Comparison of the effectiveness of chia seeds and Rosuvastatin in the modulation of lipid profile in fat-induced animal model

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Abstract:

Background: Various drug classes are available for the management of dyslipidemia but due to their toxicities the focus has been shifted to experiment herbal adjuvants to treat the condition. In this regard the current study evaluated and compared the alterations in lipid-profiles of fat-induced dyslipidemic rats when treated with chia seeds and rosuvastatin.

Methodology: It was a preclinical experimental study, conducted at Baqai medical University Karachi. Male Wistar albino rats of 9 weeks age, 200-250g weight were divided into 5 groups such as 6 rats per group. Coconut oil and Banaspati ghee were administered to induce dyslipidemia in animal groups (2, 3, 4, and 5) at the dose of 10ml/kg for 28 days and weight of animal was measured before and after the protocol. After the 28th day, intervention as per grouping of the animals was started for next 28 days, chia seed powder and rosuvastatin suspended in distilled water was administered via 20g feeding needle directly into the stomach of animals. After 8 weeks the animals were sacrificed under euthanasia (100mg/kg pentobarbital) and blood was withdrawn via cardiac puncture for evaluation of lipid profile of all animals.

Results: The paired analysis for weight displayed a significant ($p=<0.005$) increase in weight of animals after administration of high fat diet. Conversely, a significant decrease in weight was observed after administration of chia seeds powder and rosuvastatin in group 2, 3, 4, and 5. Further to this lipid profile of animals highlighted a significant ($p=<0.05$) increase in total cholesterol triglyceride and LDL level after induction of dyslipidemia however, HDL, Urea and Creatinine level remained non-significant. The anova highlighted that chia seed powder at 50mg and 100 mg dose reduced total cholesterol, triglyceride and LDL level equivalent to rosuvastatin (group 5) and did not alter the HDL, Urea and Creatinine.

Conclusion: Chia seeds at both the doses i.e. 50mg and 100mg decreased weight of animals and modulated hematological parameters equivalent to rosuvastatin.

Key Words: Chia seeds, rosuvastatin, dyslipidemia, Animal

Introduction:

Dyslipidemia is defined as high plasma levels of triglycerides (TG), increased levels of low-density lipoprotein cholesterol (LDLc) molecules, and decreased high-density lipoprotein cholesterol (HDLc) molecules (Găman et al., 2020). Continuous persistence of dyslipidemia is an established risk factor for cardiovascular diseases including coronary artery disease and peripheral artery disease, that may be fatal and can lead to heart attack or stroke (Levin and Rader, 2022). Various etiological factors predispose to dyslipidemia including a high-fat diet, obesity, and reduced physical activity. Adverse lifestyle changes play a major role in dyslipidemia's etiology and increase the complications related to dyslipidemia (Wajpeyi, 2020). Various drugs used to decrease lipid levels are statins, niacin, fibrates, and bile acid sequestrants (Rauf et al., 2022). While, statins are the most commonly used drugs for the treatment of dyslipidemia and to reduce the risk of atherosclerotic cardiovascular diseases (Hariyanto and Kurniawan, 2020). Statins act by inhibiting rate-limiting enzymes in the mevalonate pathway, that is β-hydroxy β-methylglutaryl-coenzyme (HMG-CoA), and by increasing LDLc clearance by promoting low-density lipoprotein receptor expression majorly in the hepatocytes (Mollazadeh et al., 2021). The licensed HMG-CoA reductase inhibitors include Atorvastatin, Rosuvastatin, Simvastatin, Fluvastatin, and Lovastatin (Hadi et al.). Statins being very effective lipid-lowering drugs also has multiple dose-limiting toxicities. Reported toxicities include haemorrhagic stroke, diabetes mellitus, cognition decline, tendon rupture and interstitial lung disease (Mo et al., 2019). Apart of adverse profile of statins, there is a wide range of drug interactions associated with statins (Hirota et al., 2020).

Despite having multiple drugs for the prevention of dyslipidemia, herbal medications are still preferred in various parts of the world (Ji et al., 2019). Herbal medications can be used as a adjunctive to standard drugs for increasing the efficacy of drugs and minimizing possible adverse effects (Gyawali et al., 2021). Chia seeds are edible seeds of an herbaceous plant *Salvia hispanica* which is a flowering plant belonging to the Lamiaceae family (Rubavathi et al., 2020). The *Salvia* genus consists of about 900 species that are widely distributed throughout several regions of the world, including South-East Asia, Southern Africa, Central America, North America, and South America (Grancieri et al., 2019). Over the recent years, the use of chia seeds has been significantly increased due to its various health promoting benefits related to chronic diseases such as obesity, cardiovascular diseases, diabetes, and cancer (Prathyusha et al., 2019). These health promoting effects of chia seeds are thought to be because of presence of various essential fatty acids, dietary fibers, proteins, antioxidants, vitamins, carotenoids, and minerals as bioactive constituents (Rani et al., 2021).

Pre-clinical experiments on hyperlipidemia are mostly studied on high-fat induced hyperlipidemia models (Acharya and Talahalli, 2019). In our study, we have evaluated and compared the alterations in lipid-profiles of fat-induced dyslipidemic rats when treated with chia seeds and an HMG-CoA reductase inhibitor, rosuvastatin.

Methodology:

It was a preclinical experimental study, conducted at Baqai medical University Karachi. The study was approved by the animal ethics committee of the university.

Animal grouping:

Male Wistar albino rats of 9 weeks age, 200-250g weight were purchased from the vendor. The animals were divided into 5 groups such as 6 rats per group as follows.

Group 1, negative control (No intervention),

Group 2, Positive Control (fat induction but no intervention),

Group 3, Administration of 50mg chia seed powder

Group 4, Administration of 100mg chia seed powder

Group 5, Administration of 5mg/kg rosuvastatin

Induction of Dyslipidemia:

Coconut oil and Banaspati ghee were administered to induce dyslipidemia in animal groups (2, 3, 4, and 5) at the dose of 10ml/kg for 28 days by 20g feeding needle orally and weight of animal was measured before and after the protocol by standard weight machine in grams (Zahid et al.). Coconut oil and Banaspati ghee were administered for only 28 days.

Protocol:

After the 28^{th} day, intervention as per grouping of the animals was started for next 28 days, chia seed powder and rosuvastatin suspended in distilled water was administered via 20g feeding needle directly into the stomach of animals. Furthermore, during the intervention the animals were given balanced healthy diet. After 8 weeks the animals were sacrificed under euthanasia (100mg/kg pentobarbital) and blood was withdrawn via cardiac puncture for evaluation of lipid profile of all animals.

Animal Consideration:

Animals were dealt according to CARE animal guidelines, they were given free access to food and water and a 12 hourly light and dark cycle was maintained.

Data analysis:

Numerical data was compared via SPSS v. 22, Shapiro wilk test was applied to check the normality of data. Paired t test was applied to identify pre and post intervention differences in weight. Anova followed by post-hoc Tukey test was applied to analyze inter and intra group variations. The data was analyzed at 95% confidence interval and p-value >0.05 was considered as significant.

Results:

The paired analysis for weight displayed a significant (p=<0.005) increase in weight of animals after administration of high fat diet (Coconut oil and Banaspati ghee). Conversely, a significant decrease in weight was observed in all intervened group (2, 3, 4, 5) Table 1 display the paired analysis of weight of animals.

Table 1. Paired t test analysis of weight of animal after (a) induction of dyslipidemia and (b) Intervention

Group (6 rats / group)	(a) Induction of Dyslipidemia (28 days)			(b) Intervention (28 days)		
	Before (wt in grams)	After (wt in grams)	p-value	Before (wt in grams)	After (wt in grams)	p-value
1	225 ± 10	231 ± 15	0.516	231 ± 15	247 ± 13	0.341
2	240 ± 8	318 ± 11	0.002*	318 ± 11	308 ± 17	0.172
3	237 ± 12	330 ± 18	0.015*	330 ± 18	267 ± 12	0.046*
4	259 ± 19	310 ± 15	0.003*	310 ± 15	230 ± 19	0.001*
5	213 ± 13	299 ± 10	0.009*	299 ± 10	242 ± 14	0.025*
*significant p value						

Further to this lipid profile of animals highlighted a significant (p=<0.05) increase in total cholesterol triglyceride and LDL level after induction of dyslipidemia however, HDL, Urea and Creatinine level remained non-significant. The anova highlighted that chia seed powder at 50mg and 100 mg dose reduced total cholesterol, triglyceride and LDL level equivalent to rosuvastatin (group 5) and did not alter the HDL, Urea and Creatinine as shown in table 2.

Table 2. Effects of intervention on hematological parameters

Hematological Parameter	Group 1 (Negative control)	Group 2 (Positive control)	Group 3 (50 mg chia seed powder)	Group 4 (100 mg chia seed powder)	Group 5 (5mg/kg rosuvastatin)	p-value
Total Cholesterol	131 ± 6.1	156 ± 10	142 ± 5.7	137 ± 6.1	139 ± 8.3	0.001*
Triglycerides	100 ± 10	130 ± 12	110 ± 3.1	102 ± 5.1	103 ± 2.8	0.001*
HDL	37.6 ± 4.1	39 ± 08	38 ± 1.9	39 ± 4.8	36 ± 5.7	0.519
LDL	90 ± 07.1	95 ± 07	94 ± 8.3	91 ± 5.2	90 ± 3.8	0.012*
Urea	19.31 ± 3.2	20 ± 3.7	18 ± 4.1	19 ± 5.2	20 ± 4.9	1.000
Creatinine	0.61 ± 0.23	0.58 ± 0.12	0.61 ± 0.41	0.57 ± 3.1	0.59 ± 0.21	0.918

Discussion:

The most common form of dyslipidemia is hyperlipidemia that is caused by defect in lipoprotein lipase activity as well as reported in dietary, environmental and genetic factors (Rauf et al., 2022). The characteristic raise in LDL cholesterol in hyperlipidemia is a major risk factor for well-known cardiovascular diseases (Lee et al., 2022) mainly atherosclerosis. Atherosclerosis is characterized by deposition of atherosclerotic plaque in the arterial walls that may partially or totally occlude the vascular lumen (Lee et al., 2022). In our study, we have compared the weight and lipid profile of animals before and after fat induction by administering high fat diet including coconut oil and banaspati ghee.

A significant increase in weight was observed in all the fat-induced groups. Various other studies have also reported increase in weight of the animals by inducing high-fat diet obesity (Liu et al., 2019, Moorthy et al., 2021, Li et al., 2020, Heo et al., 2021). Our results reported that the post-induction treatment with chia seeds and rosuvastatin have significantly reduced the total body weight of animals. A comparatively equal weight-reduction was observed in 50mg chia seeds group and 5mg/kg rosuvastatin group. While maximum reduction in the weight was observed in 100mg chia seed extract group. Similar results were observed in another study where a slight but significant decrease in body weight was recorded in rats (Fernández-Martínez et al., 2019). Contrary to our results a previous study has reported increase in body weight when treated with chia seeds extract (Mihafu et al., 2020). Additionally, another study reported an increase in body weight of diabetic-rats treated with black and white chia seeds extracts (Alamri, 2019). Similar to our results, a study has also reported dose-dependent weight loss by rosuvastatin (Al-Kuraishy and Al-Gareeb, 2019). Another study reported no significant difference in the final body weight of rats treated with 5mg/kg rosuvastatin alone, when compared with the control group (e Silva et al., 2020). Similar results were obtained from another study which reported a slight but significant reduction in body weight of rats after 14 days treatment with 10mg/kg rosuvastatin (Mondol et al., 2020).

Regarding the lipid profile parameters, our results showed a dose-dependent decrease in total cholesterol levels and a maximum reduction was observed in 100mg chia seeds powder group when compared with the positive control group. An equal reduction in total cholesterol level was also observed in 5mg/kg rosuvastatin group. A couple of other studies also reported the dose-dependent decline in total cholesterol levels when treated with chia seeds extracts (Aljumayi et al., 2022). Rosuvastatin has also reported a significant and dose-dependent decline total cholesterol levels (Al-Kuraishy and Al-Gareeb, 2019). Our study exhibited similar results when triglycerides were measured and a dose-dependent decline was observed in both 50mg and 100mg chia seeds powder groups when compared with the positive control group. The 5mg/kg rosuvastatin group showed equal reduction of triglycerides as of 100mg chia seeds powder group. A previous study reported a significant reduction in triglyceride levels in chia seeds treated group and related it with the inhibition of pancreatic lipase activity (Gómez-Velázquez et al., 2022). Similar results were reported from another study which showed a significant reduction in triglyceride levels when treated with chia seeds extract (Ali et al.). Regarding HDL levels, there was no significant decrease or increase in their levels when treated with 50mg and 100mg chia seeds powder. The rosuvastatin group also showed the same results as of chia seeds powder groups. Contrary to our results, a previously mentioned study has reported a significant dose-dependent increase in HDL levels when treated with chia seeds extract (Aljumayi et al., 2022). Another study reported maximum levels of HDL in chia seeds extract treated group (Veggi et al., 2021). Our results exhibited a slight but significant reduction in the LDL levels of both chia seeds powder groups and the rosuvastatin group. There was also no significant difference was observed in

urea and creatinine levels when chia seeds powder groups and rosuvastatin group were compared with the positive controls. Similar reduction in LDL levels was observed in a previously mentioned study when the chia seeds groups were compared with diabetic controls (Alamri, 2019). Another previous study reported similar LDL reduction in chia seeds extract groups but contrary to our results there was also a reduction in urea and creatinine levels (Z Mahfouz, 2020). Another previous study reported that the rosuvastatin treated group caused a significant decrease in LDL levels while no significant difference was observed In HDL levels (Al-Kuraishy and Al-Gareeb, 2019).

Conclusion: Chia seeds at both the doses i.e. 50mg and 100mg decreased weight of animals and modulated hematological parameters equivalent to rosuvastatin.

Ethical Approval: Study was approved by the ERC of University.

Conflict of interest: There was no any conflict of interest.

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