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Original Article

Effect of Dill Seed Cake on Dyslipidemia and Hormonal Imbalance against High Fructose-diet Induced Obesity in Rats

Ankita Awasthi[1], Bhaskar Kumar Gupta[1,*], Papiya Bigoniya[2]
[1]School of Pharmacy and Research, People's University, Bhopal, Madhya Pradesh, INDIA.
[2]DSKM College of Pharmacy, RKDF University, Bhopal, Madhya Pradesh, INDIA.

ABSTRACT

Background: The present study was investigated about the anti-obesity effect of dill seed cake on rats fed with high fructose diet. **Materials and Methods:** 45 days experimental study of high fructose diet feeding induced obesity, dyslipidaemia, hormonal imbalance, insulin insensitivity and increased atherogenic index. The control rat continued to receive either a control diet or high fructose diet, and the treatment groups were fed high fructose diet with 6 % of Dill Seed Cake and Dill seed Cake alone (8 %) and high fructose diet with orlistat (12mg/kg I.P.) for a period of 6 week. **Results:** In result treatment of Dill Seed Cake along with feed material decreased the weight gain, normalized the dyslipidemia, hyperlipidaemia and hormonal imbalance, and reduced the serum cholesterol level. Rats fed with high fructose diet supplemented with 8gm/kg of Dill seed Cake significantly reduced the metabolic disorder, hormonal imbalance and hypothyroidism. **Conclusion:** Intake of Dill Seed Cake supplementation can be adopted as a therapeutic strategy for the prevention of high fructose diet induced obesity complications in rat.

Key words: High fructose diet, *Dill Seed Cake*, Obesity, Dyslipidemia, Hormonal imbalance.

Correspondence

Dr. Bhaskar Kumar Gupta
School of Pharmacy and Research, People's University, Bhopal-462037, Madhya Pradesh, INDIA.

Email id: bhaskar.peoples@gmail.com

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INTRODUCTION

Obesity is an increasing, epidemic globally public health issue. More common causes of obesity are certain disease, lack of physical activity and sedentary lifestyle. Also, economic betterment and the influx of fast foods led to a rise in obesity as our per capita income improved the nutrition in a diet have fallen. Dietary component forms are very important cause a person who takes excess of carbohydrate and fat and less of protein they are at higher risk prone to obese.[1] Dietary fiber rich foods play valuable role in lowering of cholesterol, obesity and in management of hormonal imbalance where hypothyroidism changes body metabolism may cause severe obesity[1,2] In our study we use plant based dietary product *Dill seed* which is scientifically known as *Anethum graveolens* L. is the most common herbs very much useful in medicinal diseases with past times of applying as a remedy and spices in foods.

Dill seed cake is obtained from the plant *A. graveolens* (Family- Apiaceae). All segments of freshly plant including stem, leaves, seed and fruit are used in various medicinal productions. Beside many beneficial effects of *A. graveolens* including anti-cancer, anti-spasmodic, anti-hypolipidemic and anti-hypercholesterolemia. *Dill seed* and their by-products contain consequential soluble and insoluble fibre, amount after oil extraction left in the residue. Researcher suggested that *dill seed* may be useful in hormonal imbalance and reduce in complications of obesity. DSC seed contained dietary fibre, lignan and phenolic compound the residue left after oil extraction is known as *Dill Seed Cake (DSC)*, which is traditionally used as cattle feeding. Carvone, phellandrene and limonene are three main constituents present in dill essential oils.[3] Carvones are used in the food and flavor industry, Carvone and limonene has shown as suppressant effect against high-fat diet in obesity and anti-inflammatory effect.[4] Also *Dill seed* is useful in reduction of blood cholesterol, menstrual bleeding and dysmenorrheal effect and gastric changes in stomach.[5] In view the aim of Dill seed cake on major complications of obesity, the ongoing consumption of this herb against High fructose diet (HFrD) in rat model the authors determines the dill seed effect as anti-obesity agent with less side effects on body.

MATERIALS AND METHODS

Authentication and Collection of Dill Deed

Fresh *A. graveolens* seeds were purchased from the local market of Bhopal, M.P. These seeds were identified and authenticated by the experts (Dr. Saba Naaz) of taxonomy (Specimen no. 147/Bot. Saifia/Sci./College/Bpl. at the Herbarium department of Faculty of Saifia College, India.

Drugs and Chemicals

Fructose, casein, dextrose, cholesterol and methionine-DL were purchased from Fisher Scientific Chemicals Pvt. Ltd., India. Orlistat was generous gift from Aristo Pharmaceuticals Pvt Ltd, India, as capsules each capsule contains 120 mg. All other chemical reagents used in the study were of analytical grade.

Animals

Six week old laboratory bred wistar albino rats of either sex weighing between 200–450 g were selected for study and were acclimatized for 1 week before being randomly assigned into experimental groups. The animals were maintained according to guidelines given by Committee for the Purpose of Control and Supervision of the Experiments on Animals (CPCSEA). The experimental protocols were approved by the IAEC, PH/IAEC/VNS/2K21/24. The animals were housed in individual cages with free access to water in departmental animal house kept under controlled environmental conditions with 12 hr light/dark cycle at 22-24°C, relative humidity in the range of 40–50% and allowed to take water and food *ad*

libitum. During the acclimatization period, each animal were raised at regular diet *ad libitum*.

Preparation of Dill Seed Cake

Extraction of oil from multi oil seeds press machine the residue left after seed oil extraction is known as seed cake, which is traditionally used as cattle feeding. All other nutrition content was self prepared (Table 1).

Crude Extract

Dried and powdered DSC (10 g) was extracted with 200 ml of 90% ethanol for 18 hr in soxhlet extractor. The extract was filtered and concentrated using a vacuum evaporator (Jyoti Scientific, India). Weighed the residue and re-dissolved in 200 ml ethanol and stored in refrigeration for further analysis qualitatively for the presence *of* different phytochemicals.[6]

Extract Purification

30 gm of dried and powdered DSC sample was initially extracted with hexane (three times with a total of 500 ml of hexane) at room temperature. The defeated residue was washed with distilled water 3 times with a total of 500 ml of distilled water) for removing soluble sugars and proteins and dried less than 90°C. Purified residue (15gm) was extracted with 200 ml methanol for 16 hr in a soxhlet extractor. Filtered the extract, removed under vacuum to dryness, weighed and re-dissolved the residue in 100 ml of methanol to show lignin extract and phenolic compounds stored in refrigerator for further analysis.[7,8]

Isolated Lignin Authentication by HPLC Technique

The HPLC system (Waters) consisted of a pump (515), a U.V. Visible detector, a Thermo C_{18} (250 × 4.6 mm, 5µm) column, a Data Ace software, equipped with CAT-228- 39001-38 pump, 228-393000-38 photodiode array detector, and a rheodyne valve injection fitted with a 20 µl injection loop was used for the analysis. Chromatographic analysis of carvone and limonene in dill seed performed by using methanol: water (65:35v/v) solutions as mobile phase and used a flow rate of 1ml per min and absorbance at 220nm. It gave good separation of carvone at RT 6.099min. Dill seed extracts did not showed any peak at corresponding retention time of carvone (6.099 min.). (Figure 1b). The retention time of peaks was found to similar retention time of standard 6.100, which confirm the presence of carvone in dill seed extract. At 25 min, solution was sonicated was made with methanol and the final volume and mixture was then filtered with 0.45 µm filter. The stock solution was further diluted sufficiently with methanol to get sample solution of drug concentration of 10µg/mL. Sample volume of 20µl was injected and determines the retention time of carvone. The test solution was made by dissolving 200 mg substance examined in 90 ml of methanol, 10 µl were injected after filtered the solution. HPLC profile of Dill seed cake purified extract showing presence of Carvone (R*t* 6.099) and –limonene (8.462).[9]

Quantitative Determination of Dill Seed Cake

Dry Matter Determination

The dry matter was determined by oven drying with some modification at 103°C to constant Weight.[10]

Total Dietary Fiber Determination

Insoluble and soluble dietary fibres were determined by the following method described by[8] Dill seed sample (1 g) was digested with α-amylase (1 ml), protease (1 ml) and amyloglucosidase (3 ml) in a beaker, to remove, protein and starch with some modification. Heated (60°C, ph 6, 20 min) 95% ethanol was added and the solution was left precipitated at room temperature overnight. Digested samples were filtered, washed (with water, 95% ethanol and acetone), Crucibles containing residues from filtration was dried and weighed to determine the insoluble fiber.

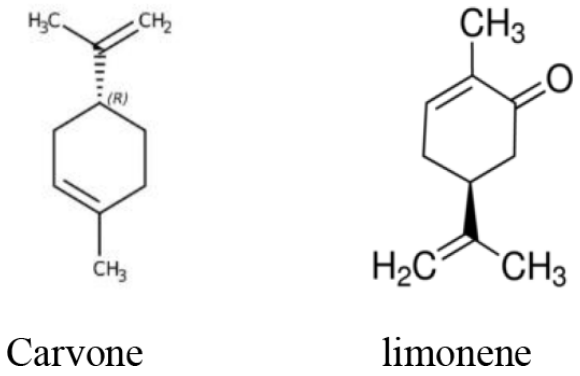

Figure 1a: Chemical structure of lignan.

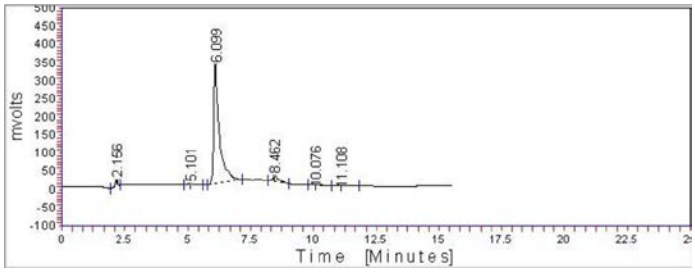

Figure 1b: Dill seed cake extract showing presence of carvone at (R_t 6.099min) and limonene at (R_t 8.462 min) in HPLC profile.

Table 1: Composition of experimental and high fructose containing diet.

CD	Quantity (gm/kg)	Experimental diet	Quantity (gm/kg)	High Fructose diet	Quantity (gm/kg)
Casein	200	Casein	100	Casein	200
Ghee	104	Ghee	104	Ghee	104
Corn flour	110	Corn flour	110	Corn flour	140
Dill seed cake	--	Dill seed cake	40	Dill seed cake	--
Vitamin	5	Vitamin	5	Vitamin	5
Mineral	15	Mineral	15	Mineral	15
Methionine-DL	3	Methionine-DL	3	Methionine-DL	3
Cholesterol	8	Cholesterol	8	Cholesterol	8
Dextrose	500	Dextrose	500	Fructose	500

The obtained values were corrected for ash and protein. 4 volumes of 90% ethanol (preheated to 60°C) were added for filtration and washing with water. Then, the precipitates were washed and filtered with 70% ethanol, 90% acetone and ethanol. After that, the (soluble fiber) residues were weighted and dried. To obtain insoluble dietary fibre and hence, soluble dietary fibre percentage the procedure was repeated.[11,12]

Total Phenolic Compound Estimation

Phenolic content was determined with some modification by Folin-Ciocalteu method by 10 mg Gallic acid was dissolved in 10 ml methanol, various aliquots of 5- 25µg/ml was prepared in methanol. Dried extract of 10mg (dill seed) was extracted and filter with 10 ml methanol. 2 ml of extract or standard was mixed with 1 ml of Folin-Ciocalteu reagent (previously diluted with distilled water 1:10 v/v) and 1 ml (7.5g/l) of sodium carbonate. The mixture was vortexes for 15s and allowed to stand for 15min at 40°C for color development. The absorbance was measured at 765 nm using a spectrophotometer. (Figure 2)[13]

Fat content: This was determined by soxhlet extraction with n-hexane for 9 hr at boiling point of the solvent (69°C). This extraction was carried out to estimate the content of oil.[14]

Experimental Design and Treatment

Animals were divided randomly into 5 groups containing 6 animals in each group. The experimental protocol was conducted in accordance with the internationally accepted principles for laboratory animal use and care as described by CPCSEA guideline after approval of IAEC, VNS Institute of Pharmacy, India. (778/PO/ReBi/S/03/CPCSEA). The control rat continued to receive either a control diet (CD) or high fructose diet (HFrD), and the treatment groups were fed a HFrD with 6g/kg of DSC for a period of 45 days. Orlistat was administered as a positive control with the High Fructose Diet at a dose of 12 mg/kg. CD, HFrD and DSC diet were own prepared and the nutritional content was same for all groups except carbohydrate content in HFrD (Table 1). CD, HFrD and DSC administered orally 8g/kg in the form of pellets while orlistat 12 (mg/kg) was given through I.P route to animals.[15] At starting of the experiment body weights and average food intake were recorded and measured at 7 days interval, for 45 days. Blood samples were collected at the end of the study, from the Retro-Orbital and the serum was separated after 30 min of stabilization by 3000 rpm centrifugation. Body total Cholesterol and triglyceride were measured using a kit (Scan lab. India) method based on an enzymatic colorimetric by[16] LDL-c concentration was followed by method[17] AI and HOMA-IR were calculated by the formula described by[18] The amount of protein was estimated by,[19] Bilirubin test was determined by using the Bilirubin (D&T) reagent kit provided by (Scan Laboratories, India). HDL-c was determined by kit Direct HDL Cholesterol, provided by (Scan Laboratories, India) based on the method.[20] Triiodothyronine, thyroxine, and thyroid stimulating hormone were determined using an (ELECSYS 1010 auto-analyzer (Thyrocare Lab, India). Liver and kidneys were isolated and store in ice cold saline, blotted and weighted. Initially one week CD to animals of all groups followed by 45 days feeding of the respective diet as per group division and drug treatment.

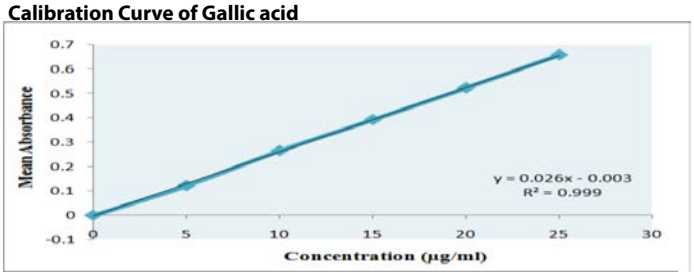

Figure 2: Total Phenolic content was calculated as Gallic acid equivalent mg/100mg using the equation based on the calibration curve: Y=0.026X- 0.003, R^2=0.999, where X is the BSA equivalent (BE) and Y is the absorbance.

Biochemical Assays

After 45 days of treatment, blood sample was collected fasting from retro-orbital puncture process under very light ether anesthesia. Biochemical investigations such as Thyroid test, ELECSYS 1010 auto-analyzer (Thyrocare Lab, India) lipid profile test, liver function test, Cholesterol test, and renal function test were carried out using commercial kits (Erba) with a fully automated clinical analyzer (ERBA-EM-200). Blood Glucose level was determined by using Accu-Chek glucometer from the orbital venous plexus at 0. (Path Vets Lab, India).

Statistical Analysis

All the data are presented as mean ± SEM. Students "*t*-test" was used for testing statistical significance between groups. Analysis of variance was used to test for differences between the groups, followed by 'Tukey's multiple comparison test. A (p) value $P < 0.05$ considered as statistically significant.

RESULTS

Quantitative Determination

Quantitative determination of *DSC* is presented in (Table 2). Chromatogram of HPLC showed the lignin presence like carvone amount present in dill is **(33**.2%-60%) and *limonene* (18%p-29.3%) with R_t (6.099) and *limonene* at (8.462) (Figures 1a and 1b).

Effect on Body Weight

Individual body weight gains were recorded before study imitation (Day 0), and weekly theremafter from the 1st week to the end of the study, a gradual increase in body weight was recorded in normal control group, whereas the rate of increase in body weight was much higher in the fructose control during study food consumptions were measured weekly per cage and mean food consumptions by individual rats were calculated. Fasting Blood Glucose levels were determined at the beginning of experiment, BG level in the HFrD rats increased rapidly due to fructose loaded diet (18%) at the termination of experiment DSC diet control BG level as compared to HFrD. The rate of increase in the body weight is depicted in (Table 3).

Effect on Liver and Kidney Organ Weight

Organ weight of rat for CD group was taken as normal values. The animals of the HFrD group showed a significant ($p < 0.05$) increase in weight of Liver and kidney. The results observed in the group that received the DSC (8 g/kg) significantly reduced weight of kidney ($p < 0.01$), respectively, as compared to HFrD+DSC diet while no significant changes showing

Table 2: Quantitative estimation of Dill seed cake.

Parameters	Quantity (mg/gm)
Total Fiber	33.37±0.210
%Dry Matter	84.36±0.238
Soluble Fiber	4.32±0.172
Insoluble Fiber	17.31±1.02
Fat	4.11±0.217
Phenolic Compound	138.23±0.367

Values are expressed in M ± SEM of three estimations

when compared to CD. As compared to the HFrD+orlistat diet, DSC (8mg/kg) treatment has moderately potent in reducing the weight of liver ($p < 0.05$). Figure 3(a) (b).

Biochemical Parameters Analysis

Plasma lipid levels in HFrD fed rats were significantly ($p < 0.05$–$p < 0.001$) increased compared to the levels in CD group (Table 4), HFrD+DSC (6gm/kg) group showed increased total cholesterol level, low-density lipoprotein (LDL), triglyceride, whereas high-density serum lipoprotein (HDL) level and total protein level, was noticeably decreased, these values appeared statistically significant when compared to control group ($P < 0.05$). Atherogenic Index by 110 fold and the insulin sensitivity resistance by 154 fold compared to those in CD group. The DSC (8 g/kg) treated groups showed significantly reduced levels of, TG ($p < 0.05$), LDL-c ($p < 0.001$), total cholesterol, ($p < 0.001$ and serum-insulin ($p < 0.01$), T3 ($p < 0.01$), TSH ($p < 0.001$), and T3/T4 ratio ($p < 0.001$) in comparison to the HFrD group. Liver function markers such as serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), and total bilirubin level in the HFrD and DSC diet group were decreased ($P < 0.05$), whereas total protein level showed a mild and statistically insignificant ($P > 0.05$) increase in HFrD group [Table 3]. The renal function markers such as serum

Table 3: Effects of Dill Seed Cake treatment and orlistat treatments on final body weight and food intake changes in rats fed high fructose diet.

Group Parameter	Control diet (CD)	Experimental diet (DSC diet)8g/kg	High Fructose diet (HFrD)	High Fructose + DSC diet (6g/kg)	High Fructose diet (HFRD) + Orlistat (12 mg/kg)
Initial Body Weight (g)	200.5	236.6	300.7	336.8	198.4
Final Body Weight (g)	210 ± 12	162 ± 13	340 ± 16	320 ± 18	160 ± 18
Food Intake (g/week)	187 ± 15	200 ± 15	210 ± 18	240 ± 19	190± 10

The weekly changes in body weight expressed in grams. All the values are means ± SD of n=6, individual observations. Significant at $p < 0.05$ with respect to normal control.

Liver Histology

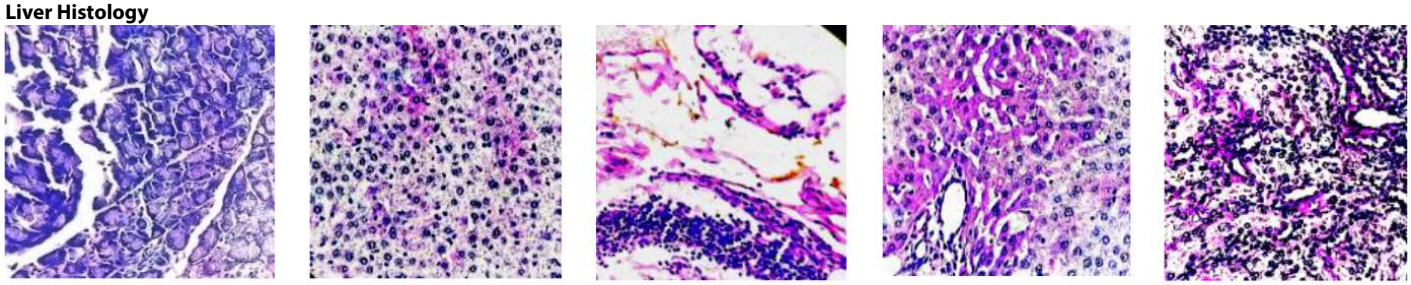

Figure 3 (a): Representative result images of histopathological changes in the Liver rats fed with high fructose diet. A. CD, B. DSC diet(8 gm/kg) C. HFrD D. HFrD+DSC (6gm/kg) E. HFrD + Orlistat (12mg/kg) for 6 weeks, A. Control group showed normal liver histology B. Std. Diet fed rats with no indication of metabolic dysfunction, no inflammation in liver, (p>0.005) C. Mild hepatic morphological changes, appearing as scattered inflammation in liver. D. Hepatocytes have some visible cytoplasmic fat vacuole. E. Both combinations shows–normal healthy liver (BD).

Kidney Histology

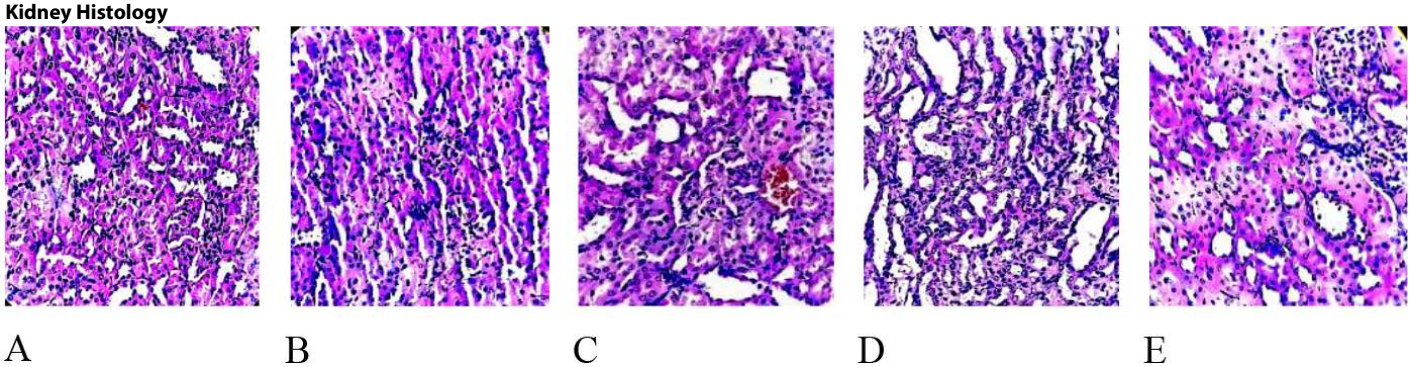

Figure 3 (b): Representative result images of histopathological changes in the Kidney in rats fed a high fructose diet: A. CD, B. DSC diet (8gm/kg) C. HFrD D. HFrD+DSC (6gm/kg) E. HFrD + Orlistat (12mg/kg) for 6 weeks, A. Control group showed healthy kidneys with normal glomeruli and tubules. B. Consumption of DSC 8gm/kg neither caused renal toxicity nor induced morphological changes in kidneys and observed normal cellular glomeruli. C. shows metabolic dysfunction-induced renal damage in red colour. D. fructose rich diet with dill extract showed some deposition of triglycerides was observed in both glomerular and tubular cells E. Orlistat shows normal weight of kidney Inhibit gastric and pancreatic lipase with proven efficacy in the augmentation and maintenance of renal function.

Table 4: Effect of *Dill seed cake* on the serum biochemical parameters of high fructose diet induced obese rats.

Group Parameter	Control diet (CD)	Experimental diet (DSC diet)	High Fructose diet (HFrD)	High Fructose + DSC diet	High Fructose diet (HFrD) + Orlistat (12 mg/kg)
Triglycerides (TG) (mg/dl)	108.40 ± 3.642	132.75 ± 9.050[b]	151.25 ± 5.114[b]	112.25 ± 7.510 [ns3]	92.50 ± 8.121 [ns3]
Total Cholesterol (TC) (mg/dl)	150.15±10.036	154.75 ± 9.020[c]	210.56 ± 5.189[c]	167.15 ±7.050[ns1]	116.95 ± 9.060 [ns1]
HDL-Cholesterol (HDL-C) mg/dl)	55.17 ± 2.032	54.01 ± 5.123[ns2]	60.00 ± 2.213[a]	56.10 ± 4.232[ns]	49.14 ± 2.128 [ns]
LDL-Cholesterol (LDL-C) (mg/dl)	74.67 ± 10.941	72.57 ± 7.709[ns1]	162.98 ± 6.216c	96.64 ± 5.739[ns1]	57.23 ± 9.123[ns1]
Total protein (mg/dl)	5.71±0.18	5.60±0.16 [ns2]	5.89±0.13 [c]	5.76±0.19[ns2]	4.99±0.13 [ns1]
Bilirubin (mg/dl)	0.01±0.0	0.02±0.01[ns1]	0.05±0.02[b]	0.04±0.03[ns1]	0.03±0.01 [ns1]
Blood urea nitrogen (BUN) (mmol/L)	11.27±1.01	11.17±1.02[ns1]	13.16±1.21[a]	14.20±1.20[ns3]	10.27±1.43[ns3]
Uric acid	1.06±0.04	1.09±0.03 [c]	2.82±0.54[a]	1.72±0.42[ns3]	1.03±0.22[ns3]
Creatinine	0.38±0.01	0.32±0.01 [a]	0.53±0.02[b]	0.68±0.02 [ns]	0.25±0.01 [ns]
SGOT	38±3.81	34±2.61[a]	151±21.75[c]	46±3.31 [ns2]	28±4.20 [ns2]
SGPT	32.15±1.83	44.32±1.93 [b]	109.83±30.14[b]	79.18±1.43 [ns2]	29.36±1.13[ns2]
ALP	108.83±30.14	105.63±19.13[c]	220.5±29.74 [a]	120.23±10.02[ns2]	114.23±20.04[ns2]
Leptin (nglml)	11.70±0.46	13.62±1.01[b]	49.74±2.49[c]	26.72±1.08[ns]	10.18±1.42[ns]
HOMA-Insulin Resistance	5.25	4.14 (+11.76%)	14.15 (+104.6%)	4.01 (+15.65%)	2.43 (-37.58%)
Atherogenic Index(AI)	1.67	3.07 (+24.00%)	5.13 (+108.2%)	2.71(+48.12%)	1.69 (23.38%)
T_3(ng/ml)	3.15 ± 1.22	3.25 ± 1.12[a]	4.18 ± 1.10 [a]	3.27 ± 1.38 [ns2]	3.67 ± 1.16 [ns3]
T_4 (µg/dl)	11.3 ± 14.1	10.2 ± 15.1 [c]	11.7± 1 8.5 [c]	10.5 ± 8.1 [ns2]	10.3 ±20.1 [ns1]
TSH (mlU/ml)	2.03 ± 1.18	2.07 ± 1.16 [c]	3.10 ± 1.20 [c]	2.43 ± 1.34 [ns3]	2.01 ± 1.08 [ns1]

Values are expressed in M ± SEM considering n = 6 animals. CD: control diet; HFrD: high fructose diet; DSC: Dill seed cake, The values in parenthesis signify percent change from the respective control (CD) values for each group.

ns – Not significant in case of both.

[a] $p < 0.001$ when compared to CD.

[b] $p < 0.01$ when compared to CD.

[c] $p < 0.05$ when compared to CD.

[1] $p < 0.001$ when compared to HFRD.

[2] $p < 0.01$ when compared to HFRD.

[3] $p < 0.05$ when compared to HFRD

creatinine and uric acid were elevated in HFrD rats and HFrD+DSC diet after compared to the control group ($P < 0.05$) and urea serum levels showed minimal and statistically insignificant increase. Here, T3 ($p < 0.01$), TSH ($p < 0.001$), and T3/T4 ratio ($p < 0.001$) were slightly higher in HFrD+DSC than DSC alone group. At the end of the experiment DSC (8 g/kg) treatment was moderately potent in reducing the biochemical parameters (19%) than orlistat (21%) as compared to HFrD and HFrD+DSC group. (Table 4).

Effect on Average Food Intake

In the last week of experiment, in HFrD group the average food intake (+8.12%) was slightly higher than the CD (-19.30%) and HFrD+Orlistat (- 28.18%) groups in the last 7 days of experiment duration, the average food intake of HFrD + DSC (6g/kg) groups was reduced by 5% in last week, DSC(8g/kg) alone was reduced by 20% as compared to other groups considering the last week value as the initial food consumption (Table 5).

DISCUSSION

Obesity has become a worldwide concern of imbalance between hypothyroidism, dyslipidaemia and hormonal imbalance and other complications like cholesterol, hypertension, cardiac arrest, cardiac hypertrophy, inflammation, atherosclerosis, etc. It is very serious human health problems and threats to health worldwide and is linked with serious complications and excessive medical expenses,[21] Rat models for diseases in human, such as obesity, diabetes, and obese related complications have been broadly used to find the prevention of the disease symptoms and possible treatment options with fewer side effects. The mostly used rat models studies for complications of obesity are those induced by hypercaloric diet. Dill seed extract consumption against HFrD diet shows effective reduction in lipid profile after 6 weeks experiment in rat. In this study after two weeks of hyper-caloric fructose supplementation HOMA-IR was increased.[22] The obesity associated with HFrD may be attributed to the hypothyroidism with elevated level of TSH and hypertriglyceridemia and also enhances in visceral adipose deposition

Table 5: Effect of *Dill seed cake* on the average food intake of high-fructose diet induced obesity in rat.

Groups		Average food intake per group in g/100 g of body wt.					
		1ST week	2nd week	3rd week	4th week	5th week	6th week
1	Control	11.29	10.16 (-10.08%)	8.56 (-24.18%)	10.53 (-6.81%)	8.98 (-20.46 %)	9.12 (-19.30%)
2	Experimental diet (DSC) 8gm/kg	10.46	9.65 (-7.74%)	10.87 (+3.10%)	11.36 (+8.74%)	8.69 (-16.10%)	8.16 (-21.98%)
3	HFrD(High Fructose Diet)	9.45	9.30 (-15.87%)	10.11 (+6.10%)	11.21 (+18.62%)	8.15 (-13.75%)	10.21 (+8.12%)
4	High Fructose + DSC diet (6gm/kg)	8.67	8.23 (-5.14%)	9.14 (+5.42%)	9.24 (+6.57%)	10.67 (+23.06%)	8.35 (-3.69%)
5	High Fructose diet (HFRD) + Orlistat (12 mg/kg)	8.80	8.34 (-5.37%)	7.34 (-16.59%)	8.21 (-6.70%)	6.32 (-28.18%)	6.21 (-18.43%)

Where, CD: control diet; HFrD: high fructose diet; DSC: *Dill seed cake*.

Values in parenthesis signify percent change compared to initial values that is average food intake in g up to 6th week.

and metabolic disturbances.[23] These metabolic disturbances commonly observed with high fructose feeding in both humans and animal models. Leptin, insulin resistance and elevated TG serum levels may promote food over consumption and contribute to the corresponding obesity. Forty five days of feeding of the experimental animals with HFrD had gradually developed a pre-cholesterol state associated with weight gain. HFrD along with DSC and DSC alone treated rats showed weight loss tendency, however, the body weight in DSC (8g/kg) treated rats were almost stable throughout the experiment.

Liver and kidney weights were reduced significantly through the administration of DSC (8g/kg) in comparison to HFrD, showing the prevention of fat deposition in adipose tissue and muscle. The dietary dill seed extract has been shown to possess hypolipidemic and enhance antioxidant activity in humans.[24] Administration of DSC extract for a period of 45 days repeatedly resulted in a significant decrease in the lipid profile in serum when compared to the HFrD group. The present investigation clearly demonstrates lipid level, thyroid level, and cholesterol lowering effects of DSC powder in obese rats. In this context, dietary fiber is rich in DSC powder and presence of phenolic compounds (lignans) could be important for cholesterol elimination.[25]

Dietary fiber lower or displace intestinal cholesterol and reduce the cholesterol absorption from the intestine.[26] Previous researchers investigated lipid-lowering activity (*in vitro*) of carvone as potential hypolipidemic agents. This fact could explain the high levels of LDL-c observed in HFrD rats the possible mechanism by which DSC brings about its anti-obesity action may be by the increasing of HDL level following administration of DSC to obese rats.[27] Studies finding that, cholesterol accumulation in adipose tissue that used in rat models and since that mostly obesity models use carbohydrates, fats and proteins to induce obesity, such as HFrD diet.[28] Major complication of obesity is high cholesterol, cardiac dysfunstion and hyperlipidaemia here findings suggested that insulin level is increased and lipid level is decreased in normal rats treated with DSC and orlistat.[29] In HFrD fed rats, DSC (6g/kg) caused a fall in HOMA-IR values, indicating improved insulin sensitivity. At the end of the last week of the experiments, finding suggested decrease in average food intake in the CD, DSC alone and HFrD with orlistat groups, whereas an Increase in the HFrD group and normal increase in HFrD + DSC group. Also, nutraceutical food shows inhibit effect of insulin released, increases leptin release and inhibit eating habits. Findings suggested that *Anethum Graveolens.* L inhibit food intake which helps in loss of appetite improves in weight loss and reduced plasma HDLc levels have been attributed to increased fractional clearance of HDL secondary to depletion of its cholesterol.[30]

Thyroid function is the major complication of obesity could be one of important factors acting in concert to determine individual body weight. Leptin produced by adipocytes has important influences on central regulation of thyroid function through stimulation of TRH.[31] The current study was specifically designed to evaluate whether fructose, when administered for a weight-maintenance diet, causes significant changes in biochemical parameters of blood lipid. Soluble fiber slows down stomach and small intestine, digestion, which helps to reduce the conversion of other carbohydrates into glucose, thus steady blood glucose levels.[32] Administration of orlistat, with high fructose diet showed significantly decreased the blood parameters as compared with HFrD.[33] The best effect is noticed in the DSC and orlistat group. These results indicate positive effects of HFrD and orlistat and DSC alone showed reduction in weight. The effect of DSC alone shows potential effect on obesity complications also extract improved the plasma lipid profile as compared to orlistat.

CONCLUSION

It could be conclude that high fructose diet cause obesity in rat showed elevated plasma lipid parameter, and body weight. *Dill seed cake (DSC)* alone exerts its effect by inhibiting LDL-c levels, pancreatic lipase and may reduce weight by suppressing appetite. There were many experimental studies in literature about fructose diet cause obesity and our studies defined the duration of treatment as 6 weeks, to detect biochemical changes in rat model. The above anti-obesity activity may be due to DSC and phenolic compound present in extract of dietary fiber and phytosterol may be beneficial as current evidence showed that DSC can regulate lipid profile, hypothyroidism, hyperthyroidism level and metabolic disorder in rat fed against high fructose rich diet. Further more studies are necessary to elucidate the medicinal mechanism of these effects.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

HFrD: High Fructose Diet; **DSC:** Dill Seed Cake; **HDL:** High Density lipoprotein; **SGOT:** serum glutamic oxaloacetic transaminase.

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