EC PHARMACOLOGY AND TOXICOLOGY
Research Article

Effect of Honey on Body Weight, Body Mass Index and Adiposity in High-Fat Diet Fed Wistar Rats

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Abstract

Increased consumption of sugars and sweetened beverages contributes to increased prevalence of obesity. The aims of this study were to investigate the effects of honey supplementation on body weight (BW), weight gain, body mass index (BMI) and adiposity in Wistar rats fed a high-fat diet (HFD). The study also investigated if administration of high doses of honey to HFD fed Wistar rats would deteriorate body weight, weight gain, BMI and adiposity. Rats were fed chow or HFD (coconut and olive oil) and 30% sucrose solution for 8 weeks. The animals were then randomly divided into 5 groups. Group 1 (fed chow) was treated with 1.0 ml/kg BW of drinking water. Group 2 (fed HFD and 30% sucrose solution) was treated with 1.0 ml/kg BW of drinking water. Groups 3, 4 and 5 (fed HFD and 30% sucrose solution) were administered 1.0, 2.0 and 3.0 g/kg BW of honey, respectively. The animals were treated for a duration of 6 weeks. Groups 1 and 2-5 were maintained on chow and HFD, respectively during treatment. The HFD fed control rats showed a higher BW ($p > 0.05$), weight gain ($p < 0.01$), BMI ($p > 0.05$), % change in BMI ($p > 0.05$), BW/body length (BL) ($p < 0.05$), adiposity index (AI) ($p < 0.05$) and % change in AI ($p < 0.01$) compared with chow fed rats. Honey-treated HFD fed rats showed no significant difference in BMI, BW/BL and AI compared with chow fed rats. Honey (1.0 g/kg BW)-treated HFD fed rats had significantly lower BMI ($p < 0.01$), % change in BMI ($p < 0.01$), BW/BL ($p < 0.05$), AI ($p < 0.05$) and % change in AI ($p < 0.01$) compared with HFD fed control rats. These results suggested that 1.0 g/kg BW of honey produced beneficial effects on obesity anthropometric parameters including BMI in HFD fed rats.

Keywords: *Honey; Body Mass Index; Obesity; Coconut Oil; Olive Oil; Rats*

Abbreviations

HFD: High Fat Diet; BW: Body Weight; BMI: Body Mass Index; BL: Body Length; AI: Adiposity Index; CAM: Complementary and Alternative Medicine; SEM: Standard Error of Mean; ANOVA: Analysis of Variance

Introduction

Obesity constitutes a main global health problem and its prevalence has increased considerably in children and adults in both developed and developing countries [1]. Several factors such as increased consumption of sugars, sweetened beverages, highly saturated fats and physical inactivity contribute to increased incidence of overweight and obesity [2-3]. Obesity is characterized by excessive weight gain and adiposity resulting from an imbalance between energy consumption and expenditure. In addition to regular exercise, changes in lifestyle and dietary habits are vital in the management of obesity [4]. Even though anti-obesity drugs are effective in suppressing weight gain, these drugs have low benefit to risk ratio [5]. There is therefore an urgent need for the discovery of additional agents which are more therapeutic and beneficial for obesity. There has been an increased interest in the use of complementary and/or alternative medicine (CAM) for the treatment of various ailments including obesity in the past decade [6-7]. This may be attributed to commonly held beliefs that CAM treatments are safer and cheaper. The accuracy of some of these beliefs still remain controversial especially in view of limited data on the efficacy and safety of CAM [7].

Honey has been used in traditional medicine as far back as 2100 - 2000 BC. The increased patronage of honey in treating diverse ailments in the recent past is attributed to a rise in availability of evidence-based data on the health benefits of honey [8]. Honey has been shown to prevent weight loss or improve weight gain in diabetic rats induced by chemicals such as streptozotocin [9]. However, some studies found no such effects [10]. The reasons for the inconsistency on the effect of honey on body weight in alloxan- or streptozotocin-induced diabetic rats remain unclear. The role of botanical sources and geographical origins of those honeys may be a factor. Alloxan- or streptozotocin-induced diabetes, a model of type 1 diabetes, is associated with weight loss – a consequence of reduced insulin secretion from pancreas [11]. Therefore, prevention of weight loss or promotion of weight gain is a desirable effect of honey in this type of diabetes. There is no doubt that amelioration of hyperglycemia may contribute to body weight improvement in honey-treated diabetic rats. However, reduced hyperglycemia alone does not entirely explain improved weight gain in honey-treated diabetic rats. This is based on the fact that glibenclamide-treated diabetic rats with improved glycemia showed no body weight gain whereas diabetic rats administered glibenclamide and honey exhibited both lower hyperglycemia and improved body weight [12]. This therefore suggests that honey enhances weight gain through a mechanism independent of its hypoglycemic effect.

In healthy rats, the data on the effect of honey on body weight are likewise inconsistent. While most studies showed that honey caused no significant change in body weight in normal rats [13-14] and hypertensive rats [15], honey has been found to promote weight gain in normal rats [10]. In that same study, honey also enhanced weight gain in fructose-fed rats [10]. Compared to sucrose, available data indicated that honey supplementation caused lower weight gain [16-17]. In obesity (a disorder characterized by increased weight gain), the body weight-enhancing effect of honey is undesirable or unwanted. Moreover, if honey ingestion is combined with consumption of HFD or excessive sugar, this potential weight gain-promoting effect of honey may be of grave concern in obesity. As a result of lack of data on the effects of honey on obesity anthropometric parameters, this preliminary study was carried out to investigate the effects of honey supplementation on body weight, weight gain, BMI and adiposity in Wistar rats fed a HFD (an animal model of obesity). The study also investigated if administration of high doses of honey to HFD fed Wistar rats would deteriorate body weight, weight gain, BMI and adiposity.

Materials and Methods

Animals

Male Wistar rats (aged 12 weeks) were purchased from animal house unit, Nsukka, Enugu State, Nigeria. The rats were allowed to acclimatize to the animal room for at least a week. The animal room was well ventilated with temperature of 25-27°C and 12:12-h light:dark cycle. During the one-week acclimatization period, the rats were given free access to rat chow and drinking water *ad libitum*. The study protocol was approved by University Research Ethics Committee of Ebonyi State University. The animals were humanely handled and in strict compliance with institutional and international guidelines on the Use and Handling of Experimental Animals. The rats (referred to as experimental animals or rats) were fed a HFD and 30% sucrose solution for 8 weeks. The HFD comprised coconut oil and olive oil which were mixed together in the ratio 1:1. The oil was administered to the experimental rats at a dose of 5 ml/kg BW via an oral gavage once daily.

Honey

The honey used in this study was purchased from a bee farm in Abakaliki, Ebonyi State, Nigeria. It was registered with National Agency for Food and Drug Administration Control (NAFDAC). The honey was dissolved in drinking water not more than 30 minutes before administration.

Treatment

At the end of the 8 weeks of feeding with a HFD and 30% sucrose solution, the experimental rats were randomly divided into 4 groups. Each group consisted of five rats. The randomization was performed such that the average body weight of rats in each group was comparable. Another group of rats fed rat chow served as control. The control rats had similar body weight as the experimental groups. Hence, there was no difference in body weight between the experimental and control groups of rats before the commencement of treatment. With the aid of an oral canula, the rats were treated with drinking water or honey once daily for 6 weeks as follows:

Group 1: Chow fed rats administered 1 mL/kg BW of drinking water

Group 2: Experimental rats administered 1 mL/kg BW of drinking water

Group 3: Experimental rats treated with 1.0 g/kg BW of honey

Group 4: Experimental rats treated with 2.0 g/kg BW of honey

Group 5: Experimental rats treated with 3.0 g/kg BW of honey

An hour after treatment each day, the experimental rats were administered the HFD (coconut and olive oil; 5 mL/kg BW). Before the commencement of treatment, body weight and body length of rats were measured using a weighing scale and tape rule, respectively. The measurements obtained were used as baseline data. Thereafter, the body weight was weighed weekly. After treatment for 6 weeks, body weight and body length were measured. The body weight and body length measurements were used for the estimation of BMI and adiposity index. The BMI was determined using the formula: BMI = Body weight (g) / body length^2 (cm^2). Adiposity index was calculated using the formula for Lee index of obesity: Adiposity index = cube root of body weight (g) / body length (cm) [18]. The rats were sacrificed under diethyl ether anesthesia.

Statistical Analysis

The results were analyzed using SPSS version 16. Data are expressed as mean ± SEM. One-way analysis of variance (ANOVA) and Tukey's post hoc test were used to assess differences among the groups.

Results and Discussion

Effect of Honey on Body Weight and Weight Gain during the 6 Weeks of Treatment

There was no significant difference in body weight at week 0, 1, 2, 3, 4, 5 and 6 between the HFD fed groups of rats and chow fed rats despite the fact that the HFD fed rats had higher body weight (Figure 1). The body weight was not statistically significantly ($p > 0.05$) different in the honey-treated HFD fed rats compared with HFD fed control rats though the honey-treated rats had lower body weight than the HFD fed control rats. Total weight gain was significantly ($p < 0.01$) higher in HFD fed control rats than in chow fed rats (Figure 2). The HFD fed rats treated with 3 g/kg BW of honey showed significantly greater weight gain compared with chow fed rats. Weight gain in HFD fed rats treated with 1 or 2 g/kg BW of honey was not significantly ($p > 0.05$) different from that of the chow fed rats.

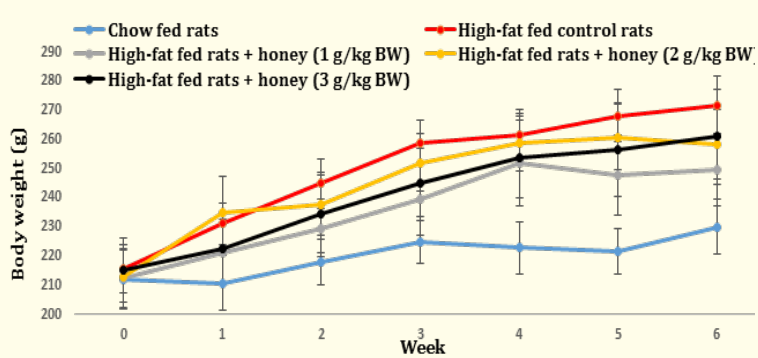

Figure 1: *Effect of honey on body weight during the 6 weeks of treatment.*

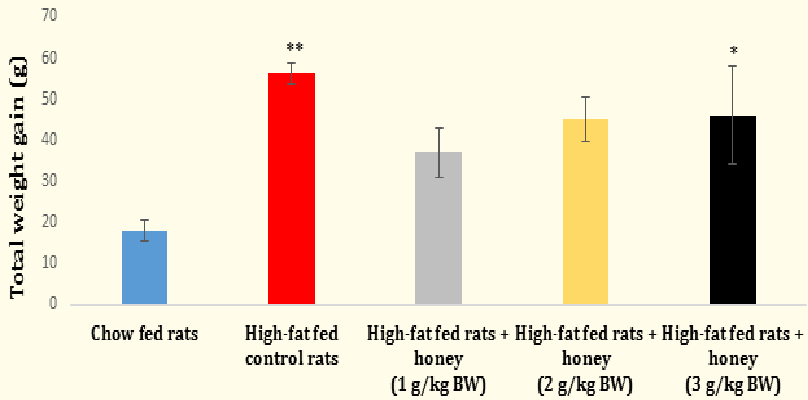

Figure 2: *Effect of honey on total weight gain after 6 weeks of treatment.*

** p < 0.05 & ** p < 0.01 compared with chow fed rats*

Effect of Honey on Body Mass Index and % Change in Body Mass Index after 6 Weeks of Treatment

The BMI was similar among all the groups before treatment (Figure 3). After treatment, BMI was non-significantly ($p = 0.069$) higher in HFD fed control rats than in chow fed rats. The HFD fed rats treated with 1 g/kg BW of honey had significantly ($p < 0.01$) lower BMI than HFD fed control rats. The HFD fed rats treated with 2 g/kg BW of honey had borderline ($p = 0.058$) lower BMI than HFD fed control rats. The HFD fed rats treated with 1 g/kg BW of honey had significantly ($p < 0.01$) lower % change in BMI compared with HFD fed control rats (Figure 4).

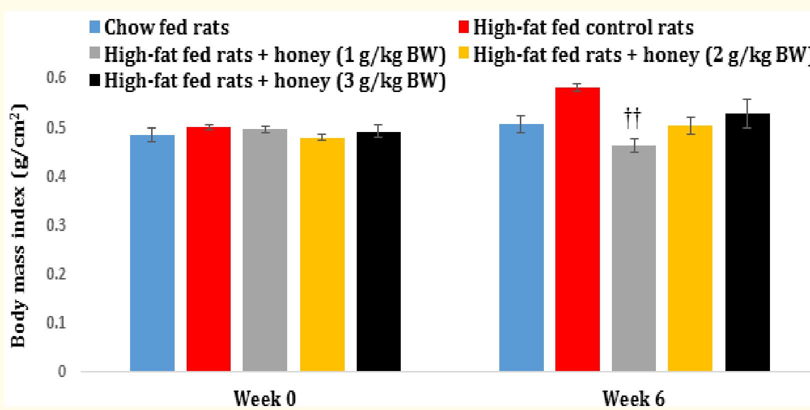

Figure 3: *Effect of honey on body mass index after 6 weeks of treatment.*

†† p < 0.01 compared with high-fat fed control rats at week 6.

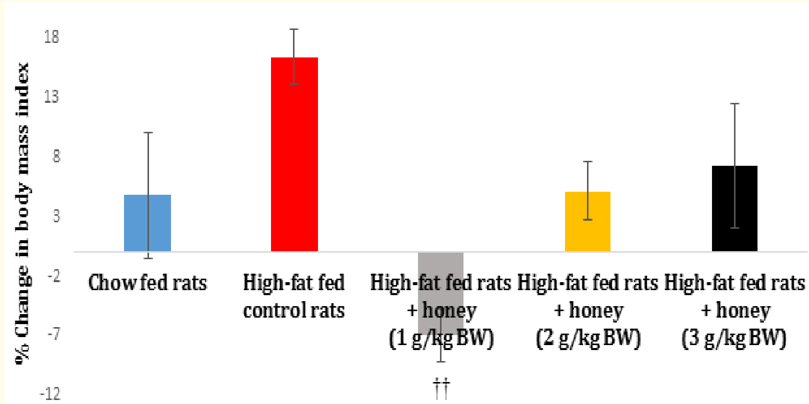

Figure 4: *Effect of honey on % change in body mass index after 6 weeks of treatment.*

†† p < 0.01 compared with high-fat fed control rats

Effect of Honey on Body Weight/Body Length, Adiposity Index and % Change in Adiposity Index after 6 Weeks of Treatment

There was no significant difference in body weight/body length among all the groups before treatment commenced (Figure 5). After treatment, body weight/body length was significantly ($p < 0.05$) higher in HFD fed control rats than in chow fed rats. The HFD fed rats treated with honey (1 g/kg BW) had significantly ($p < 0.05$) lower body weight/body length compared with HFD fed control rats. The adiposity index was significantly ($p < 0.05$) higher in the HFD fed control group than in chow fed rats. The HFD fed rats administered honey (1 g/kg BW) had markedly ($p < 0.05$) lower adiposity index compared with HFD fed control rats (Figure 6). The % change in adiposity index was significantly ($p < 0.01$) greater in HFD fed control rats than in chow fed rats (Figure 7). Honey (1 g/kg BW) supplementation produced significantly ($p < 0.01$) lower % change in adiposity index.

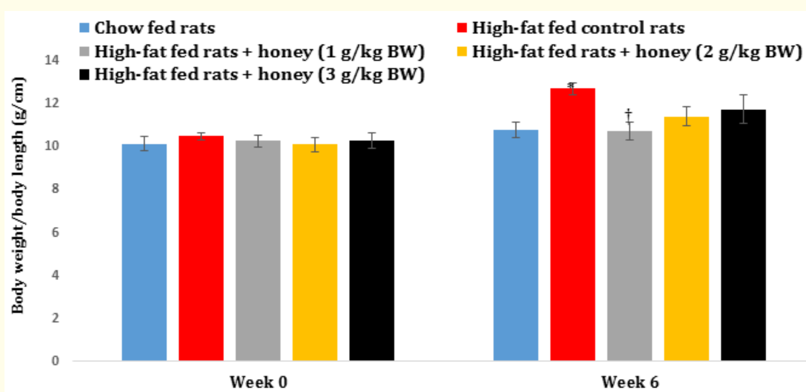

Figure 5: *Effect of honey on body weight/body length after 6 weeks of treatment.*

** p < 0.05 compared with chow fed rats at week 6; † p < 0.05 compared with high-fat fed control rats at week 6.*

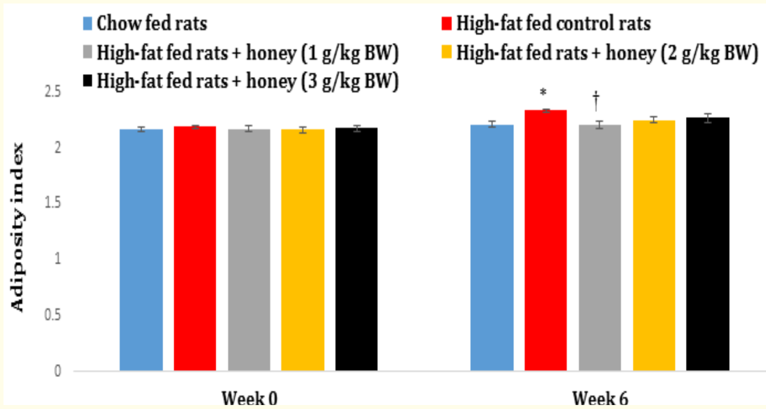

***Figure 6:** Effect of honey on adiposity index after 6 weeks of treatment.*

** p < 0.05 compared with chow fed rats at week 6; † p < 0.05 compared with high-fat fed control rats at week 6*

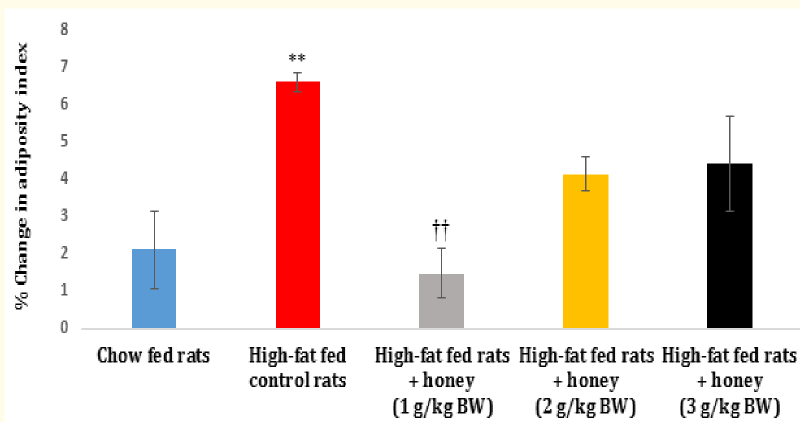

***Figure 7:** Effect of honey on % change in adiposity index after 6 weeks of treatment.*

*** p < 0.01 compared with chow fed rats; †† p < 0.01 compared with high-fat fed control rats*

This study investigated the effects of honey on body weight, weight gain, BMI and adiposity in HFD fed Wistar rats. The potential deteriorating effects of high doses of honey on body weight, weight gain, BMI and adiposity in HFD fed Wistar rats were also assessed. To the best of the authors' knowledge, it is worth mentioning that this is the first study to investigate the effects of honey in HFD fed rats (a rodent model of obesity). The results showed that the Wistar rats fed HFD had non-significant greater body weight than chow fed rats starting from week 1 till week 6. Total weight gain over the period of 6 weeks was significantly higher in HFD fed control rats than in chow fed rats. These observations are similar to previous reports that demonstrated higher body weight and/or total weight gain in rats fed HFD [19-20]. Beginning from week 2, all the honey-supplemented HFD fed groups of rats exhibited non-significantly lower body weight compared with the HFD fed control rats. With the exception of the HFD fed rats treated with 3 g/kg BW of honey, the total weight gain in the honey-treated HFD fed rats was not significantly different from that of the chow fed rats. These data corroborate previous findings showing that honey administration to healthy rats resulted in lower body weight and weight gain [16,21]. The findings on body weight and total weight gain revealed that the lower the dose, the greater the suppressing effect of honey. With respect to this negative dose dependent effect of honey on body weight and total weight gain in HFD fed rats, it is difficult to draw a comparison with previous studies. This is because no study has determined the effect of honey in HFD fed rats. Similarly, previous studies that investigated the effect of honey in fructose-fed rats or compared the effect of honey with other sugars on body weight and weight gain in healthy rats utilized only one dose of honey [10,16-17].

The study found non-significantly higher BMI in HFD fed control rats than in chow fed rats. Other previous reports have also documented non-significantly or significantly higher BMI in HFD fed rats [22-23]. In humans, BMI reflects fat mass and a higher BMI is associated with an increased cardiovascular risk and all-cause mortality [24]. All the honey-supplemented HFD fed rats had comparable BMI as the chow fed rats. Similar to data on weight gain, the results of the effect of honey on BMI in HFD fed rats indicated a lower dose-greater response relationship. This negative dose dependent effect of honey on BMI in HFD fed rats is reinforced by the fact that the HFD fed rats treated with 1 g/kg BW of honey showed significantly lower BMI compared with the HFD fed control rats. The % change in BMI in HFD fed control rats was non-significantly higher than in chow fed rats. The HFD fed rats treated with honey showed similar % change in BMI as the chow fed rats. The lowest dose of honey produced a significant lower % change in BMI compared with the HFD fed control group, a demonstration of negative dose dependent effect of honey on % change in BMI.

Like the BMI, the body weight/body length and adiposity index represent additional indicators of body fatness. Higher adiposity has been demonstrated in HFD fed rats [23]. In this study, the body weight/body length and adiposity index were significantly higher in HFD fed control group than in chow fed group. The % change in adiposity index was also significantly higher in the HFD fed control group than in chow fed group. These data are in agreement with previous findings [23,25]. Administration of honey suppressed body weight/body length, adiposity index and % change in adiposity index towards those of the chow fed rats. However, of the three administered doses of honey, only 1 g/kg BW dose produced significantly lower body weight/body length, adiposity index and % change in adiposity index compared with the HFD fed control rats. These data are again consistent with the results on weight gain and BMI demonstrating a negative dose response relationship. At the moment, it remains unclear if the negative dose response of honey on weight gain, BMI and adiposity in Wistar rats fed HFD would also manifest on the lipid profile. Additional research is needed to clarify this even though there is a positive correlation between BMI and triglycerides [26].

The issue of negative dose-dependent effects of honey on all the parameters examined in this study becomes relevant in view of previously reported findings and propositions. In a previous study, honey supplementation was found to exert a dose-dependent hypoglycemic or glucose-lowering effect [27]. However, the maximal dose for the glucose-lowering effect of honey was recently reported [28]. Honey is predominantly sugars – consisting primarily of fructose and glucose as well as other classes of carbohydrate including disaccharides and oligosaccharides. Some of these sugars especially fructose and oligosaccharides are proposed to contribute to glucose-lowering effect of honey [29-30]. It is therefore not surprising that increasing the dose of honey resulted in greater lowering of hyperglycemia in diabetic rats [27]. That is, honey administration demonstrated a positive (glucose-lowering) dose response relationship in diabetic rats. This is in contrast to negative dose response found in HFD fed rats in this study. It is worthy of note that in spite of this negative dose-dependent effect of honey in obese rats, neither 2 nor 3 g/kg BW of honey caused greater body weight, weight gain, BMI or adiposity in HFD fed rats compared with HFD fed control rats. Based on existing data in the literature, honey is considered a better alternative to artificial sweeteners in diabetic diets [31-32]. The fact that high doses of honey (2 or 3 g/kg BW) did not deteriorate obesity parameters as observed in this study suggests that honey has a potential to serve as a viable functional food or substitute to synthetic sweeteners in obese diets.

The role of fructose in the development of obesity still remains controversial. Findings from animal studies revealed that administration of high doses of fructose is detrimental to health and may enhance the development of obesity features [33-34]. In humans, while evidence suggests that fructose (if consumed within the normal and accepted range of human consumption) may not constitute an increased risk of obesity [2], several studies have demonstrated the beneficial effects of fructose restriction or reduction in obese subjects [35-36]. By and large, in spite of the debate on the association of fructose with obesity, there seems to be convincing evidence in support of the benefits of lower doses of fructose or fructose reduction in obesity. This is important with regards to the data obtained in this study. As reported, neither 2 nor 3 g/kg BW of honey produced a significantly lower BMI, % change in BMI, body weight / body length, adiposity index and % change in adiposity index compared with HFD fed control rats. In contrast, significantly beneficial effects of 1 g/kg BW of honey on these obesity parameters were demonstrated. Therefore, it is possible that at high doses, the high sugar content of honey especially fructose may render honey less beneficial in obesity. This may provide a plausible explanation for the negative dose response of honey observed in this study.

It is important to note that obesity is a lifestyle and chronic disorder. Hence, its treatment requires a long-term intervention. In such a chronic disorder, despite the positive beneficial effects of honey demonstrated in this study, 6 weeks of honey supplementation may be considered inadequate or acute. This view is based on the findings from a previous study which showed that the acute beneficial effects of honey might not be observed in a chronic study [37]. The researchers reported that rats administered honey (500 or 800 mg) for 2 days had significantly higher calcium absorption. In contrast, long-term (8 weeks) honey administration showed no such effect. Consequently, studies on long-term effects of honey supplementation in HFD fed rats are recommended. Such studies are necessary to demonstrate the sustainability of the reported beneficial effects of honey on weight gain, BMI and adiposity in HFD fed rats. Besides, considering that variations in honey composition (which influence its biological responses) pose a great challenge to reproducibility [8], it is recommended that further studies that utilize honeys of other botanical or geographical sources are also carried out to confirm the reproducibility of these findings.

Conclusions

This study showed that 6 weeks of honey supplementation resulted in beneficial effects of honey (1 g/kg BW) on obesity parameters in HFD fed Wistar rats. The study revealed that high doses of honey (2 or 3 g/kg BW) did not increase body weight, weight gain, BMI and adiposity. However, the findings indicated that honey supplementation exerted a negative dose response in an animal model of obesity. By and large, it can be suggested that honey has a potential to serve as a viable functional food or a substitute for artificial/synthetic sweeteners in obese diets. Long-term studies are needed to demonstrate the sustainability of these reported beneficial effects of honey in HFD fed rats. Further studies that utilize honeys of other botanical and/or geographical sources are also desirable to confirm the reproducibility of these findings.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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Volume 3 Issue 1 January 2017