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EFFECT OF BITTER MELON (*Momordica charantia Linn.*) EXTRACT ON GROSS MORPHOLOGY AND WEIGHT OF SOME METABOLIC TISSUES IN MICE

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Abstract. Obesity is often accompanied by increased risk of metabolic disorders. Increased body and tissue weight is a hallmark of obesity. In the current study, we assessed if bitter melon extract supplement attenuated the high-fat diet induced obesity. Male Swiss mice fed a high-fat diet for 11 weeks parallelly with a bitter melon extract supplement via arbitrarily drinking and were compared with the nonsupplemented control group. Bitter melon extract significantly decreased high-fat diet induced body weight gain. This was paralleled with decrease in size and weight of adipose tissues, including axillary and epididymal adipose tissues. Moreover, bitter melon extract tendentiously reduced decrease in percent of skeletal muscle (quadriceps and soleus) weight per body weight of high-fat diet fed mice. These findings suggest that bitter melon extract may have positive effects in the prevention of the high-fat diet-induced obesity (DIO) and its related disorders.

Keywords: High-fat diet, bitter melon extract, body weight, adipose tissues, skeletal muscle tissues.

1. Introduction

Chronic high-fat diet feeding usually leads to obesity and its related metabolic dysfunctions such as dyslipidemia, fatty liver diseases, insulin resistance and type 2 diabetes [1]. Obesity is characterized by an increase in body weight and adipose tissue weight [2-3].This is accompanied by increases in production of adipocytokines (e.g., interleukin-6 [IL-6, tumor necrosis factor-α [TNF-α], and chemoatractant protein-1 [MCP-1]). These adipocytokines, in turn, burden lipid metabolism and insulin signaling in the cells that at least partly contributing to aforementioned disorders [4]. Changes in tissue weight, especially increased adipose tissue weight, are an important sign of obesity [5]. And, thus, strategy to protect from high-fat diet induced adipose tissue weight gain is a good candidate to prevent obesity and its related metabolic syndromes.

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It has been reported that nutrients from bitter melon have several beneficial effects on diminishing some metabolic dysfunctions such as hyperlipidemia, hyperglycemia [6-7]. They, therefore, may also have positive effects on protection against obesity and its metabolic disorders. In the present study, we prepared bitter melon extract and treated mice. As a result, Bitter melon extract significantly lowered high-fat diet induced body weight gain and decreased size and weight of adipose tissues, including axillary and epididymal adipose tissues. Additionally, bitter melon extract tendentiously reduced decrease in percent of skeletal muscle weight per body weight of high-fat diet fed mice. These results indicate that bitter melon extract may have promise effects in the prevention of the high-fat diet-induced obesity and its related metabolic dysfunction.

2. Content

2.1. Materials and methods

2.1.1. Animals and diets

Four-week of age male Swiss mice were purchased from the National Institute of Hygiene and Epidemiology (NIHE). Mice were caged in an animal facility with 12-12 h light-dark cycle maintaining. For 11 weeks, the mice were fed a regular diet (RD) (5% energy from lipid) or a high-fat diet (HFD) (60% energy from lard) on the RD base. The RD was also purchased from the NIHE. The mice were fed restrictedly with food and arbitrarily with tap water or with fluid of bitter melon extract (BME). Bitter melons (*momordica charantia linn***)** were collected in Lang Son province and were cut into 1 mm-thick slides. The bitter melon slides were dried naturally by the sun light. Bitter melon extract was prepared by boiling 50 gram of dried bitter melon in 1000 mL water for 1 hour. The mice were weighted weekly to observer their body weight. After 11days, the animals were killed by decapitation. White adipose tissues and skeletal muscle tissues were dissected and measured.

2.2.2. Statistical analysis

The results were shown as means ± standard error of the mean (SEM). Comparisons of variables were carried out by using Student's t test or analysis of variation (ANOVA) with Duncan's multiple-range examination. Differences were considered to be significant when $P < 0.05$.

2.2. Results and discussion

2.2.1. Effect of BME on high-fat diet induced body weight gain

The mice were fed with a regular diet (RD) or a high-fat diet (HFD) in the same amount of food. Two groups arbitrarily drank tap water and other two groups arbitrarily drank bitter melon extract (BME). We found that the HFD feeding significantly induced body weight gain in mice compared with the RD feedings and that BME supplement reduced HFD-induced body weight gain. However, this observation was not seen in the RD + BME group compared to RD group (Figure 1).

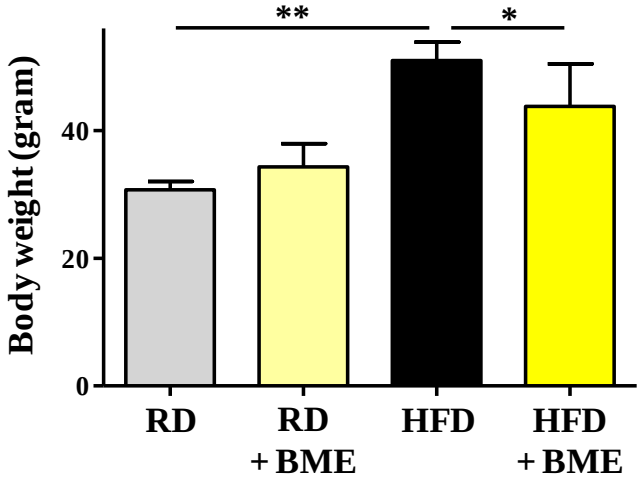

Figure 1. Bitter melon extract reduces high-fat diet induced body weight gain

*Four week-old male Swiss mice were fed a regular diet (RD) or a high-fat diet (HFD), and HFD supplemented with bitter melon extract (HFD+BME) for 11 weeks. Body weight changes among groups are monitored. Data are presented as means ± SEM; n = 6 in each group. *P < 0.05, ** P < 0.01 compared between HFD-fed mice with other groups.*

It is worth to note that, lipid metabolic dysfunction such as increased lipid synthesis but decreased lipid lipolysis is associated with obesity. Nutrients derived from bitter melon have been shown to reduce lipid metabolic malfunction [6]. Hence, BME may give a protection from HFD-induced body weight gain by increased lipid lipolysis that leading to lowered lipid accumulation in the tissues.

2.2.2. Effect of BME on axillary adipose tissue weight

To test whether BME supplement reduced HFD-induced body weight gain is associated with the reduction of adipose tissue weight, we measured axillary adipose tissue weight and saw that the HFD + BME group had significantly lower axillary adipose tissue weight than did the HFD group. There was no difference in axillary adipose tissue weight between the RD + BME group and the RD group (Figure 2B). Consistent with this, the HFD + BME group showed smaller axillary adipose tissue size than the HFD group did (Figure 2A).

Previous study has demonstrated that BME has potential effect on inhibition of adipogenesis. This effect may be related with the upregulation of key molecules, especially AMP-Activated Protein Kinase (AMPK) that control adipogenesis in adipose tissues [8-10]. Moreover, axillary adipose tissue is distributed under the skin which is a major site of adipose tissue distribution.

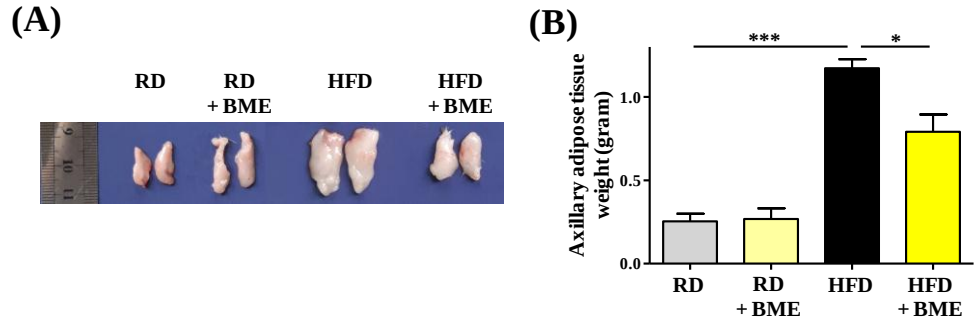

Figure 2. Bitter melon extract reduces high-fat diet induced increased axillary adipose tissue weight

*Four week-old male Swiss mice were fed a regular diet (RD) or a high-fat diet (HFD), and HFD supplemented with bitter melon extract (HFD+BME) for 11 weeks. (A) gross morphology of axillary adipose tissue. (B) axillary adipose tissue weight changes. Data are presented as means ± SEM; n = 6 in each group. *P < 0.05, *** P < 0.001 compared between HFD-fed mice with other groups.*

2.2.3. Effect of BME on epididymal adipose tissue weight

The next was to examine if BME can give the similar effect on adipose tissue at another position in mouse body, we also measured the epididymal adipose tissue that is distributed around the testis. Similarly, the HFD + BME group had smaller epididymal adipose tissue size than the HFD group had (Figure 3A). This was proven by a significant decreased in the tissue weight of the HFD + BME group compared with that in the HFD group (Figure 3B). There was also no difference in the gross morphology and weight of epididymal adipose tissue between the RD group and RD + BME group (Figure 3A and 3B). All together, these data suggested that BME supplement reduced HFD-induced obesity may be at least partly attributed to the inhibition of adipogenesis in adipose tissues.

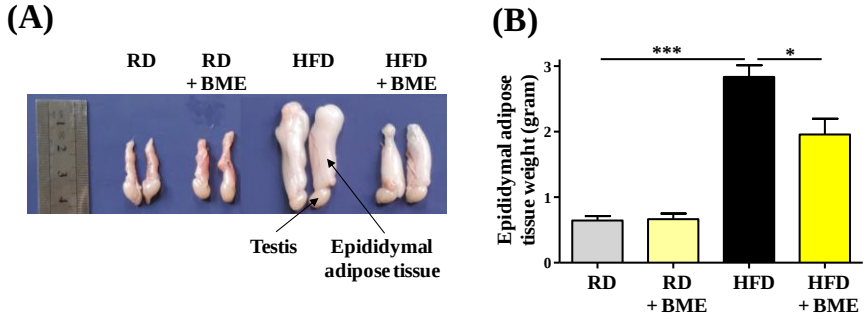

Figure 3. Bitter melon extract reduces high-fat diet induced increased epididymal adipose tissue weight

*Four week-old male Swiss mice were fed a regular diet (RD) or a high-fat diet (HFD), and HFD supplemented with bitter melon extract (HFD+BME) for 11 weeks. (A) gross morphology of epididymal adipose tissue. (B) epididymal adipose tissue weight changes. Data are presented as means ± SEM; n = 6 in each group. *P < 0.05, *** P < 0.001 compared between HFD-fed mice with other groups.*

2.2.4. Effect of BME on quadriceps skeletal muscle weight

It is interested to note that skeletal muscle is the biggest tissue in the body, thus, it becomes very important site to regulate lipid and glycemic metabolism. Indeed, decreased skeletal muscle tissue weight leads to higher risk of diabetes [11]. Previous study has been reported that percent of skeletal muscle weight per body weight is decreased in the obese individuals [12]. Here, we found that HFD-fed mice showed tendentious decrease in the percent of quadriceps skeletal muscle weight per body weight and BME supplement reduced this effect of HFD feeding (Figure 4B). The size of quadriceps skeletal muscle was not differed among the groups (Figure 4A).

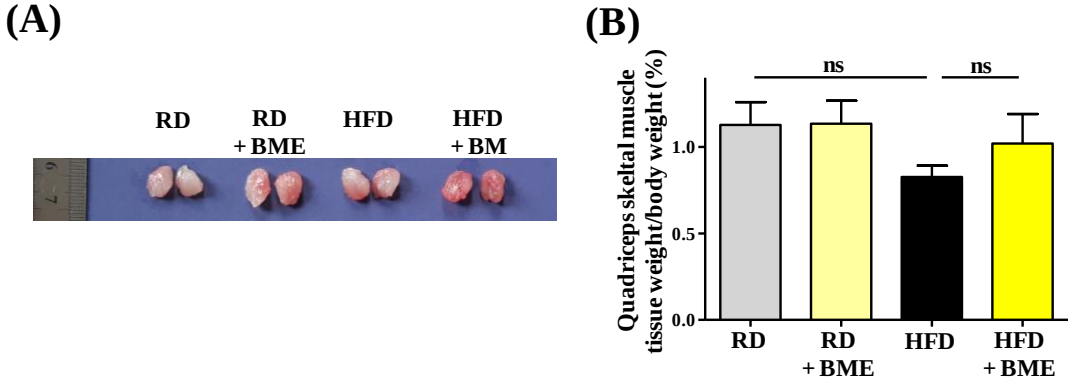

Figure 4. Effect of bitter melon extract on quadriceps skeletal muscle weight

Four week-old male Swiss mice were fed a regular diet (RD) or a high-fat diet (HFD), and HFD supplemented with bitter melon extract (HFD+BME) for 11 weeks. (A) gross morphology of quadriceps skeletal muscle. (B) quadriceps skeletal muscle weight changes. Data are presented as means ± SEM; n = 6 in each group. ns = not significant compared between HFD-fed mice with other groups.

It has been known that BME downregulates the expression of IL-6 and TNFα who are key inducers of skeletal muscle sarcopenia [13-14]. Hence, our observation of the BME effect on quadriceps skeletal muscle may be at least partly related with the regulation of AMPK signaling.

2.2.5. Effect of BME on soleus skeletal muscle weight

To confirm the effect of BME on skeletal muscle, we here also tested the changes in soleus skeletal muscle which is used in several studies to research about metabolic functions. In concomitant with the data observed in quadriceps skeletal muscle, the HFD + BME group tendentiously showed higher percent of soleus skeletal muscle weight per body weight than did the HFD group (Figure 5B). The size of soleus skeletal muscle weight had no difference among the groups (Figure 5A). Consequently, our current data showed that BME supplement may have a beneficial effect on protection of obesity-related skeletal muscle dystrophy. It, in turn, may be deal with the positive effect on obesity-related metabolic dysfunctions such as insulin resistance and type 2 diabetes.

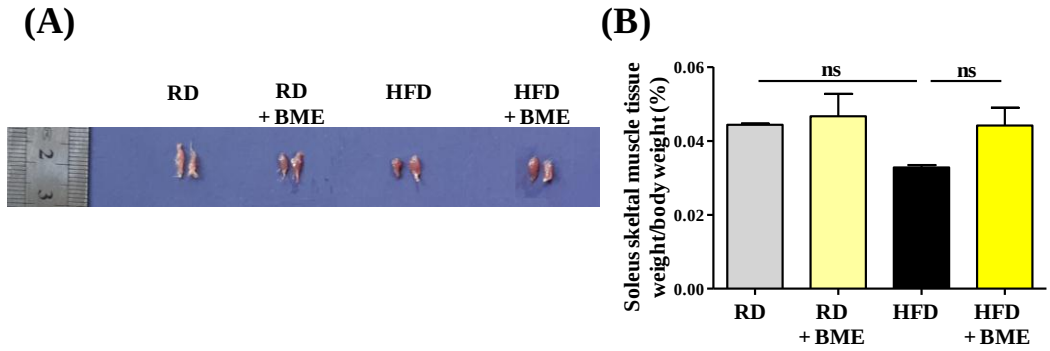

Figure 5. Effect of bitter melon extract on soleus skeletal muscle weight. *Four week-old male Swiss mice were fed a regular diet (RD) or a high-fat diet (HFD), and HFD supplemented with bitter melon extract (HFD+BME) for 11 weeks. (A) gross morphology of soleus skeletal muscle. (B) soleus skeletal muscle weight changes. Data are presented as means ± SEM; n = 6 in each group. ns = not significant compared between HFD-fed mice with other groups.*

3. Conclusions

The current study demonstrates that BME supplement for 11 weeks led to significant reduction of body weight and axillary- and epididymal-adipose tissue weight gain in the HFD-fed mice. Besides, BME supplement tendentiously diminished HFD-induced decrease in percent of quadriceps- and soleus-skeletal muscle tissue weight per body weight. These observed changes may be attributed to inhibition of adipogenesis and skeletal muscle dystrophy. As a consequence, our data may support a promise ability to use BME supplement in the battle against of obesity and its related metabolic dysfunctions.

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