ORIGINAL ARTICLE

Effect of Tualang Honey Supplementation in Weight Reduction and Dyslipidaemia in High Cholesterol Diet- induced Obese Rats

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ABSTRACT

INTRODUCTION: Obesity is a key risk factor for many chronic diseases. Malaysia records the highest prevalence of obesity in Southeast Asia. Tualang honey has been proven to treat many chronic diseases but its effect on weight reduction has yet to be well-studied. This study aimed to investigate the effects of Tualang honey (TH) supplementation on body weight and lipid profile in a 12% high cholesterol diet (HCD) induced obesity rat model. **MATERIALS AND METHODS:** Forty male Sprague-Dawley rats were assigned to five groups (n=8): Group 1 (normal diet), Group 2 (normal diet + TH 3.0 g/kg), Group 3 (12% HCD), Group 4 (12% HCD + TH 3.0 g/kg), and Group 5 (12% HCD + Orlistat 10 mg/kg). Diets were administered for 12 weeks, followed by treatments for six weeks. Body weight was measured weekly, and blood was collected for lipid analysis at the end of the study. **RESULTS:** We demonstrated a significantly lower final body weight of rats in Group 2 (328.25 ± 25.49 g) compared to Group 1 (409.13 ± 16.33g) ($p<0.001$) and in Group 4 as compared to Group 3 (343.88 ± 44.24 g vs 471.00 ± 19.55g, $p<0.001$). The administration of TH also significantly reduces the cholesterol (Med=1.8 mmol/L, IQR=0.7 vs Med=3.2 mmol/L, IQR=0.8, $p<0.05$) and triglyceride level (Med=0.9 mmol/L, IQR=0.3 vs Med=1.5 mmol/L, IQR=1.0, $p=0.001$) in Group 4 compared to Group 3. **CONCLUSION:** Tualang honey supplementation has been shown to reduce body weight and improve lipid profiles in 12% HCD-induced obese rats.

Keywords
Obesity, tualang honey, high cholesterol diet, dyslipidaemia, body weight

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INTRODUCTION

Obesity and overweight are pathological states marked by an elevated body mass index (BMI) and/or increased fat accumulation.[1] A BMI of 25 kg/m² or more is classified as overweight, whereas obesity is indicated by a BMI of 30 kg/m² or above.[2] Currently, obesity has risen to epidemic levels globally, with its prevalence expected to continue rising across both developed and developing countries due to shifts in dietary patterns and reduced physical activity.[3] As global standards of living improve, overweight and obesity have become prominent and pressing nutritional issues in many regions.

Research has shown that from 1975 to 2015, global obesity rates rose significantly, from 3.2% to 10.8% among men and from 6.4% to 14.9% among women.[4] With this accelerated increase in prevalence, it is projected that by 2025, more than 18% of men and 21% of women worldwide becoming overweight or obese.[5] Among South Asian countries, Malaysia ranks highest in overweight and obesity rates, with 64% of men and 65% of women being classified as either overweight or obese.[6] These statistics highlight a growing health and economic burden, as the rising obesity rates directly contribute to an increase in obesity-related health complications. Recent studies have demonstrated that obesity and excess body weight are correlated with elevated mortality rates and are contributors to numerous health complications, including cardiovascular problem, liver disease, kidney failure, and diabetes mellitus (Figure 1).[7]

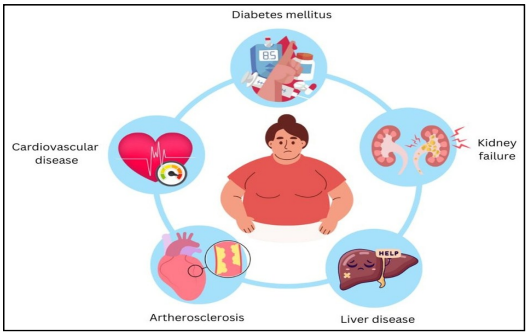

Figure 1: Health complications related to obesity.

Obesity management primarily involves lifestyle interventions, including dietary adjustments and exercise. Pharmacological treatments, such as orlistat, and surgical procedures like bariatric surgery are also employed as therapeutic strategies.[8] However, these methods are often associated with potential risks and adverse effects. Consequently, there has been growing interest in exploring natural products, such as honey, as alternative approaches for managing obesity due to their potential to minimize side effects.[9] In modern contexts, honey is valued as a nutritious supplement with recognized medicinal benefits. As reported by the Food and Agriculture Organization of the United Nations (FAO), honey production in Asia rose substantially, from 600 tonnes in 2007 to nearly 1,000 tonnes in 2017. In 2021, the amount of honey produced is nearly 1.8 million tonnes, reflecting a notable increase in honey consumption.[10]

Honey is a natural mixture composed of numerous constituents, including both simple and complex sugars, water, organic acids, proteins, vitamins, and minerals, as well as amino acids, phenolic acids, and flavonoids.[11] It has been shown to offer varieties of physiological benefits, such as antibacterial, anticancer, anti-inflammatory, and antioxidant effects.[12] By the late 20th century, honey gained popularity as a weight management aid, either alone or paired with other nutritious foods. Various studies have also demonstrated anti-obesity effects of honey, [13–15] with its active compounds, such as phenols and flavonoids, believed to impact fat metabolism by stimulating lipolysis and inhibiting lipogenesis.[16]

One of the most recognized honey varieties is Tualang honey (TH), which was selected as the primary focus of this study. It is produced by the rock bee (*Apis dorsata*), which builds its hives high in the branches of the Tualang tree (*Kompassia excelsa*). This wild, multi-floral honey is renowned in Malaysia for its medicinal properties. TH contains over 200 components, including various sugars such as fructose, glucose, maltose, and sucrose, along Zwith organic acids, vitamins, minerals, proteins, phenolic acids, flavonoids, enzymes, and other bioactive compounds.[17] TH stands out from other honey varieties lies on its notably high concentration of flavonoids and phenolic acids, which contribute to its antioxidant and anti-inflammatory effects.[18] These properties are particularly important in the context of obesity, where oxidative stress[19] and chronic inflammation[20] are key mechanisms driving the development of metabolic complications. Oxidative stress can lead to cellular damage, while prolonged inflammation has been closely associated with insulin resistance and lipid metabolism disturbances. TH, known for its antioxidant and anti-inflammatory qualities, helps to reduce oxidative stress by neutralizing free radicals and preventing cellular damage and may help to reduce chronic inflammation, which is commonly associated with obesity and metabolic disorders.

Additionally, the natural sweetness of TH may help to regulate appetite and reduce overall calorie intake.[21] Its consumption has also been suggested to promote satiety, which could support weight management efforts. Furthermore, TH may positively regulate gut microbiota composition, which plays a vital role in metabolic health and obesity prevention.[22] While TH has been widely investigated for its beneficial effects in several metabolic disorders, studies focusing on its role in obesity management remain limited.

In addition, in human studies, body mass index (BMI) is a widely accepted measure of obesity, however, its applicability in animal models, particularly rodents, is limited due to species-specific differences in body composition and shape. Unlike BMI, the Lee Obesity Index (LOI) was specifically developed for rodents and accounts for variations in body size and shape. This makes LOI a more accurate and reliable tool for assessing obesity in rats, as it better reflects the body fat percentage in rodents subjected to dietary-induced obesity.[23]

Therefore, by utilizing LOI, this study aimed to assess the impact of Tualang honey's antioxidant and anti-inflammatory effects on weight reduction in rats with obesity induced by a high-cholesterol diet.

MATERIALS AND METHODS

Animals

In this study, forty male Sprague-Dawley rats, each weighing between 200-250g, were selected as the experimental animal model. The rats were obtained from A-Sapphire Enterprise, located in Seri Kembangan, Selangor, Malaysia. They were individually housed in controlled conditions with a temperature of 22 ± 2ºC, a relative humidity of 60 ± 5%, and a 12-hour light/dark cycle. Food and water were provided *ad libitum*. The rats were acclimatized for a week period with a commercial rat pellet diet prior to the beginning of the experiment. All experimental procedures were approved by the Animal Care and Use Committee of the International Islamic University Malaysia (IIUM/504/14/2/IACUC).

Preparation of High Cholesterol Diet

The 12% high-cholesterol diet (HCD) was formulated by blending 1 kg of powdered commercial rat pellets (Gold Coin, Malaysia) with 120 grams of analytical-grade cholesterol powder (Nacalai-Tesque, Japan; Code 08721-75). To promote the absorption of cholesterol, 3 grams of cholic acid (Nacalai-Tesque, Japan; Code 08843-72) were incorporated into the mixture. To prevent oxidative modifications of the cholesterol, the high-cholesterol diet was freshly prepared daily.

Preparation of Tualang Honey and Orlistat

Tualang honey (TH) (AgroMas, Malaysia) was sourced from the Federal Agricultural Marketing Authority (FAMA), Kedah, Malaysia. A daily dose of 3.0g/kg[24] was prepared by dissolving the honey in warm water immediately before administration. The dose was calculated by converting the human equivalent dose to a rat equivalent using the Km factor method, based on the following formula:

Human Equivalent Dose (HED) = (Animal Km factor / Human Km factor) × Animal dose.[25]

Xenical Orlistat (Roche, Basel, Switzerland) was obtained from a local drugstore and was administered at a dose of 10 mg/kg[26] body weight, also freshly prepared in warm water before use.

Animal Experimental Design

The study was conducted in two phases: the induction phase (12 weeks) and the treatment phase (6 weeks). Following a one-week acclimatization period, their initial bodyweight was measured, and the rats were randomly assigned to five groups, with eight rats per group.

Group 1 served as the control and was provided with standard commercial rat pellets and drinking water, with no treatment administered throughout the study. Group 2 also received a standard commercial rat pellet diet, but was treated with Tualang honey (TH) during the treatment phase. Groups 3, 4, and 5 were given with a high-cholesterol diet (HCD) during the induction phase to induce obesity. Group 3 did not receive any treatment during the treatment phase, however Groups 4 and 5 were treated daily via oral gavage with TH (3.0g/kg) and Orlistat (10mg/kg), respectively.

At the end of the experimental period, the rats were fasted overnight and their final weight were recorded before sacrifice. Blood was collected via retro-orbital bleeding and centrifuged for 10 min at 2500 x g for serum separation and stored at -80°C until further biochemical obesity-related parameters analysis.

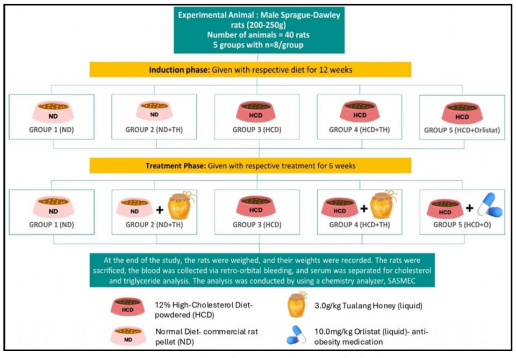

Figure 2: Animal experimental design.

Assessment of Obesity Parameter

The Lee obesity index (LOI) was calculated following the method described in previous studies, with a value greater than 315 indicating obesity.[27] To compute the LOI, the

cube root of the body weight (in grams) was divided by the naso-anal length (in centimetres), and the resulting value was multiplied by 1000.

Lipid Profile Analysis

Lipid profile measurements were conducted on the serum samples, including total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c). These parameters were analysed using the Cobas Integra 400 Plus Analyser (Roche, Switzerland) at the Sultan Ahmad Shah Medical Centre (SASMEC), Kuantan, Malaysia.

Statistical Analysis

Data that followed a normal distribution were analysed using one-way analysis of variance (ANOVA), with post-hoc comparisons performed using the Tukey test. Results are presented as the mean ± standard deviation. For non-normally distributed data, the Kruskal-Walli's test was applied, followed by the Dunn-Bonferroni test, and results are reported as the median with interquartile range. A p-value<0.05 was considered statistically significant.

RESULTS

Bodyweight, Lee Obesity Index and Adipose Tissue Weight

Table 1 presents significant differences across the dietary and treatment groups. Initial bodyweights were comparable among all groups, indicating no significant baseline differences (p>0.05). At the end of the study, rats in the HCD-only group (Group 3) had the highest final bodyweight and bodyweight gain percentage, significantly greater than those in the other groups (p<0.05). In contrast, the normal diet group (Group 1) showed significantly lower final bodyweight and bodyweight gain percentage compared to Group 3 (p<0.05). Additionally, rats on a normal diet with TH (Group 2) had significantly lower final bodyweight and bodyweight gain percentage compared to Group 1 (p<0.05). Among the HCD groups receiving treatment, both Group 4 and Group 5 had significantly lower final bodyweight and bodyweight gain percentage compared to Group 3 (p<0.05).

Table 1: Comparison of Bodyweight, Adipose tissue weight and Lee Obesity Index results among the rat groups

Groups	Group 1 ND only	Group 2 ND + TH	Group 3 HCD only	Group 4 HCD + TH	Group 5 HCD + Orlistat
Initial bodyweight (g)	210.5 ± 23.1	196.0 ± 23.7	191.6 ± 13.3	191.0 ± 18.2	192.5 ± 17.7
Final bodyweight (g)	409.1 ± 16.3	328.3 ± 25.5[a]	471.0 ± 19.5[a]	343.9 ± 44.2[b]	351.0 ± 27.1[b]
Bodyweight gain (%)	96.4 ± 23.1	70.5 ± 30.4	146.3 ± 9.7 [a]	82.8 ± 37.4[b]	84.9 ± 19.5[b]
Lee's Obesity Index	304.8 ± 16.3	294.3 ± 20.3	335.3 ± 11.3[a]	302.8 ± 8.2[b]	308.4 ± 7.4[b]
Adipose Tissue Weight (g)	15.7 ± 2.1	12.3 ± 1.7[a]	19.8 ± 2.2[a]	11.9 ± 1.7[b]	12.3 ± 1.7[b]

Normal distributed data was presented as mean ± standard deviation.
a. Significant difference when compared to Group 1 (p < 0.05).
b. Significant difference when compared to Group 3 (p < 0.05).

Lee Obesity Index (LOI), a measure of obesity in obese-animal model, was also highest in Group 3 compared to Group 1 (p<0.05). Nevertheless, when supplemented with TH, rats in Group 2 showed significantly lower LOI compared to Group 1 (p<0.05). Similar with Group 4, when treated with TH, those rats exhibit significantly lower LOI compared to Group 3 (p<0.05). However, there is no significance different of LOI between the HCD-treated groups, Groups 4 and 5 (p>0.05).

As for the weight of adipose tissue, the HCD-treated group, Groups 4 and 5 showed significantly lower adipose tissue weights (p<0.05) compared to Group 3. Similarly, adipose tissue weight in Group 2 which was treated with TH is significantly lower compared to Group 1 (p<0.05).

Lipid Profile Parameters

Table 2 presents the lipid profile results across the groups. Total cholesterol levels were significantly higher in rats receiving the HCD (Group 3) compared to those on the normal diet (Group 1) (p<0.05). In contrast, rats in the HCD groups receiving treatment (Groups 4 and 5) had significantly lower total cholesterol levels compared to Group 3 (p<0.05). A similar trend was observed for triglyceride levels, with Group 3 exhibiting significantly higher levels compared to Groups 1, 4, and 5 (p<0.05). No significant difference was observed between the TH and Orlistat treatments in the HCD groups (Groups 4 and 5, p>0.05). Nevertheless, there were no significant differences among the groups in LDL-c and HDL-c levels.

Table 2: Lipid profile result for each group

Groups	Group 1 ND only	Group 2 ND + TH	Group 3 HCD only	Group 4 HCD + TH	Group 5 HCD + Orlistat
Total cholesterol (mmol/L)	1.8 (0.2)	1.4 (0.1)[b]	3.2 (0.8)[a]	1.9 (0.7)[b]	1.9 (0.4)[b]
Triglyceride (mmol/L)	0.8 (0.4)	0.7 (0.2)[b]	1.5 (1.0)[a]	0.9 (0.3)[b]	0.9 (0.4)[b]
HDL-c (mmol/L)	1.0 (0.2)	0.9 (0.4)	0.9 (0.2)	1.3 (0.2)	1.3 (0.4)
LDL-c (mmol/L)	0.3 (0.3)	0.4 (0.3)	0.8 (0.2)	0.5 (0.3)	0.7 (0.6)

Non-normal distributed data was presented as median (interquartile range)
a. Significant difference when compared to Group 1 ($p < 0.05$).
b. Significant difference when compared to Group 3 *($p < 0.05$).*

Gross of Adipose Tissue

Figure 3 shows the visceral adipose tissue deposition in rats across five experimental groups, demonstrating differences influenced by dietary interventions. Group 1 exhibits minimal adipose tissue deposition around the abdominal cavity. In contrast, Group 3 shows markedly excessive visceral fat accumulation, characterized by prominent fat accumulation surrounding the intestines and organs. Groups 2, 4 and 5 reveal varying degrees of fat reduction compared to Group 3. Notably, Group 4 which was supplemented with TH has displayed a substantial decrease in visceral adiposity, while Group 5 also shows reduced fat deposition.

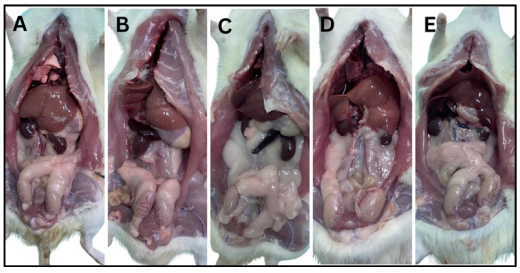

Figure 3: Gross anatomical representation of the rat's adipose tissue among the five groups; A (Group 1- showing minimal fat accumulation), B (Group 2- displaying reduced visceral fat deposition compared to Group 1), C (Group 3- demonstrating excessive visceral fat accumulation, indicative of obesity development), D (Group 4- showing a marked reduction in visceral fat compared to Group 3), E (Group 5- decreased visceral fat deposition, comparable to Group 4).

DISCUSSION

A high-cholesterol diet was used in research to induce obesity and dyslipidaemia in animal models, as it promotes excessive fat accumulation and disrupts lipid metabolism, leading to conditions associated with metabolic syndrome and cardiovascular disease. In this study, we investigated the effect of Tualang honey (TH) supplementation on body weight and lipid profile in a 12% high-cholesterol diet (HCD)-induced obesity rat model and observed that HCD-alone group led to significant increases in body weight, Lee Obesity Index (LOI), and unfavourable lipid profiles, which aligns with previous studies using similar dietary models to induce obesity and related metabolic disorders.[24] The HCD model employed in this study effectively induced obesity in rats, as evidenced by significant weight gain and an increased LOI in the HCD-only group. These results are in line with previous research, which shows that high-fat diets lead to increased adiposity, weight gain, and metabolic disturbances, confirming the effectiveness of the diet in inducing obesity within this timeframe.[28,29] In contrast, TH supplementation significantly reduced body weight, bodyweight gain percentage, and LOI in HCD-fed rats, suggesting that TH has a beneficial impact on body weight regulation in an obesity-rat model. These results align with findings from other studies, where supplementation of honey for six weeks has improved the anti-obesity parameters in high-fat diet induced obese rats.[30]

The weight-modulating effects of TH may be largely attributed to its unique composition. TH contains 35–40% fructose and 30–35% glucose, sugars that differ significantly from refined sugars in metabolic effects.[31] Unlike sucrose, the fructose in honey is absorbed more gradually, leading to a lower glycaemic response and reduced insulin spikes, which can reduce fat storage and appetite.[21] This was further proven by a study that observed rats fed honey, rather than sucrose, showed reduced weight gain and lower body fat percentage over the study period.[32] The moderate absorption rate of honey's sugars may help regulate blood glucose levels and avoid excessive insulin release, factors associated with obesity prevention.[21]

In this study, obese rats treated with TH (Group 4) showed significantly lower final bodyweight. Additionally, TH is rich in polyphenolic compounds and flavonoids such as quercetin, kaempferol, and luteolin, which have been shown to possess anti-obesity effects.[33] A study has demonstrated that rats on an high-fat diet treated with Gelam and Acacia honey for 4 weeks exhibited significantly lower weight gain compared to the untreated group.[34] Their findings suggested that honey's polyphenol content may inhibit fat deposition and adipogenesis.[34] This

was further explained by another study that stated flavonoid-rich honey reduced weight gain in rats on a high-fat diet, presumably via improving fat oxidation and energy expenditure.[35]

The weight and accumulation of adipose tissue in rats which were supplemented with TH (Group 2 and 4) is significantly lower compared to rats in Groups 1 and 3. The findings may be attributed to the antioxidant properties of TH, which can exert its effect on body weight and adiposity. Obesity is associated with elevated oxidative stress, which can impair mitochondrial function and fat oxidation, leading to fat accumulation.[36] A study had suggested that honey's antioxidant activity helps to combat oxidative damage in obese individuals, which could indirectly support weight management.[37] Findings from the current research suggest that TH's antioxidants, including phenolic acids and flavonoids, help to counter oxidative stress and may enhance mitochondrial function, thus supporting metabolic health and reducing fat storage.

TH also showed significant effects on lipid profile parameters. In Group 3, we observed elevated total cholesterol, triglycerides, and LDL-c, with a reduction in HDL-c, which align with the dyslipidaemia profile typically seen in high-fat or high-cholesterol diets. TH supplementation in Groups 2 and 4, significantly reduced total cholesterol, triglycerides, and LDL-c, while increasing HDL-c levels, indicating an overall improvement in lipid profile.

The findings were in accordance with previous research which suggests that Kelulut honey significantly lowered LDL-c and total cholesterol levels in high-fat diet-induced models, lending further support to TH's potential in cholesterol management.[38] Another study proposed that Acacia tree honey (*Desi kikar*) may reduce triglyceride, total cholesterol, and LDL levels in albino mice.[39] Studies suggest that the lipid-modulating effects of TH are likely due to its bioactive compounds, such as phenolics and flavonoids, which are known to influence cholesterol metabolism and enhance reverse cholesterol transport.[40] This was further supported by another study which demonstrated that polyphenols inhibit HMG-CoA reductase, a crucial enzyme in cholesterol biosynthesis, resulting in decreased circulating cholesterol levels.[41]

Other experimental data further confirm these recent findings, where supplementation of Gelam honey in Sprague-Dawley rats improved lipid profiles and reduced oxidative stress markers, supporting honey's role in managing lipid dysregulation.[42] This aligns with the findings of the present study, which indicate that TH can mitigate HCD-induced dyslipidaemia and support healthier lipid profiles. Among the benefits highlighted from previous study is the honey's ability to facilitate weight loss and reduce blood triglyceride levels in obese rats.[39] In this study, the triglyceride-lowering effect of TH is also noteworthy, as elevated triglycerides are associated with increased cardiovascular risk. The high flavonoid content in TH may activate lipoprotein lipase, which is involved in triglyceride breakdown, facilitating triglyceride clearance and contributing to a more favourable lipid profile.[43]

Human subjects have also been studied to see how different honey variations affect their lipid profiles. Previous study found that consuming honey for 48 days improved lipid profiles in obese adult participants.[44] In addition, a study has discovered that patient with diabetic neuropathy supplemented with probiotic honey for 12 weeks has significant improvement in their lipid profile while not causing weight gain in overweight or obese participants.[45] Furthermore, a clinical study revealed that the supplementation of honey in human subjects led to a reduction in serum total cholesterol and LDL-c, accompanied by an increase in HDL-c, suggesting that honey's lipid-modulating effects are applicable across species.[46]

The effects observed with TH in this study were comparable to those of Orlistat, a pharmacological anti-obesity agent, suggesting that honey may offer similar benefits through natural mechanisms that improve metabolism and lipid utilization. A study comparing the effect of Pauttika honey and Orlistat has shown that both have exerted similar effects in reducing fat accumulation in obesity.[47] These current findings suggest that TH may be a promising natural intervention for managing diet-induced obesity and dyslipidaemia.

This aligns with a growing interest in using natural products to manage metabolic diseases since natural interventions often have fewer side effects than pharmaceuticals.

However, further clinical studies are required to verify the effects of TH in human. Additionally, long-term studies could also evaluate the sustainability of honey's benefits and any potential side effects associated with prolonged consumption. Although the present study demonstrated a significant reduction in adipose tissue weight following TH supplementation, it is recommended that future studies utilize body composition analysis methods, such as DEXA scan, to further validate whether the weight reduction is specifically due to fat loss rather than changes in muscle or water content. Moreover, gut microbiome dysbiosis has been strongly associated with obesity and high-fat diets,[22,48] while antioxidant supplementation has demonstrated the potential to improve gut microbiota composition and mitigate obesity-related effects.[49] Therefore, exploring this connection further is encouraged to develop a more comprehensive strategy for managing obesity and its associated health complications.

CONCLUSION

Tualang honey supplementation has been shown to reduce body weight and improve lipid profiles in 12% HCD-induced obese rats.

CONFLICT OF INTEREST

There are no conflicts of interest among the authors.

ACKNOWLEDGEMENT

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