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Research Article

CORN SILK OFFERS MULTIMECHANISTIC APPROACHES IN MITIGATING OBESITY IN RODENTS

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ABSTRACT

Objective: The current study aimed to investigate the effect of corn silk extracts (aqueous and methanolic) against obesity in an animal model.

Methods: Animals were fed high-cholesterol diet (HCD) for 12 W to induce obesity and then treated either with Orlistat, corn silk extracts (aqueous and methanolic) for 6 W. Anthropometric measurements (abdominal circumference [AC], thoracic circumference [TC], and body mass index [BMI]) were recorded. Biochemical parameters including lipid profile (serum total cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein, and lipase), glucose, insulin, and homeostasis model assessment of basal insulin resistance were assayed. Inflammatory cytokines visfatin, haptoglobin (Hp), afamin, endothelin-1, calprotectin, and protein S100B levels were quantified.

Results: Significant decrease in TC, AC, and BMI was detected in HCD-fed groups treated with corn silk extracts with respect to HCD-fed group. Biochemical analyses indicated marked hypolipidemic and hypoglycemic effects of corn silk extracts. Treatment of HCD-fed groups with corn silk extracts experienced significant regression of visfatin, Hp, endothelin-1, calprotectin, and protein S100B levels relative to HCD-fed group.

Conclusion: In conclusion, the current findings revealed the antiobesity potential of corn silk extracts. This effect may be attributed to its hypolipidemic, hypoglycemic, and anti-inflammatory properties of the active phytochemicals present in the extracts.

Keywords: Obesity, Corn silk, Insulin resistance, Hyperlipidemia, Inflammation, Rodents.

INTRODUCTION

Obesity, a health problem which is relevant in the worldwide, affects more than 185 million adults in the industrialized nations, 115 million in the developing countries, and more than 18 million children under the age of five [1]. The current health crisis was focused in weight control via many ways such as diet, exercise, surgery, and pharmaceuticals administration. 5-10% weight loss could reduce the risk factor of cardiovascular disease, blood pressure improvements, cholesterol level, Type-2 diabetes, and inflammation. This is because of the association between obesity and many diseases as coronary heart disease, Type-2 diabetes, dyslipidemia, hypertension as well as cancer has been documented [2].

Pharmacologically, orlistat has been revealed to stimulate weight loss and weight maintenancein obese cases through prevention of gastric as well as pancreatic lipase, the enzyme which promotes long chain triglycerides (TG) digestion [3]. Drew *et al*. [3] have been found that orlistat at a dose of 120 mg three times daily could inhibit about 30% of fat absorption. Nevertheless, till now, the effect of orlistat on the clinical outcomes of other diseases not known. Karamadoukis *et al*. [4] have been found that orlistat has side effects as insomnia, constipation, headache, increased blood pressure as well as dry mouth.

Sustainable agents from natural sources could serve as viable alternatives to currently available synthetic drugs in the management of obesity. This is of special importance owing to the adverse effects of most synthetic drugs and their high costs which make them not readily accessible to many patients in developing countries-like Egypt.

Corn (*Zea mays* Linnaeus), also known as maize, is a member of the family Gramineae. Now, it is widely cultivated all over the world [5]. Corn silk is ascribed as stigmata of maize; it is yellowish thread-like strands from the female flowers of *Z. mays* L. (Gramineae) with 10-20 cm long. It is a waste material from corn cultivation and available in abundance. Corn silk contains phytochemicals of medical benefits such as proteins, vitamins, carbohydrates and natural sugars, fibers, mineral salts such as Ca, K, Mg, and Na salts, fixed and volatile oils, steroids such as sitosterol and stigmasterol, alkaloids, saponins, tannins, and phenolic compounds, particularly flavonoids as well as chlorogenic acid, p-coumaric, ferulic acid, phytosterols, fixed oil, resin, and allantoin [6]. The methanol extract of corn silk showed antioxidant activity on the level of lipid peroxidation because of its high content of flavonoids which are effective antioxidant [7].

Corn silk has been consumed for a long time as a therapeutic remedy for various illnesses and is important as an alternative natural-based treatment. It has been used as traditional medicine in many parts of the world such as China, Turkey, United States, and France. It is used for the treatment of cystitis, edema, kidney stones, diuretic, prostate disorder, and urinary infections as well as bedwetting [8].

The focus of our interest was to explore the potency of corn silk aqueous as well as methanolic extract against obesity induced in experimental animals with special concern to its mode of action.

MATERIALS AND METHODS

Materials

Chemicals and drugs

Cholesterol and orlistat drug were purchased from Sigma Chemical Co. USA. All other chemicals and solvents were of analytical grade.

Plant material

Fresh corn silk was obtained from local market Giza, Egypt. Corn silk was washed with distilled water, and dried for 24 hrs using a hot air oven at 60°C until it turned brown and powdered using a grinder, and then stored in a drying cabinet at 4°C until used.

Preparation of corn silk extract

Preparation of corn silk aqueous extract

Aqueous corn silk extract was prepared according to the method described by Velazquez *et al*. [9]. Briefly, aqueous extraction of corn silk was performed by adding 100 ml boiling water to 10 g corn silk powder, and the extract was filtered after 20 minutes and then lyophilized using freeze drier (LABCONCO) freeze dry system/Lyph Lock 4.5, Model 38028, made in England, Kansas City, MO.

Preparation of corn silk methanolic extract (CSME)

Methanolic extract of corn silk was prepared by extracting 25 g of powdered corn silk in 100 ml methanol/water (80% v/v), left at room temperature for 24 hrs, and then filtered. The filtrates were evaporated under reduced pressure at 45°C in a rotatory evaporator (Heidolph, Germany) till dryness [10].

Experimental protocol

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.

A total of 40 adult female albino rats of Wistar strain, weighing 130±10 g at 90 d of age, were enrolled in the present study. The animals were obtained from the Animal House Colony of the National Research Centre, Cairo, Egypt. The animals were housed 8 rats/cage in polypropylene cages in an environmentally controlled clean air room with a temperature of 24±1°C, a 12 hrs light/12 hrs dark cycle, a relative humidity of 60±5% and free access to tap water and standard rodent chow. Rats were allowed to adapt to these conditions for 2 W before the commencement of the experiment. After the acclimatization period, eight rats were fed a standard rodent chow with 26.5% protein, 3.8% fat, 40% carbohydrate, and 4.5% crude fiber in 100 g of chow according to Buettner *et al*. [11] during 18 W of the experimental period and served as lean control group (control group). The other 32 rats were fed a high-cholesterol diet (HCD) with 19.93% protein, 15% cholesterol, 57.50% carbohydrate, and 2.81% dietary fiber in 100 g of chow following the modified method of Soliman *et al*. [12]. Eight rats were then taken, left untreated for other 6 weeks and served as an obese group (obese group). The last 24 rats were assigned into three equal groups that orally administered orlistat (200 mg/kg b.wt.) daily according to Nishioka *et al*. [13] for 6 W (Ob+Orlistat); Corn silk aqueous extract (400 mg/kg b.wt.) daily for 6 W (Ob+CSAE); and CSME (400 mg/kg b.wt.) daily according to Bhaigyabati *et al*. [14] for 6 W (Ob+CSME).

Samples collection

After animal treatment was over, the animals were fasted overnight (12-14 hrs), and the blood samples were collected, under diethyl ether anesthesia, from the retroorbital venous plexus in a clean dry centrifuge tubes without any anticoagulant agent and allowed to coagulate for 45 minutes at room temperature to obtain sera to be used for biochemical analysis. Serum samples were separated by centrifugation at 1800 × g for 15 minutes at 4°C using cooling centrifuge. Aliquots of serum were frozen and stored at −20°C pending further biochemical analyses. After collection of the blood samples, the animals were scarified by cervical dislocation.

Methods

Anthropometric measurements

The abdominal circumference (AC) (immediately anterior to the forefoot), thoracic circumference (TC) (immediately behind the foreleg), and body length (nose-to-anus or nose-anus length) were measured in anesthetized rats at the end of the experimental period (18 W). Body weight and body length were measured to be used for determination of body mass index (BMI) [15].

$$BMI\ (g/cm^2) = (Body\ weight\ (g)/Length^2\ (cm^2))$$

Biochemical determinations

Serum total cholesterol, TG, high-density lipoprotein (HDL), and glucose levels were determined by colorimetric method using kits purchased from Reactivos GPL (Barcelona, Spain) following the methods of Meiattini [16], Bucolo and David [17], Naito [18], and Young [19], respectively. Quantitative determination of serum lipase activity was done using kinetic kit purchased from Chronolab Co. (Barcelona, Spain) according to the method described by Young [19]. Serum insulin level was quantified using enzyme-linked immunosorbent assay (ELIZA) kit purchased from Immunospec Co. (Netherlands) following the method of Eastham [20]. The homeostasis model assessment of basal insulin resistance (HOMA-IR) was used to calculate the index from the product of the fasting concentration of serum glucose (mmol/L) and serum insulin (mU/ml) divided by 22.5 according to the method of Duncan *et al*. [21]. Serum visfatin, afamin, endothelin-1, and calprotectin levels were estimated by ELIZA using kits purchased from Glory Science Co., Ltd, USA, according to manufacturer's instructions. Quantitative estimation of the serum haptoglobin (Hp) level was carried out using ELIZA kit purchased from Assaypro LLC (USA) according to Van Vlierberghe *et al*. [22] method. Quantitative determination of serum protein S100B level was performed using ELIZA kit purchased from Wuhan Eiaab Science Co., Ltd., China according to manufacturer's instruction.

Statistical analysis

The experimental results were represented as arithmetic means with their standard errors (se) (mean±SE). Data were analyzed by one-way analysis of variance using the Statistical Package for the Social Sciences program, version 14 followed by least significant difference to compare significance between groups [23]. The level of significance was set at $p<0.05$. Percentage difference representing the percent of variation with respect to the corresponding control group was also calculated using the following formula:

% difference = (Treated value-control value)/control value)×100

RESULTS

Anthropometrical measurements

The results of the present study recorded significant increase ($p<0.05$) in the TC, AC, and BMI in HCD-fed group with respect to the placebo group. Meanwhile, there is significant decrease ($p<0.05$) in TC, AC, and BMI in HCD-fed groups treated with orlistat, corn silk aqueous or methanolic extract relative to the untreated HCD-fed group (Table 1).

Biochemical determinations

Table 2 illustrated the impact of orlistat, aqueous or methanolic extract of corn silk on lipid profile (cholesterol, TG, HDL, low-density lipoprotein [LDL], and lipase) of HCD-fed rats. The current study showed significant elevation ($p<0.05$) in cholesterol, TG, LDL serum levels, and lipase activity in HCD-fed group comparing with placebo group. Significant depletion ($p<0.05$) was observed in serum HDL in HCD-fed group comparing with placebo group. Treatment of HCD-fed group with orlistat, aqueous or methanolic extract of corn silk elicited significant depletion ($p<0.05$) in cholesterol as well as LDL serum levels as compared to with the HCD-fed group. Treatment of HCD-fed group with orlistat elicited significant depletion ($p<0.05$) in TG serum level as well as lipase activity comparing with the HCD-fed group. However, treatment of HCD-fed groups with aqueous or methanolic extracts of corn silk elicited insignificant depletion ($p<0.05$) in TG as well as lipase serum levels comparing with the HCD-fed group. Regarding serum HDL level, treatment of HCD-fed group with orlistat, aqueous or methanolic extract of corn silk experienced a significant increase ($p<0.05$) in serum HDL level comparing with HCD-fed group (Table 2).

The current study results recorded significant increase ($p<0.05$) in serum glucose, insulin levels, insulin resistance value, and visfatin level in the HCD-fed group versus the placebo group. Meanwhile, treatment of HCD-fed group with orlistat, aqueous or methanolic extract of corn

silk produced significant depletion ($p<0.05$) in glucose, insulin serum levels, insulin resistance value as well as visfatin level comparing with those in the HCD-fed group (Table 3).

The results recorded in Table 4 showed significant elevation ($p<0.05$) in Hp as well as endothelin-1 serum levels in the HCD-fed group comparing with the placebo group. Afamin serum level recorded insignificant depletion ($p<0.05$) in the HCD-fed group comparing with the placebo group. Meanwhile, treatment of HCD-fed group with orlistat elicited significant depletion ($p<0.05$) in Hp as well as endothelin-1 serum levels comparing with the HCD-fed group. However, treatment of HCD-fed group with orlistat elicited insignificant increase ($p<0.05$) in serum afamin level comparing with that in the HCD-fed group. Significant depletion ($p<0.05$) in serum endothelin-1 level has been observed in HCD-fed rats treated with aqueous or methanolic extract of corn silk when compared with those in the HCD-fed group. While insignificant depletion ($p<0.05$) in Hp serum level has been observed in HCD-fed rats and treated with aqueous or methanolic extract of corn silk when compared with that in the HCD-fed group. Afamin serum level recorded insignificant increase ($p<0.05$) in HCD-fed group administered aqueous or methanolic extract of corn silk as compared to the HCD-fed group.

The data illustrated in Table 5 showed the effect of treatment with orlistat, aqueous or methanolic extract of corn silk on serum calprotectin B; calcium-binding protein (S100B) levels have been recorded in HCD-fed rats. Significant elevation ($p<0.05$) in calprotectin B as well as S100B serum levels of HCD-fed rats comparing with the placebo group. Meanwhile, treatment of HCD-fed group with orlistat, aqueous or methanolic extract of corn silk elicited significant decrease ($p<0.05$) in serum calprotectin B level when compared with that in the HCD-fed group. Treatment of HCD-fed group with orlistat or aqueous extract of corn silk induced significant depletion ($p<0.05$) in S100B serum level comparing with the HCD-fed group. However, treatment of HCD-fed group with methanolic extract of corn silk caused insignificant

Table 1: The impact of orlistat, corn silk aqueous or methanolic extract on anthropometric measurements of HCD-fed rats

Parameters groups	Thoracic (cm)	Abdominal (cm)	BMI (g/cm^2)
Placebo group	14.50±0.25	11.66±0.36	0.68±0.02
HCD-fed group	17.5±0.25^a (20.69%)	13.6±0.15^a (17.14%)	0.94±0.08^a (38.34%)
HCD+Orlistat	15.83±0.35^b (−9.52%)	12.58±0.34^b (−7.92%)	0.69±0.04^b (−25.84%)
HCD+CSAE	15.98±0.19^b (−8.67%)	12.75±0.125^b (−6.7%)	0.72±0.066^b (−23.72%)
HCD+CSME	16.0±0.31^b (−8.57%)	13.0±0.26 (−4.88%)	0.72±0.04^b (−22.86%)

Results were expressed as mean±SE (8 rats/group). a: The significant at $p>0.05$ comparing with the placebo group, b: The significant at $p>0.05$ comparing with the HCD-fed group, c: The significant at $p>0.05$ comparing with the HCD+orlistat group, %: The percent of change with respect to its corresponding control. CSAE: Corn silk aqueous extract, CSME: Corn silk methanolic extract, HCD: High-cholesterol diet, BMI: Body mass index, SE: Standard error

Table 2: The impact of orlistat, corn silk aqueous or methanolic extract on lipid profile of HCD-fed rats

Parameters groups	Cholesterol (mg/dL)	TG (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	Lipase (U/L)
Placebo group	60.61±1.78	55.3±2.23	38.5±1.37	18.27±0.38	14.94±0.26
HCD-fed group	111.16±1.85^a (83.39%)	78.36±2.39^a (41.7%)	20.18±0.79^a (−47.58%)	27.67±2.19^a (51.46%)	23.05±2.49^a (54.24%)
HCD+Orlistat	69.19±4.36^b (−37.75%)	66.58±5.1^b (−15.03%)	25.31±0.39^b (25.43%)	19.94±1.93^b (−27.95%)	18.66±0.39^b (−19.01%)
HCD+CSAE	74.25±4.5^b (−33.19%)	69.77±2.73 (−10.96%)	29.92±0.2^{bc} (48.27%)	21.39±1.57^b (−22.69%)	19.67±0.6 (−14.65%)
HCD+CSME	79.12±3.77^b (−28.82%)	76.19±1.37^c (−2.77%)	32.65±1.44^{bc} (61.83%)	23.17±0.57^b (−16.26%)	20.9±1.67 (−9.27%)

Results were expressed as mean±SE (8 rats/group). a: The significant at $p>0.05$ comparing with the placebo group, b: The significant at $p>0.05$ comparing with the HCD-fed group, c: The significant at $p>0.05$ comparing with the HCD+orlistat group, %: The percent of change with respect to its corresponding control. CSAE: Corn silk aqueous extract, CSME: Corn silk methanolic extract, LDL: Low-density lipoprotein, HCD: High-cholesterol diet, SE: Standard error, HDL: High-density lipoprotein

Table 3: The impact of orlistat, corn silk aqueous or methanolic extract on serum glucose, insulin levels, insulin resistance value, and visfatin level of HCD-fed rats

Parameters groups	Glucose (mg/dL)	Insulin (µU/ml)	Insulin resistance value	Visfatin (µg/L)
Placebo group	49.71±3.93	12.07±0.39	0.66±0.027	1.98±0.16
HCD-fed group	116.83±3.77^a (134.99%)	18.3±0.35^a (49.43%)	1.1±0.025^a (66.6%)	2.97±0.15^a (49.61%)
HCD+Orlistat	58.12±4.48^b (−50.25%)	13.11±0.52^b (−28.1416%)	0.726±0.034^b (−34%)	2.11±0.05^b (−28.86%)
HCD+CSAE	69.97±4.47^b (−40.11%)	14.1±1.0^b (−22.71%)	0.799±0.054^b (−27.3%)	2.25±0.19^b (−24.27%)
HCD+CSME	70.89±5.25^{bc} (−39.32%)	14.93±1.52^b (−18.19%)	0.838±0.0805^b (−2381%)	2.36±0.2^b (−20.42%)

Results were expressed as mean±SE (8 rats/group). a: The significant at $p>0.05$ comparing with the placebo group, b: The significant at $p>0.05$ comparing with the HCD-fed group, c: The significant at $p>0.05$ comparing with the HCD+orlistat group, %: The percent of change with respect to its corresponding control. CSAE: Corn silk aqueous extract, CSME: Corn silk methanolic extract, HCD: High-cholesterol diet, SE: Standard error

Table 4: The impact of orlistat, corn silk aqueous or methanolic extract on serum Hp, afamin, and endothelin-1 levels of HCD-fed rats

Parameters groups	Hp (µg/mL)	Afamin (Pg/mL)	Endothelin-1 (ng/L)
Placebo group	1.57±0.01	6517.5±457.2	761.43±11.56
HCD-fed group	1.72±0.08^a (9.15%)	5962.5±407.7 (−8.51%)	841.64±7.06^a (10.53%)
HCD+Orlistat	1.59±0.018^b (−7.41%)	6207.5±152.5 (4.11%)	780.0±13.49^b (−7.32%)
HCD+CSAE	1.61±0.003 (−6.06%)	6095.0±966.64 (2.22%)	794.28±9.42^b (−5.62%)
HCD+CSME	1.65±0.04 (−3.82%)	6198.7±238.1 (3.96%)	779.3±11.65^b (−7.41%)

Results were expressed as mean±SE (8 rats/group). a: The significant at $p>0.05$ comparing with the placebo group, b: The significant at $p>0.05$ comparing with the HCD-fed group, c: The significant at $p>0.05$ comparing with the HCD+orlistat group, %: The percent of change with respect to its corresponding control. CSAE: Corn silk aqueous extract, CSME: Corn silk methanolic extract, HCD: High-cholesterol diet, SE: Standard error

Table 5: The impact of orlistat, corn silk aqueous or methanolic extract on serum calprotectin B and S100B levels of HCD-fed rats

Parameters groups	Calprotectin B (Pg/ml)	S100B (Pg/ml)
Placebo group	436.0±6.97	7.35±0.28
HCD-fed group	619.5±9.14[a] (42.1%)	22.33±1.1[a] (203.66%)
HCD+Orlistat	506.4±8.75[b] (−18.25%)	15.44±1.24[b] (−30.83%)
HCD+CSAE	554.3±8.92[bc] (−10.51%)	18.47±1.11[b] (−17.27%)
HCD+CSME	539.5±7.19[bc] (−12.91%)	19.84±1.39[c] (−11.16%)

Results were expressed as mean±SE (8 rats/group). a: The significant at p>0.05 comparing with the placebo group, b: The significant at p>0.05 comparing with the HCD-fed group, c: The significant at p>0.05 comparing with the HCD+orlistat group, %: The percent of change with respect to its corresponding control, HCD: High-cholesterol diet. CSAE: Corn silk aqueous extract, CSME: Corn silk methanolic extract, SE: Standard error

depletion (p<0.05) in S100B serum level comparing with the HCD-fed group.

DISCUSSION

The present study showed encouraging findings on the hypolipidemic, hypoglycemic, and anti-inflammatory influence of corn silk aqueous and methanolic extract which qualifies corn silk extracts to be promising candidates for mitigating obesity.

Herein, we recorded a significant increase in anthropometric measurements (TC, AC, and BMI) in the HCD-fed group with respect to the placebo group. These results were in agreement with Hasanudin *et al*. [5], who have been stated that HCD causes fat accumulation in both thoracic as well as the abdominal region. Thus, the body weight was increased because of the increment of energy intake and accumulation of adipose tissue. As BMI has been revealed to be a reliable measurement of body fat and obesity in rats[15]. Thus, the positive correlations between daily lipid intake and BMI and fat deposition have been reported [24].

There was a significant decrease in the anthropometric measurements in HCD-fed groups treated with orlistat, corn silk aqueous or methanolic extract versus the HCD-fed group. It has been revealed that lipstatin saturated derivative, orlistat, an important pancreatic lipases inhibitor from natural source isolated from *Streptomyces toxytricini* bacteria. Thus, orlistat is documented as an antiobesity drug rather than lipstatin because of its simplicity as well as stability [25]. Orlistat causes weight loss more than that caused *via* an individual on a fat-restricted diet replacement because orlistat can decrease the dietary fat absorption by up to 30% [26].

The corn silk extract has been found to have total flavonoids which showed the hypolipidemic effect on experimental animals. It has been suggested that flavonoids from corn silk extract possessed protective properties against atherogenesis. The mechanism by which flavonoids extract lowered TG could be either by decreasing very LDL synthesis through increase lipoprotein lipase activity. The observed hypolipidemic effect might be the synergistic action of these compounds by controlling the hydrolysis of lipoprotein and inhibition of cholesterol absorption [27].

The current study revealed that there is an obvious hyperlipidemia in HCD-fed group versus the placebo group. The obtained data are in agreement with Son *et al*. [28], who observed high cholesterol as well as TG level in HCD-fed rats. Furthermore, Fruchart *et al*. [29] have demonstrated that adipose tissue lipid is mostly derived from circulating TG, especially during HCD feeding. Furthermore, Novelli *et al*. [15] have been documented that serum LDL level increased in both obese rats as well as HCD-fed rats. Moreover, depletion in HDL has been reported by Raveh *et al*. [30], in accordance with the current study results, due to depletion of the reverse cholesterol transport from blood to the liver. HCD administration leads to oxidative stress which causes increment of reactive oxygen species (ROS) production. The excess of ROS leads to cellular damage through oxidation of critical cellular components as membrane lipids, proteins, and DNA [31].

Treatment of HCD-fed group with orlistat elicited a significant decrease in serum cholesterol, TG, LDL levels, and lipase activity when compared with those in the HCD-fed group. Regarding serum HDL level, treatment of HCD-fed group with orlistat showed a significant elevation in HDL serum level comparing with that recorded in the HCD-fed group. Orlistat had the ability to reduce lipid profile such as cholesterol, TG, LDL, and elevate HDL [1]. The improvement in concentrations of cholesterol and triacylglycerols resulted from treatment with orlistat is attributed to its effect on the body's ability to absorb dietary fats; orlistat therapy is known to be associated with an increased incidence of gastrointestinal events in its users [32]. The pharmacological function of orlistat in stimulating weight loss in obese subjects is through gastric as well as pancreatic lipase prevention and lipid profile depletion [1]. It has been revealed that orlistat inhibits a gastric as well as pancreatic lipase and disturb the energy balance via inhibition the gastrointestinal tract absorption of TG as well as cholesterol. Moreover, orlistat made a covalent bound with the serine residue, the active site on lipase, which in turn causing inhibition of the enzyme [33]. Orlistat blocked lipase activity and inhibited hydrolysis of TG from diet to absorbable free fatty acids and excreted undigested instead. The primary route of elimination is through the feces. Furthermore, it was reported that orlistat reduced fat absorption which indicating a depletion of LDL cholesterol in serum. It has been reported that orlistat therapy causes inhibition of cholesterol absorption by about 25% and fat absorption by about 30% [34].

Treatment of HCD-fed groups with aqueous or methanolic extract of corn silk experienced significant hypolipidemic effect as indicated by decreasing serum cholesterol, TG, whereas increasing HDL in comparison with those recorded in the HCD-fed group. These results are in agreement with Kaup *et al.* [35]. It has been demonstrated that treatment of diabetic rats with corn silk extract causes improvement of lipid profile, and this may be related to the flavonoid compounds of corn silk extract that may have potential antihyperlipidemic effects. Weggemans and Trautwein [36] reported that flavonoids intake decrease LDL and increased HDL that may enhance removal of cholesterol from peripheral tissue to the liver for catabolism and excretion. Moreover, several studies revealed that isoflavones are able to decrease cholesterol in serum via increasing of LDL receptor activity. It has been reported that many natural products as well as medicinal plants are lipase inhibitor agents. Corn silk extract decreases serum lipase activity due to its bioactive compounds that reported to inhibit porcine lipase such as polyphenols, tannins, proanthocyanidin, and flavonoids contents [37].

The present results recorded a significant increase in serum glucose, insulin levels, insulin resistance value, and visfatin level in the HCD-fed group comparing with the placebo group. These results are in agreement with Galisteo *et al*. [38]. Ginsberg and Stalenhoef [39] have been reported that increased lipolytic activity in fat accumulation leads to increase free fatty acids flux to the liver which causing stimulation of gluconeogenesis as well as depletion of insulin effect on peripheral glucose. Furthermore, it has been recorded that obesity is caused low-grade chronic systemic inflammation which may be led to insulin resistance. Conditions as lipid disturbances, hypertension, and diabetes as well as insulin resistance may cause increasing the morbidity which is associated obesity [40]. Insulin signaling in adipose tissue plays a key role in the storage of lipid as well as glucose homeostasis regulation. Furthermore, adipocytes insulin signaling is critical for obesity development and its associated metabolic abnormalities, and abrogation of insulin signaling in fat unmasks a heterogeneity in adipocyte response in terms of gene expression as well as the storageof TG [41]. The linkage between obesity and systemic inflammation has

been evidenced. Visfatin can be considered a new pro-inflammatory adipocytokine. Visfatin, pre-B cell colony-enhancing factor, has been identified as adipocytokine which affecting insulin resistance via binding to the insulin receptor. Visfatin secretes from visceral adipose tissue, its level in plasma linked with the amount of visceral fat in humans as well as experimental animals and the elevated visceral body fat is correlated to insulin resistance in adults. A great line of evidence indicated a role for visfatin in glucose homeostasis [42]. It has been reported that there is a significant positive correlation between plasma visfatin and anthropometric markers including weight, BMI, and waist-hip circumferences in obese subjects. Moreover, significant positive correlation between visfatin and fasting insulin, HOMA, and lipid parameters in obese subjects has been manifested [43]. Accordingly, visfatin possesses an insulin-like activity in obesity insulin-resistant milieu. As visfatin imitates the effects of insulin through a binding site on the insulin receptor. Thus, visfatin exerts insulin-mimetic effects in muscle and adipocyte glucose transport stimulation and in hepatocyte glucose production inhibition. Noteworthy, visfatin as well as insulin did not compete for binding to the insulin receptor, indicating that the two proteins were recognized by different regions of the receptor [44]. Visfatin plasma level increased in obesity and accompanied with LDL as well as low HDL cholesterol level elevation. The negative correlation of visfatin, as well as HDL, has occurred in diabetic and obese patients. Finally, visfatin serum levels elevated in obesity gives evidence that central obesity correlated with physical inactivity, higher glucose, insulin, amino acids, and triacylglycerols as well as inflammation due to visfatin increment [45].

Treatment of HCD-fed group with orlistat, aqueous or methanolic extract of corn silk produced a significant decrease in serum glucose, insulin levels, insulin resistance value, and visfatin level when compared with those in the HCD-fed group. A significant effect of orlistat treatment on insulin and glucose levels has been revealed by Shalaby *et al*. [1]. Obesity is accompanied insulin resistance with hyperinsulinemia as well as lipid metabolism disturbance. Insulin-resistance as well as hyperinsulinemia occurred due to vascular dysfunction because of reversing endothelium-dependent vasodilating and vasoconstrictor, insulin are shifted toward a permanent vasoconstriction in obese patients. Thus, orlistat addition to a conventional weight loss regimen revealed significant improvement of oral glucose tolerance and diminished the progression to the development of impaired glucose tolerance and Type-2 diabetes [1].

The administration of aqueous or methanolic extract of corn silk showed hypoglycemic and hepatoprotective effects in rabbits [6]. In our study, methanol corn silk extract administration showed hypoglycemic effect which is consistent with the reports of Ajali *et al*. [46], who reported that corn silk extract phytochemicals cause significant reduction in blood glucose and Guo *et al*. [47], who found that the extract corn silk deplete hyperglycemia in diabetic mice. The effect of corn silk extract on the metabolism of glucose *via* elevating the sensitivity of insulin and the injured β-cells recovery. Guo *et al*. [47]revealed that the extract of corn silk could use as a hypoglycemic food or medicine for hyperglycemic people. The aqueous extract of corn silk also decrease glucose concentration and inhibit glucose-induced insulin secretion *via* inhibition of glucokinase enzyme [47].

Treatment of HCD-fed group with orlistat, aqueous or methanolic extract of corn silk caused significant depletion in visfatin serum level comparing with that in the HCD-fed group. This effect may contribute to the role of visfatin in glucose homeostasis [42] and due to the significant positive correlations between visfatin and fasting insulin, HOMA, and lipid parameters [48].

The data of the current study showed a significant elevation in Hp as well as endothelin-1 serum levels in HCD-fed group comparing with the placebo group. Afamin serum level recorded insignificant decrease in the HCD-fed group as compared to the placebo group. Hp is a glycoprotein produced by many cytokines, LPS as well as by inflammation. Significant upregulation of Hp in the obese animals has been revealed [48]. Hp expression is occurred in adipocytes and its level in the circulation is considered as a marker of adiposity because of the relation between Hp serum levels with body weight elevation. Moreover, the association of circulating Hp concentration with BMI has been reported, which could be dependent on the Hp expression in adipose tissue. Moreover, serum Hp levels increased with increased insulin resistance and obesity [49].

Obesity contributes to the imbalance between increase calorie intake as well as decrease physical activity is one of the emerging global health issues and is linked with an activated endothelin system in humans with or without hypertension [50]. Levels of the endothelium-derived peptide endothelin-1 (ET-1) are increased in obese subjects, and ET-1 mediated vascular tone is elevated. Blood vessels of obese rats contain an elevated expression of ET-1 gene as well as ETA receptor protein, but the effect of elevated body weight on the responsiveness to the vasoconstrictor peptide is not homogenous among murine conduit arteries [51]. The increased ET-1 may be due to NO release as a result of activation of endothelial ETB receptors. Furthermore, the increased plasma ET-1 concentrations in human obesity could depend on fasting insulin concentrations, abnormal peptide clearance, or both [52].

Afamin vitamin E binding protein (a member of the albumin gene family) that is associated with several key parameters of the metabolic syndrome. Afamin concentration is also positively correlated with increasing BMI, obesity, systolic as well as diastolic blood pressure, diabetes, and LDL as well as HDL-cholesterol, TGs, free fatty acids, and glucose as well as HbA1c plasma level. Moreover, it has been revealed that afamin strongly linked with TGs as well as waist circumference in adults [53].

Treatment of HCD-fed group with orlistat elicited significant depletion in Hp and endothelin-1 serum levels accompanied with insignificant elevation in afamin serum level comparing with the HCD-fed group. However, HCD-fed group treated with aqueous or methanolic extract of corn silk elicited an insignificant decrease in Hp and significant decrease in endothelin-1 in association with in significant increase in serum afamin when compared with those in the HCD-fed group.

Kesh *et al*. [54] have been reported that high-fat diet (HFD) induced systemic oxidative stress insults an imbalance between oxidants derivatives production and antioxidants defenses. Furthermore, Hp could be due to oxidative stress as well as low-grade chronic inflammation. This is linked with the syndrome of polycystic ovary, obesity as well as glucose tolerance disturbance [55]. Moreover, it has been demonstrated that the expression of Hp in white adipose tissue (WAT) is elevated in obesity in experimental animals and TNF-α is an important signal for this regulation [48]. Corn silk has been reported to inhibit tumor necrosis factor TNF-α and lipopolysaccharide (LPS)-induced cell adhesion [56]. This is a suggested mechanism for reducing serum Hp level because of the treatment of HCD-fed rats with the extract of corn silk.

It has been found that in hypertensive obese subjects possess enhanced vascular activity to endogenous ET-1. Recently, a correlation between ET-1 gene and blood pressure levels was reported in obese Japanese subjects. Orlistat has been found to cause a significant reduction in systolic and diastolic blood pressure with consequent suppression in serum ET-1 level [57].

Corn silk extract was used in the Chinese traditional medicine for the treatment of dropsy as well as hypertension [58]. Thus, the decrease in serum ET-1 level due to treatment with corn silk extract might be attributed to the antihypertensive action of corn silk extract.

The treatment of HCD-fed group with orlistat, aqueous or methanolic extract of corn silk experienced insignificant increase in serum afamin when compared with that in the HCD-fed groups. The slight effect of

the selected treatments on serum afamin level could possibly ascribe to the insignificant reduction in serum TG level in the treated groups. As afamine strongly correlates with TG levels [53].

Significant increase in serum calprotectin B and S100B levels in HCD-fed rats as compared to the control counterparts has been observed in the present experiment. Meanwhile, treatment of HCD-fed group with orlistat, aqueous or methanolic extract of corn silk induced a significant decrease in serum calprotectin B and S100B levels versus the HCD-fed group. Calprotectin plasma levels are increased in many inflammatory diseases. It has been revealed that calprotectin plasma level could be elevated in patients with low-grade systemic inflammation, i.e. either obese or with Type-2 diabetes [59]. Calprotectin has been documented as a new biomarker of obesity, and its level elevated in obese subjects [60]. Moreover, inflammation stimulates releasing of calprotectin subunits (S100A8&A9) from monocytes through energy-dependent pathway *via* activation of protein kinase C. Furthermore, it has been reported that calprotectin found in inflammation *via* stimulation of CD11b gene expression in monocytes as well as participation in the mechanism of the transendothelial migration and causing monocytes accumulation in the inflammation site [60].

The inflammatory response initiator in obesity, visceral adipose tissue (VAT), could produce and secrete many proteins, which participate in obesity-related derangementsdevelopment [61]. Because calprotectin has emerged as an important mediator of chronic inflammation, circulating concentrations and visceral adipose tissue (VAT) expression of calprotectin subunits (S100A8 and S100A9) complex were elevated in Type-2 diabetic obese and normoglycemic patients. The elevation of calprotectin level in obesity and obesity-associated Type-2 diabetes is due to its positive association with inflammation [62].

S100 calcium binding protein B (S100B), as an adipokine, plays a role in the interaction between adipocytes and macrophages [63]. Elevated blood levels of S100B reflect the increased or dysfunction of adipose tissue. The levels of S100B were linked with BMI, leptin levels as well as adipocyte-type fatty acid-binding protein (A-FABP/FABP4) that are well-known adipose-related factors. Physiologically, S100B humans levels are associated with adipose tissue mass, which considered as an important confounding factor in clinical studies examining the role of S100B [64].

Treatment of HCD-fed group with orlistat, aqueous or methanolic extract of corn silk produced a significant decrease in serum calprotectin B and S100B levels when compared with those in the HCD-fed group. This effect may be attributed to the anti-inflammatory effect of corn silk extract [56]. The therapeutic properties of orlistat in the stomach lumen as well as small intestine through constructing a covalent bond with the active serine residue site of gastric as well as pancreatic lipases. The inactivated enzymes are thus not found to induce dietary fat hydrolysis in the form of TG into absorbable free fatty acids as well as monoglycerides. As undigested TG is not absorbed, the resulting caloric deficit may have a positive effect on weight control. Similarly, a weight reducing the influence of corn silk extract may implicate in the effect of this extract on serum level of S100B. This is because plasma S100B levels are increased by obesity and weight gain. In white adipose tissue (WAT), it has been documented that obesity causes stimulation of the expression S100B gene and weight loss could reverse this stimulation [65].

Taken collectively, our results could indicate that the effective role of corn silk extracts in the management of obesity was rather agreeable. The present data provided a novel aspect on the preferable therapeutic effect for corn silk on obesity as it targeted multiple systems. This evidenced by antihyperlipidemic and hypoglycemic as well as anti-inflammatory activity of its active phytochemicals.

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