 85 kcal/100 grams, lipid 45 kcal/100 grams.

After that, mice with high-fat diet were divided randomly into two groups and one group fed the standard diet for 6 weeks:

- Normal group (SD): mice were fed the standard diet for 8 weeks, continued to eat the standard diet and drank water.
- Control group (HFD): mice were fed a high-fat diet for 8 weeks, continued to eat a high-fat diet and drank water.
- Mangosteen peel extract group (HFD+ME): mice were fed a high-fat diet for 8 weeks, continued to eat a high-fat diet and drank ME at a dose of 200 mg/kg body weight.

Mice were maintained daily and checked for the body weight changes weekly. Twenty-four hours after the last day of the experiment, all mice were sacrificed, adipose tissue including visceral adipose tissue, epididymal white adipose tissue, subcutaneous adipose tissue, was collected for mass determination.

2.5. Data analysis

The results were analyzed using the SPSS version 16.0 by applying the analysis of Variance (ANOVA). P value below 0.05 was considered as statistically significant. The data were expressed as the mean ± standard deviation.

3. RESULT

3.1. Acute toxicity test results

<table>
<thead>
<tr>
<th>Number of mice</th>
<th>Oral dose</th>
<th>Number of mice alive/dead after 72 hours</th>
<th>Number of mice alive/dead after 7 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>300 mg/kg</td>
<td>6/0</td>
<td>6/0</td>
</tr>
<tr>
<td>6</td>
<td>2000 mg/kg</td>
<td>6/0</td>
<td>6/0</td>
</tr>
<tr>
<td>6</td>
<td>5000 mg/kg</td>
<td>6/0</td>
<td>6/0</td>
</tr>
<tr>
<td>6</td>
<td>6000 mg/kg</td>
<td>6/0</td>
<td>6/0</td>
</tr>
</tbody>
</table>

After taking the extract in large amounts, no abnormal symptoms (fatigue, anorexia) were observed in all the mice. After continuously 24 hours, 72 hours, and 7 days, observing the experimental mice showed that the mice returned to activity, eating normally, the pupils of the eyes were normal, and there was no expression of cyanosis, or difficulty breathing. Therefore, the ME caused no mortality and behavioral changes in the mice, the LD50 was estimated to be above 6000 mg/kg (Table 1).
Through the above experiments, it was shown that xanthone extract from mangosteen peel was not toxic to experimental mice.

### 3.2. Effect of extract from mangosteen peel on body weight

The body weight of mice after 8 weeks of eating different diets is shown in Figure 1. The mean weights of the standard diet and high-fat diet at week 1 were 37.175 grams and 37.325 grams, respectively. This difference was not significant statistical. Significant changes in body mass of mice fed a HFD occurring from week three onwards are shown by the path in Figure 1. After eight weeks, the weight in both groups increased significantly, the SD group reached 50.335 grams while the HFD group reached 57.8 grams. This suggests that a high-fat diet led to weight gain and obesity in these mice.

*Figure 1. Change in body weight of mice from week 1 to week 8*

The results in Figure 2 showed that, from week 12 onwards the path on the chart has changed. The mean weight of the HFD group increased much more than the other 2 groups, the SD group was almost unchanged, the HFD + ME group had a significant reduction in average weight. The above results show that xanthone extract from mangosteen peel can reduce weight and obesity in laboratory mice.

When mice eat HFD, it will lead to lipid metabolism disorders, for example, reducing lipolysis or increasing lipid synthesis in the body. Leads to lipid accumulation in adipose tissue causing obesity. The xanthone compound in ME has the effect of reducing bad cholesterol, effectively fighting obesity. Therefore, xanthone extract from mangosteen peel can help the body fight lipid accumulation when eating high-fat foods (HFD).

Another natural food that is also known for its slimming effect is bitter melon, scientifically known as Momordica charantia Linn, belonging to the Gourd family. Some studies have found that bitter melon contains an abundant amount of beta carotene, and vitamins C, B1, B2, B3, phosphorus, and amino acids in bitter melon can neutralize fats from food. Prevents fat accumulation, excess fat and suppress appetite so as not to overeat food, reducing the amount of newly formed fat (Chaturvedi et al., 2004). However, the
substances in bitter melon have a different mechanism of impact on the control of weight gain and obesity than that of xanthone from the mangosteen skin.

3.3. Effect of extract from mangosteen peel on subcutaneous adipose tissue

Experimental results in Figure 3 show that the size of subcutaneous adipose tissue, hips is the largest in the group of mice fed a high-fat diet but not taking xanthone extract (HFD), followed by the group of mice fed a diet. Following a high-fat diet and taking xanthone extract finally, the smallest size was the group of mice reared on a normal diet (SD). Observing the results in Figure 4 was found that the weight of subcutaneous adipose tissue in the hip of the experimental group of mice was as follows: the largest was in the HFD group, the second group was raised on HFD+ME group, and the last one, was raised on a normal diet.

The results of the subcutaneous fat mass was completely consistent with the results of comparing the weights of these three groups of mice. It can be seen that the extract has the effect of inhibiting the process of adipogenesis, reducing the mass of adipose tissue, thereby reducing weight gain in the body of laboratory mice. A study showed that the mangosteen pericarp ethanolic extract has the effect of reducing the concentration of free fatty acids leading to weight loss in rats (John et al., 2021). Similarly, previous research has also demonstrated that mangosteen and its xanthones have good potential to design human studies to control and modulate metabolic syndrome and related disorders such as obesity.

3.4. Effect of extract from mangosteen peel on epididymal white adipose tissue

The effect of ME on epididymal white adipose tissue has shown in Figure 5. It can be seen that the size of adipose tissue in the testes of the group of mice fed the normal diet (SD), followed by the size of adipose tissue of the group of mice fed the fatty diet and drank xanthone extract (HFD+ME) and the largest was the testicular adipose tissue size of the group of mice fed a fatty diet but did not drink xanthone extract (HFD). Figure 6 shows that the fat mass of the group of mice fed the fatty diet but did not drink the xanthone extract (HFD) was the largest, the second was the fat mass of the group of mice raised on the fatty diet.

The above comparison results are also part of the evidence to show that xanthone extract has the effect of inhibiting the growth of testicular adipose tissue cells. This result
also adds a part to show that xanthone extract has an inhibitory effect on lipid synthesis in adipose tissue. A study of mangosteen pulp supplementation reducing morphological changes in the liver and kidneys of obese mice induced by a high-fat diet showed that ME has potential use for the treatment of obesity and inhibitory activity on pancreatic lipase. Mangosteen pulp supplementation for 7 weeks in obese mice reduced their body weight, increased total oxidative capacity, improved lipid profile and glutathione peroxidase levels, and decreased plasma pro-inflammatory markers (TNF-α and IL-6) (p < 0.05). In addition, mangosteen pulp supplementation reduced abnormalities of kidney and liver tissue caused by a high-fat diet. Taken together the findings suggest that *Garcinia mangostana* supplementation may be able to ameliorate the biochemical changes of obesity and help reduce body weight induced by a high-fat diet in mice (Muhamad et al., 2019).

![Figure 5. Size of epididymal white adipose tissue](image)

![Figure 6. Weight of epididymal white adipose tissue](image)

4. CONCLUSION

The results of this study showed that the ME was not toxic to mice. The body weight of the HFD + ME group of mice was smaller than that of the HFD group. There was a significant difference in white adipose tissue in subcutaneous adipose tissue, epididymal white adipose tissue between the HFD and HFD + ME groups. The weight of the HFD + ME group of mice were smaller than that of the HFD group.

Therefore, xanthone extract from mangosteen peel has the effect of reducing obesity in HFD-fed mice by reducing body weight, white adipose tissue mass. The effect of xanthone extract from mangosteen peel was demonstrated in the difference between mice that did not drink xanthone extract and mice that used xanthone extract from mangosteen peel. Thus, our study has contributed to the data showing that xanthone extract from mangosteen peel has a slimming effect, is a natural medicine that can be used to fight obesity and other metabolic disorders.

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REFERENCES


TÁC DỤNG CỦA CAO CHIẾT TỪ VỎ QUẢ MĂNG CỤT TRONG VIỆC GIẢM CÂN VÀ KHÔI LUỘNG MÔ MỞ Ở CHUỘT NHẤT TRANG

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Tóm tắt. Vỏ măng cụt (Garcinia mangostana L.) chứa nhiều chất chuyển hóa thứ cấp, điển hình là các chất thuộc nhóm xanthones. Nghiên cứu này được tiến hành nhằm đánh giá tác dụng giảm cân và giảm khối lượng mỡ mô của cao chiết từ vỏ măng cụt trên những con chuột được cho ăn chế độ ăn giàu chất béo. Những con chuột được cho ăn chế độ ăn giàu chất béo trong 8 tuần rồi sau đó được bổ sung cao chiết từ vỏ măng cụt (200 mg/kg/ngày) trong 6 tuần nữa trong khi những con chuột được cho ăn chế độ ăn tiểu chuẩn được sử dụng làm nhóm chứng. Kết quả cho thấy uống cao chiết từ vỏ quá măng cụt làm giảm khối lượng cơ thể và khối lượng mỡ mô bao gồm mỡ mô nội tạng, mỡ mô trạng cảnh tinh hoàn. Như vậy, cao chiết từ vỏ quá măng cụt có hiệu quả trong việc giảm khối lượng cơ thể và khối lượng mỡ mô ở những con chuột được nuôi bằng chế độ ăn giàu chất béo.

Từ khóa: Cao chiết vỏ măng cụt, giảm cân, mỡ mô, chuột nhất trang.

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