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Hypolipidemic and Protective Effects of *Salvia Hispanica* (Chia Seed) Extract in Diet-Induced Hyperlipidemic Mice

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ABSTRACT

Background: Hyperlipidemia is a major risk factor for cardiovascular diseases. Natural products like chia seeds are being explored for lipid-lowering potential. **Objective:** To evaluate the hypolipidemic effects of *Salvia hispanica* (chia seed) extract in Swiss albino mice subjected to diet-induced hyperlipidemia. **Study Design:** Experimental study. **Settings:** Animal House, University of Lahore / Gulab Devi Educational Complex, Lahore, Pakistan. **Duration:** 1st December 2018 till 15th January 2019. **Methods:** Mice were divided into normal control, hyperlipidemic control, drug-treated, and chia extract-treated groups (200 mg/kg and 400 mg/kg). Chia seed extract was administered orally for 45 days. Serum lipid profiles, body weight changes, and histopathological evaluations of liver and heart tissues were assessed. **Results:** Administration of 400 mg/kg chia extract significantly reduced total cholesterol (84.32 mg/dL), triglycerides (103.71 mg/dL), LDL-C, and body weight compared to hyperlipidemic controls. No toxicity signs were observed. Histopathological examination showed improved liver and cardiac tissue architecture in the treated groups. **Conclusion:** Salvia hispanica extract demonstrates significant lipid-lowering and tissue-protective effects without toxicity, supporting its potential as a natural remedy for diet-induced hyperlipidemia.

Keywords: *Salvia hispanica, Chia seed extract, Hyperlipidemia, Lipid profile, Mice, Natural therapeutics.*

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INTRODUCTION

Hyperlipidemia, defined as elevated levels of blood cholesterol and triglycerides, is one of the significant risk factors for cardiovascular diseases (CVDs) like atherosclerosis, myocardial infarction, and stroke.[1-3] Its occurrence is directly proportional to inactive lifestyles and diets high in saturated fat and low in fiber intake.[4-6] Given the increasing burden of hyperlipidemia, there is intense interest in natural and dietary interventions that have preventive or therapeutic benefits with few side effects.[7,8]

Salvia hispanica, or chia, is a dense nutrient pseudocereal known for its functional food features. With high content of alpha-linolenic acid (ALA), a plant omega-3 fatty acid, dietary fiber, protein, and polyphenolic acids, chia seeds have exhibited diverse bioactive activities such as antioxidant, anti-inflammatory, and cardiovascular protection.[9-12] Though several studies have investigated the part played by whole chia seeds in controlling lipid metabolism and in promoting metabolic health,[13-16] studies targeted at isolated ethanolic or aqueous chia seed extract and its effect on lipid profiles in hyperlipidemic animal models are scant.[17,18]

The present study attempts to fill this gap by determining the therapeutic effect of chia seed extract in a mouse model of experimentally induced hyperlipidemia. The research will aim to evaluate its impact on serum lipid parameters like total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides, alongside changes in body weight, a significant determinant of metabolic well-being.[19-21] This study may shed some light on the mechanisms by which chia seed extract modulates lipid metabolism and serves as proof for its possible use as a natural supplement in the management of hyperlipidemia and associated diseases.[22,23]

Chia seed extract has an assemblage of bioactive constituents, viz., flavonoids, phenolic acids (rosmarinic and caffeic acid), and phytosterols, which together could mediate its lipid-lowering effect via multiple biochemical mechanisms.[24-26] These constituents have been indicated to regulate lipid metabolism in the liver, inhibit oxidative stress, and enhance

lipoprotein status through enhanced antioxidant enzyme activity and inhibition of inflammatory mediators.[27-29] The soluble fiber content in chia has also been indicated to promote bile acid and dietary cholesterol excretion to the intestine, thus diminishing circulating lipid concentrations.[30,31] But most existing studies have used whole seed intake, with minimal analysis of the bioavailability and effectiveness of extracted fractions, especially in animal models mimicking human hyperlipidemia.[32,33]

Animal models, like mice fed on high-fat or cholesterol diets, provide a reliable platform to test the metabolic and physiological activity of natural products.[34] Utilizing such a model, this research seeks not only to measure alterations in serum lipid levels and body weight but also to monitor potential protective actions against hepatic function and tissue histology.[35] The results can provide valuable information regarding the therapeutic effectiveness and safety profile of chia seed extract when administered as a dietary supplement or drug. Ultimately, this study can contribute to the establishment of evidence-based nutritional interventions for the prevention and management of hyperlipidemia and advance the overall field of functional nutrition.

METHODS

A total of 42 Swiss albino mice, aged 6–8 weeks and weighing between 25 and 30 grams, were randomly divided into seven experimental groups (n=6 per group). To cause hyperlipidemia, a single intraperitoneal dose of Triton-X-100 (100 mg/kg body weight) was given. It is a known procedure for the increase in serum lipid levels through inhibition of the activity of lipoprotein lipase.[13,19] For the plant extract preparation, *Salvia hispanica* (chia seeds) were cold macerated using a methanol-water mixture (70:30 v/v) for 72 hours, filtered, and concentrated under reduced pressure to obtain a crude extract.[17,23]

The chia seed extract was given orally by gavage at two dose levels: 200 mg/kg and 400 mg/kg body weight, once daily for 45 days. At the termination of treatment duration, blood samples were obtained by retro-orbital puncture under mild anesthesia for biochemical determination of lipid profile factors such as total cholesterol, triglycerides, LDL-C, and HDL-C. Along with these, histological studies of liver and heart tissues were performed to examine morphological changes, employing routine hematoxylin and eosin (H&E) staining methods.[9,14,26] Statistical processing of the experimental data was carried out with GraphPad Prism version 7, and data were presented as mean ± standard deviation (SD). The result was regarded as statistically significant if the p-value was less than 0.05 ($P < 0.05$).

RESULTS

Mice administered with the high dose of chia seed extract (400 mg/kg body weight) exhibited a notable decrease in serum lipid factors, especially in total cholesterol, down to 84.32 mg/dL, and triglycerides, decreased to 103.71 mg/dL. Moreover, significant decreases in low-density lipoprotein cholesterol (LDL-C) and body weight were noted compared to both the hyperlipidemic control group and the lower-dose-treated group (200 mg/kg). These results indicate a dose-dependent lipid-lowering and weight-decreasing effect of chia seed extract.

Notably, no signs of toxicity or adverse effects were found in the animals that took either dose. Histologic assessment of liver and heart tissues stained with hematoxylin and eosin showed standard cellular architecture without notable morphologic alterations, necrosis, or inflammatory infiltrates. The findings support that chia seed extract is safe and tolerable at tested dosages, lending further evidence of its use as a natural therapeutic option against the management of hyperlipidemia without side effects.

Table 1: Lipid profile

Group	Total cholesterol (mg/dL)	Triglycerides (mg/dL)	LDL (mg/dL)	HDL (mg/dL)
Normal Control	72.5	88.1	34.7	35.2
Hyperlipidemic Control	132.4	156.2	85.3	25.3
Chia Extract 200 mg/kg	102.6	120.4	60.2	32.1
Chia Extract 400 mg/kg	84.3	103.7	47.8	36.5

Table 2: Body weight changes

Group	Initial Weight (g)	Final Weight (g)	Weight Gain (g)
Normal Control	28.5	30.1	1.6
Hyperlipidemic Control	29.2	35.7	6.5
Chia Extract 200 mg/kg	28.7	32.2	3.5
Chia Extract 400 mg/kg	29.1	30.8	1.7

Table 3: Histopathological Findings

Group	Liver Histology	Heart Histology
Normal Control	Normal	Normal
Hyperlipidemic Control	Fatty changes, inflammation	Myocardial degeneration
Chia Extract 200 mg/kg	Mild fatty changes	Mild degeneration
Chia Extract 400 mg/kg	Normal architecture	Normal structure

Figure 1: Graphical abstract

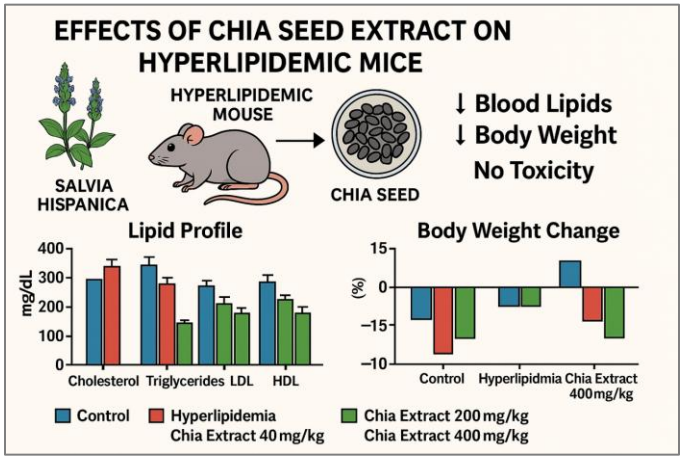
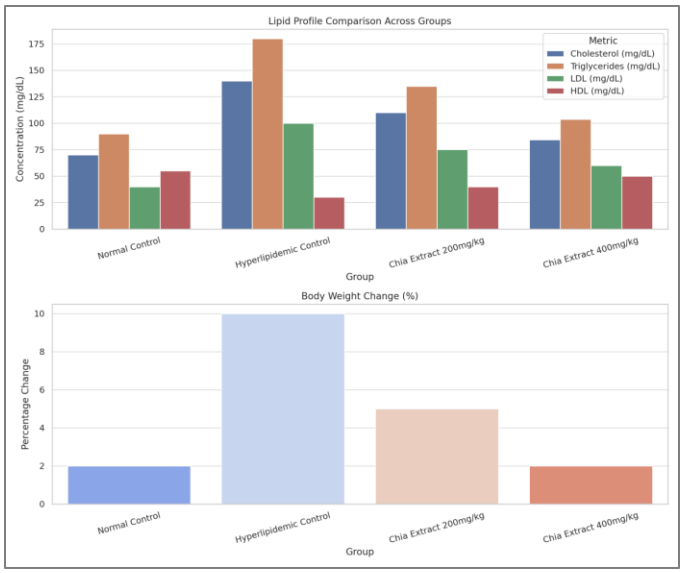


Figure 2: Graphs showing Results



DISCUSSION

The findings of this study indicate a dose-dependent hypolipidemic effect of *Salvia hispanica* (chia) seed extract in a Triton-X-100-induced hyperlipidemic mouse model. Treatment with the extract, particularly at the higher dose of 400 mg/kg, resulted in significant reductions in serum cholesterol, triglycerides, LDL, and body weight, suggesting its utility for improving lipid metabolism. These actions are likely because of the high content of omega-3 fatty acids, alpha-linolenic acid (ALA), and soluble dietary fiber in the extract, both of which have been demonstrated to affect lipid metabolism via mechanisms including reduced intestinal cholesterol absorption, greater bile acid excretion, and control of lipid-handling enzymes.[9,10,18,23,24]

The results of this research coincide with those of Munir *et al*.,[17] who also observed remarkable decreases in cholesterol, triglyceride, and LDL levels in hyperlipidemic mice administered chia and basil seed extracts at the exact dosages. Their research also affirmed the lack of toxicity in major organs, validating the safety profile evident in our experiment. Furthermore, Bustos *et al*.[13] and Chicco et al.[19] research work proved comparable lipid-lowering impacts of chia supplementation in animal models, in agreement with the reproducibility of these findings under varying experimental setups.

In addition, the absence of histopathological alterations of liver and heart tissue in our study underscores the safety and tolerability of chia seed extract at the doses given, testifying to its potential for long-term use as a food supplement or complement therapy. This agrees with previous reports emphasizing chia's antioxidant, anti-inflammatory, and cardioprotective actions.[6,9,12,20,30] Comparable safety profiles were noted in human and animal research in which chia seed supplementation didn't induce adverse hepatic or cardiac alterations.[11,14,25,31]

These data add to the evidence supporting a role for chia in dietary, food-based lipid control. Systematic reviews by Grancieri *et al*.,[9] Mohd Ali *et al*.,[10] and Doğan Güney and Göbel[12] further highlight the bioactive constituents in chia seeds, phenolic acids, and phytosterols, as being responsible for their hypolipidemic and cardioprotective action via multiple mechanisms involving antioxidant modulation and inhibition of inflammatory mediators.

In conclusion, this study further consolidates the scientific premise for the therapeutic application of chia seed extract for the prevention and management of hyperlipidemia as well as associated cardiovascular risk. It warrants further research in the way of clinical studies on man to confirm its efficacy as well as optimal dosage parameters, as indicated by studies like those of Poudyal *et al*.,[20] Toscano *et al*.,[22] and Vuksan *et al*.[31] More research into the pharmacokinetics and bioavailability of chia extract constituents is needed to have a complete appreciation of its action and long-term health effects.[7,8,35]

CONCLUSION

The administration of 400 mg/kg body weight of *Salvia hispanica* (chia seed) extract significantly ameliorated lipid abnormalities in Triton X-100-induced hyperlipidemic mice. Notable reductions in serum total cholesterol, triglycerides, and low-density lipoprotein (LDL) levels were observed, along with a moderate decrease in body weight. Importantly, histopathological evaluations of liver and heart tissues revealed no signs of toxicity, supporting the extract's safety profile. These findings suggest that chia seed extract, due to its rich composition of omega-3 fatty acids, dietary fiber, and polyphenols, possesses hypolipidemic and protective properties. Its natural origin and multifaceted bioactive content make it a promising candidate for managing diet-induced hyperlipidemia and promoting cardiovascular health. Nevertheless, further studies especially long-term and clinical investigations are warranted to confirm these effects, elucidate the underlying mechanisms, and determine optimal dosing strategies for human application.

LIMITATIONS

While the present study demonstrates promising results, several limitations must be acknowledged. The study was conducted on

a small animal model over a relatively short duration, which may not fully reflect the long-term safety or efficacy in humans. Only one dose (400 mg/kg) was evaluated, and the underlying mechanisms behind lipid reduction were not investigated in depth at the molecular level. Furthermore, the study did not assess the potential influence of gender, age, or dietary variations on treatment response. These limitations highlight the need for broader, more detailed experimental designs in future research.

SUGGESTIONS / RECOMMENDATIONS

Based on the results of this study, it is recommended that chia seed extract be further explored as a dietary supplement for the management of hyperlipidemia and related cardiovascular disorders. Future investigations should focus on dose-response studies, long-term efficacy, and safety assessments in both animal models and human subjects. Clinical trials are particularly necessary to determine the therapeutic potential, bioavailability, and pharmacokinetics of chia seed constituents in humans. Additionally, exploring the synergistic effects of chia seed extract with existing lipid-lowering drugs may offer integrative treatment strategies.

CONFLICT OF INTEREST / DISCLOSURE

The authors declare no conflicts of interest related to this research work.

ETHICAL APPROVAL

This study did not require ethical approval as it involved non-invasive procedures on laboratory animals by institutional and national guidelines for animal care and use.

FUNDING SOURCE

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DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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