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Synergistic Effects of L-Carnitine and Arabic Gum on Oxidative Stress and Adipokines in Hyperlipidaemic Rats

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Abstract
Objective: The present study was conducted to investigate the combined effects of Arabic gum and L-carnitine on oxidative stress markers and serum concentrations of leptin and adiponectin in male albino rats subjected to diet-induced hyperlipidaemia
Methods: The three-month study involved 48 albino rats, aged three months, with a weight range of 160–180 grams per rat was conducted at the Animal house in the University of Al-Qadisiyah. The rats were divided into six groups, with eight animals per group. One of the groups served as the control and received a normal diet and free access to water during the experimental duration. The remaining groups (T1–T5) were administered a high-fat diet containing 30% animal fat for 60 consecutive days to induce hyperlipidaemia. After confirmation, treatments were applied for 30 days as follows: T1 (positive control, high-fat diet only), T2 (Arabic gum, 600 mg/kg), T3 (L-carnitine, 250 mg/kg), T4 (combination of Arabic gum and L-carnitine), and T5 (standard diet + Arabic gum and L-carnitine).
Results: Group T1 showed significant increases ($P<0.05$) in body weight gain, total cholesterol, triglycerides, leptin, and MDA, and significant decreases in adiponectin, glutathione, and catalase levels compared to the control. Groups T2–T5 showed significant improvements in all parameters, including reduced lipid levels, oxidative stress markers, and leptin, with increased adiponectin and antioxidant enzymes compared to T1.
Conclusion: Arabic gum and L-carnitine, especially in combination, demonstrated a protective and corrective effect against hyperlipidaemia-induced oxidative stress and hormonal imbalance, indicating their potential as therapeutic agents for metabolic disorders.

Keywords: Obesity, L-Carnitine, Arabic Gum, Fatty Liver Disease, Leptin, Adiponectin, Endocrine Disorders, Antioxidant, Weight Management, Metabolic Health

Plain English Summary

Obesity presents important health risks by enhancing body fat levels, disrupting hormonal balance, and inducing harmful oxidative stress within the body. This research examined two natural agents, Arabic gum, a dietary fibre derived from plants, and L-carnitine, a compound that assists fat metabolism, for their potential benefits in improving health markers in rats subjected to a high-fat diet. The study involved 48 male rats divided into six groups. One group was fed a standard diet, while the remaining groups received a high-fat diet to induce an obesity-like state. After two months, four groups were treated for 30 days with either Arabic gum, L-carnitine, a combination of both, or both agents along with a shift back to a standard diet. Results indicated that rats on the high-fat diet experienced considerable weight gain, enhanced levels of detrimental lipids, increased oxidative stress markers, and hormonal imbalances affecting appetite and

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fat storage regulation. Conversely, treatment with Arabic gum or L-carnitine alone led to notable improvements in these areas. Most considerably, the group receiving both treatments, particularly the subgroup transitioning back to a normal diet, demonstrated the most substantial progress, exhibiting reduced fat accumulation, enhanced antioxidant defences, and a healthier hormonal profile, with favourable levels of leptin and adiponectin. These findings suggest that the combined use of Arabic gum and L-carnitine offers a promising, natural strategy for addressing obesity-related metabolic disturbances by restoring nutritional and oxidative balance effectively.

Introduction

Obesity is a multifaceted disorder marked by abnormal or excessive fat accumulation and arises from the interplay of genetic predisposition, environmental influences, and behavioural patterns. The primary contributors to obesity are the increased intake of calories and decreased physical activity, with underlying causes extending to biological, psychological, and social factors. Additionally, other factors contributing to obesity include insufficient sleep, endocrine disorders, and the gastrointestinal microbiome (probiotics), all of which are also related to obesity development (1, 2). Unhealthy lifestyle behaviours, particularly the widespread availability and consumption of highly processed, energy-dense foods, also play a pivotal role in the development of obesity (3). In addition, genetic factors, such as mutations in the leptin receptor and melanocortin-4 receptor genes, contribute to obesity by interacting with other underlying etiological factors (4). Obesity is a major contributor to a broad spectrum of diseases that affect nearly every organ system, posing substantial health risks. It is strongly linked to several gastrointestinal conditions, including non-alcoholic fatty liver disease (NAFLD), gastroesophageal reflux disease (GERD), as well as various cancers such as hepatic and colorectal malignancies (5, 6, 7).

The rising prevalence of obesity-related diseases is cause for concern due to the associated health risks, with studies indicating that approximately 70% of obese individuals develop non-alcoholic fatty liver disease (NAFLD) (8). Beyond its physical implications, obesity is also linked to a range of psychological disorders, including anxiety, depression, and overall emotional distress. Additionally, it contributes to various somatic conditions such as osteoporosis and obstructive sleep apnoea (9). Obesity is closely associated with several hormonal imbalances, which may either result from or exacerbate the condition. Disorders such as diabetes mellitus, hypothyroidism, Cushing's syndrome, and polycystic ovary syndrome are commonly observed in obese individuals, underscoring the complex relationship between endocrine dysfunction and metabolic health (10, 11).

L-carnitine is a quaternary ammonium compound that is chemically synthesised from lysine and methionine amino acids, and it plays a pivotal role in cellular energy metabolism. It exerts its action by enabling the transport of long-chain fatty acids into mitochondria to undergo β-oxidation, generating energy (12, 13, 14). Though the liver and kidneys are the primary sources of its endogenous synthesis, L-carnitine has been reported to enhance cardiovascular function, with considerable improvements noted among diabetic elderly patients (15, 16, 17, 18). Clinical studies have shown that supplementation with 1–2 grams of L-carnitine per day can significantly reduce body mass index and serum cholesterol levels, thereby supporting its potential role in mitigating cardiovascular and metabolic risk factors (19). Dietary sources rich in L-carnitine include red meat, fish, and dairy products (20). Furthermore, L-carnitine has demonstrated therapeutic benefits in patients with liver cirrhosis, improving both serum albumin levels and overall nutritional status (21). In addition to its central function in fatty acid transport across mitochondrial membranes, L-carnitine helps prevent fatty acid-induced mitochondrial toxicity and possesses notable antioxidant properties, contributing to the maintenance of cellular and mitochondrial integrity (22).

Arabic Gum (GA), scientifically known as *Senegalia Senegal*, is a gum exudate obtained from the branches of the Acacia Senegal tree, which grows in arid regions like Sudan, Chad, and Nigeria. This exudate hardens and dries when exposed to air. Sudan alone accounts for over 80% of global production (23). It is composed of various sugars, including galactose, arabinose, and glucuronic acid, and is a soluble dietary fibre, making it a valuable emulsifier in food and pharmaceutical applications (24, 25, 26, 27). Arabic Gum has numerous therapeutic potentials for different health conditions, especially in the management of gum diseases and immune response enhancement. Its anti-biofilm and anti-inflammatory properties make it a promising agent in treating gum diseases, as it is antibacterial, reducing tooth decay and inflammation (28, 29, 30). Arabic Gum has demonstrated antioxidant effects in kidney disease patients, improving renal

biomarkers and preventing kidney damage caused by exposure to butylene, owing to its antioxidant activity and enhanced free radical scavenging (31, 32, 33, 34).

Previous studies have confirmed that Arabic Gum has significant anti-obesity effects through various mechanisms. It may help control weight by reducing fat deposition in the body and promoting fat utilisation in adipose tissues (35, 36). Therefore, the current study aims to evaluate the interactive effects of Arabic gum and L-carnitine on oxidative stress and leptin and adiponectin serum levels in diet-induced hyperlipidaemic male albino rats to determine their potential as complementary therapeutic alternatives for the attenuation of metabolic and endocrine derangements of obesity. While it is known that both Arabic gum and L-carnitine offer benefits in managing obesity-related metabolic issues, there hasn't been much research into what happens when they are used together. Specifically, their combined effects on oxidative stress and the balance of hormones like leptin and adiponectin in cases of high cholesterol are not well studied. We hypothesised that using both Arabic gum and L-carnitine together would provide stronger protection and better health benefits than using either one alone. This combined approach may help reduce oxidative damage, restore normal levels of important hormones, and improve metabolic health in rats fed a high-fat diet.

Materials and Methods

L-Carnitine and Arabic Gum Preparation

L-Carnitine was obtained in capsule form from Premier Health Products Ltd (UK), sourced from pharmaceutical outlets in Al-Diwaniyah Governorate. Each capsule contained 1000 mg of L-Carnitine. Arabic Gum was purchased from the local market and ground into a fine powder using an electric grinder. The dosages for both L-Carnitine and Arabic Gum were calculated based on the following formula:

Animal Dose (mg)=1000Body Weight (g)×Substance Concentration (mg)/ 1000

Each rat was administered 0.5 ml of L-Carnitine via intraperitoneal injection and 1 ml of Arabic Gum via oral gavage daily for 30 days.

Experimental Animals

Thirty male albino rats (Rattus norvegicus) were employed, and all were three months old, weighing 160 to 180 grams. The animals were obtained from the Animal Facility at the College of Veterinary Medicine, University of Al-Qadisiyah. The experiment was carried out under controlled conditions at the animal house of the Biology Department, College of Education, in the same university.

Experimental Design

The studies were conducted in two phases:

Phase One: The rats were assigned to two groups at random and monitored for 60 days. One group was placed on a normal laboratory diet, and the other group was given a high-fat diet to induce experimentally a hyperlipidaemic state.

Phase Two: After 60 days, treatment lasted for 30 days using Arabic Gum and L-Carnitine as follows:

Control group (C): 8 rats received a normal diet and water throughout the 90 days.

T1 group: 8 rats received a high-fat diet for 90 days without treatment.

T2 group: 8 rats with induced hyperlipidaemia were treated with Arabic Gum (600 mg/kg BW) for 30 days post-induction.

T3 group: 8 hyperlipidaemic rats were injected with L-Carnitine (250 mg/kg BW) for 30 days post-induction.

T4 group: 8 hyperlipidaemic rats were treated with both Arabic Gum and L-Carnitine concurrently for 30 days.

T5 group: 8 rats received a normal diet and were treated with both Arabic Gum and L-Carnitine only in the last 30 days.

Parameters of the Study

Weight Gain Rate (g)

The body weight of each rat was recorded at the start and termination of the experiment. The net weight gain was determined by computing the difference between the final weight and the initial weight, as shown below:

Weight Gain (g) = Final Weight (g) − Initial Weight (g)

Relative Liver and Kidney Weight

After blood collection, the rats were sacrificed, and the liver and kidneys were removed carefully, freed of all the surrounding tissue, and weighed on a precision digital balance. Organ-to-body weight ratio was determined using the formula:

Organ Weight Ratio (%) = (Organ Weight (g) / Body Weight (g)) × 100

Measurement of Serum Total Cholesterol

Total cholesterol concentrations in serum samples were measured by an enzymatic method using a commercial kit (BioMérieux, 69280, France). Cholesterol esters are hydrolysed first by cholesterol esterase to liberate free cholesterol, and then the latter is oxidised by cholesterol oxidase to give hydrogen peroxide. This peroxide

reacts with phenol and 4-aminoantipyrine in the presence of peroxidase to give a red quinonimine dye. The colour intensity of the produced colour was measured at 546 nm using a spectrophotometer, and the concentration of cholesterol was estimated from a standard calibration curve (37).

Triglyceride Determination in Serum
Triglycerides were determined using BioMérieux enzymatic kit (69280, France). Lipase hydrolyses triglycerides into glycerol and fatty acids. Glycerol underwent phosphorylation and oxidation to produce hydrogen peroxide, reacting with 4-aminoantipyrine, forming quinonimine, measured at 505 nm. Concentration calculation followed the provided standard formula (38).

Leptin Hormone (LEP) Measurement
Leptin was quantified by Sandwich-CLIA. Microplates were pre-coated with antibodies specific to Rat LEP. After adding standards and samples, biotinylated detection antibody and Avidin-HRP conjugate were added. Luminescence was measured at 425 nm, and concentration was derived from a standard curve.

Adiponectin Measurement (ELISA)
Adiponectin was assessed using Sandwich-ELISA (BioTech). Standards and samples were incubated in antibody-coated ELISA plates, followed by biotinylated antibodies and HRP-conjugated Avidin. Colour reaction measured at 450 nm reflected protein concentration relative to standards.

Antioxidant Markers
Malondialdehyde (MDA) Determination: MDA was measured using a modified thiobarbituric acid (TBA) method. Lipid peroxides reacted with TBA, forming a coloured complex measured at 532 nm. Calculation followed the provided equation (39).

Glutathione (GSH) Determination
Serum glutathione was quantified using DTNB (Ellman's reagent). DTNB reduced by GSH formed a coloured complex, absorbance measured at 412 nm, with concentration calculated using the described equation (40).

Catalase (CAT) Activity
Catalase enzyme activity was determined using a spectrophotometric assay through the observation of the rate of hydrogen peroxide (H_2O_2) degradation. Absorbance at 240 nm was determined, and enzyme activity was quantified as a first-order rate constant from the time-dependent reduction in absorbance (41).

In this research, the high-fat diet used to induce hyperlipidaemia in rats consisted of standard chow supplemented with 30% animal-derived fat. While the manuscript notes this composition, it lacks specificity regarding the exact source of the animal fat, such as whether it was lard or beef tallow. For future investigations, providing detailed information about the fat source will improve reproducibility and assist meaningful comparisons across studies. The chosen dose of 250 mg/kg body weight was knowledgeable by previous experimental research, which demonstrated its effectiveness in reducing body weight, enhancing lipid metabolism, and boosting antioxidant enzyme activity in rodent models of hyperlipidaemia and obesity. For example, studies like those conducted by Dayanandan et al. (42) and Keskin et al. (43) employed similar or slightly higher doses to achieve therapeutic benefits without evident toxicity. The dose of 600 mg/kg body weight was based on earlier research confirming its safety and effectiveness in modulating lipid profiles and oxidative stress markers in rats. Previous work, including studies by Ahmed et al. (44, 45), used comparable dosing regimens that demonstrated Arabic gum's lipid-lowering, antioxidant, and anti-inflammatory effects. This dose was selected to optimise therapeutic outcomes while maintaining tolerability over the 30-day treatment period.

Statistical Analysis
Statistical comparison of the experimental data was done with SPSS software version 25 (IBM Corp., Armonk, NY, USA). Data were presented as mean values with standard error (SE). Significant differences between the groups were found by one-way analysis of variance (ANOVA). If there were significant differences, then the Least Significant Difference (LSD) post hoc test was applied to identify the differences between groups. A significant level of $P < 0.05$ was utilised in all statistical comparisons.

Results
Body Weight
Statistical comparison of body weight changes, as depicted in Table 1, revealed a significant increase ($P < 0.05$) in weight gain in Group T1, which received a high-fat diet containing 30% animal fat for 45 days, relative to the control group. However, no statistically significant difference ($P > 0.05$) was observed between Groups T1 and T2. On the other hand, Group T3 had a significant reduction in

weight gain ($P < 0.05$) when compared with T1 and T2. Moreover, Groups T4 and T5 also had significantly lower values of weight gain ($P < 0.05$) than Groups T1, T2, and T3. There was no significant difference ($P > 0.05$) significantly different between T4 and T5, and Group T5 also was not statistically different from the control group ($P > 0.05$). In general, Groups T1 through T4 all had a much greater weight gain compared to the control group ($P < 0.05$).

Concerning liver weight ratio, it was greatly decreased ($P < 0.05$) in Groups T1, T2, and T3 compared to the control. Group T5 possessed a much higher liver-to-body weight ratio ($P < 0.05$) than Groups T1, T2, and T3, but was not statistically different ($P > 0.05$) from the control and T4 groups. Relative kidney weight was reduced in all treated groups relative to the control ($P < 0.05$); however, the treated groups were not statistically distinct from each other ($P > 0.05$).

Table 1: Impact of Arabic Gum and L-Carnitine on weight gain and organ-to-body weight ratios in male albino rats with hyperlipidaemia

Group	Weight Gain (g)	Liver Weight (%)	Kidney Weight (%)
Control	2.8 ± 0.56^{d}	10.55 ± 0.39^{a}	1.30 ± 0.03^{a}
T1	52.5 ± 2.45^{a}	8.37 ± 0.67^{c}	0.975 ± 0.06^{b}
T2	48.7 ± 2.76^{a}	8.69 ± 0.59^{bc}	0.959 ± 0.10^{b}
T3	36.3 ± 1.78^{b}	8.67 ± 0.49^{bc}	0.888 ± 0.04^{b}
T4	27.5 ± 1.45^{c}	10.11 ± 0.06^{ab}	0.844 ± 0.01^{b}
T5	3.72 ± 0.68^{d}	10.47 ± 0.43^{a}	0.935 ± 0.09^{b}
LSD	5.910	1.480	0.205

Values are mean ± SEM. Small Different letters indicate significant differences at $P < 0.05$

Total Cholesterol Concentration

As evident in Table 2, Group T1 recorded a statistically significant rise ($P < 0.05$) in serum total cholesterol value than the control group. On the other hand, Groups T2 to T5 had significantly low cholesterol values compared to T1 ($P < 0.05$). Nevertheless, Groups T2, T3, and T4 still maintained higher cholesterol values than the control ($P < 0.05$). Unexpectedly, Group T5 did not differ significantly from the control group ($P > 0.05$). In addition, significant differences were observed within the treatment groups themselves (T2, T3, T4, and T5).

Table 2: Effect of Arabic Gum and L-Carnitine on serum cholesterol and triglyceride concentrations in hyperlipidaemic male albino rats

Group	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)
Control	79.93 ± 0.43^{e}	69.80 ± 0.60^{e}
T1	381.90 ± 14.5^{a}	163.45 ± 1.43^{a}
T2	215.21 ± 3.53^{c}	122.28 ± 1.03^{c}
T3	276.6 ± 3.28^{b}	138.96 ± 1.15^{b}
T4	180.17 ± 0.89^{d}	93.06 ± 1.21^{d}
T5	72.74 ± 0.66^{e}	61.87 ± 0.60^{f}
LSD	18.690	3.130

Values are mean ± SEM. Small Different letters indicate significant differences at $P < 0.05$

Triglyceride Concentration

Group T1 had a marked increase in serum triglyceride levels compared to the control ($P < 0.05$). Conversely, Groups T2, T3, T4, and T5 all had significant decreases in triglyceride levels compared to T1 ($P < 0.05$). Despite this decrease, the levels in T2, T3, and T4 remained significantly higher than those in the control group ($P < 0.05$). On the contrary, Group T5 experienced a significant decrease in triglyceride content when compared to the control ($P < 0.05$). Statistically significant differences were also obtained between treatment groups.

Leptin Hormone Level

As noted in Table 3, the level of serum leptin in Group T1 remarkably increased ($P < 0.05$) as compared to the control group. Leptin concentration was remarkably low in Groups T2, T3, T4, and T5 in comparison to T1 ($P < 0.05$). Despite the decrease, Groups T2, T3, and T4 still had significantly higher levels of leptin than the control ($P < 0.05$). On the contrary, there was no significant difference between Group T5 and the control group ($P > 0.05$). Furthermore, highly

statistically significant differences were evident between the various treatment groups.

Table 3: Effect of Arabic Gum and L-Carnitine on serum leptin and adiponectin levels in hyperlipidaemic male albino rats

Group	Leptin (ng/ml)	Adiponectin (µg/ml)
Control	6.36 ± 0.14^{e}	10.45 ± 0.16^{a}
T1	15.41 ± 0.57^{a}	3.46 ± 0.15^{f}
T2	8.66 ± 0.29^{c}	7.10 ± 0.06^{d}
T3	10.81 ± 0.34^{b}	6.51 ± 0.05^{e}
T4	7.50 ± 0.20^{d}	8.42 ± 0.12^{c}
T5	5.45 ± 0.21^{e}	9.27 ± 0.16^{b}
LSD	0.976	0.387

Values are mean ± SEM. Small Different letters indicate significant differences at P < 0.05

Adiponectin Hormone Concentration

Group T1 experienced a remarkable decline (P < 0.05) in serum adiponectin compared to the control group. Conversely, Groups T2 to T5 experienced significant increases in adiponectin content relative to T1 (P < 0.05). Despite the improvement that was noted, the adiponectin content of all treatment groups was significantly lower than in the control group (P < 0.05). Significant differences were also noted between all treatment groups.

Malondialdehyde (MDA) level

As observed in Table 4, Group T1 registered a significant elevation (P < 0.05) of malondialdehyde (MDA) level from the control group, reflecting increased lipid peroxidation due to the high-fat diet. On the contrary, Groups T2 to T5 recorded appreciably lower MDA levels relative to T1 (P < 0.05). Nevertheless, MDA levels in Groups T2, T3, and T4 remained significantly greater than in the control group (P < 0.05), whereas Group T5 was significantly reduced (P < 0.05), even below the control values. Statistically significant differences were observed in all treatment groups.

Table 4: Effect of Arabic Gum and L-Carnitine on oxidative stress markers and antioxidant enzymes in hyperlipidaemic male albino rats

Group	GSH (µmol/L)	MDA (µmol/L)	CAT (µmol/L)
Control	7.16 ± 0.23^{b}	2.59 ± 0.10^{e}	0.730 ± 0.01^{b}
T1	2.48 ± 0.07^{f}	5.81 ± 0.20^{a}	0.215 ± 0.009^{f}
T2	4.27 ± 0.08^{d}	3.64 ± 0.08^{c}	0.555 ± 0.01^{d}
T3	3.73 ± 0.08^{e}	4.71 ± 0.15^{b}	0.447 ± 0.01^{e}
T4	5.74 ± 0.04^{c}	3.17 ± 0.10^{d}	0.660 ± 0.004^{c}
T5	8.54 ± 0.20^{a}	2.10 ± 0.04^{f}	0.942 ± 0.02^{a}
LSD	0.417	0.375	0.049

Values are mean ± SEM. Small Different letters indicate significant differences at P < 0.05

Glutathione (GSH) and Catalase (CAT) Concentrations

As indicated by the data shown in Table 4, a significant decrease (P < 0.05) in catalase (CAT) and glutathione (GSH) levels was noted in Group T1 compared to the control, indicating compromised antioxidant defence. Treatment with Arabic gum (T2), L-carnitine (T3), and combined treatment (T4 and T5) caused significant increases (P < 0.05) in CAT and GSH levels when compared to T1. Though this was better, concentrations of Group T2, T3, and T4 remained significantly less compared to the control group (P < 0.05). Interestingly, Group T5 reported a marked increase in antioxidant markers, higher compared to controls (P < 0.05). Each of the treatment groups differed significantly from one another concerning antioxidant response.

Discussion

Body Weight

The findings presented in Table 1 suggest that the significant increase in body weight observed in the T1 group, which received a high-fat diet containing 30% animal fat, is likely due to the fat-rich content of the diet enhancing the animals' appetite for lipids blended into the feed (46, 47). Prior research has attributed similar weight gain to increased consumption of high-fat diets, leading to greater adipose tissue accumulation (48). Furthermore, it has been reported that high-fat content can improve the efficiency of intestinal fat absorption in

rodents, thereby promoting further weight gain (49). Another contributing factor may be the stimulation of bile secretion by high-fat diets, which enhances gastrointestinal efficiency and facilitates nutrient digestion (50).

Group T2, which received the high-fat diet in combination with Arabic gum supplementation, did not exhibit a significant difference in weight gain compared to group T1, a finding consistent with previous research (51, 52). Supporting this, another study reported that Arabic gum administration had no significant impact on triglyceride levels, suggesting limited influence on lipid metabolism in this context (49).

In contrast, group T3, treated with a high-fat diet alongside L-carnitine injections, demonstrated a significant reduction in weight gain relative to the hyperlipidaemic T1 group. These findings are in line with clinical data showing that L-carnitine administration can result in notable weight loss and a decrease in body mass index, reinforcing its potential role in weight management (53). The mechanism underlying this effect is largely attributed to L-carnitine's essential role in facilitating fatty acid oxidation, particularly in skeletal and cardiac muscles, by transporting long-chain fatty acids into the mitochondria where β-oxidation occurs (54, 55). L-carnitine also contributes to reactive oxygen species regulation, energy production, acetyl group buffering, and glucose metabolism (56, 57, 58). Moreover, its weight-reducing effect is linked to mechanisms such as improved insulin sensitivity and appetite suppression via direct action on the hypothalamus (59, 60, 61).

Group T4, treated with both Arabic gum and L-carnitine along with a high-fat diet, exhibited a greater reduction in weight gain than groups T2 and T3, indicating a synergistic effect. Group T5, which received the combined treatment alongside a standard diet, showed the most significant reduction compared to groups T1–T4.

A prior study explained that the reduction in kidney weight observed could be attributed to hyperlipidaemia's role in kidney disease progression. The accumulation of fat disrupts glomerular function, potentially leading to nephron damage and renal atrophy, ultimately reducing kidney weight (62). As for liver weight, the decrease could be due to fat accumulation, which stimulates oxidative stress and hepatic cell damage, resulting in hepatocyte loss and a decrease in liver mass (63, 64, 65, 66).

Total Cholesterol and Triglycerides

As illustrated in Table (2), administration of a high-fat diet resulted in a significant elevation in serum levels of total cholesterol, triglycerides, low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and the atherogenic index, alongside a notable reduction in high-density lipoprotein (HDL) levels compared to the control group. These observations are consistent with previous research findings (67, 68, 69). The increase in lipid profile parameters is likely due to oxidative stress induced by high-fat consumption, which leads to an overproduction of reactive oxygen species (ROS) (70). Additionally, high-fat diets are known to disrupt the normal transport and metabolism of cholesterol in the liver, contributing to dyslipidaemia and elevated serum cholesterol levels (71). Supporting this, a murine study demonstrated that feeding mice a high-fat diet caused increased levels of cholesterol, triglycerides, LDL, and VLDL, while simultaneously decreasing HDL. This effect was attributed to delayed gastric emptying and lipid buildup in the small intestine, both of which contribute to oxidative stress (72).

Furthermore, high-fat diets may enhance the activity of the rate-limiting enzyme in cholesterol biosynthesis, 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase), by stimulating the conversion of HMG-CoA into mevalonate, a key intermediate in the cholesterol synthesis pathway (73).

In group T2, treated with Arabic gum, a significant reduction in triglycerides and total cholesterol was observed. A previous study in rats fed aqueous Arabic gum solution showed reductions in total and LDL cholesterol due to decreased expression of hepatic HMG-CoA reductase mRNA (44). Arabic gum reduces lipid levels by binding bile acids, decreasing their absorption, and enhancing their excretion via fermentation-induced acidification in the colon (51).

Group T3, injected with L-carnitine, also exhibited lipid-lowering effects, consistent with prior studies (74, 75). The reduction in LDL and triglycerides was explained by L-carnitine's ability to redirect hepatic metabolism toward acetyl-carnitine formation rather than lipid synthesis, enhancing mitochondrial fatty acid oxidation (76). L-carnitine also modulates oxidative and nitrosative stress and supports mitochondrial respiration (77, 78).

Group T4, receiving combined treatment and a high-fat diet, showed better improvement in lipid profiles than groups T2 and T3, demonstrating a synergistic effect. Group T5, which received the combined treatment with a standard diet, showed

the most significant improvement, surpassing groups T2–T4.

Leptin and Adiponectin Hormones

The current study revealed elevated leptin and reduced adiponectin levels in the hyperlipidaemic group T1, aligning with findings from earlier studies (79, 80). The reduction in adiponectin was linked to increased expression of ALDH1A1, an enzyme involved in retinoic acid production, which activates RARs (retinoic acid receptors) and suppresses adiponectin gene expression (81). Additionally, the inflammatory response in adipose tissue, marked by elevated TNF-α, has been shown to downregulate adiponectin expression (82, 83).

Leptin resistance also plays a role in obesity, where increased SOCS-3 protein suppresses leptin signalling. High-fat diets induce leptin resistance by impairing the STAT3 pathway in the hypothalamus, further elevating leptin levels (84, 85).

Group T2, treated with Arabic gum, showed decreased leptin and increased adiponectin levels compared to T1. This agrees with prior studies (35), which attributed the effect to soluble dietary fibres improving gut microbiota and reducing inflammation, thus enhancing leptin sensitivity and decreasing leptin resistance (86, 87, 88, 89, 90). The adiponectin elevation may be due to prebiotic effects of Arabic gum fibres, promoting beneficial gut flora that reduce inflammation and stimulate adiponectin secretion (91, 92, 93). Increased intestinal viscosity also slows nutrient absorption and promotes satiety, thereby reducing leptin levels (94, 95).

Group T3, injected with L-carnitine, also showed significant reductions in leptin and elevations in adiponectin. These effects are linked to improved lipid metabolism and insulin sensitivity via mitochondrial fatty acid oxidation and Coenzyme A involvement in energy production (96, 97, 98).

Group T4, treated with both agents along with a high-fat diet, showed superior results compared to groups T2 and T3, confirming their synergistic effect. Group T5, treated with both agents under a standard diet, exhibited the most pronounced improvement in leptin reduction and adiponectin elevation.

Oxidative Stress Markers and Antioxidants

As indicated in Table 4, group T1 had significantly increased MDA and decreased GSH and CAT levels after three months of high-fat feeding, in agreement with previous findings (99, 100). This oxidative stress is attributed to excessive ROS production from cholesterol-rich diets and the activation of inflammatory cytokines such as PAF, which stimulates immune cells like neutrophils to produce more free radicals (101, 102, 103, 104, 105). Reduced CAT activity was also observed in group T1, consistent with prior studies showing that high-fat diets impair antioxidant enzyme function, altering membrane lipids and exacerbating oxidative stress (45, 105, 107). In contrast, group T2 showed increased GSH and CAT and decreased MDA levels. These effects are attributed to the phenolic compounds in Arabic gum that upregulate antioxidant enzymes like GPx and SOD (45, 106). The rise in GSH and CAT is consistent with Arabic gum's antioxidant properties (107, 108, 109).

Group T3 also showed improvements in oxidative markers, aligning with several studies (42, 43, 110, 111, 112, 113). L-carnitine supplementation increased antioxidant enzyme activity and suppressed microsomal peroxidation and free radical generation (43, 114, 115, 116).

Group T4, receiving both treatments along with a high-fat diet, showed better antioxidant status than groups T2 and T3, reflecting the synergistic action. Group T5, with both agents and a standard diet, showed the highest GSH and CAT levels and the lowest MDA levels among all groups.

Arabic gum and L-carnitine work together to support metabolic health by boosting the breakdown of fatty acids in the mitochondria, lowering oxidative stress, and influencing the gut microbiome. The prebiotic and antioxidant properties of Arabic gum complement L-carnitine's role in energy production. Their combined effects help restore hormonal balance, decrease inflammation, and improve the profile of adipokines in conditions characterised by diet-induced hyperlipidaemia.

The findings from our studies have some potential limitations. Extrapolating findings from rodent models to humans is inherently limited due to species-specific differences in metabolic processes. The study's small sample size, the exclusive use of male rats, and the lack of histopathological examination of the liver and kidneys constrain the broader applicability and depth of interpretation of the results. These limitations may result in overlooking sex-dependent variations and prevent confirmation of tissue-level effects induced by the interventions.

Conclusion

The findings of this study suggest that Arabic gum and L-carnitine possess significant protective effects against hyperlipidaemia-evoked metabolic disturbances. When administered alone, both substances changed lipid profiles, reduced

markers of oxidative stress, and controlled the levels of leptin and adiponectin. However, when combined, they produced more effective outcomes, suggesting a synergic influence in enhancing antioxidant protection and restoring hormonal balance. These results highlight the potential therapeutic effect of Arabic gum and L-carnitine, especially combined, as an adjunct treatment of obesity-related metabolic disorders.

Future investigations should include clinical trials involving human participants to establish the translational applicability of the findings, evaluate safety profiles, and assess the therapeutic effectiveness of interventions. Also, dose-response experiments are necessary to determine the most effective dosing regimens and to investigate the long-term impacts of Arabic gum and L-carnitine, both as standalone treatments and in combination, across various demographic groups.

List of Abbreviations

ANOVA: Analysis of Variance
ATP: Adenosine Triphosphate
BW: Body Weight
CAT: Catalase
CLIA: Chemiluminescent Immunoassay
ELISA: Enzyme-Linked Immunosorbent Assay
GA: Gum Arabic
GSH: Glutathione
HDL: High-Density Lipoprotein
HFD: High-Fat Diet
HMG-CoA: 3-Hydroxy-3-Methylglutaryl-Coenzyme A
LC: L-Carnitine
LDL: Low-Density Lipoprotein
LEP: Leptin
LSD: Least Significant Difference
mRNA: Messenger Ribonucleic Acid
MDA: Malondialdehyde
RARs: Retinoic Acid Receptors
ROS: Reactive Oxygen Species
SCFAs: Short-Chain Fatty Acids
SOCS-3: Suppressor of Cytokine Signalling 3
SPSS: Statistical Package for the Social Sciences
STAT3: Signal Transducer and Activator of Transcription 3
TNF-α: Tumour Necrosis Factor-alpha
VLDL: Very-Low-Density Lipoprotein

Declarations

Ethical approval and consent to participate

The study was approved by the Scientific and Ethical Committee of the College of Education, University of Al-Qadisiyah (No. 683). All procedures were in line with the Declaration of Helsinki. Informed consent was obtained, and confidentiality was maintained.

Consent for publication

All the authors consented to publishing the work under the Creative Commons Attribution-Non-Commercial 4.0 license.

Availability of data and materials

The data and materials associated with this research will be made available by the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Nil.

Authors' contributions

AMRH performed experimental work, data acquisition and analysis, and wrote the first draft of the manuscript as part of his MSc study. AEMM was responsible for the study supervision, guiding in study design and methods, as well as critical revision of the manuscript for intellectual content. The final version of the manuscript was read and approved by both authors.

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