

EFFECT OF LEPIDIUM SATIVUM ON BLOOD LEVELS OF APELIN AND SOME METABOLIC AND OXIDATIVE PARAMETERS IN OBESE MALE RATS

By

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ABSTRACT

Background: Obesity is a major health problem worldwide characterized by excessive fat accumulation that presents a risk to health. Apelin is a biologically active peptide identified as one of the adipokines. Insulin is considered one of the main regulators of apelin production. Oxidative stress reflects an imbalance between body antioxidant capacity and toxic oxidant products. *Lepidium sativum* (LS) is an annual herb with antioxidant and antidiabetic activity.

Objective: To study the effect of LS on blood apelin levels and some metabolic and oxidative parameters in 2 strains of albino rats fed on high fat diet (HFD).

Material and Methods: Sixty adult male albino rats, 30 Wistar rats and 30 Sprague Dawely (SD) rats, divided into six equal groups . Group I (Wistar control), group II (Wistar rats fed on HFD), group III (Wistar rats fed on HFD and LS), group IV (SD control rats), group V (SD rats fed on HFD) and group VI (SD rats fed on HFD and LS). The body weights were measured and recorded weekly. At the end of the experiment, blood samples were collected for estimation of the serum levels of apelin, fasting glucose, insulin, insulin resistance, lipid profile, reduced glutathione (GSH), and malondialdehyde (MDA). The adipose tissue was dissected for estimation of the adiposity index.

Results: HFD fed rats showed increase in the body wights and adiposity index in both strains when each was compared to their corresponding control group. Feeding by LS seeds powder showed: A- In Wistar rats: Significant increase in their body weight gain, adiposity index, serum level of GSH and HDL-C. On the other hand, there was significant decrease in serum levels of apelin, glucose, insulin, insulin resistance, total cholesterol (TC), triglycerides (TG), low density lipoprotein-C (LDL-C), very low density lipoprotein (VLDL) and MDA when compared to HFD wistar rats.

B- In SD rats: There were insignificant changes in their weight gain and adiposity index. In addition significant decrease was observed in serum levels of apelin, glucose, insulin, insulin resistance, TC, TG, LDL- C, VLDL and MDA. Also, there were significant increases in serum levels of GSH and HDL-C when compared to the HFD SD rats.

Conclusion: LS could ameliorate the metabolic and oxidative disturbances induced by HFD in both strains. Apelin and VLDL levels returned almost back to normal after addition of LS seeds powder to HFD fed SD rats. LS in the studied dose increase the body weight significantly in Wistar rats. However, it decreased VLDL and triglycerides close to their control levels.

Keywords: apelin, GSH, HFD, LS, LDL-C, MDA, SD, TC, TG and VLDL.

INTRODUCTION

Obesity is associated with metabolic disorders including insulin resistance, type 2 diabetes, dyslipidemia, cardiovascular diseases and cancer, resulting in decreased lifespan (Kalupahana *et al.*, 2011). Increased consumption of dietary fat is one of the leading causes of obesity as fat contains more calories than protein and carbohydrate (Klockener *et al.*, 2011).

The predisposition to gain weight on a HFD is partially genetically determined (Wardle *et al.*, 2008).

White adipose tissue is recognized as a dynamic endocrine organ able to release numerous bioactive polypeptides known as adipokines which play an important role in the development of diseases related to obesity (Leal and Mafra, 2013).

Apelin is a biologically active peptide, identified in 1998 as a member of the adipokines (Tatemoto *et al.*, 1998). Also, apelin mRNA is highly expressed in various tissues, including adipose tissue (Shirasuna *et al.*, 2008).

Insulin is considered one of the main regulators of apelin production, as it increases expression and secretion of apelin in adipocytes (Xu *et al.*, 2011). Apelin expression was found to participate in regulation of blood pressure, cardiac contractility, fluid balance and stimulation of ACTH release from the anterior pituitary gland (Zhu *et al.*, 2013).

Oxidative stress reflects an imbalance between body antioxidant capacity and oxidant toxic nitrogen derived products, causing tissue damage. In humans, oxidative stress is thought to be involved

in the development of complications associated with obesity (Pham-Huy *et al.*, 2008). Chemically, oxidative stress is associated with increased levels of oxidative parameters such as MDA or significant decrease in the effectiveness of antioxidant defenses, such as glutathione (Rahman, 2007).

LS or Garden cress is a fast growing annual herb that is native to Egypt and west Asia, although it is currently cultivated in the entire World (Doke and Guha, 2014). LS seeds are known to be effective against diabetes (Mishra *et al.*, 2017).

This work aimed to study the effect of LS on blood apelin levels, some metabolic and oxidative parameters in Wistar and SD rats fed on HFD. Also to study the response of each strain to the HFD and to LS administration regarding the body weight and the adiposity index.

MATERIALS AND METHODS

Animals and experimental design: This study was performed on sixty adult male albino rats, 30 Wistar rats and 30 SD rats, obtained from Helwan farm, Cairo, Egypt. Their body weight ranged from 140-170 g. The experimental protocol and procedures were done at the animal house of Research Institute of Oncology, Cairo University. Rats were housed every 3 rats in a cage measuring 80×40×30 cm at room temperature on normal light-dark cycle. Before the start of the experiment, rats were left 10 days for adaptation and had free access to food and water. The biochemical analysis was performed in Biochemistry Department, Faculty of Medicine, Cairo University.

Rats were divided into six equal groups. All rats were exposed to experimental intervention for eight weeks.

Group I (Wistar control): rats were kept on the balanced diet of the ordinary rat chow.

Group II (Wistar HFD): Rats were kept on a HFD (Akkol et al., 2009).

Group III (Wistar HFD and LS): Rats were kept on HFD mixed with LS seeds powder (6 g/kg) as described by Chauhan et al. (2012).

Group IV (SD control): Rats were kept on the balanced diet of the ordinary rat chow.

Group V (SD HFD): Rats were kept on HFD (Akkol et al., 2009).

Group VI (SD HFD and LS): Rats were kept on HFD mixed with LS seeds powder (6 g/kg) as described by Chauhan et al. (2012).

Diets and Plant material: I. Commercial rat chow diet (balanced diet):

The composition of the commercial rat chow diet was 5.4% fat, 53.8% carbohydrate, 21.9% protein, 2.9% fiber, 15.8% minerals, added vitamins A, D, and E, and 0.2% cholesterol (a total of 350 kcal per 100 g) (Yang et al., 2012). II. HFD consisted of 80% balanced diet and 20% beef tallow (Akkol et al., 2009). Plant material: LS seeds used in this study was purchased from local market in Cairo. LS seeds were freshly grinded as fine powder, then added to the diet (Chauhan et al., 2012).

Measurement of the body weight: The weight of the animals were measured and recorded weekly for each rat. At the end of the experimental period the weight gain was expressed by using the following equation: The body weight gain (g) = Final body weight (g) - initial body weight (g) (David and Richard, 1984).

Blood sampling: At the end of the experiment blood samples were collected from retro- orbital sinuses by heparinized capillary tubes under light ether anesthesia then centrifuged at 3000 rpm for 15 minutes. Serum was separated from each sample and stored frozen at -80 °C until the time of analysis (Simmons and Brick, 1970).

Biochemical analysis: -Serum apelin levels (Porstmann and Kiessig, 1992).

- Fasting serum glucose (Tietz, 1995).

- Fasting serum insulin level (Carlsson et al., 2010).

- Insulin resistance (IR) index: It was calculated by homeostasis model assessment for insulin resistance (HOMA-IR) formula (Matthews et al., 1985): $HOMA\ IR = \frac{\text{Fasting insulin (}\mu\text{IU/L)} \times \text{fasting glucose (mmol/L)}}{22.5}$.

- Lipid profile: Serum TC, TG, HDL-C, VLDL and LDL-C (Friedewald and Fredrickson, 1972; Flegg, 1973; Bergmeyer & Grassl, 1990 and Tietz, 1998).

- Serum glutathione level (Beutler et al., 1963).

- Serum MDA level (Erdelmeier, 1997).

Adiposity index: After blood collection, each animal was sacrificed by decapitation, and adipose tissue was isolated from the epididymal, visceral and retroperitoneal pads. Adiposity index of each rat was determined by the sum of epididymal, visceral and retroperitoneal fat weights divided by body weight and multiplied by 100, and expressed as adiposity percentage (Li *et al.*, 1997).

Statistical analysis was done by using Statistic Package for Social Science version 18 (SPSS, 18) for windows (Alan and Duncan, 2012). Quantitative data were expressed as mean \pm standard deviation of the mean (Hill, 1977).

Comparison of the groups were done using Student's t-test for quantitative data of 2 independent samples. Level of significance was considered at P value < 0.05 .

RESULTS

The results of this study showed that administration of HFD to rats for eight weeks caused significant increase in their body weight gain and adiposity index in both strains. When compared to their corresponding control rats (Table 1). SD rats gained weight more than Wistar rats.

Table (1): Effect of lepidium sativum on body weight gain and adiposity index of obese Wistar and Sprague Dawely rats (Mean \pm SD).

| Groups Parameters | Group 1 (Control) | Group 2 (HFD) | Group 3 (HFD+LS) | Group 4 (Control) | Group 5 (HFD) | Group 6 (HFD+LS) |
|----------------------|----------------------|------------------------------------|---|----------------------|-------------------------------------|---|
| Weight gain (g) | 75.8 \pm 14.3 | 110.5 \pm 7.0 $P_a < 0.001^*$ | 159.5 \pm 40.17 $P_b < 0.001^*$ $P_c < 0.003^*$ | 95.4 \pm 7.5 | 188.6 \pm 12.1 $P_a < 0.001^*$ | 224.0 \pm 62.4 $P_b < 0.001^*$ $P_c > 0.05$ |
| Adiposity index (%) | 2.55 \pm 0.17 | 3.85 \pm 0.77 $P_a < 0.001^*$ | 5.15 \pm 0.53 $P_b < 0.001^*$ $P_c < 0.001^*$ | 2.85 \pm 0.15 | 5.7 \pm 0.64 $P_a < 0.001^*$ | 5.2 \pm 0.68 $P_b < 0.001^*$ $P_c > 0.05$ |

P_a = group 1 vs group 2, P_b = group 1 vs group 3, P_c = group 2 vs group 3 *Significant p-value. n = 10 rats.

HFD caused significant increases in serum TC, TG, VLDL, LDL-C and significant decrease in serum level of

HDL-C, in both strains when each was compared to their corresponding control rats (Table 2).

Table (2): Effect of lepidium sativum on lipid profile of obese Wistar and Sprague Dawely rats.

| Parameters | Groups | | | | | |
|---|--------------------------------|---------------------------------|---|-------------------|---------------------------------|--|
| | Group 1 (Control) Mean ± SD | Group 2 (HFD) Mean ± SD | Group 3 (HFD+LS) Mean ± SD | Group 4 (Control) | Group 5 (HFD) | Group 6 (HFD+LS) |
| Serum total cholesterol (TC) (mg/dl) | 155.2 ± 13.7 | 212.7 ± 12.7 $P_a < 0.001^*$ | 182.1 ± 13.2 $P_b < 0.001^*$ $P_c < 0.001^*$ | 143.3 ± 9.48 | 208.9 ± 25.8 $P_a < 0.001^*$ | 178.3 ± 14.1 $P_b < 0.001^*$ $P_c < 0.001^*$ |
| Serum triglycerides (mg/dl) | 88.5 ± 12.13 | 124.5 ± 15.6 $P_a < 0.001^*$ | 86.8 ± 8.9 $P_b > 0.05$ $P_c < 0.001^*$ | 86.1 ± 10.5 | 112.2 ± 10.1 $P_a < 0.001^*$ | 97.7 ± 10.7 $P_b < 0.05^*$ $P_c < 0.05^*$ |
| Serum HDL-C (mg/dl) | 55.1 ± 4.2 | 31.9 ± 4.3 $P_a < 0.001^*$ | 42.4 ± 4.4 $P_b < 0.001^*$ $P_c < 0.001$ | 57.5 ± 3.08 | 33.3 ± 7.37 $P_a < 0.001^*$ | 46.0 ± 7.07 $P_b < 0.001^*$ $P_c < 0.05^*$ |
| Serum VLDL (mg/dl) | 17.3 ± 2.05 | 24.9 ± 2.4 $P_a < 0.001^*$ | 17.57 ± 1.6 $P_b > 0.05$ $P_c < 0.001^*$ | 17.48 ± 2.0 | 22.0 ± 2.1 $P_a < 0.001^*$ | 19.28 ± 2.4 $P_b > 0.05$ $P_c < 0.05^*$ |
| Serum LDL-C (mg/dl) | 87.08 ± 13.4 | 152.8 ± 12.2 $P_a < 0.001^*$ | 123.17 ± 19.0 $P_b < 0.001^*$ $P_c < 0.001^*$ | 67.6 ± 8.8 | 159.5 ± 27.8 $P_a < 0.001^*$ | 129.5 ± 18.6 $P_b < 0.001^*$ $P_c < 0.05^*$ |

P_a = group 1 vs group 2, P_b = group 1 vs group 3, P_c = group 2 vs group 3 *Significant p-value. n = 10 rats.

Significant increases occurred in serum apelin, glucose, insulin levels and IR in rats of both strains after intake of HFD when compared to their corresponding control rats. The addition of LS to the HFD significantly decreased serum apelin,

glucose, insulin and insulin resistance in both strains when each was compared to their corresponding HFD fed rats. In Wistar rats, these parameters still significantly higher when compared to their control group (Table 3).

Table (3): Effect of LS on serum apelin, glucose, insulin, IR index, GSH and MDA of obese Wistar and Sprague Dawley rats (Mean \pm SD).

| Parameters \ Groups | Group 1 (Control) | Group 2 (HFD) | Group 3 (HFD+LS) | Group 4 (Control) | Group 5 (HFD) | Group 6 (HFD+LS) |
|---------------------------------|-------------------|--|---|-------------------|---|---|
| Serum apelin (ng/dl) | 4.48 \pm 1.6 | 20.25 \pm 5.9 P _a < 0.001* | 11.5 \pm 3.77 P _b < 0.001* P _c = 0.001* | 5.9 \pm 2.7 | 15.9 \pm 3.3 P _a < 0.001* | 7.27 \pm 1.8 P _b > 0.05 P _c < 0.001* |
| Serum Glucose (mmol/l) | 5.68 \pm 0.54 | 15.8 \pm 2.4 P _a < 0.001* | 10.4 \pm 1.2 P _b < 0.001* P _c < 0.001* | 5.5 \pm 1.0 | 12.0 \pm 1.3 P _a < 0.001* | 8.2 \pm 1.4 P _b < 0.001* P _c < 0.001* |
| Serum Insulin (?IU/l) | 11.36 \pm 2.0 | 18.3 \pm 2.4 P _a < 0.001* | 13.18 \pm 1.4 P _b < 0.05* P _c < 0.001* | 10.69 \pm 1.19 | 18.6 \pm 3.13 P _a < 0.001* | 12.5 \pm 1.57 P _b < 0.05* P _c < 0.001* |
| Insulin resistance index (HOMA) | 2.9 \pm 0.57 | 12.9 \pm 2.15 P _a < 0.001* | 5.5 \pm 1.16 P _b < 0.001* P _c < 0.001* | 2.6 \pm 0.38 | 10.8 \pm 2.5 P _a < 0.001* | 4.5 \pm 1.0 P _b < 0.001* P _c < 0.001* |
| Serum GSH (mmol/ml) | 60.87 \pm 5.3 | 21.28 \pm 4.9 | 40.9 \pm 4.7 | 53.14 \pm 3.4 | 28.0 \pm 6.67 P _a < 0.001* | 45.66 \pm 3.5 P _b < 0.001* P _c < 0.001* |
| Serum MDA (mmol/ml) | 1.37 \pm 0.3 | 16.58 \pm 2.8 | 6.2 \pm 2.1 | 9.05 \pm 2.2 | 112.4 \pm 12.8 P _a < 0.001* | 85.32 \pm 12.39 P _b < 0.001* P _c < 0.001* |

P_a = group 1 vs group 2, P_b = group 1 vs. group 3, P_c = group 2 vs group 3 *Significant p-value. n = 10 rats.

The addition of LS to the HFD led to significant increase body weight gain and adiposity index in both strains when each was compared to their corresponding control rats. Also, LS led to significant increase in the body weight in Wistar rats, but insignificant change in SD rats when each was compared to their corresponding HFD fed rats. This combination led to significant decreases in serum TC, VLDL, TG and LDL-C, and significant increase in serum level of HDL-C when compared to their corresponding HFD fed rats. Administration of LS to HFD of Wistar

rats caused significant increases in serum TC and LDL-C and significant decrease in serum level of HDL-C, but insignificant change in serum VLDL and triglycerides when compared to their corresponding control rats. In SD rats, addition of LS caused significant increases in serum TC, triglycerides and LDL-C and significant decrease in serum level of HDL-C, but insignificant change in serum VLDL when compared to their corresponding control rats. Also, significant increase in serum malondialdehyde (MDA) and significant decrease in serum level GSH in

both strains when compared to their corresponding control rats. On the other hand addition of LS to HFD resulted in significant increase in serum GSH and

significant decrease in serum MDA in both strains when each was compared to their corresponding HFD rats (Table 4).

Table (4): Comparison between different parameters in all groups.

| Groups Parameters | Group 1 (Control) | Group 2 (HFD) | Group 3 (HFD+LS) | Group 4 (Control) | Group 5 (HFD) | Group 6 (HFD+LS) | ANOVA F= P<0.001* | p value |
|---------------------------------|----------------------|------------------|---------------------|----------------------|------------------|---------------------|-------------------------|---------|
| Weight gain (g) | 75.8 ± 14.3 | 110.5± 7.0 | 159.5±40.1 | 95.4 ± 7.5 | 188.6 ± 12.1 | 224.0 ± 62.4 | 31.266 | 0.0001 |
| Adiposity index (%) | 2.55 ± 0.17 | 3.85 ± 0.77 | 5.15 ± 0.53 | 2.85 ±0.15 | 5.7 ±0.64 | 5.2 ± 0.68 | 58.873 | 0.0001 |
| Total cholesterol (TC) (mg/dl) | 155.2 ± 13.7 | 212.7 ± 12.7 | 182.1 ± 13.2 | 143.3 ± 9.48 | 208.9 ± 25.8 | 178.3 ± 14.1 | 31.987 | 0.0001 |
| triglycerides (mg/dl) | 88.5 ± 12.13 | 124.5 ± 15.6 | 86.8 ± 8.9 | 86.1 ± 10.5 | 112.2 ± 10.1 | 97.7 ± 10.7 | 18.774 | 0.0001 |
| HDL-C (mg/dl) | 55.1 ± 4.2 | 31.9 ± 4.3 | 42.4 ± 4.4 | 57.5 ± 3.08 | 33.3 ± 7.37 | 46.0 ± 7.07 | 40.376 | 0.0001 |
| VLDL (mg/dl) | 17.3 ± 2.05 | 24.9 ± 2.4 | 17.57 ± 1.6 | 17.48 ± 2.0 | 22.0 ± 2.1 | 19.28 ± 2.4 | 20.736 | 0.0001 |
| LDL-C (mg/dl) | 87.08 ± 13.4 | 152.8 ± 12.2 | 123.17 ± 19.0 | 67.6 ± 8.8 | 159.5 ± 27.8 | 129.5 ± 18.6 | 41.539 | 0.0001 |
| Serum apelin (ng/dl) | 4.48 ± 1.6 | 20.25 ± 5.9 | 20.25 ± 5.9 | 5.9 ± 2.7 | 15.9 ± 3.3 | 7.27 ± 1.8 | 31.178 | 0.0001 |
| Serum Glucose (mmol/l) | 5.68 ± 0.54 | 15.8 ± 2.4 | 15.8 ± 2.4 | 5.5 ± 1.0 | 12.0 ± 1.3 | 8.2 ± 1.4 | 74.076 | 0.0001 |
| Serum Insulin (?IU/l) | 11.36 ± 2.0 | 18.3 ± 2.4 | 18.3 ± 2.4 | 10.69 ± 1.19 | 18.6 ± 3.13 | 12.5 ± 1.57 | 27.961 | 0.0001 |
| Insulin resistance index (HOMA) | 2.9 ± 0.57 | 12.9 ± 2.15 | 12.9 ± 2.15 | 2.6 ± 0.38 | 10.8 ± 2.5 | 4.5 ± 1.0 | 78.562 | 0.0001 |
| Serum GSH (mmol/ml) | 60.87 ± 5.3 | 21.28 ± 4.9 | 21.28 ± 4.9 | 53.14 ± 3.4 | 28.0 ± 6.67 | 45.66 ± 3.5 | 92.840 | 0.0001 |
| Serum MDA (mmol/ml) | 1.37 ± 0.3 | 16.58 ± 2.8 | 16.58 ± 2.8 | 9.05 ± 2.2 | 112.4 ± 12.8 | 85.32 ± 12.39 | 407.747 | 0.0001 |

n = 10 rats.

DISCUSSION

The results of the present study showed that administration of high fat diet to rats caused significant increase in their body weight (in the form of increase of body weight gain and adiposity index) in both strains when each was compared to their corresponding control rats. Induction of

obesity by HFD was reported by **Kim et al. (2012)** who demonstrated that obesity was induced in male mice fed on HFD for 2 weeks. There was a correlation between the present results and that reported by **Sour et al. (2015)** where administration of HFD for 12 weeks in male Wistar rats

showed significant increase in the body weight.

In the present study, SD rats gained weight more than Wistar rats. This most probably due to the genetic tendency of SD rats to be obese when fed on HFD (**Rada et al., 2010**). HFD increased gene expression of galanin (GAL), the opioid peptides, enkephalin (ENK), dynorphin (DYN), and orexins (ORX), in SD rats as they stimulate ingestion of fat and in turn the feeding behavior that lead to the development of diet induced obesity (**Gaysinskaya et al., 2007**).

The present study showed that addition of LS powder led to significant increase in their body weight (in the form of increase of body weight gain and adiposity index), in both strains when each was compared to their corresponding control rats. Also addition of LS powder to HFD led to significant increase in the body weight in Wistar rats, The results of the present study were in agreement with **Al Hamedan (2010)** who reported that aquatic extract of LS (20 mg/kg body weight) and LS powder added to hypercholeslerolemic diet increase weight gain and decrease total cholesterol, LDL cholesterol and triglycerides in SD rats. Also, **Sahane et al. (2014)** reported an increase in the body weight in diabetic rats treated with ethanolic extract of LS They explained the ability of LS seeds to recover the body weight loss to be due to its hypoglycemic effect and increase of insulin sensitivity as insulin stimulates lipogenesis and storage of fat in adipose tissue.

El-Dakak et al. (2013) reported that the administration of aqueous extract of LS to diabetic rats reversed the weight loss. This

ability to recover body weight loss seems to be due to its antihyperglycemic effect. The significant increment in body weight of rats received LS mixed with HFD, in comparison to their corresponding control groups, may be due to its palatable and spicy taste and this might led to increase appetite in these rats. Also the hypolipidemic effect of LS may be responsible for the action of LS on body weight through increasing storage of fat in adipose tissue (**Chauhan et al., 2012**).

The results of the present study showed significant increase in serum apelin, glucose, insulin levels and insulin resistance (IR) in rats of both strains after intake of HFD, when each was compared to their corresponding control rats. **Hussien et al. (2016)** reported that fasting blood glucose, insulin, the glycated hemoglobin (HbA1c) and homeostasis model assessment of HOMA-IR were higher in obese patients. The same findings were observed by **Assaad et al. (2015)** who confirmed the association between hyperinsulinemia and obesity. Insulin resistance was often linked to obesity, as excess adipose tissue plays a central role in the induction of insulin resistance (**Vandanmagsar et al., 2011**). These results were in agreement with **Buettner et al. (2007)** who reported hyperglycemia and hyperinsulinemia in HFD fed to C57BL/6J mice.

The results of the present study were in agreement with **Hancock et al. (2008)** who reported that administration of HFD to male Wistar rats induced insulin resistance of muscle glucose transport. Also, **Liu et al. (2015)** reported that administration of HFD to C57BL/6J mice induced hepatic insulin resistance. These

results were in agreement with the study of **Cekmez et al. (2011)** and **Altinkaya et al. (2014)**. They reported that hyperinsulinemia has a close correlation with apelin levels. Furthermore, the expression of apelin increased by hyperinsulinemia in obese condition with IR in rats and humans. These studies suggested a compensatory response of apelin to insulin resistance. **Cavallo et al. (2012)** and **Abd-Elbaky & Abo-ElMatty (2015)** who found that apelin levels showed higher significant values in obese diabetic groups compared to healthy subjects.

The results of the present study showed significant positive correlation between apelin levels and the calculated HOMA-IR in HFD groups. It has been postulated that the apelin levels are directly proportional to the degree of insulin resistance (**Yu et al., 2012**). **El-Dakak et al. (2013)** reported significant reduction in the blood glucose level after the administration of aqueous extract of LS to diabetic rats. In addition, LS contain alpha-linolenic acid which has an anti-inflammatory activity (**Diwakara et al., 2008**).

The present study showed that addition of LS powder to HFD significantly decreased serum apelin, glucose, insulin and insulin resistance in both strains when each was compared to their corresponding HFD fed rats, while in Wistar rats caused significant increases in serum apelin, glucose, insulin and insulin resistance when each was compared to their corresponding control rats. Also, in SD rats, it caused significant increase in serum glucose, insulin and insulin resistance. LS possess insulin mimetic

properties because of its biologically active substances, as alkaloids, that enhance glucose uptake by activating insulin receptor kinase activity and autophosphorylation of the insulin receptor (**Prajapati et al., 2014**). **Al-Kazraji (2012)** reported significant reduction in the blood glucose level and enhancement of insulin sensitivity by oral administration of aqueous extract LS to diabetic rats. He explained the possible mechanism of the extract could be by promoting insulin secretion via closure of K^+ ATPase channels, membrane depolarization and stimulation of Ca^{++} influx, an initial key step in insulin secretion.

The LS administration decreased serum apelin in this study may be due to the decrease in serum insulin as a parallel correlation between them has been reported by studies of (**Cekmez et al. 2011** and **Altinkaya et al. 2014**). Moreover, if LS treatment more than 8 weeks or with a higher dose, it might be possible to observe significant increase in serum apelin levels. AS obesity is probably not the main determinant of increased plasma apelin concentrations since circulating apelin levels are not necessary significantly correlated to the body mass index (BMI) in many studies (**Soriguer et al., 2009; Aydin, 2010** and **Telejko et al., 2010**).

The present study showed that administration of HFD caused significant increases in serum lipid profile in the form of total cholesterol, VLDL, triglycerides and LDL-C and significant decrease in serum level of HDL-C, in both strains when each was compared to their corresponding control rats. **Sour et al.**

(2015) showed significant increase in the serum concentrations of TG, TC and LDL-C after administration of HFD in male Wistar rats. **Ma et al. (2012)** reported that the TC and LDL-C levels of mice on the HFD increased dramatically in the first two weeks, followed by a slower increase. As regards serum level of HDL, the results of this study were in agreement with **Lavie and Milani (2003)** who reported that the reduction in HDL cholesterol level in animals fed HFD may be due to the decrease in lecithin-cholesterol acyltransferase (LCAT) activity, the key enzyme for extracellular cholesterol metabolism. This enzyme facilitates uptake of cholesterol from peripheral tissues to HDL particles by maintaining a concentration gradient for the efflux of free cholesterol, moreover, it is important in the maturation of HDL particles. So, decrease LCAT leads to decrease mature HDL generation with augmentation of atherosclerosis (**Kunnen and Van Eck, 2012**).

The present study showed that addition of LS powder to HFD diet of rats in both strains caused decrease in serum lipid profile in the form of total cholesterol, VLDL, triglycerides, LDL-C and significant increase in serum level of HDL-C when each was compared to their corresponding HFD fed rats. These results were in line with **Al Hamedan (2010) and Umesha and Naidu (2012)** who reported the hypolepidemic effect LS and LS powder added to hypercholesterolemic diet for in SD rats. Also, **Amawi & Aljamal (2012)** studied the effect of LS seed aqueous extract on lipid profiles and blood glucose levels of hypercholesterolemic and alloxan induced diabetic albino rats. They reported better

lipid profile and reduction in blood glucose level in both cases.

The hypolipidemic effect of LS might be attributed to inhibition of absorption and enhanced excretion of lipids (**Chauhan et al., 2012**). The hypocholesterolemic effect of LS might be attributed to inhibition of cholesterol biosynthesis. This is through the inhibition of hydroxymethylglutaryl co-enzyme A (HMG-CoA) reductase, the rate-limiting enzyme that mediates the first step in cholesterol biosynthesis (**Russell and DeBose-Boyd, 2008**).

The present study showed that administration of HFD caused significant increase in serum malondialdehyde (MDA) and significant decrease in serum level of reduced glutathione (GSH) in both strains when each was compared to their corresponding control rats. The results of the present study were in agreement with **Patel et al. (2007)** who reported that a diet high in fat and carbohydrates induces significant increase in oxidative stress (OS) parameters and inflammation in obese persons. The increase in obesity-associated OS is probably due to the presence of excessive adipose tissue itself, because adipocytes and preadipocytes have been identified as a source of proinflammatory cytokines, including TNF- α , IL-1, and IL-6. Thus, obesity is considered a state of chronic inflammation (**Fonseca-Alaniz et al., 2007**).

Obesity increases the mechanical load and myocardial metabolism. Therefore, oxygen consumption is increased. One negative consequence of increased oxygen consumption is the production of ROS as superoxide, hydroxyl radical, and hydrogen peroxide derived from the

increase in mitochondrial respiration and from the loss of electrons produced in the electron transport chain, resulting in the formation of superoxide radical (Amirkhizi et al., 2007).

The present study showed that administration of LS powder with HFD to rats for 8 weeks, showed significant increase in serum GSH and significant decrease in serum MDA, in both strains when each was compared to their corresponding HFD rats. Significant decrease occurred in serum GSH and significant increase in MDA, in both strains when each was compared to their corresponding control rats. These results were in agreement with the study of Qusti et al. (2016) who reported significant increase in the levels of GSH and significant decrease in the levels of MDA in serum and kidney tissue homogenate in rats received methanolic LS extract for 4 weeks. Also, these results were in correlation with the study of Mohamed and Safwat (2016). They reported that a diet supplemented with of LS seed powder restored the levels of myocardial MDA and GSH. They attributed this effect to its high content in antioxidants (vitamin C, E, carotenoids, polyphenols and flavonoids).

Choi et al. (2014) attributed the antioxidant activity of LS to the presence of total polyphenolic compounds. These polyphenolic compounds include flavonoids, anthraquinones, anthocyanidins, xanthenes and tannins. These compounds can scavenge free radicals, superoxide and hydroxyl radical by single electron transfer.

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تأثير حب الرشاد على مستويات الأبلين وبعض مقاييس الأيض والتأكسد في دم ذكور الجرذان السمينية

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خلفية البحث: البدانة مشكلة صحية كبرى في جميع أنحاء العالم تتميز بتراكم الدهون الزائدة التي تشكل خطراً على الصحة. وأبيلين هو ببتيد نشط بيولوجياً تم تحديده باعتباره واحداً من مؤشرات الدهون. ويعتبر الإنسولين أحد المنظمين الرئيسيين لإنتاج الأبيلين ويعكس الإجهاد التأكسدي عدم التوازن بين قدرة الجسم المضادة للأكسدة والمنتجات المؤكسدة السامة. وأظهرت بذور حب الرشاد تأثيراً مضاداً للأكسدة ونشاطاً مضاداً للبول للسكري.

الهدف من الدراسة: تهدف هذه الدراسة إلى معرفة تأثير بذور حب الرشاد على مستويات الأبيلين وبعض مقاييس الأيض والتأكسد في دم ذكور الجرذان السمينية.

مواد وطرق البحث: تم إجراء هذه الدراسة على ستين فأراً: ثلاثين من فصيلة فيستر وثلاثين من فصيلة سبريج داولي، بواقع عشر فئران لكل مجموعته مقسمة كالتالي:

المجموعة الأولى: (المجموعة الضابطة من فئران فصيلة فيستر)، والمجموعة الثانية: (المجموعة عالية الدهون من جرذان فصيلة فيستر)، والمجموعة الثالثة (المجموعة عالية الدهون المعالجة ببذور حب الرشاد من جرذان فصيلة فيستر)، والمجموعة الرابعة (المجموعة الضابطة من جرذان فصيلة سبريج داولي)، والمجموعة الخامسة (المجموعة عالية الدهون من جرذان فصيلة سبريج داولي) والمجموعة السادسة (المجموعة المعالجة ببذور حب الرشاد من جرذان فصيلة سبريج داولي). وقد تم قياس الوزن أسبوعياً، وفي نهاية التجربة تم جمع عينات الدم وفصل المصل لقياس مستويات الجلوكوز، والإنسولين، والأبيلين، ومعدل مقاومة الإنسولين، ومستوى الدهون في الدم (نسب الكوليسترول الكلى، الكوليسترول في البروتينات الدهنية منخفضة الكثافة ومنخفضة الكثافة جداً، والكوليسترول في البروتينات الدهنية عالية الكثافة والدهون الثلاثية)، ومستوى الجلوتاثيون ومستوى المالونديالدهيد.

النتائج: أظهرت النتائج أن إضافة بذور حب الرشاد إلى الفئران من فصيلة فيستر أدى إلى زيادة في وزن الجسم المكتسب، مؤشر الدهون، ومستوى الجلوتاثيون والكوليسترول في البروتينات الدهنية عالية الكثافة، مع انخفاض ذو دلالة إحصائية في مستويات: الجلوكوز، والإنسولين، والألبين، ومعدل مقاومة الأنسولين، والكوليسترول الكلى، والكوليسترول في البروتينات الدهنية منخفضة الكثافة، والكوليسترول في البروتينات الدهنية منخفضة الكثافة جداً، والدهون الثلاثية ومستوى المالموندايالدهيد. كما أظهرت النتائج أن إضافة بذور حب الرشاد إلى الفئران من فصيلة سبريج داوولي قد أدى إلى زيادة ذات دلالة غير إحصائية في وزن الجسم المكتسب، ومؤشر الدهون، مع انخفاض ذا دلالة إحصائية في مستويات الجلوكوز، والإنسولين، والألبين، ومعدل مقاومة الأنسولين، والكوليسترول الكلى، والكوليسترول في البروتينات الدهنية منخفضة الكثافة، والكوليسترول في البروتينات الدهنية منخفضة الكثافة جداً، والدهون الثلاثية ومستوى المالموندايالدهيد. وعلى العكس من ذلك فقد ارتفع مستوى كلاً من الجلوتاثيون والكوليسترول في البروتينات الدهنية عالية الكثافة ارتفاعاً ذا دلالة إحصائية.

الإستنتاج: يمكن لبذور حب الرشاد تقليل إضطرابات الايض والأكسدة الناتجة من الغذاء عالي الدهون بدليل عودة الألبين والكوليسترول في البروتينات الدهنية منخفضة الكثافة جداً إلى مستواهم الطبيعي تقريبا بعد إستخدام بذور حب الرشاد في الفئران من فصيلة سبريج داوولي. ولكن أدى إستخدام بذور حب الرشاد بجرعة الدراسة إلى زيادة في الوزن في فئران الفصيلتين.