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Anethum graveolens, and Allium Polyanthum extracts suppress obesity in HFD-fed rats

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A R T I C L E I N F O

Keywords:
Obesity
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Anethum graveolens
Allium polyanthus
Anti-obesity

Abstract

Objective: The objective of this study was to evaluate the anti-obesity effects of **Anethum graveolens** (AGE) and **Allium polyanthus** (APE) extracts on high-fat diet (HFD)- induced obesity in male Wistar rats.

Methods: Twenty-four male Wistar rats were randomly assigned to four groups: Normal Control (NC), High-Fat Diet Control (HFD-C), HFD + AGE, and HFD + APE. Obesity was induced in all groups except the NC by feeding them HFD for eight weeks. The treatment groups received intragastric administration of AGE or APE (300 mg/kg BW) daily for eight weeks. Weekly measurements of body weight and food intake were recorded. At the end of the study, serum biochemical parameters, including triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), glucose, malondialdehyde (MDA), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were analyzed.

Results: Compared to the NC group, HFD-fed rats exhibited significant increases in body weight, hyperlipidemia, hyperglycemia, hepatic dysfunction, and oxidative stress. Treatment with APE significantly reduced body weight gain and improved biochemical markers compared to the HFD-C group. AGE treatment significantly improved biochemical parameters but did not significantly affect body weight gain.

What is already known about the topic? It is already known that **Anethum graveolens** (dill) and **Allium polyanthum** (wild garlic) have bioactive compounds with potential health benefits, including anti-inflammatory and antioxidant properties. Previous studies suggest that these extracts may help regulate lipid metabolism, reduce fat accumulation, and improve metabolic functions, making them candidates for managing obesity, particularly in high-fat diet (HFD)-fed animals.

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INTRODUCTION

Obesity is a complex and multifaceted condition characterized by an excessive accumulation of body fat due to an imbalance between energy intake and expenditure (Kim et al., 2016). It has emerged as a significant global public health concern, affecting individuals across developed and developing countries (Mabrouki et al., 2020). The World Health Organization (WHO) reports that approximately 39% of the global population is overweight, and 13% is obese (Piragine et al., 2020). Recent estimates suggest that over 500 million adults and 40 million children worldwide are classified as obese, highlighting the escalating prevalence of this condition (Bati et al., 2020).

Obesity is closely associated with several chronic health conditions, including cardiovascular disease, fatty liver disease, hyperlipidemia, hypertension, diabetes, and certain forms of cancer (Li et al., 2013). The rising incidence of these obesity-related conditions is primarily attributed to modern lifestyle factors such as an abundant supply of nutrient-rich foods and a decline in physical activity (Woo et al., 2008). Traditional approaches to managing obesity, including dietary regimens, exercise, and pharmacological interventions, often yield limited success and may be accompanied by adverse side effects and rebound weight gain (Rahman et al., 2017; Mopuri et al., 2015).

In contrast, the use of medicinal plants for the prevention and treatment of obesity has gained attention due to their potential efficacy and lower risk of side effects (Oluyemi et al., 2007). Plant-based treatments have been employed for centuries in various cultures to address various health conditions. These natural remedies are often preferred over synthetic drugs because they tend to have fewer contraindications and adverse effects (Oluyemi et al., 2007). The current study investigated the potential anti-obesity effects of **Anethum graveolens** and **Allium polyanthum** extracts in a high-fat diet (HFD)-induced obesity model in rats. The study aimed to assess the impact of these plant extracts on body weight gain and vital biochemical markers associated with obesity and its related metabolic disturbances.

MATERIAL AND METHOD

Plant Materials:

In March 2021, fresh Anethum graveolens and Allium polyanthum plants were collected in the region of Ranyah. The plants were shade-dried at room temperature, ground into powder, and sold.

Plant Extract Preparations

Anethum graveolens, and *Allium polyanthum* powders were Soxhlet extracted with 95% ethanol. Each plant's extracts were filtered and concentrated by distillation after ten cycles of 100 gm/250 ml solvent extractions. Yields were ~13.3 and 11.8 grams. The extracts were refrigerated until use.

Animals Used in the Experiment

Twenty-four male albino rats (Rattus norvegicus) were used. The medical laboratory science department/ College of Science/ Raparin University's animal house housed the experiment from March to July 2021. The animals were housed at 24 ±2 °C in plastic cages with hardwood chips with 12-hrs light/dark cycles and fed according to study design with water ad libitum.

Dosing Regimen

Every morning at 9:30–10:30, rats received intragastric administration. NC and model groups received normal saline; the others received the test treatments. Weekly rat weights were used to modify treatment doses.

Acute Toxicity Study:

For the acute toxicity study, 12 h fasted animals (n=12) were randomly selected and divided into two groups of 6 rats each. AGE and APE in 300 mg/kg BW were administered orally. The animals were continuously examined for three hours; overnight mortality, if any, was recorded (Sharma, 2011).

Induction of Obesity:

The administration of HFD-induced obesity was prepared according to a study (Wilding *et al*., 1992) by mixing 33% standard chow, 33% Nestle milk powder, 7% sucrose, and 27% tap water by weight. This diet provides 68% of energy as carbohydrate, 20% as protein, and 12% as fat, whereas the ND provides 65% of energy as carbohydrate, 20% as protein, and 4% as fat (Brown *et al*., 2001).

Experimental Design:

Following an acclimation period of one week, the rats were arbitrarily split up into four groups, each consisting of six rats.

First group (NC): Fed ND for eight weeks.

Second group (HFD-C): Fed HFD for eight weeks.

Third group (HFD + AGE): Fed HFD + Received AGE (300 mg/kg b.w., six days/week) for eight weeks using oral gavage.

Fourth group (HFD + APE): Fed HFD + Received APE (300 mg/kg b.w., six days/week) by oral gavage over eight weeks.

Each group, except NC, was maintained throughout the experiment on the HFD. Water was readily available for all the animals. The HFD-C group received an exact volume of distilled water via oral gavage as the model control group for eight weeks. Body weight and food intake were regularly measured weekly during the experimental period. After fasting overnight, all animals were anesthetized with diethyl ether. Cardiac puncture was used to collect blood samples. The serum was separated by centrifuging at 2500 rpm for 15 min and tested for several biochemical characteristics.

Serum Parameter Measurements:

Using a full-auto analyzer, the levels of glucose, total cholesterol, high-density lipoprotein (HDL), and liver enzymes AST and ALT were calculated (Cobas C-111). Spectrophotometric analysis using a TBA solution was used to determine serum MDA according to the methodology given by (Hassan et al., 2018), and the Friedewald formula was used indirectly to calculate the LDL and VLDL levels, as shown in the following: LDL = [TC – (HDL + (TG/5)] and VLDL = [TC – (HDL + LDL)] (El-shiekh *et al*. 2019).

Statistical Analysis:

Data were analyzed using SPSS (Version 26.0). Results are reported as mean ± standard error (mean ± SE). Duncan's test for multiple comparisons was applied following analysis of variance to identify statistically significant differences (ANOVA). The level of significance was fixed at $P<0.05$.

RESULTS

AGE and APE Effects on Body Weight Gains and Food Consumption

When the study began, the average body weight of each experimental group was roughly equivalent. Administration of HFD for eight successive weeks was linked to a significant increase ($p < 0.05$) in the final BW of the HFD-C group.when, in comparison to the NC samples, the percentage of gain in BW was 83.243% and 70.531%, respectively. (Table 1, Fig. 1 & 2).

Daily treatment of AGE for rats fed HFD for eight weeks showed more BW gain (87.47%), but the difference was not statistically significant ($p > 0.05$). The APE treatment group had gained a significant ($p < 0.05$) less BW (69.79%) than HFD-C rats. (Table 1, Fig. 1 and 2). Between the HFD-C and NC samples, there were no significant differences in the amount of food consumed. Although there were slight differences between the HFD-C and the treatment groups (AGE and APE), they were not statistically significant ($p > 0.05$). (Table 1).

Effects of AGE and APE on the Biochemical Parameters of Serum

Table 2 summarizes the effects of AGE and APE on the biochemical parameters of serum in HFD-induced obese rats. Rats fed on an HFD for eight weeks were associated with a significant ($p < 0.05$) increase in the levels of serum glucose, TC, TG, LDL, VLDL, and MDA levels compared with rats fed on ND, while serum HDL level was decreased but did not reach

RESULT

statistically significant ($p > 0.05$) (Fig 3, 4, 5, 6, 7, 8, 9, 10 & 11).

Compared with the HFD-C group, the AGE treatment group revealed a significant ($p < 0.05$) drop in serum, TG, TC, LDL, HDL, VLDL, MDA, and ALT levels. In contrast, serum glucose and AST levels exhibited no significant alteration ($p > 0.05$). Treatment of APE caused a significant ($p < 0.05$) decrease in all serum parameters in comparison with the HFD-C group, except for serum HDL and AST levels, which exhibited no significant change ($p > 0.05$). (Fig 3, 4, 5, 6, 7, 8, 9, 10 & 11).

Table (1) Effects of AGE and APE on gain in BW and food intake in rats fed on HFD for eight weeks.

Parameters	NC	HFD-Fed obese induced Rats		
		HFD-C	Extracted of the Plant (300mg/kg BW)	
			AGE	APE
Initial Body Wt. (gm)	195.63 ± 4.53 [a]	198.25 ± 7.20 [a]	201.18 ± 3.48 [a]	203.66 ± 3.42 [a]
Final Body Wt. (gm)	333.61 ± 4.95 [a]	363.28 ± 7.94 [b]	377.17 ± 5.75 [b]	335.81 ± 4.68 [a]
Body Wt. gain (%)	70.531	83.243	87.47	64.88
Food intake (g/week)	129.32 ± 4.28 [a]	129.47 ± 7.77 [a]	130.69 ± 7.04 [a]	125.11 ± 2.32 [a]

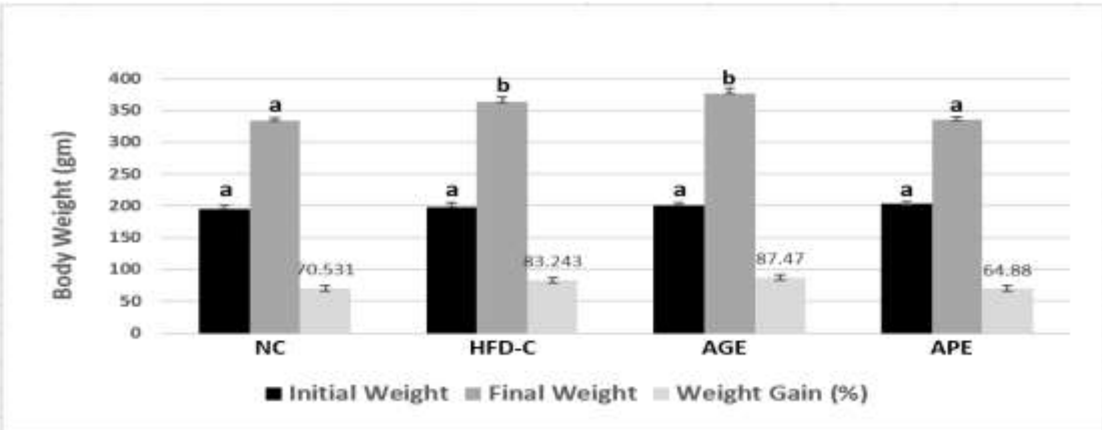

Figure 1: Effects of AGE and APE on body weight gain in rats fed on HFD for eight weeks.

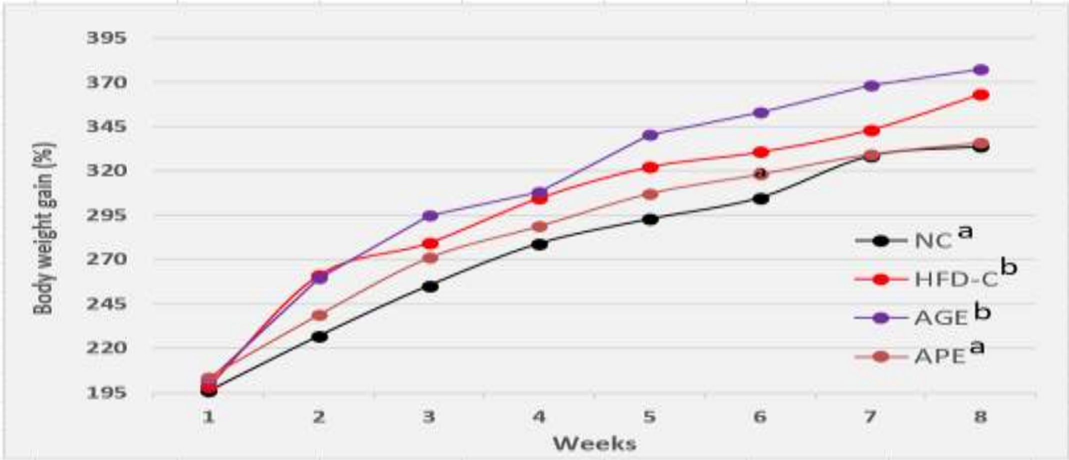

Figure 2: Effects of AGE and APE on body weight gain/week in rats fed on HFD for eight weeks.

Table 2: Effects of AGE and APE on various rats' biochemical parameters fed an HFD for eight weeks.

Parameters		High-fat diet-induced obese groups		
			Plant extracts (300mg/kg BW)	
	NC	HFD-C	AGE	APE
Glucose (mg/dl)	92.65 ± 5.71 [a]	147.03 ± 8.52 [b]	149.26 ± 11.72 [b]	111.41 ± 15.12 [a]
TC (mg/dl)	49.66 ± 2.52 [b]	72.66 ± 5.02 [c]	35.53 ± 4.91 [a]	45.73 ± 2.58 [ab]
TG (mg/dl)	38.50 ± 3.59 [a]	75.20 ± 1.88 [b]	39.60 ± 5.27 [a]	42.28 ± 3.39 [a]
HDL (mg/dl)	24.30 ± 1.82 [b]	21.31 ± 3.66 [b]	13.59 ± 2.18 [a]	19.96 ± 1.58 [ab]
LDL (mg/dl)	7.70 ± 0.71 [a]	36.30 ± 3.66 [c]	14.01 ± 3.35 [ab]	17.31 ± 1.60 [b]
VLDL (mg/dl)	7.73 ± 0.88 [a]	15.04 ± 0.37 [b]	7.92 ± 1.05 [a]	8.45 ± 0.67 [a]
MDA (µmol/l)	1.695 ± 0.04 [a]	3.411 ± 0.08 [c]	2.47 ± 0.19 [b]	1.99 ± 0.23 [a]
AST (IU/L)	86.53 ± 6.38 [a]	112.41 ± 4.49 [ab]	91.03 ± 9.31 [a]	138.61 ± 3.14 [b]
ALT (IU/L)	23.56 ± 0.98 [a]	54.31 ± 1.98 [c]	27.36 ± 2.61 [a]	39.61 ± 3.82 [b]

The similar letters indicate that there are no significant differences, but different letters indicate that there are significant differences.

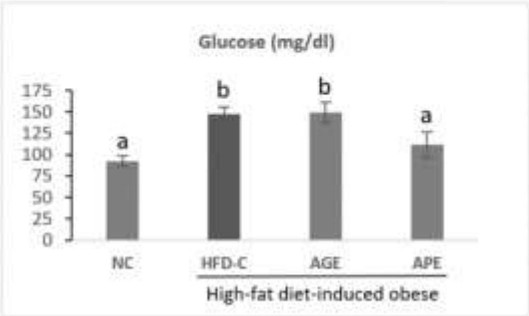

Figure 3: Eight weeks Effects of AGE and APE on serum glucose rats fed a HFD

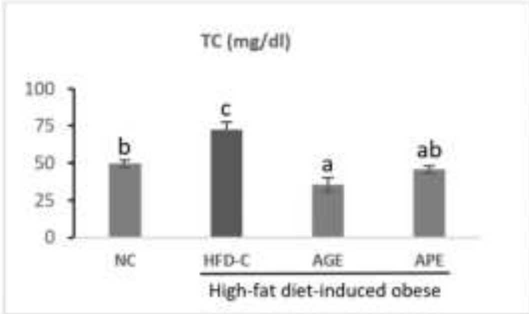

Figure 4: Eight-week effects of AGE and APE on serum TC in rats fed a HFD.

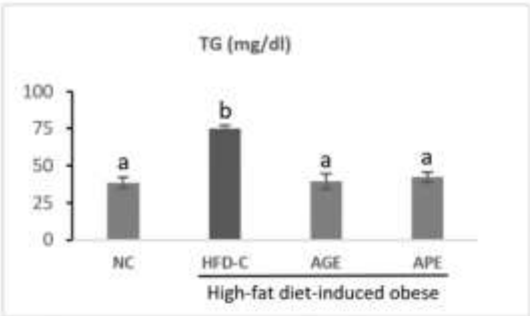

Figure 5: Eight weeks effects of AGE and APE on serum TG in rats fed a HFD.

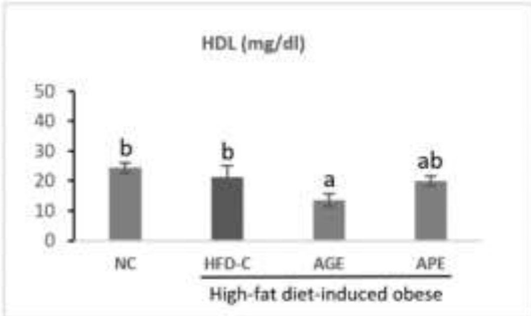

Figure 6: Eight weeks effects of AGE and APE on serum HDL in rats fed a HFD.

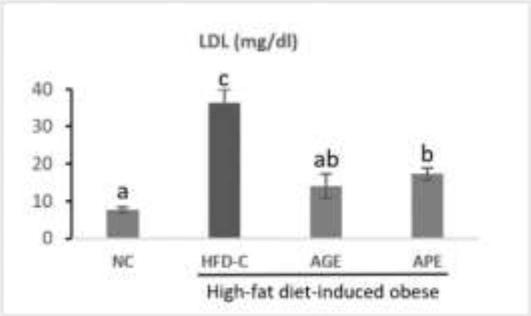

Figure 7: Eight weeks effects of AGE and APE on serum LDL in rats fed a HFD.

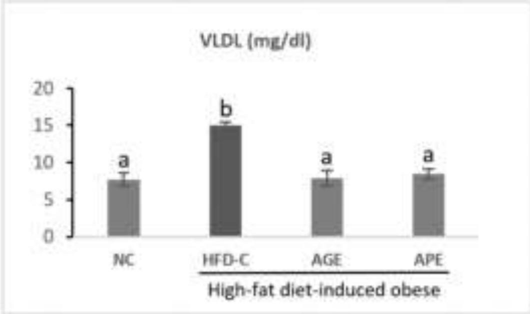

Figure 8: Eight weeks effects of AGE and APE on serum VLDL in rats fed a HFD.

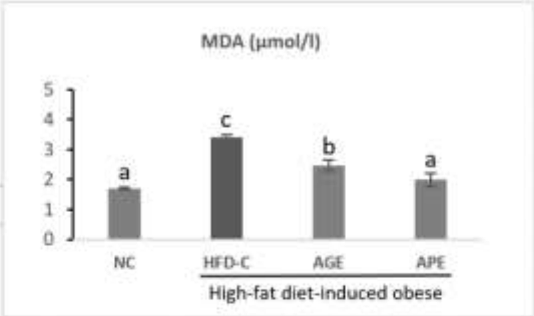

Figure 9: Eight weeks effects of AGE and APE on serum MDA in rats fed a HFD

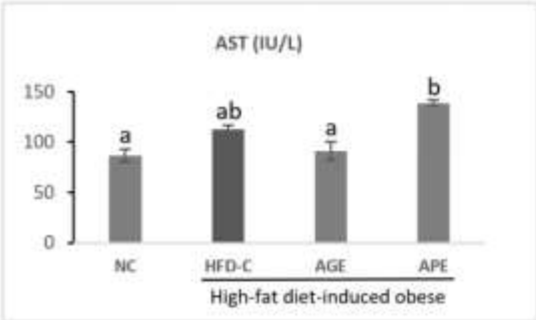

Figure 10: Effects of AGE and APE on serum AST in rats fed a HFD

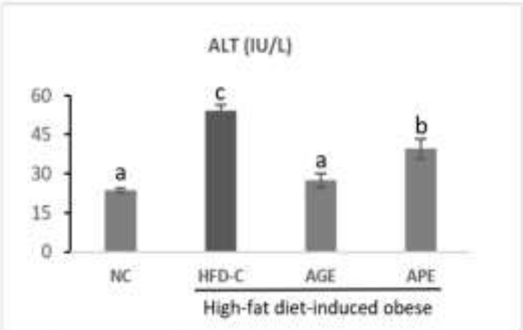

Figure 11: Eight weeks effects of AGE and APE on serum ALT in rats fed a HFD

DISCUSSION

The development of an adequate obesity model is necessary for the investigation of natural compounds with anti-obesity activities (Boqué *et al.*, 2013). Induction of obesity through HFD in rodents pathophysiologically very similar to human obesity five better than the genetic obese models (Sharma, 2011), which could provide a positive energy balance and is considered a significant risk factor for the development of obesity (Li *et al.*, 2013), besides rodents were developed visceral adiposity, hyperglycemia, dyslipidemia, insulin resistance and hepatic steatosis when fed on HFD (Oluyemi *et al.*, 2007).

Despite the availability of several hypolipidemic medications in the market, people avoid the use of chemical drugs for the management of overweight and obesity because of their adverse side effects on health (Bahramikia & Yazdanparast, 2008). many studies have focused on the use of medicinal plants as a new anti-obesity drug that could minimize these side effects (Lim *et al.*, 2013). Hence, the first objective of this study was to establish a diet-induced obesity model in male Wistar rats. This work's second and primary objective was to test and differentiate the potential anti-obesity properties of Anethum graveolens and Allium polyanthum plant extracts in diet-induced obese animals, as assessed by the observed results on body weight gain and blood biochemical parameters.

The HFD feeding for eight weeks successfully induced obesity, hyperglycemia, and dyslipidemia in the rats, as evidenced by a significant increment in the body weight gain, serum glucose, TC, TG, LDL, and VLDL with a decrease in serum HDL level as compared with rats from NC without significant changes in the amount of food intakes. These results were in agreement with data previously reported by (Lei *et al.*, 2007), (Mabrouki *et al.*, 2020), (Kim *et al.*, 2016), (Mopuri *et al.*, 2015), (El-Shiekh *et al.*, 2019) (Othman *et al.*, 2019). Furthermore, a study (Piragine *et al.*, 2020) documented that HFD administration in rodents could promote body weight gain, hyperlipidemia, and alteration in glucose homeostasis. Because of the higher fat content, the energy intake was significantly higher in HFD-fed rats even if the amount of food intake did not significantly differ (Woo *et al.*, 2008) & (Lim *et al.*, 2013). High-fat diet (HFD) consumption is associated with hyperglycemia because it reduces glucose absorption and inhibits insulin-stimulated hepatic glucose synthesis. (Sharma 2011) and glucose intolerance (Rahman *et al.*, 2017).

The liver plays a vital role in lipid metabolism. It controls the accumulation of fat tissue and serum lipid levels (Li *et al.*, 2013). Essential markers of the functional condition of the liver are liver function tests. (Mopuri *et al.* 2015). As observed in the current study, a change in liver metabolic function and hepatocellular injury are indicated by elevated serum levels of AST and ALT in the HFD group compared to the NC group. The similar results were confirmed by (Bati *et al.*, 2020) (El-Shiekh *et al.*, 2019). Study (Abliz *et al.*, 2014) It was also confirmed that rats consume hyperlipidic foods with hepatic complications. Furthermore, The association between oxidative stress and excess fat consumption is well-known (Jang et al., 2012). Therefore, one of the significant consequences of the induction of obesity is oxidative stress (El-Shiekh *et al.*, 2019), and data on serum MDA in HFD-C rats by this study strongly supported that claim since serum level of

MDA is a quantitative marker of lipid peroxidation by ROS.

Our results demonstrated that administration of APE to rats fed on HFD significantly suppressed BW gain and improved sugar and lipid profiles with oxidative stress and hepatic misfunctioning exerted by HFD feeding compared to untreated HFD-fed rats after eight weeks independent of food or energy intake since all rats received the same amount of diet; On the other hand, treatment of AGE on obese rats showed no significant change on BW gain, whereas significantly improved the HFD-induced changes in serum biochemical parameters. Current results were consistent with data from (Al-Snafi, 2017) and (Lim *et al*., 2013) studies.

Natural products could develop weight-reducing effects of anti-obesity through five basic mechanisms (Jamous *et al*., 2018), including inhibiting pancreatic lipase activity (Seyedan *et al*., 2015), promoting lipolysis (Kim *et al*., 2012), preventing adipogenesis, promoting thermogenesis and lipid metabolism (Shen *et al*., 2014) and controlling appetite (Yang e.a. 2016).

A study (Woo *et al*., 2008) belonged these combined effects to phytochemical or plant components (Boqué *et al*., 2013) argued that polyphenols from plant extracts could act as inhibitors of adipocyte differentiation, lipogenesis, lipolysis or intestinal lipid absorption as well as inducers of fatty acid oxidation or antagonist at cannabinoid receptors. In addition (Boqué *et al*. 2013) thought the anti-obesity activities of plant extracts are through metabolic modulation or increased energy expenditure. However, additional experimentation is needed to clarify this issue further.

Several previous studies described the role of plant polyphenols; plant extracts that contain a mixture of polyphenols could help prevent obesity and related disorders (Othman *et al*., 2019). Polyphenols have antioxidant, anti-inflammatory, and glucose and lipid metabolizing properties (Layman *et al*., 2019), and many authors have confirmed a strong correlation between phenolic compounds and antioxidant activities (Mabrouki *et al*., 2020).

The restorations in serum parameters by treatments of the current study could guarantee the presence of anti-hyperglycemic, anti-hyperlipidemic, and antioxidant properties, and this could belong to the availability of bioactive compounds, especially polyphenols within these two plants.

CONCLUSION

The abovementioned discussion concludes that HFD-induced increases in BW gain and their associated physiological effects were reduced by APE treatment. Treatment of AGE had marked effects on diminishing the obesity-related consequences (Hyperlipidemia, hyperglycemia, hepatocellular damage, and oxidative stress) but was not effective in BW control.

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AUTHOR'S CONTRIBUTIONS

Study the concept and write and review the final edition by all authors.

DISCLOSURE STATEMENT:

The authors report no conflict of interest

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