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## Regulation of Obesity and Lipid Disorders by *Foeniculum vulgare* Extracts and *Plantago ovata* in High-fat Diet-induced Obese Rats

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### ABSTRACT

Obesity is a condition in which excess body fat is accumulated to an extent that health may be negatively affected and in spite of the number of studies to prevent or treat obesity, its prevalence continues to rise in developed as well as in developing countries. It has become one of the most serious public health challenges of the 21st century. The current study was undertaken to evaluate efficacy of *Foeniculum vulgare* (fennel) methanolic, aqueous and oil extracts and *Plantago ovata* (*Plantago*) seeds-supplemented diet in management of obesity in high fat diet-fed rats. Adult female sprague Dawley rats were classified into six groups. The first group was kept on standard rodent chow for 24 weeks (lean control). The other groups received high fat diet for 24 weeks. These animals were assigned as obese control group, fennel methanolic extract-treated group, fennel aqueous extract-treated group, fennel oil extract-treated group and *Plantago* seeds-treated group. The results revealed significant increase in thoracic (TC) and abdominal (AC) circumferences and Body Mass Index (BMI) in obese rats. Dyslipidemia, hyperinsulinemia, hyperglycemia and hyperleptinemia have been demonstrated in obese rats. Serum malondialdehyde (MDA) level significantly increased in obese rats compared with control rats. Treatment with fennel extracts or *Plantago* seeds reduced food intake and BMI as well as ameliorated the dyslipidemia, hyperinsulinemia and hyperglycemia in obese rats. Serum leptin level showed significant improvement in obese rats due to treatment with fennel methanolic ( $p < 0.01$ ), aqueous ( $p < 0.05$ ) and oil ( $p < 0.05$ ) extracts or *Plantago* seeds ( $p < 0.05$ ). Significant inhibition ( $p < 0.01$ ) in serum MDA level was detected as a consequence of treatment with either fennel extracts or *Plantago* seeds in obese rats. In conclusion, the data of the current study confirms the anti-obesity effect of fennel extracts, particularly, methanolic extract and *Plantago* seeds supplemented diet. Thus, present findings reinforce the advice recommending consumption of natural products and/or diets with a high fiber content to modulate obesity and its metabolic complications.

**Key words:** Obesity, *Foeniculum vulgare*, *Plantago ovata*, hypolipidemic, antioxidant, antiinflammatory, rats

### INTRODUCTION

Obesity is the result of an energy imbalance caused by an increased ratio of caloric intake to energy expenditure. In spite of the number of studies to prevent or treat obesity, its prevalence

continues to rise and it has become one of the major threats to health throughout the world (Lopez-Jimenez and Cortes-Bergoderi, 2011). In fact, the dysregulated energy homeostasis stems from a societal reduction in physical activity, energy-dense foods, combined with a myriad of genetic, social and economic complicating factors (Mitchell *et al.*, 2005). High fat diet is certainly of importance to obesity incidence and to its negative consequences such as type II diabetes (Samaras and Campbell, 2000), dyslipidemia (Novelli *et al.*, 2007), cardiovascular disease (Diniz *et al.*, 2005), aging (Hart *et al.*, 1999) and cancer (Bianchini *et al.*, 2002). Adipose tissue has been considered as a highly specialized, endocrine and paracrine organ producing an array of mediators called adipokines. One of the most important adipokines is leptin which significantly correlates with the amount of fat tissue in humans and animals (Maffei *et al.*, 1995). Ordinary, leptin functions to reduce food intake and maintain energy homeostasis but in obesity, the development of a state of leptin resistance results in a dysfunctional energetic state (Sahu, 2004).

Oxidative stress was found to be associated with obesity. There is a growing awareness that obesity is a prime risk factor for the development of dyslipidemic profile and that oxidative stress may play a role in various adverse effects of obesity (Diniz *et al.*, 2005). Pharmacologic therapy used for the treatment of obesity is formulated to reduce energy intake or increase energy output (Fujioka, 2002). However, the effectiveness and tolerableness of these medications are limited because they have well recognized potential side effects (Sindler, 2001). American Association of Clinical Endocrinologists reported that natural therapies for obesity may be beneficial but studies were needed to prove their safety and efficacy (AAACE/ACE obesity Task Force, 1998).

*Foeniculum vulgare* (Fennel) fruits and their essential oil are used as flavoring agents in food products such as liqueurs, bread, pickles, pastries and cheese. They are also used as a constituent of cosmetic and pharmaceutical products (Piccaglia and Marotti, 2001). The anti-inflammatory and antioxidant activities of fennel have been reported (Choi and Hwang, 2004). There are three species of *Plantago*, *Plantago ovata*, *Plantago psyllium* and *Plantago indica*. The seeds of this plant are used for medical purposes from many thousand years (Kritchevsky *et al.*, 1995). It has been reported that obese patients treated with a rational diet supplemented with 15 g *Plantago psyllium* for two months lost their weight significantly compared with the untreated obese ones (Moran *et al.*, 1997). It has been demonstrated that *Plantago ovata* husk-supplemented diet prevents endothelial dysfunction, hypertension and ameliorates dyslipidemia and hyperinsulinemia in obese Zucker rats (Galisteo *et al.*, 2005).

The current study was designed to evaluate the therapeutic potential and the possible mode of action of *Foeniculum vulgare* (fennel) extracts as well as *Plantago ovata* (*Plantago*) in the treatment of obesity in adult female rats. This goal could be achieved through using anthropometrical parameters and testing the hypothesis that the anthropometrical index may predict obesity adverse effects on lipid profile and oxidative stress and may assess the effectiveness of the herbal therapy in the treatment of obesity in rats.

## MATERIALS AND METHODS

### A: Phytochemical study

**Plant materials:** *Foeniculum vulgare* fruits and *Plantago ovata* seeds were obtained from local market at Harraz Herbal Drugstore (2 Cairo, Egypt) in September 2010 and identified by Prof. Dr Ibrahim Elgarf, Department of Botany, Faculty of Science, Cairo University, Cairo, Egypt. A voucher specimen has been deposited at the Herbarium of the National Research Centre, Cairo, Egypt.

Preparation of fennel extracts and *Plantago* seeds:

- Methanol extract, 3 kg powder of fennel fruit was mixed five times with 5 L methanol. Extraction continued until the extraction solvents became colorless. The obtained extracts were filtered over Whatman No. 1 paper and the filtrate was collected, then methanol was removed by a rotary evaporator at 50°C to give 150 g
- Water extract, 3 kg of fennel fruit was grounded into a fine powder in a mill and mixed with 5 L boiling water obtained using an ultrasonic bath for 1/2 h to ensure an exhaustive extraction. Then the extract was filtered over Whatman No. 1 paper. The filtrate was frozen and lyophilized to give 250 g
- Essential oil was obtained by hydrodistillation of the powdered dry fennel fruits (1 kg) according to Shahat *et al.* (2011). The oil phase was separated, dried over anhydrous sodium sulfate and kept in a dark glass bottle at 4°C until the analyses and biological evaluation
- *Plantago ovata* seeds are grounded using the electric blender and added on the pulverized standard diet of rats in a dose of 35 g kg<sup>-1</sup> diet

**B: Biological study:** This study was conducted in accordance with the principles and guidelines of the Ethical Committee for animal care and protection of the National Research Centre, Egypt.

**Animals and experimental protocol:** The present study was conducted on sixty adult female sprague Dawley rats weighing 130±10 g at 90 days of age obtained from the animal house colony of the National Research Centre, Cairo, Egypt in October 2010. The animals were housed 5/cage in polypropylene cages in an environmentally controlled clean air room with a temperature of 24±1°C, a 12 h light/12 h dark cycle, a relative humidity of 60±5% and free access to tap water and food. Rats were allowed to adapt to these conditions for two weeks before beginning the experimental protocol.

After the acclimatization period, ten rats were given water *ad libitum* and were fed a standard rodent chow with 26.5% protein, 3.8% fat, 40% carbohydrate, 4.5% crude fibre in 100 g of chow during 24 weeks of the experimental period and served as lean control group. The other fifty rats were received water *ad libitum* and were fed a High-fat Diet (HFD) with 19.93% protein, 15.39% fat, 57.50% carbohydrate, 2.81% dietary fibre in 100 g of chow. The dietary ingredients were homogenized in distilled water at 60°C and the homogenate was used to prepare the pellets. Diets were given fresh each day as dry pellets; therefore there was no spillage (Novelli *et al.*, 2007). These rats were randomly assigned to five groups (10 rats group<sup>-1</sup>) as follows; group one in which the rats were fed a HFD diet, for induction of obesity (Soliman *et al.*, 2012), for 24 weeks and served as obese control group, the groups two and three in which the rats were fed a HFD diet for 24 weeks but at the 12th week, they were orally administered with fennel methanolic extract in a dose of 200 mg kg<sup>-1</sup> b.wt., fennel aqueous extract in a dose of 300 mg kg<sup>-1</sup> b.wt. by Choi and Hwang (2004) and Birdane *et al.* (2007), respectively daily for 12 weeks. Group four in which the rats were fed a HFD diet for 24 weeks but at the 12th week the HFD was supplemented with 100 mg fennel oil kg<sup>-1</sup> diet (Schone *et al.*, 2006) and the rats were fed this fennel oil supplemented diet for the other 12 weeks and group five in which the rats were fed a HFD diet for 24 weeks but at the 12th week, the HFD diet was supplemented with grounded *Plantago ovata* seeds in a dose of 35 g kg<sup>-1</sup> diet (Galisteo *et al.*, 2005) and the rats were fed this *Plantago ovata*-supplemented diet for the other 12 weeks. Food intake was measured after 12 weeks and also after 24 weeks i.e., at the end of the experiment at the same time (09:00-10:00 h).

**Anthropometrical determinations:** The Abdominal Circumference (AC) (immediately anterior to the forefoot), Thoracic Circumference (TC) (immediately behind the foreleg), body length (nose-to-anus or nose-anus length) were determined in all rats at the end of the experimental period (24 weeks). The measurements were made in anaesthetized rats (0.1 mL intraperitoneally of 1% sodium barbiturate). The body weight and body length were used to determine the body mass index (Novelli *et al.*, 2007):

$$\text{BMI} = \frac{\text{Body weight (g)}}{\text{Length}^2 \text{ (cm}^2\text{)}}$$

**Biochemical determinations:** After obtaining anthropometrical measurements, rats were fasted overnight (12-14 h) and the blood samples were withdrawn, under diethyl ether anaesthesia, from the retro-orbital pleux in a clean dry centrifuge tubes and allowed to clot to obtain the sera. Serum samples were separated by centrifugation at 800 xg for 10 min at 4°C. Aliquots of serum were frozen and stored at -20°C for further determinations of biochemical markers.

Serum Total Cholesterol (TC) and Triglycerides (TG), High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL) were assayed by enzymatic method using StanBio Laboratory kits (Boerne, Texas, USA) according to Allain *et al.* (1974) Fossati and Prencipe (1982), Lopes-Virella *et al.* (1977) and Assmann *et al.* (1984) methods respectively. Serum malondialdehyde (MDA) was determined by colorimetric methods using Biodiagnostic kit (Egypt) according to the method described by Satoh (1978). Serum insulin was estimated by enzyme linked immunosorbent assay (ELIZA) procedure using DRG kit (Germany) according to the method of Temple *et al.* (1992). Serum glucose was measured by colorimetric method using Biodiagnostic kit (Egypt) according to the method described by Trinder (1969). Serum leptin was assayed by ELIZA technique using DRG kit (Germany) according to Considine *et al.* (1996) method.

**Statistical analysis:** The statistical analysis was performed using SPSS/PC statistical program (version 11.0 for Windows; SPSS, Inc). Descriptive data were expressed as Mean±SE. Differences between each two groups were analyzed by the student unpaired t-test. A probability of 0.05 was chosen as the significant level (Steel and Torrie, 1984).

## RESULTS

This study was constructed to evaluate the anti-obesity influence of fennel methanolic, aqueous and oil extracts as well as *Plantago* seeds in high fat diet-fed rats. Table 1 illustrates the results of average food intake in the different studied groups after 12 and 24 weeks from starting the experiment. It was observed that there was significant increase (p<0.01) in average food intake of obese rats after 12 or 24 weeks when compared with that in lean control rats. In contrast, the

Table 1: Effect of fennel extracts and *Plantago* seeds on the average food intake in female rats after 12 and 24 weeks

Food consumption (g day <sup>-1</sup> )	Group					
	<i>Plantago</i> seeds	Fennel oil extract	Fennel aqueous extract	Fennel methanolic extract	Control obese	Control lean
12 weeks	26.00±2.2**	25.0±2.0**	23.0±2.5**	30.0±2.0**	50.0±3.0**	15.0±1.1
24 weeks	17.06±1.7**	14.7±1.2**	10.3±1.3**	20.0±1.5**	50.0±4.0**	15.0±1.5

Values are Mean±SE for 8 animals group<sup>-1</sup>, \*\*\*Significant at p<0.05 and p<0.01, respectively

average food intake of obese rats treated with either one of fennel extracts or those treated with *Plantago* seeds showed significant decrease ( $p < 0.01$ ) after 12 or 24 weeks when compared with that of obese rats at each time interval.

The results of the current study revealed that there was significant increase in Thoracic Circumference (TC) ( $p < 0.01$ ) and Abdominal Circumferences (AC) ( $p < 0.05$ ) of obese group that supplemented with HFD when compared with lean control one kept on standard rodent chow. However, there was significant decrease ( $p < 0.01$ ) in TC of obese rats treated with either fennel methanolic extract or fennel oil extract when compared with obese control rats. Also, *Plantago* seeds-treated group showed significant decrease ( $p < 0.05$ ) in TC when compared with obese control group. Significant decrease ( $p < 0.05$ ) in AC was detected only in obese rats treated with fennel oil extract. Meanwhile, obese rats treated with *Plantago* seeds showed insignificant decrease ( $p > 0.05$ ) in AC when compared with AC of obese control rats. Body Mass Index (BMI) of obese group showed significant increase ( $p < 0.01$ ) when compared with that of lean control group. However, significant decrease ( $p < 0.01$ ) in BMI was recorded in obese groups treated with each one of the three fennel extracts and also in a group of rats treated with *Plantago* seeds when compared with BMI of obese control group (Table 2).

The results depicted in Table 3 showed the effect of treatment with either one of fennel extracts or *Plantago* seeds on lipid profile of obese female rats. The data revealed that there was significant increase ( $p < 0.01$ ) in serum cholesterol and LDL levels in obese rats compared with lean control rats. Triglycerides showed insignificant increase ( $p > 0.05$ ) in obese rats as compared with that in lean control rats. While, serum HDL level recorded significant decrease ( $p < 0.01$ ) in obese rats when compared with lean control rats (Table 3). However, treatment of obese rats with either one of fennel extract or with *Plantago* seeds resulted in significant decrease ( $p < 0.01$ ) in serum cholesterol level when compared with that in obese control rats. Serum LDL level revealed significant decrease ( $p < 0.05$ ) only in rats treated with either fennel methanolic extract or *Plantago* seeds when compared with that in obese control rats. Triglycerides level in serum of the all treated groups showed insignificant decrease ( $p > 0.05$ ) when compared with that in untreated obese control rats. Serum HDL level recorded significant increase only in rats treated with fennel methanolic extract ( $p < 0.01$ ) and in those treated with *Plantago* seeds ( $p < 0.05$ ) as compared with that recorded in obese control rats (Table 3).

The data illustrated in Table 3 also revealed that serum lipid peroxide level represented by malondialdehyde (MDA) recorded significant increase ( $p < 0.01$ ) in obese rats compared with lean control rats. On the other hand, treatment of obese rats with fennel methanolic extract or fennel aqueous extract or fennel oil extract or even *Plantago* seeds produced significant decrease ( $p < 0.01$ ) in serum MDA level as compared with that in untreated obese control rats (Table 3).

Table 2: Effect of fennel extracts and *Plantago* seeds on anthropometric parameters of female rats

Parameters	Group					
	<i>Plantago</i> seeds	Fennel oil extract	Fennel aqueous extract	Fennel methanolic extract	Control obese	Control lean
Thoracic circumference (cm)	10.4±0.240*	9.5±0.200**	9.8±1.200	9.8±0.200**	11.4±0.400**	9.5±0.200
Abdominal circumference (cm)	7.4±0.150	6.6±0.180*	7.3±0.200	7.2±0.180	7.7±0.400*	6.5±0.170
Body mass index ( $g\ cm^{-2}$ )	0.6±0.016**	0.5±0.008**	0.6±0.019**	0.6±0.017**	0.7±0.023**	0.5±0.009

Values are Mean±SE for 8 animals group<sup>-1</sup>, \*\*Significant at  $p < 0.05$  and  $p < 0.01$ , respectively

Table 3: Effect of fennel extracts and *Plantago* seeds on lipid profile of female rats

Contents (mg dL <sup>-1</sup> )	Group					
	<i>Plantago</i> seeds	Fennel oil extract	Fennel aqueous extract	Fennel methanolic extract	Control obese	Control lean
Cholesterol	79.30±2.10**	81.00±3.10**	89.25±3.50**	74.6±2.90**	124.00±2.40**	66.96±1.60
Triglycerides	89.90±5.00	88.40±4.90	89.50±5.50	84.1±4.20	93.61±5.90	79.08±4.50
High density lipoprotein	24.10±1.90*	21.10±1.30	23.30±2.10	26.5±1.80**	19.80±0.30**	30.50±0.90
Low density lipoprotein	19.00±1.10*	20.90±1.60	20.50±1.80	18.5±1.10*	24.36±2.30**	14.30±0.40
MDA (nmol mL <sup>-1</sup> )	3.12±0.29**	2.60±0.23**	2.30±0.21**	2.2±0.20**	4.50±0.35**	2.10±0.17

Values are Mean±SE for 8 animals group<sup>-1</sup>, \*\*\*Significant at p<0.05 and p<0.01, respectively

Table 4: Effect of fennel extracts and *Plantago* seeds on biochemical parameters of female rats

Parameters	Group					
	<i>Plantago</i> seeds	Fennel oil extract	Fennel aqueous extract	Fennel methanolic extract	Control obese	Control lean
Insulin (µIU mL <sup>-1</sup> )	14.30±1.1*	17.00±1.2	16.50± 1.0	15.10±0.9*	18.30±0.9**	13.13±0.7
Glucose (mg dL <sup>-1</sup> )	82.50±2.9**	90.50±4.0	92.00±4.3	83.00±2.1**	100.19±3.3**	81.89±2.5
Leptin (ng mL <sup>-1</sup> )	35.10±2.7*	35.90±2.1*	33.70±2.9*	29.40±2.1**	43.52±2.1**	15.00±0.9

Values are Mean±SE for 8 animals group<sup>-1</sup>, \*\*\*Significant at p<0.05 and p<0.01, respectively

Serum insulin level showed significant increase (p<0.01) in obese rats compared with lean control rats. Significant decrease (p<0.05) in serum insulin level was detected only in obese rats treated with fennel methanolic extract. Similarly, obese rats treated with *Plantago* seeds showed significant decrease (p<0.05) in serum insulin level compared with that in obese control rats (Table 4).

Serum glucose level showed significant increase (p<0.01) in obese rats as compared with that in lean control rats. In contrast, significant decrease (p<0.01) in serum glucose level was recorded only in obese rats treated with fennel methanolic extract. Similarly, significant decrease (p<0.01) in serum glucose level was demonstrated in obese rats treated with *Plantago* seeds as compared with that in obese control rats (Table 4).

Concerning serum leptin level, obese rats showed significant increase (p<0.01) compared with serum leptin level in lean control rats. However, serum leptin level showed significant depletion in obese rats treated with fennel methanolic extract (p<0.01) or with fennel aqueous extract (p<0.05) or with fennel oil extract (p<0.05) or even with *Plantago* seeds (p<0.05) when compared with that in obese control rats (Table 4).

## DISCUSSION

In the present study, the potential effects of fennel methanolic, fennel aqueous and fennel oil extracts as well as *Plantago* seeds on food intake, anthropometric measures, lipid profile, oxidative stress marker, insulin, glucose and leptin circulating levels in obese rats were investigated.

The present data revealed that food intake in obese rats was significantly increased after 12 or 24 weeks, this finding is in agreement with that of Galisteo *et al.* (2005). This means that the total energy intake was higher in obese rats than that in the lean control one. This indicates that diet is certainly of importance to obesity incidence. The diminished food intake in rats treated with either one of the fennel extracts agreed with the previous report of Schone *et al.* (2006). In this

respect, it can be proposed that trypsin inhibitors in fennel reduce food intake and stimulate cholecystokinin release, increasing satiety and that is the reason for fennel's association with weight control. Regarding the effect of *Plantago* seeds on reducing food intake in obese rats, Galisteo *et al.* (2005) attributed this effect to the reduction in ghrelin production and also to the low energy intake of *Plantago* seeds due in part to dilution of nutrients by fiber incorporation.

The present data revealed that both TC and AC were significantly increased in obese rats. In addition, BMI showed significant increase in obese rats when compared with lean control rats. These results indicate that there was fat accumulation in the thoracic and abdominal regions due to high fat diet (Novelli *et al.*, 2007). This means that the increased body weight due to excessive energy intake was the adipose tissue. There were positive correlations between daily lipid intake and BMI as well as fat deposition (Rodrigues *et al.*, 2012) demonstrating that BMI is a simple reliable estimate of body fat and obesity in rats (Novelli *et al.*, 2007). Treatment of obese rats with the different fennel extracts, particularly fennel oil extract, resulted in a reduction in both TC and AC. Methanolic extract of fennel and *Plantago* seeds exerted their reducing effects on TC only. In general, treatment with the different fennel extracts as well as *Plantago* seeds exhibited significant reduction in BMI of obese rats. These findings indicate that fennel extracts could reduce body fat percentage in obese rats. This might be explained by the capacity of fennel active ingredients to reduce the expression of sterol regulatory element binding protein 1 which inhibits lipid accumulation and expression of lipogenic genes, resulting in the reduction in body fat. In addition, promoting satiation and altering secretion of gut hormones might be the possible mechanisms involved in weight loss and BMI regulation associated with the treatment with fennel extracts in obese rats (Schone *et al.*, 2006). The observed reduction in TC and BMI of obese rats treated with *Plantago* seeds was due, at least in part, to a reduced food intake. The weight reducing effect of *Plantago* was previously asserted by Galisteo *et al.* (2005).

The current results revealed significant increase in serum cholesterol and LDL levels accompanied with insignificant increase in serum triglycerides level in obese rats. While, significant depletion in serum HDL level was recorded in obese rats as compared to lean control rats. Hypercholesterolemia and hypertriglyceridemia have been previously detected in obese rats (Son *et al.*, 2012). It has been demonstrated that lipids in adipose tissue are largely derived from circulating triglycerides especially during high-fat diet feeding (Fruchart *et al.*, 1998) and the reduction in serum triglycerides leads to decreased adipose tissue mass (Jeong *et al.*, 2004). The increased serum LDL level in obese rats has been also recorded in high fat diet supplemented rats (Novelli *et al.*, 2007). This fact was explained by the decreased HDL level, as recorded in our study, thus decreasing the reverse cholesterol transport from the blood stream to the liver (Raveh *et al.*, 2001). Different fennel extracts and *Plantago* seeds used in the present study could reduce serum cholesterol level in obese rats. Nonappreciable reduction in serum triglycerides level was recorded in obese rats treated with either one of fennel extracts or with *Plantago* seeds. Fennel methanolic extract and *Plantago* seeds treatment could significantly decrease serum LDL level and increase serum HDL level in obese rats. The other fennel extracts could insignificantly reduce LDL level and rise HDL level in obese rats. These results indicated that the constitution of fennel and *Plantago* seeds plays an important role in improving blood lipid profile. This could be explained as fennel methanolic extract (Choi and Hwang, 2004) and *Plantago* seeds (Ziai *et al.*, 2005) could significantly increase HDL level. This type of lipoprotein could stimulate the reverse cholesterol transport from the blood stream to the liver (Raveh *et al.*, 2001). Furthermore, it has been shown that fennel, involved in herbal formulation, could delay upper gastrointestinal transit which



promotes a decrease in fat and sugar absorption (Capasso *et al.*, 2007). Regarding the hypolipidemic effect of *Plantago* seeds, our results are in agreement with those of Galisteo *et al.* (2005). The possible hypocholesterolemic mechanisms of *Plantago* were related to decreased cholesterol absorption or inhibition of the enterohepatic circulation of bile acids, due to the physicochemical properties of *Plantago* and also to the increasing meal viscosity (MacMahon and Carless, 1998). The hypotriglyceridemic effect of *Plantago* is consistent with a possible delay in the absorption of triglycerides and sugars from the small intestine (Ebihara and Schneeman, 1989).

The present data revealed that the lipid peroxidation product (MDA) recorded significant elevation in obese rats when compared with the lean control one. This result agrees with that of Prasanna and Purnima (2011). The increased MDA level in obese rats could be explained as the increased caloric intake represents an important factor in decreasing the mitochondrial membrane fluidity and increasing the generation of ROS (Esposito *et al.*, 1999). The study of Novelli *et al.* (2007) revealed that there was a positive correlation between BMI and lipid peroxidation products concentration. The significant reduction in serum MDA level observed in obese rats treated with either one of the fennel extracts could be attributed to the anti-lipid peroxidative capacity of fennel constituents in its methanolic extract (Choi and Hwang, 2004). Augmentation of the antioxidant defense system and the anti-lipid peroxidative activity of aqueous fennel extract has been also reported (Birdane *et al.*, 2007). The efficacy of fennel oil extract to decrease the percentual feed intake in pigs (Schone *et al.*, 2006) and in rats as shown in our study indicated that fennel oil could reduce the production of ROS and in turn oxidative stress indirectly via decreasing the caloric intake. Treatment of obese rats with *Plantago* seeds resulted in significant reduction in serum MDA level. The effect of *Plantago* in lowering food intake and energy intake in obese rats has been previously reported (Galisteo *et al.*, 2005). This effect of *Plantago* could be responsible for the depletion of oxidative stress and lipid peroxidation product (MDA) observed in the current study.

Our results revealed that there was significant increase in serum insulin level in obese rats compared with that in lean control one. This finding is in agreement with that of Galisteo *et al.* (2005). This could be explained as obesity is associated with low-grade chronic systemic inflammation which potentially leads to insulin resistance (Mori *et al.*, 2011). Treatment of obese rats with fennel methanolic extract significantly decreased serum insulin level compared with that in obese control rats. This result could be explained via the powerful antiinflammatory action of fennel methanolic extract (Choi and Hwang, 2004). This property contributed in reducing the proinflammatory cytokine production and promoting the antiinflammatory mediators. In this way, fennel methanolic extract could reduce hyperinsulinemia in obese rats. *Plantago* seeds supplementation has been found to reduce serum insulin level significantly in obese rats. This result agreed well with that of Galisteo *et al.* (2005) who explained this phenomenon by the ability of *Plantago* seeds to reduce food intake and ghrelin concentration in obese rats.

The present results showed that obese rats recorded significant elevation in serum glucose level. This finding is in agreement with that in the study of Galisteo *et al.* (2005). This result could be explained by the presence of high lipolytic activity in fat accumulation that results in high free fatty acids mobilization to the liver. The elevated fatty acids flux to liver accelerates gluconeogenesis and decreases the effect of insulin on peripheral glucose disposal (Ginsberg and Stalenhoef, 2003). The ability of fennel methanolic extract to reduce serum glucose level in obese rats could be attributed to the effect of this extract in lowering fat accumulation and hence improving the glycemic status of obese rats via reducing the gluconeogenesis process and elevating the efficacy of insulin on glucose disposal. Obese rats supplemented with *Plantago* seeds

recorded significant reduction in serum glucose level in comparison with that in obese control one. *Plantago* has been found to have glucose lowering effect in serum via its ability to inhibit glucose absorption from the small intestine (Hannan *et al.*, 2006). Additionally *Plantago* could reduce the concentration free fatty acids which promote gluconeogenesis and inhibit the effect of insulin on peripheral glucose disposal (Galisteo *et al.*, 2005).

Serum leptin level showed significant increase in obese rats as compared with lean control one. Leptin is a cytokine like polypeptide produced by the adipocytes and it is overproduced during obesity (Assal *et al.*, 2007). The observed significant lowering effect of either fennel methanolic, aqueous or oil extract or even *Plantago* seeds on serum leptin level in obese rats indicates that both fennel and *Plantago* seeds have an ability to reduce fat mass in the treated groups. Thus, the reduction in fat mass, due to fennel administration (Choi and Hwang, 2004) or *Plantago* seeds supplementation (Ziai *et al.*, 2005), attenuates the proinflammatory environment associated with obesity (Cottam *et al.*, 2002) leading to depletion of leptin production and hence serum leptin level.

## CONCLUSION

In conclusion, the present study showed that the prolonged intake of fennel extracts or *Plantago* seeds-supplemented diet retards obesity. The effect that was accompanied by improvement of BMI, amelioration of the dyslipidemia, hyperinsulinemia and hyperleptinemia, modulation of glycemic status and reduction of the oxidative stress in high-fat diet-induced obesity in rats. The observed effects of fennel extracts or *Plantago* seeds could be attributed to their properties such as hypolipidemic, antioxidant and antiinflammatory. Thus, fennel extracts, particularly, methanolic extract and *Plantago* seeds may be useful for treating obese patients with hypercholesterolemia and hypertriglyceridemia. Further studies will be necessary to identify and characterize active compounds responsible for these effects.

## REFERENCES

- AACE/ACE Obesity Task Force, 1998. AACE/ACE position statement on the prevention, diagnosis and treatment of obesity. *Endocr. Pract.*, 4: 297-350.
- Allain, C.C., L.S. Poon, C.S. Chan, W. Richmond and P.C. Fu, 1974. Enzymatic determination of total serum cholesterol. *Clin. Chem.*, 20: 470-475.
- Assal, H.S., M. Fath-Allah and A. Elsherbiny, 2007. Serum leptin and adiponectin in obese diabetic and non-diabetic. *J. Med. Sci.*, 7: 865-869.
- Assmann, G., H.U. Jabs, U. Kohnert, W. Nolte and H. Schriewer, 1984. LDL-cholesterol determination in blood serum following precipitation of LDL with polyvinylsulfate. *Clin. Chim. Acta.*, 140: 77-83.
- Bianchini, F., R. Kaaks and H. Vainio, 2002. Overweight, obesity and cancer risk. *Lancet Oncol.*, 3: 565-574.
- Birdane, F.M., M. Cemek, Y.O. Birdane, I. Gulcin and M.E. Buyukokuroglu, 2007. Beneficial effects of *Foeniculum vulgare* on ethanol-induced acute gastric mucosal injury in rats. *World J. Gastroenterol.*, 13: 607-611.
- Capasso, R., F. Savino and F. Capasso, 2007. Effects of the herbal formulation ColiMil on upper gastrointestinal transit in mice *In vivo*. *Phytother. Res.*, 21: 999-1101.
- Choi, E.M. and J.K. Hwang, 2004. Antiinflammatory, analgesic and antioxidant activities of the fruit of *Foeniculum vulgare*. *Fitoterapia*, 75: 557-565.

- Considine, R.V., M.K. Sinha, M.L. Heiman, A. Kriauciunas and T.W. Stephens *et al.*, 1996. Serum immunoreactive-leptin concentrations in normal weight and obese humans. *N. Engl. J. Med.*, 334: 292-295.
- Cottam, D.R., P.A. Schaefer, G.W. Shafiq, L. Velcu and L.D. Angus, 2002. Effect of surgically-induced weight loss on leukocyte indicators of chronic inflammation in morbid obesity. *Obes. Surg.*, 12: 335-342.
- Diniz, Y.S., L.A. Faine, C.M. Galhardi, H.G. Rodrigues and G.X. Ebaid *et al.*, 2005. Monosodium glutamate in standard and high-fiber diets: Metabolic syndrome and oxidative stress in rats. *Nutrition*, 21: 749-755.
- Ebihara, K. and B.O. Schneeman, 1989. Interaction of bile acids phospholipids, cholesteryl and triglycerides with dietary fibers in the small intestine of rats. *J. Nutr.*, 119: 1100-1106.
- Esposito, L.A., S. Melov, A. Panov, B.A. Cottrell and D.C. Wallace, 1999. Panov Mitochondrial disease in mouse results in increased oxidative stress. *Proc. National Acad. Sci.*, 96: 4820-4825.
- Fossati, P. and L. Prencipe, 1982. Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. *Clin. Chem.*, 28: 2077-2080.
- Fruchart, J.C., H.B. Brewer and E. Leitersdorf, 1998. Consensus for the use of fibrates in the treatment of dyslipoproteinemia and coronary heart disease. Fibrate Consensus Group. *Am. J. Cardiol.*, 81: 912-917.
- Fujioka, K., 2002. Management of obesity as a chronic disease: Nonpharmacological, pharmacological and surgical options. *Obes. Res.*, 10: 116S-123S.
- Galisteo, M., M. Sanchez, R. Vera, M. Gonzalez, A. Anguera, J. Duarte and A. Zarzuelo, 2005. A diet supplemented with husks of *Plantago ovata* reduces the development of endothelial dysfunction, hypertension and obesity by affecting adiponectin and TNF- $\alpha$  in obese Zucker rats. *J. Nutr.*, 135: 2399-2404.
- Ginsberg, H. and A. Stalenhoef, 2003. The metabolic syndrome targeting dyslipidemia to reduce coronary risk. *J. Cardiovasc. Risk*, 10: 121-128.
- Hannan, J.M.A., L. Ali, J. Khaleq, M. Akhter, P.R. Flatt and Y.H.A. Abdel-Wahab, 2006. Aqueous extracts of husks of *Plantago ovata* reduce hyperglycaemia in type 1 and 2 diabetes by inhibition of intestinal glucose absorption. *Br. J. Nutr.*, 96: 131-137.
- Hart, R.W., R. Dixi, J. Seng, A. Turturro and J.E. Leakey *et al.*, 1999. Adaptive role of caloric intake on degenerative disease process. *Toxicol. Sci.*, 52: 3-12.
- Jeong, S., M. Han, H. Lee, M. Kim and J. Kim *et al.*, 2004. Effects of fenofibrate on high-fat diet-induced body weight gain and adiposity in female C57BL/6J mice. *Metabolism*, 53: 1284-1289.
- Kritchevsky, D., S. Tepper and D. Kiufeld, 1995. Influence of Psyllium preparations on plasma and liver lipids of cholesterol-fed rats. *Artery*, 21: 303-311.
- Lopes-Virella, M.F., P. Stone, S. Ellis and J.A. Colwell, 1977. Cholesterol determination in high-density lipoproteins separated by three different methods. *Clin. Chem.*, 23: 882-884.
- Lopez-Jimenez, F. and M. Cortes-Bergoderi, 2011. Update: Systemic diseases and the cardiovascular system (i): Obesity and the heart. *Rev. Esp. Cardiol.*, 64: 140-149.
- MacMahon, M. and J. Carless, 1998. Ispaghula husk in the treatment of hypercholesterolaemia: A double-blind controlled study. *J. Cardiovasc. Risk*, 5: 167-172.
- Maffei, M.J., J. Halaas, E. Rayussin, R.E. Pratley and G.M. Lee *et al.*, 1995. Leptin levels in human and rodent: Measurement of plasma leptin and ob mRNA in obese and weight reduced subjects. *Nat. Med.*, 1: 1155-1161.

- Mitchell, M., D.T. Armstrong, R.L. Robker and R.J. Norman, 2005. Adipokines: Implications for female fertility and obesity. *Reproduction*, 130: 583-597.
- Moran, S., M. Uribe, M.E. Prado, G. de la Mora and R.M. Munoz *et al.*, 1997. Effects of fiber administration in the prevention of gallstones in obese patients on a reducing diet. A clinical trial. *Rev. Gastroenterol. Mex.*, 62: 266-272.
- Mori, N., P. Lee, I. Yamamoto, S. Nozawa and T. Arai, 2011. Insulin Treatment-Induced Daily Changes to Plasma Adiponectin and TNF- $\alpha$  Level and Lipid Metabolism Parameters in Dogs Suffering from Type 1 Diabetes Mellitus *Asian J. Anim. Vet. Adv.*, 6: 844-850.
- Novelli, E.L., Y.S. Diniz, C.M. Galhardi, G.M. Ebaid and H.G. Rodrigues *et al.*, 2007. Anthropometrical parameters and markers of obesity in rats. *Lab Anim.*, 41: 111-119.
- Piccaglia, R. and M. Marotti, 2001. Characterization of some Italian types of wild fennel (*Foeniculum vulgare* Mill.). *J. Agric. Food Chem.*, 49: 239-244.
- Prasanna, G.S. and A. Purnima, 2011. Protective effect of leaf extract of *Trichilia connaroides* on hypercholesterolemia induced oxidative stress. *Int. J. Pharmacol.*, 7: 106-112.
- Raveh, O., I. Pinchuk, M. Fainaru and D. Lichtenberg, 2001. Kinetics of lipid peroxidation in mixture of HDL and LDL, mutual effects. *Free Radic. Biol. Med.*, 31: 1486-1497.
- Rodrigues, A., P.C. Pereira, A.F. Vicente, J.A. Brito, M.A. Bernardo and M.F. Mesquita, 2012. Food intake, body mass index and body fat mass in elderly. *Asian J. Clin. Nutr.*, 4: 107-115.
- Sahu, A., 2004. Minireview: A hypothalamic role in energy balance with special emphasis on leptin. *Endocrinology*, 145: 2613-2620.
- Samaras, K. and L.V. Campbell, 2000. Increasing incidence of type 2 diabetes in the third millennium: Is abdominal fat the central issue?. *Diabetes Care*, 23: 441-442.
- Satoh, K., 1978. Serum lipid peroxide in cerebrovascular disorders determined by a new colorimetric method. *Clin. Chem. Acta*, 90: 37-43.
- Schone, F., A. Vetter, H. Hartung, H. Bergmann and A. Biertumpfel *et al.*, 2006. Effects of essential oils from fennel (*Foeniculiaetheroleum*) and caraway (*Carviaetheroleum*) in pigs. *J. Anim. Physiol. Anim. Nutr.*, 90: 500-510.
- Shahat, A.A., A.Y. Ibrahim, S.S. Hendawy, E.A. Omar, F.M. Hammoud, F. Abdel-Rahman and M.A. Saleh, 2011. Chemical composition and biological evaluation of essential oils from three Egyptian organic cultivation fennel varieties. *Molecules*, 16: 1366-1377.
- Sindler, B.H., 2001. Herbal therapy for management of obesity: Observations from a clinical endocrinology practice. *Endocr. Pract.*, 7: 443-447.
- Soliman, M.M., H.F. Attia, S.A. El-Shazly and O.M. Saleh, 2012. Biomedical effects of cinnamon extract on obesity and diabetes relevance in Wistar rats. *Am. J. Biochem. Mol. Biol.*, 2: 133-145.
- Son, E.L., U.K. Pal, P.K. Mandal, G.E. Hong, S.K. Kim and C.H. Lee, 2012. Hypolipidaemic effect of processed sulfur, *Allium tuberosum* rottl. and fermented *Allium tuberosum* Rottl in rat. *Asian J. Anim. Vet. Adv.*, 7: 812-821.
- Steel, R.G.D. and J.H. Torrie, 1984. *Principles and Procedures of Statistics*. McGraw Hill Book Co. Inc., New York, USA.
- Temple, R., P.M.S. Clark and C.N. Hales, 1992. Measurement of insulin secretion in type 2 diabetes: Problems and pitfalls. *Diabetic Med.*, 9: 503-512.
- Trinder, P., 1969. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. *Ann. Clin. Biochem.*, 6: 24-27.
- Ziai, S.A., B. Larijani, S. Akhoondzadeh, H. Fakhrzadeh and A. Dastpak *et al.*, 2005. Psyllium decreased serum glucose and glycosylated hemoglobin significantly in diabetic outpatients. *J. Ethnopharmacol.*, 102: 202-207.