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RESEARCH ARTICLE

Protective Effects of *Fagonia cretica* L. Extract in Cafeteria Diet Induced Obesity in Wistar Rats

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Abstract

Obesity is one of the major life style disorders which may lead to undesirable effects on cholesterol, triglycerides, blood pressure and insulin resistance and eventually increases the risk of various adverse conditions like ischemic heart disease, stroke, coronary artery disease & type 2 diabetes. The present investigation was undertaken to explore protective effects of aerial parts of *Fagonia cretica* L. extract in cafeteria diet induced obesity in Wistar rats. Female Wistar rats were provided with cafeteria diet (CD) for the period of 10 weeks to induce obesity. *Fagonia cretica* L. methanolic extracts (200 & 400 mg/kg) & standard drug orlistat (30 mg/kg) were administered for last 6 weeks along with the continuation of CD. Various primary metabolic indicators of obesity like daily food consumption, body weight, lipid profile, fecal fat content & fat pads were studied. Administration of methanolic extract of *Fagonia cretica* L. significantly stopped increase in daily food consumption & body weight gain as compared to obese control group. Improvement in lipid profile was also observed in the all treatment groups rats as compared to obese control group rats. Obtained results validate that supplementation of *Fagonia cretica* L. methanolic extracts in obese rats resulted in significant protection against various indicators of obesity.

Keywords: Cafeteria Diet, *Fagonia cretica* L. Lipid Profile, Obesity

1. Introduction

Obesity is a cosmetic disorder described as proximal or immoderate fat accumulation in adipose tissue along with major indispensable organs like heart, liver & skeletal muscles. It is considered as a significant hazard factor to the wellbeing and prosperity of human beings[1]. In majority of cases drug treatment of obesity is related with bounce back weight increase after the suspension of medication admission, adverse effects caused by medicine and potential for sedate maltreatment[2].

Fagonia cretica L. (Zygophyllaceae) is a small vertical spiked undershrub with slim branches, terete striates, inadequately glandular puberulous growing annually mainly in north-west regions of India[3]. In traditional medicine, this plant is mentioned for anti-bilious, antiseptic and blood purifying actions. Internally, it is used in the form of decoction, as a gargle in stomatitis and other diseases of the mouth; externally its paste is applied to boils, wounds and scrofulous glands[4]. In Indo-Pak subcontinent region this plant is used for the treatment of typhoid, scabies, fever, asthma, urinary discharges, bronchitis, tumors, liver problems, piles and digestive disorders[5-6]. Preliminary phytochemical investigations revealed the presence of flavonoids, alkaloids, terpenoids, tannins, saponins, sterols, coumarins and glycosides in different extracts of powdered plant material[7-8]. Various *in vivo* and/or *in vitro* experiments showed a wide range of pharmacological actions of

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Fagonia cretica L. crude extracts like, anti-oxidant, anti-cancer, anti-inflammatory, hepatoprotective, anti-microbial and immunomodulatory activity[9-14]. According to Ayurvedic literature this plant has fat diminishing property[15]. However, till date there is no scientific proof demonstrating this activity, therefore current investigation was intended to demonstrate the protective effects of *Fagonia cretica* L. methanol extract on cafeteria diet-induced obesity in Wistar rats.

2. Materials & Methods

2.1 Collection, Identification & Authentication of Plant Material

Fagonia cretica L. aerial parts was collected from local market in Vadodara, Gujarat, India. Identification of sample was done by comparing its morphological characters described in various standard texts. Further authentication was done by botanist Dr. P K Patel, Head of Botany Department, Sheth P.T Arts & Science College, Godhra (Gujarat) bearing voucher specimen number PPDC/COG/2015/001. It was dried under sunlight for 2 days to minimize moisture content. Then it was powdered, passed through sieve 60# and stored at room temperature in airtight container until further use.

2.2 Methanol Extract Preparation

Powdered aerial parts of *Fagonia cretica* L. (1 kg) were extracted by using methanol (2.5 L) as a solvent by maceration method for 7 days. Contents were filtered by passing through filter paper. Dried marc was again extracted with methanol (2.5 L) by same method for 7 days. Both percolates were combined, concentrated and evaporated up to dryness.

2.3 Animals

Healthy Female Wistar rats were kept in clean polypropylene cages (3 rats /cage) and maintained under controlled room temperature (22 ± 2°C) and humidity (55 ± 5%) with 12 hours light and 12 hours dark cycle. They were provided normal pellet diet and water *ad libitum* before dietary manipulation. Study was performed according to the guidelines prescribed by the Committee for Purpose of Control & Supervision of Experiments on Animals (CPCSEA). The protocol for study was approved by the Animal Ethics Committee of Institute bearing protocol number OGECT/PPDC/IAEC/2018/15/2.

2.4 Cafeteria Diet Composition[16-17]

Female Wistar rats weighing about 220- 250 gm were selected for study. They were given a cafeteria diet for the period of 10 weeks for induction of obesity.

Cafeteria diet comprised of three eating regimens; (i) Condensed milk + bread + peanuts powder + pellet chow powder (3:2:3:2) (ii) Grated cheese + mashed potatoes (boiled) + chips + pellet chow powder (3:3:3:2) and (iii) Chocolate powder + biscuits powder + dried coconut + pellet chow powder (3:2:3:2). The three eating regimens were presented in the form of balls to the group of six rats on the day 1, 2 & 3 respectively following repetition for 10 weeks in similar progression.

2.5 Experimental Protocol

Total 30 rats were divided into 5 groups of six rats in each group.

Group I: Normal control rats were given standard chow diet and water *ad libitum* for 10 weeks & given orally 0.5% CMC once daily. **Group II:** Obese control rats were fed only cafeteria diet for 10 weeks for induction of obesity & given orally 0.5% CMC once daily. **Group III:** Standard drug Orlistat (30 mg/kg/day) suspended in 0.5% CMC was given orally to the rats for last six weeks along with cafeteria diet. **Group IV:** MEFC (200 mg/kg/day) suspended in 0.5% CMC was given orally to rats for last six weeks along with cafeteria diet. **Group V:** MEFC (400 mg/kg/day) suspended in 0.5% CMC was given orally to rats for last six weeks along with cafeteria diet.

The treatments were given daily in the morning by oral feeding tube. Body weights and food consumptions were recorded every day by using digital weighing balance.

2.5.1 Biochemical Parameters Estimation

On the last day of 10th week, blood sample was withdrawn through retro-orbital plexus of the rats under mild ether anesthesia. Lipid profile parameters like; Total Cholesterol (TC), Triglycerides (TG), Low Density Lipoprotein Cholesterol (LDL-C), High Density Lipoprotein Cholesterol (HDL-C), & Very Low-Density Lipoprotein Cholesterol (VLDL-C) levels were measured by standard commercial kits.

2.5.2 Fecal Fat Analysis

The fecal matter of animals was collected on last day and dried in hot air oven at 60°C temperature for 1 hour, followed by extraction of total fat contents in the 5 ml of solvent mixture of chloroform: methanol (2:1) for 30 min at 60°C temperature for 2 times. Both the solvent fractions were combined and evaporated to complete dryness. The fat analysis was done gravimetrically and calculated as % weight of dry fecal matter[18].

2.5.3 Fat Pad Study

On the last day of study, rats were sacrificed by excess of ether anesthesia. The perioverian White Adipose Tissue (WAT) and interscapular Brown Adipose Tissue (BAT) were removed from rat's body, rinsed with ice cold saline, weighed immediately and compared between groups.

2.6 Statistics

All the results were expressed as mean ± SEM. Analysis of obtained data was done by One Way ANOVA followed by Dunnett's test. Results were considered to be significant when value of $p<0.05$ or $p<0.001$.

3. Results

Total % yield of methanol extract of *Fagonia cretica* L. (MEFC) was found to be 4.87 % w/w.

3.1 Effect of Treatments on Body Weight Gain

10 weeks feeding with cafeteria diet induced obesity in normal rats. At the beginning of experiment mean body weights were almost same in all experimental groups. A significant increase in body weight gain was seen in rats of obese control group rats after 10 weeks, when compared with normal control group rats. Standard drug Orlistat (30 mg/kg) treatment once daily for last six weeks produced significant ($p<0.001$) reduction in the body weight gain when compared with obese control group rats. MEFC (200 & 400 mg/kg) treatment once daily for last six weeks, resulted in significant ($p<0.001$) reduction in body weight gain when compared with obese control group rats (Table 1).

3.2 Effect of Treatment on Food Consumption

Daily food consumption was recorded in all the group's animals for 10 weeks treatment period. In obese control group rats significant increase ($P<0.001$) in daily food consumption was seen as compared to normal control group rats. MEFC (200 & 400 mg/kg) treatment reduced food consumption considerably as compared to obese control group rats ($P<0.001$). Treatment with orlistat (30mg/kg) also produced a significant ($P<0.001$) reduction in food consumption (Table 1).

Table 1. Effects of Treatment on Body Weight Gain & Food Consumption

Groups	Body Weight (g) (Last Day)	Average Daily Food Consumption (g/group)
Normal control	275.18 ± 4.68	133.48 ± 0.55
Obese control	371.53 ± 3.40$^{a\#}$	162.64 ± 1.50$^{a\#}$
Orlistat	278.68 ± 2.51$^{b\#}$	124.91 ± 1.43$^{b\#}$
MEFC 200	291.70 ± 3.72$^{b\#}$	131.01 ± 1.27$^{b\#}$
MEFC400	283.47 ± 2.47$^{b\#}$	126.37 ± 1.57$^{b\#}$

Values are expressed as mean ± SEM, n = 6, * $p < 0.05$ statistically significant
# $p < 0.001$ statistically significant
a: compared to normal control group
b: compared to disease control group

3.3 Effect of Treatment on Biochemical Parameters

Lipid profile analysis of all experimental animals was done on last day of study. The obese control group which was fed with only cafeteria diet for all 10 weeks, showed statistically significant ($p<0.001$) elevated levels of total cholesterol

(TC), triglycerides (TG), low density lipoprotein (LDL), very low density lipoprotein (VLDL) and significantly lowered levels of high density lipoprotein (HDL) as compared to normal control group rats. MEFC (200 & 400 mg/kg) treatment for last 6 weeks significantly lowered the levels of TC, TG, VLDL, LDL and significantly increased levels of HDL-cholesterol as compared to obese control animals. Similar results were seen in orlistat treated group (Table 2).

3.4 Fecal Fat Analysis

The amount of total fats excretion in the fecal matter was significantly ($p<0.001$) lowered in rats of obese control group which were fed with cafeteria diet for 10 weeks as compared to normal control group rats. MEFC (200 and 400 mg/kg) and orlistat treatment for last 6 weeks showed significantly higher fat content excretion in fecal matter as compared to obese control group (Table 3).

3.5 Fat Pad Analysis

In the group of rats which were kept on CD (obese control) for all 10 weeks, there was higher significant ($p<0.001$) deposition of perioverian and interscapular fat tissues. MEFC (400 mg/kg) and standard orlistat treatment resulted in significant ($p<0.001$) reduction in deposition of the perioverian (Visceral WAT) and interscapular (BAT) fat mass when compared with obese control group rats. Thus, MEFC showed protective effect in increased adipose tissue (Table 3).

4. Discussion

Obesity is now a days increasing in developing countries; predominantly in urban areas. It is now considered as a chronic disease that is reaching epidemic proportions in the developed world[19]. Cafeteria diet is moderately a vigorous option to induce constant hyperphagia and increased energy consumption which in turn leads to

Table 2. Effects of Treatment on Biochemical Parameters

Groups	TC (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)
Normal control	120.95± 7.55	53.37± 4.99	52.90± 3.60	33.15± 3.57	10.67±0.99
Obese control	189.22 ±9.31$^{a\#}$	173.25±7.07$^{a\#}$	35.10± 4.18$^{a\#}$	96.29± 5.36$^{a\#}$	34.65 ±1.41$^{a\#}$
Orlistat	124.42±5.77$^{b\#}$	80.28±5.53$^{b\#}$	63.18 ±4.43$^{b\#}$	41.94 ±4.94$^{b\#}$	16.05 ±1.10$^{b\#}$
MEFC 200	136.11± 6.96$^{b\#}$	87.81±7.01$^{b\#}$	52.35±7.12 $^{b\#}$	57.07 ±6.20^{b*}	17.56 ±1.40$^{b\#}$
MEFC400	129.19±7.13$^{b\#}$	77.84±7.13$^{b\#}$	65.26 ±7.91$^{b\#}$	46.40 ±4.87$^{b\#}$	15.56 ±1.43$^{b\#}$

Values are expressed as mean ± SEM, n = 6, * $p < 0.05$ statistically significant
\# $p < 0.001$ statistically significant
a: compared to normal control group
b: compared to disease control group

Table 3. Effect of Treatment on Fecal Fat Content & Fat Pad Weight

Groups	Fecal Fat Content (%)	Perioverian Fat (g)	Interscapular Fat (g)
Normal control	3.36 ± 0.38	2.71 ± 0.51	0.56 ± 0.06
Obese control	4.74 ± 0.51^{a*}	8.20 ± 0.75$^{a\#}$	1.59 ± 0.18$^{a\#}$
Orlistat	6.70 ± 0.39$^{b\#}$	3.80 ± 0.43$^{b\#}$	0.64 ± 0.11$^{b\#}$
MEFC 200	6.43 ± 0.47$^{b\#}$	5.43 ± 0.69$^{b\#}$	0.77 ± 0.02
MEFC400	7.45 ± 0.77$^{b\#}$	4.20 ± 0.48$^{b\#}$	0.72 ± 0.03^{b*}

Values are expressed as mean ± SEM, n = 6, * $p < 0.05$ statistically significant
\# $p < 0.001$ statistically significant
a: compared to normal control group
b: compared to disease control group

obesity in experimental rats similar to human beings[20]. In addition, CD provides a considerable intake of sugar and salt, which raises the appetite[21]. Maceration method of extraction was used for the preparation of methanol extract of *Fagonia cretica* L. Cafeteria diet was provided to rats to induce obesity for 10 weeks and treatment by standard drug orlistat and MEFC started by the end of 4th week along with cafeteria diet. Results obtained in our experiment indicated that rats fed with only cafeteria diet for 10 weeks provoked significant increase in body weight gain, food consumption, total cholesterol, triglycerides, LDL-cholesterol and VLDL-cholesterol along with correspondent increase in fat pad weights. MEFC treatment for last 6 weeks showed significant reduction in body weight gain in CD fed rats signifying that MEFC possess weight reducing action. MEFC treatment for last 6 weeks resulted in significant reduction in levels of total-cholesterol, triglycerides, LDL-cholesterol and VLDL-cholesterol along with significant increase in HDL-cholesterol levels in CD fed rats. Treatment with MEFC also caused significant decrease in weight of white adipose tissue (WAT) as well as brown adipose tissue (BAT) in CD fed rats, suggesting that MEFC reduces adipose tissue weight in rats. Increased amount of fat excretion in fecal matter was seen in the rats treated with MEFC indicating inhibition of fat metabolizing enzymes. The present study indicates MEFC has significant reduction in daily food consumption, body weight gain and fat pads weight along with improved lipid profile and increased fecal fat excretion. These positive results may be due to higher saponins and flavonoids contents in this plant. Further more studies are required to find out mechanism of the chemical constituent/s responsible for anti-obesity action.

5. Conclusion

The present study indicates that methanol extract of *Fagonia cretica* L. showed significant protection towards various obesity indicators in cafeteria diet induced obesity in Wistar rats. Any prior report on protective effects of *Fagonia cretica* L. in obesity has not been reported so far. The current investigation has shown positive result that *Fagonia cretica* L. methanol extract shows weight reduction in rats and exhibits anti-obesity activity.

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7. Conflicts of Interests

None.

8. References

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