

Original Research Article

Weight loss potential of Chia seeds as dietary supplement with Orlistat in an obese rat model

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Abstract

Purpose: To evaluate the biochemical impact of *Salvia hispanica* L. (chia seeds) as a dietary supplement when used alone or in combination with Orlistat (a weight-loss drug) in a rodent model of obesity.

Methods: Forty (40) male Wistar rats were divided into five groups, namely: control, which received standard diet, obesity group which was fed high-fat diet (HFD), chia seeds group which was fed HFD along with chia seed powder, Orlistat group which received HFD and Orlistat, and chia + Orlistat group which was fed HFD + chia seed powder + Orlistat. Body weight and feed intake were monitored over an eight week-trial period. Phytochemical analysis of chia seeds and biochemical analyses of serum lipid profile, liver function indices and inflammatory markers were performed.

Results: The occurrence of obesity in rats fed HFD was inferred from increases in body weight, when compared to control group ($p < 0.05$). The best weight reduction results were observed in chia + Orlistat group, thereby demonstrating synergistic effect when compared with the other treated groups. Chia + Orlistat group manifested significant decreases in body weight, triglycerides, LDL, and inflammatory markers (CRP, TNF- α , and IL-6), with minor increase in HDL. Chemical analysis revealed high levels of roughage ($34 \pm 2\%$), omega-3 fatty acids ($18 \pm 1.2\%$) and antioxidant activity ($72 \pm 3\%$) which were associated with the observed significant positive effects on weight, lipid profiles, and inflammatory response, when compared to HFD group ($p < 0.05$).

Conclusion: The combination of chia seeds with Orlistat may effectively contribute to reducing obesity, inflammation, lipid disorders, and the associated complementary effects on metabolic regulation. This synergy opens prospects for further clinical studies to confirm the findings and elucidate the associated mechanisms.

Keywords: Chia, Inflammation, Lipids, Orlistat, Obesity

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INTRODUCTION

One of the most prominent global health challenges in the 21st century is obesity. It causes multiple metabolic disorders such as insulin resistance, high triglyceride and LDL levels, as well as decreased HDL levels [1].

Orlistat is a popular and effective weight-loss drug that prevents digestion and absorption of approximately 30 % of dietary fats and inhibits gastric and pancreatic lipases, thereby improving lipid profiles and reducing calorie intake [2].

Orlistat is used as part of a therapy plan that involves reduction in calorie intake, a low-fat diet, and increased physical activity. Studies in animals and humans have shown that Orlistat lowers body weight and levels of triglycerides and LDL while moderately increasing HDL levels [3].

There is increasing interest in studying effective dietary supplements that may contribute to greater benefits in the treatment or enhanced prevention of metabolic complications related to obesity. Due to the fact that the seeds of *Salvia hispanica* L contain high percentages of soluble dietary fiber, plant Ω -3 fatty acids (especially α -linolenate), polyphenols, and natural antioxidants, they have been used as an effective dietary supplement [4,5]. These components form a theoretical basis for understanding potential effects of chia seeds on blood lipid levels and function. Studies in rodent models have shown that adding chia seeds to a high-fat diet improved biomarkers associated with lipids and inflammation [6].

Furthermore, chemical analysis of chia seeds revealed variability in contents of fiber, total lipids, protein, phenolics, and bioactive compounds. This supports the idea of evaluating the effect of chia seeds in a double-blind trial design that includes a comparison between a supplement and a drug [7,8].

Reviews and meta-analyses have established that chia seeds may be responsible for lowering levels of triglycerides and some cholesterol markers, despite conflicting results in human studies [9]. Therefore, combining chia seeds with Orlistat in an obese rat model represents a suitable experimental approach for studying the individual effects of the supplement and the drug, as well as testing for a synergistic interaction and changes in hematological and tissue markers (TC, LDL, HDL, TG, and inflammatory markers), in rats fed a high-fat diet. Thus, this study was done to fill a gap in the scientific literature by providing preliminary evidence on the effectiveness of a natural nutritional supplement as part of a multidimensional strategy for addressing obesity and lipid disorders. The research presents a comprehensive analysis that combines analytical chemistry, animal experiments, and integrative therapeutic use.

EXPERIMENTAL

Animals and design

The study was conducted in the Physiology and Biochemistry laboratory at the College of

Pharmacy, University of Thi-Qar, from February, 2025 to May, 2025. Forty (40) male Wistar rats with initial weights ranging from 150 – 170 g served as experimental animals. The animals were kept in well-ventilated plastic cages maintained at normal lighting status (12-hour light /12-hour dark cycle) at a mean temperature of 22 ± 2 °C, with *ad libitum* availability of drinking water and feed.

Following a 7-day acclimatization, the animals were arbitrarily assigned to five cohorts (8 rats per group). While group 1 (control group) was administered regular diet only, group 2 (obesity group) was fed an HFD (45 % fat) for 8 weeks, while group 3 (chia seed + HFD group) was fed an HFD containing chia seed powder (5 % of the diet). Group 4 (Orlistat + HFD group) was fed an HFD and Orlistat (a weight-loss drug) at a dose of 30 mg/kg orally daily, while group 5 (chia seed + Orlistat + HFD group) was fed an HFD containing Orlistat and 5 % chia at a dose of 30 mg/kg orally daily.

Treatment was continued for 8 weeks, during which daily feed consumption and weekly body weight were monitored.

Determination of the dose of Orlistat for rats

The dose of Orlistat for rats was determined based on the normal human dose (120 mg three times daily, equivalent to about 1.7 mg/kg/day for a 70-kg person). Using the interspecific conversion factor (6.2) based on the allometric scaling principle, the equivalent dose in rats was approximately 10.5 mg per kg daily, which was increased to 30 mg per kg daily to ensure a therapeutic effect in the obesity model while monitoring weight and side effects [10]. A gastric cannula was used to administer Orlistat orally, and the weight of each rat was determined daily in order to adjust the Orlistat dose and to ensure dosing accuracy and treatment consistency.

Preparation of chia seed extract

Chia seeds obtained from a store in Nasiriyah, Iraq, were thoroughly cleaned and then ground using an electric grinder to obtain a fine powder. The resultant powder was preserved in tightly sealed dark glass containers at 4 °C until use. For chemical analysis, 5 g of seed powder was weighed and extracted with 50 mL of 70 % ethanol for 24 h using a continuous shaker. The extract was filtered and subjected to the determination of total phenolic and flavonoid contents and antioxidant activity.

Determination of phytochemical contents of chia

The phytochemical properties of the seeds of chia were analyzed using standard methods. Moisture, ash, protein, and lipid contents were determined according to AOAC procedures: moisture was measured using oven drying to constant weight at 105 °C, ash was estimated by incineration at 550 °C, protein was determined via the Kjeldahl method, while lipids were measured using the Soxhlet extraction technique [11]. Total carbohydrates were calculated by difference by subtracting the contents of protein, fat, fiber, and ash. Fatty acids were identified through gas chromatography of lipid methyl esters, while phenolic compounds, along with antioxidant activity, were evaluated using the Folin-Ciocalteu assay and DPPH method, respectively [12]. All analyses were performed in three replicates to ensure accuracy and reliability.

Assessment of serum biomarkers

At the end of the study period, blood samples were collected from laboratory animals after a 12-h fast, and serum was separated for analysis of biomarkers such as lipids, glucose, total protein, albumin, liver enzymes, and inflammatory markers (CRP, TNF- α , and IL-6). Commercially available test kits were used according to the manufacturers' instructions to ensure the accuracy and reliability of the results.

Statistics

Data was analyzed using SPSS version 26. Results are expressed as mean $\pm$ standard deviation. Analysis of Variance test was used for group comparisons. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Chemical analysis data in Table 1 show that moisture content of chia seeds was approximately 6.5 %, while total fat was 30 %, protein was 20 %, and dietary fiber was 34 %. Additionally, there was a high level of total phenolic compounds (8,200 μ g GAE per g) and total flavonoid compounds (5,600 μ g QE per g), with a strong antioxidant potential of 72 %, when compared to DPPH, and an omega-3 fatty acid (ALA) content of approximately 18 %. The obese group showed a significant weight gain, when compared to control group, with the rat weight increasing from approximately 162 to 230 g after 8 weeks, a net gain of approximately 68 g (Table 2). In contrast, chia seed group showed a partial

reduction in weight, with a final weight of approximately 210 $\pm$ 7 g, representing a net gain of 49 g. The Orlistat group showed a greater reduction in weight, with a final weight of 200 g, which represents a net gain of 37 g.

Table 1: Data on chemical analysis of chia seeds

Component	Value
Moisture (%)	6.5 $\pm$ 0.3
Total fat (%)	30 $\pm$ 2.0
Protein (%)	20 $\pm$ 1.5
Dietary Fiber (%)	34 $\pm$ 2.0
Total phenolic compounds (mg GAE/g)	8.2 $\pm$ 0.5
Total flavonoids (mg QE/g)	5.6 $\pm$ 0.4
Antioxidant activity (% DPPH)	72 $\pm$ 3.0
Omega-3 acids (ALA, %)	18 $\pm$ 1.2

Table 2: Effect of chia seeds and orlistat on the weights of rats

Group	Initial weight (g)	Final weight (g) after 8 weeks	Net increase
Control (C)	160 $\pm$ 5	180 $\pm$ 6 ^{*c}	+20
HFD	162 $\pm$ 4	230 $\pm$ 8 ^{*a}	$\uparrow$ +68
HFD + Chia	161 $\pm$ 5	210 $\pm$ 7 ^{*b}	$\uparrow$ +49
HFD + Orlistat	163 $\pm$ 6	200 $\pm$ 5 ^{*b}	$\uparrow$ +37
HFD + Chia + Orlistat	162 $\pm$ 5	185 $\pm$ 6 ^{*c}	+23

Differences in superscript values mean statistical significance ($p < 0.05$)

Table 3 shows results for blood lipid profiles. High-fat diet (HFD) led to significant increases ($p < 0.05$) in total cholesterol, triglycerides, and LDL, while HDL was markedly decreased when compared to control group. Specifically, total cholesterol was increased from 85 mg/dL in control group to 150 mg/dL in the obesity group; triglycerides from 70 to 140 mg/dL, and LDL from 35 to 95 mg/dL, while HDL was decreased from 50 to 35 mg/dL. However, Chia seed consumption reversed these increases, with total cholesterol decreasing to 120 mg/dL, triglycerides to 110 mg/dL, and LDL to 70 mg/dL, while HDL was increased to 42 mg/dL. Orlistat alone reduced total cholesterol to 110 mg/dL, triglycerides to 95 mg/dL, and LDL to 60 mg/dL, while HDL was increased to 40 mg/dL. The best effect was seen in chia + Orlistat group, with reductions in total cholesterol levels approaching 90 mg/dL, triglycerides reaching 75 mg/dL, and LDL reaching 40 mg/dL, while HDL was raised to 48 mg/dL. These values were comparable to the corresponding levels in control group. The HFD feeding significantly increased fasting glucose (140 $\pm$ 12 mg/dL), ALT (70 $\pm$ 8 U/L), and AST (85 $\pm$ 10 U/L) while slightly reducing total protein (6.0 $\pm$ 0.4 g/dL) and albumin (3.4 $\pm$ 0.3 g/dL), when compared to control group. Supplementation with chia and Orlistat partially mitigated these

changes by lowering glucose to 120 ± 10 and 115 ± 9 mg/dL, respectively; ALT to 50 ± 6 and 55 ± 5 U/L, respectively, and AST to 60 ± 7 and 65 ± 6 U/L, respectively. Total protein levels showed no significant differences among the groups. In contrast, albumin levels varied significantly, with the HFD group having lower values (3.4 ± 0.3 g/dL) than control (3.8 ± 0.2 g/dL) and Chia + Orlistat groups (3.8 ± 0.2 g/dL, $p < 0.05$). Notably, the combination of chia and Orlistat almost restored all parameters to control levels, as shown in Table 4. Inflammatory markers (CRP, TNF- α and IL-6) were significantly elevated in the obese cohort, when compared to control group (Table 5): CRP was

approximately 4.8 mg/L in the obese group, relative to 1.2 mg/L in control group, TNF- α was increased from 15 to 45 pg/mL, and IL-6 rose from 12 to 38 pg/mL. Chia seed consumption partially mitigated these increases, with CRP reduced approximately to 3.2 mg/L, TNF- α to 30 pg/mL, and IL-6 to 25 pg/mL. Orlistat alone had a similar effect, while chia + Orlistat combination reduced these markers to approximately the same levels as control group (values for CRP, TNF- α , and IL-6 were 1.5 mg/L, 18 pg/mL, and 14 pg/mL, respectively).

Table 3: Effect of chia seeds and orlistat on blood lipoproteins (mg/100 mL)

Group	TC	TG	LDL	HDL
Control (C)	85 ± 5^c	70 ± 6^c	35 ± 4^c	50 ± 5^a
HFD	150 ± 8^a	140 ± 10^a	95 ± 7^a	35 ± 4^c
HFD + Chia	120 ± 7^b	110 ± 8^b	70 ± 6^b	42 ± 5^b
HFD + Orlistat	110 ± 6^b	95 ± 7^b	60 ± 5^b	40 ± 4^b
HFD + Chia + Orlistat	90 ± 5^c	75 ± 6^c	40 ± 4^c	48 ± 5^a

Differences in superscript values mean statistical significance ($p < 0.05$)

Table 4: Effect of chia seeds and orlistat on fasting glucose, liver enzymes and blood protein levels

Group	Fasting glucose (mg/dL)	ALT (U/L)	AST (U/L)	Total protein (g/dL)	Albumin (g/dL)
Control (C)	95 ± 5^c	35 ± 4^c	40 ± 5^c	6.5 ± 0.3^a	3.8 ± 0.2^a
HFD	140 ± 12^a	70 ± 8^a	85 ± 10^a	6.0 ± 0.4^a	3.4 ± 0.3^c
HFD+Chia	120 ± 10^b	50 ± 6^b	60 ± 7^b	6.3 ± 0.3^a	3.6 ± 0.2^b
HFD+Orlistat	115 ± 9^b	55 ± 5^b	65 ± 6^b	6.2 ± 0.3^a	3.5 ± 0.2^b
HFD+Chia+Orlistat	100 ± 8^c	40 ± 4^c	45 ± 5^c	6.5 ± 0.3^a	3.8 ± 0.2^a

Differences in superscript values mean statistical significance ($p < 0.05$)

Table 5: Influence of Orlistat and chia seeds on inflammatory markers

Group	CRP (mg/L)	TNF- α (pg/mL)	IL-6 (pg/mL)
Control (C)	1.2 ± 0.2^c	15 ± 2^c	12 ± 1^c
HFD	4.8 ± 0.4^a	45 ± 5^a	38 ± 4^a
HFD+Chia	3.2 ± 0.3^b	30 ± 3^b	25 ± 2^b
HFD+Orlistat	3.5 ± 0.4^b	32 ± 4^b	28 ± 3^b
HFD+Chia + Orlistat	1.5 ± 0.2^c	18 ± 2^c	14 ± 2^c

Values with different superscripts differ significantly ($p < 0.05$)

DISCUSSION

This study was aimed at evaluating the effects of chia seeds (*Salvia hispanica* L.) as a dietary supplement, either alone or in combination with the weight-loss drug (Orlistat), on body weight, blood lipid profiles, inflammation, and biochemical profiles in an obese rat model. Chemical analysis of chia seeds revealed high levels of dietary fiber, protein, beneficial fats, phenolic compounds, flavonoids and omega-3 fatty acids (ALA), which may explain the observed protective and therapeutic effects on obesity and lipid imbalances. Although some studies have shown that chia seeds reduced

weight and lipid profiles, better results were achieved when the seeds were combined with a balanced diet or medication [13]. The results of the study demonstrated that chia seeds effectively reduced weight gain when compared with the obese group, despite maintenance on an HFD. This is consistent with previous findings demonstrating that chia seeds have the capacity to reduce weight gain by increasing satiety and limiting calorie absorption [14]. This effect is attributable to the presence of soluble fiber and plant omega-3 fatty acids in chia seeds. Furthermore, the combination of chia seeds with Orlistat resulted in a greater reduction in weight gain.

Moreover, chia seed supplementation produced significant metabolic improvements in the obese rats. The reduction in body weight is consistent with the results in a study that demonstrated that chia promotes healthy regulation of adiposity by modulating lipid-handling enzymes and reducing visceral fat accumulation in diet-induced obesity models [15]. These results agree with findings in previous research [7,8]. These metabolic benefits seem to go beyond weight control by reflecting improvements in core biochemical processes altered by high-fat consumption.

Significant improvements in lipid profiles were noticed in chia and chia + Orlistat groups, such as reduction in total cholesterol, triglycerides, and LDL, along with increase in HDL, which agrees with previous reports. For instance, similar outcomes were seen in high-fat-fed and metabolic syndrome rat models fed with chia seed or chia seed flour and oil [16]. These outcomes are attributable to the high contents of alpha-linolenic acid and bioactive phytochemicals, which enhance lipid metabolism and reduce hepatic stress under obesogenic conditions.

High-fat diet (HFD) consumption led to significant imbalances in metabolic and hepatic parameters, such as increased fasting glucose levels and elevated liver enzymes, thereby indicating potential insulin resistance and hepatic stress [17]. Chia seed supplementation demonstrated beneficial effects on glucose tolerance and insulin signaling pathways, because of omega-3 fatty acid content and antioxidant properties [5]. Similarly, it has been reported that administration of Orlistat, a pancreatic lipase inhibitor, reduced liver fat content and improved liver function through mechanisms involving enhanced insulin sensitivity and decreased hepatic inflammation, particularly in patients with non-alcoholic fatty liver disease [18]. Notably, the combination of chia seeds and Orlistat produced a synergistic effect, which resulted in more pronounced improvements in glucose metabolism and liver function when compared to a single intervention.

Significant decreases in levels of C-reactive protein (CRP), tumor necrosis factor-alpha (TNF- α), and interleukin-6 (IL-6) were observed in the groups that took chia seeds, with a greater effect when the seeds were combined with medication, which is in tandem with the antioxidant and anti-inflammatory properties of the phenols and flavonoids in the seeds [19]. The reductions in inflammation marker levels in chia groups reinforce the hypothesis that phytochemicals in chia seeds possess potent anti-inflammatory properties. A study showed that chia mediated

down-regulation of NF- κ B and PPAR γ pathways, thereby reducing inflammation-driven metabolic disturbances [20].

Finally, chia seeds exerted multi-target metabolic modulation by improving lipid regulation and reducing oxidative and inflammatory stress. These mechanisms may encourage further evaluation of chia as a supportive dietary intervention for obesity and its complications.

CONCLUSION

The use of chia seeds as a dietary supplement effectively contributed to limiting weight gain, reducing TG and LDL, and decreasing inflammatory markers in an obese rat model. The combined use of chia seeds and Orlistat was the most effective, thereby demonstrating a synergistic effect. Data from chia seed chemical analysis support its vital role in the prevention and management of obesity-related metabolic disturbances. Therefore, more attention should be given to the strategy of combining natural nutritional supplements with weight-loss medications in the management of obesity and improvement of metabolic health.

DECLARATIONS

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Ethical approval

The ethical guidelines established by the College of Pharmacy, University of Thi-Qar, were adhered to during this study, under registration number IQR2025N140.

Conflict of interest

No conflict of interest is associated with this study.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Wafa S Abdulredha and Amena L Muttlaq planned the study design. Data collection, material preparation, and subsequent analysis were handled by Nuha S Falgoos and Amal H Anatheil. Wafa S Abdulredha prepared the initial

draft of the manuscript. The manuscript was reviewed by the authors and all authors approved its submission for publication.

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