

Protective Effects of Aqueous Extracts of Cinnamon and Ginger Herbs Against Obesity and Diabetes in Obese Diabetic Rat

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Abstract: The effects of cinnamon aqueous extract (CAE) and ginger aqueous extract (GAE) on body weight and fats, serum levels of liver enzymes, blood lipids, glucose, leptin and insulin and on the activity of tissue antioxidant enzymes in obese diabetic rats were evaluated. Fifty four male Sprague Dawley rats were randomized into 6 equal groups. Group (1) was fed on basal diet, while the other 5 groups were fed on high-fat diet (HFD) for 6 weeks to induce obesity and acute hyperlipidemia. The obese rats were then rendered diabetic by intraperitoneal injection of alloxan (120 mg/kg/day) for 5 days. After induction of diabetes, group (2) was kept obese diabetic and the other 4 groups were orally given CWE in doses 100 and 200 mg/kg or GWE in doses 100 and 200 mg/kg, respectively, for 6 weeks. Blood samples were collected for separating the serum for biochemical analyses. Kidneys were dissected out and prepared to assay activities of tissue antioxidant enzymes. The results showed that oral administration of CAE and GWE to obese diabetic rats significantly reduced body weight and fats; decreased serum levels of aspartate aminotransferase, alanine aminotransferase and gamma-glutamyl transpeptidase enzymes, total cholesterol, triglycerides and low density lipoprotein and reduced atherogenic index (LDL-c/HDL-c). There were significant decreases in blood glucose and leptin hormone and increase in insulin in obese diabetic rats given CAE and GWE. The extracts also increased activities of superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) antioxidant enzymes in kidney tissues of obese diabetic rats. In conclusion, cinnamon and ginger extracts produce anti-obesity, antidiabetic, hypolipidemic and antioxidant effects in obese diabetic rats. These results provide scientific evidence to substantiate the traditional use of cinnamon and ginger as a drink in treating obesity, hyperlipidemia and diabetes.

Key words: Cinnamon • Ginger • Obesity • Diabetes • Body fats • Liver enzymes • Blood lipids • Glucose • Insulin • Leptin • Antioxidant

INTRODUCTION

Obesity is an excessive fat accumulation in the body that results from an imbalance between energy intake and energy expenditure. It is associated with genetic, metabolic and behavioral components. Despite of a major contribution of genetic susceptibility, the rapid development of obesity might reflect great changes of other factors such as dietary habit [1]. The prevalence of obesity is rising dramatically among all ages due to the changes of lifestyles and dietary fat intake [2]. Obesity represents a serious health problem that increased the risk for many diseases such as cardiovascular diseases, hypertension and diabetes mellitus [3]. Obesity and

diabetes are among the most challenging global health problems. There is a strong association between obesity, insulin resistance and infiltration of the adipose tissues by inflammatory cells. Insulin resistance, a common accompaniment of obesity, is a major risk factor for diabetes mellitus [4, 5]. Diabetes mellitus is a chronic metabolic disease characterized by hyperglycemia due to insulin deficiency, or insulin resistance, or both. Hyperglycemia occurs when the cells become unable to utilize glucose and/or the liver and skeletal muscles cannot store glycogen [6]. The increased extracellular and intracellular glucose concentrations result in oxidative stress due to increased production of reactive oxygen species (ROS) and sharp decrease in antioxidant body

defenses [7]. Oxidative stress plays a key role in the onset and development of diabetes complications, notably diabetic nephropathy [8]. Because the synthetic chemical drugs prescribed for treating obesity and diabetes has many adverse side effects, therefore there is a great need to search for alternative safe natural agents from medicinal plants, herbs and spices. Cinnamon (*Cinnamomum zeylanicum* L., Family Lauraceae) is one of the most important spices that used to flavor most foods in Arabian countries. In animal studies, dried aqueous cinnamon extracts potentiated insulin-regulated glucose utilization via enhancing insulin signaling [9] and prevented the insulin resistance induced by a high-fructose diet in part by enhancing the insulin signaling pathway [10]. Cinnamon extracts and polyphenols have been reported to have beneficial effects in reducing fasting plasma glucose [11]. Cinnamon extracts were also reported to produce hepatoprotective [12], antioxidant [13, 14], anti-obesity [15], hypolipidemic [16, 17] and antidiabetic [18, 19] activities in man and experimental animals. Ginger rhizomes (*Zingiber officinale* Roscoe, Family *Zingiberaceae*) are commonly used as culinary spice and have a long history for its health benefits. The main active antioxidants in ginger are gingerols and shogaols beside some phenolic ketone derivatives. Ginger is used medicinally for its hepatoprotective and antioxidant [20], antidiabetic and hypolipidemic [21, 22] and anti-obesity [23, 24] effects.

The present study aimed to evaluate effects of the aqueous extract of cinnamon and ginger herbs on body weight and fats, serum levels of liver enzymes, blood lipids, glucose, leptin and insulin hormones as well as the activity of renal tissue antioxidant enzymes in obese diabetic rats.

MATERIALS AND METHODS

Plant Materials: Dried barks of cinnamon (*Cinnamomum zeylanicum* L., Family Lauraceae) and ginger rhizomes (*Zingiber officinale*, Family *Zingiberaceae*) were purchased from local market of Agricultural Herbs, Spices and Medicinal Plants, Cairo, Egypt. The dried plant materials were grinded using an electric mixer into a fine powder and thereafter subjected to preparation of aqueous extracts.

Alloxan and Biochemical Kits: Alloxan was purchased from El-Gomhoryia Company for Chemicals; Cairo, Egypt as a white powder packed bottles each containing 25g alloxan monohydrate. Glucose enzymatic kit for estimating

blood glucose and radioimmunoassay kits for leptin and insulin hormones were purchased from Gamma Trade Company, Egypt. The other biochemical kits were obtained from Biodiagnostic Company, Dokki, Egypt.

Rats: Fifty four adult male Sprague-Dawley rats weighing 200-210 g body weight and 10-12 weeks old were used in this study. Animals were obtained from the Laboratory Animal Colony, Agricultural Research Center, Egypt. Rats were housed in a well ventilated animal room under standard conditions of 24°C temperature, 50% relative humidity and 12 hr light/12 hr dark cycles. Basal diet and water were provided *ad libitum*. Rats were acclimatized to the laboratory environment for 7 days before start of the experiment.

Preparation of Basal Diet: The dietary supply of protein, fat, carbohydrates, vitamins and minerals was in accordance with the recommended dietary allowances for rats as described by Reeves *et al.* [25]. Basal diet was consisted of 20% protein, 10% sucrose, 5% corn oil, 2% choline chloride, 1% vitamin mixture, 3.5 % salt mixture and 5% fibers. The remainder was corn starch up to 100%.

Preparation of Plant Aqueous Extracts: Two hundred grams of the powder of either cinnamon barks or ginger rhizomes were dissolved in 1000 ml distilled water and boiled for 10 minutes, cooled and filtered using Whatman No. 1 filter paper to obtain 20% aqueous extract as described by Shalaby and Hamowieh [26].

Induction of Obesity and Diabetes: Obesity and acute hyperlipidemia were induced by feeding rats on high-fat diet (HFD) which supplies 45% calories from fat (lard) for 6 weeks. A 4- to 6-week HFD feeding is sufficient to induce obesity and acute hyperlipidemia and this obese model in rats closely resembles the reality of obesity in humans according to Bhatt *et al.* [27]. The obese rats were then rendered diabetic intraperitoneal injection of alloxan in a dose of 120 mg/kg/day for 5 days according to Ashok *et al.* [28].

Experiment Protocol: The experiment was performed on fifty four mature Sprague Dawley rats randomly distributed into 6 groups, of 9 rats each. Group (1) was fed on basal diet and kept negative control, while the other 5 groups were fed on HFD for 6 weeks to induce obesity. The obese rats were then rendered diabetic by intraperitoneal injection of alloxan (120 mg/kg/day) for

5 days. Thereafter, group (2) was kept obese diabetic (positive control), while groups (3), (4) (5) and (6) were orally given the aqueous extract of cinnamon in doses 100 and 200 mg/kg and ginger in doses 100 and 200 mg/kg, respectively, daily for 6 weeks. At the end of feeding period, initial and final body weights of rats were recorded and body fats were carefully removed and weighed. The adiposity index was calculated by dividing the total weight of mesenteric, visceral, epididymal and retroperitoneal adipose tissues by the body weight and multiplied by 100 i.e. (Ad.I = fat weight/body weight x100) according to Pichon *et al.* [29]. Rats were then euthanized by prolonged exposure to ether anesthetic and blood samples were withdrawn via cardiac puncture. Blood was left to clot and centrifuged at 4000 rpm for 15 min. at 4°C for separating the serum which kept frozen until biochemical analyses. Kidneys were dissected out for assaying the activity of tissue antioxidant enzymes.

Serum Analyses: Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) [30]; gamma-glutamyl transpeptidase (GGT) [31], total cholesterol (TC) [32]; triglycerides (TG) [33] and high density lipoprotein (HDL) cholesterol [32] were chemically determined using specific diagnostic kits and measured using a spectrophotometer (model T80, UV/visible, double beam, UK). Low density lipoprotein (LDL) cholesterol was calculated according to Friedewald formula: LDL-c = TC – (TG/5) – HDL-c). Blood glucose (BG) was determined using glucose enzymatic kit according to Siest *et al.* [34]. Insulin was estimated using specific antibody radioimmunoassay (RIA) kit according to Yallow and Bauman [35]. Leptin hormone was determined using enzyme-linked immunosorbent assay (ELISA) according to Xiong *et al.* [36].

Renal Antioxidant Enzymes: One gram of kidney tissue was washed with ice-cooled 0.9% NaCl solution and homogenized in 100 ml of ice-cooled 1.5% solution of potassium chloride and 50 mMol potassium phosphate buffer solutions (pH 7.4) to yield 1% homogenate (w/v). Homogenization was performed using Sonicator, 4710 Ultrasonic Homogenizer. Kidney homogenates were centrifuged at 4000×g for 10 min. at 4°C and the supernatants were used to assay the activity of antioxidant enzymes glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase (CAT) according to Paglia and Valentine [37], Spitz and Oberley [38] and Sinha [39], respectively.

Statistical Analysis: Data were presented as mean ± SE.

Statistical analysis was carried out using one-way analysis of variance (ANOVA) followed by Duncan's multiple range test [40] with SPSS computer program (version 15). Differences between the controls and treated groups were considered significant at $P < 0.05$ level.

RESULTS

Feeding of rats on high-fat diet (HFD) for 6 weeks significantly ($P < 0.05$) increased the body weight, fats weight and adiposity index when compared to negative control rats fed on basal diet. Oral administration of cinnamon aqueous extract (100 and 200 mg/kg) and ginger aqueous extract (100 and 200 mg/kg) to obese diabetic rats for 6 weeks caused significant ($P < 0.05$) decreases in the body weight, fats weight and adiposity index when compared to positive (obese diabetic) control rats, in a dose-dependent manner, as recorded in Table 1. Rats fed on HFD for 6 weeks had significant ($P < 0.05$) increases in serum levels of liver enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyl transpeptidase (GGT) when compared with negative control rats fed on basal diet. Aqueous extracts of cinnamon and ginger in doses 100 and 200 mg/kg when given to obese diabetic rats significantly ($P < 0.05$) reduced the high serum levels of AST, ALT and GGT enzymes when compared to the positive control group, in a dose dependent fashion, as illustrated in Fig. 1.

As demonstrated in Fig. 2, feeding of rats on HFD for 6 weeks produced significant ($P < 0.05$) increases in serum levels of total cholesterol (TC) and triglycerides (TG) when compared to rats fed on basal diet. Oral administration of the aqueous extract of cinnamon and ginger in doses of 100 and 200 mg/kg to obese diabetic rats for 6 weeks significantly ($P < 0.05$) decreased the elevated levels of serum TC and TG when compared to the positive control group. The effect of cinnamon and ginger aqueous extracts on serum TC and TG seemed to be a dose-dependent.

The results showed that feeding of rats on HFD for 6 weeks caused a significantly ($P < 0.05$) decreased serum high density lipoprotein (HDL), increased both low density lipoprotein (LDL) and atherogenic index (AI) when compared to negative control rats. Oral administration of aqueous extracts of cinnamon and ginger in doses of 100 and 200 mg/kg to obese diabetic rats for 6 weeks significantly ($P < 0.05$) increased serum HDL-c, decreased both LDL-c and AI when compared with the positive control groups as depicted in Table 2.

Table 1: Effects of cinnamon aqueous extract (CAE) and ginger aqueous extract (GAE) on body weight (B.wt), fats weight (F.wt) and adiposity index (Ad.I) in obese diabetic rats.(n= 9 rats)

Parameters			
Groups	B. wt (g)	F. wt (g)	Ad. I (%)
Group (1) Negative control	245.0 ± 11.0 ^d	6.55 ± 0.12 ^e	2.67 ± 0.10 ^d
Group (2) Negative control	300.0 ± 12.5 ^a	14.50 ± 0.52 ^a	4.83 ± 0.35 ^a
Group (3) CAE (100 mg/kg)	288.0 ± 10.5 ^b	10.20 ± 0.45 ^b	3.54 ± 0.24 ^b
Group (4) CAE (200 mg/kg)	278.0 ± 11.0 ^c	9.50 ± 0.37 ^c	3.41 ± 0.22 ^b
Group (5) GAE (100 mg/kg)	280.0 ± 12.5 ^b	8.40 ± 0.30 ^b	3.00 ± 0.25 ^c
Group (6) GAE (200 mg/kg)	270.0 ± 11.0 ^c	7.80 ± 0.15 ^c	2.88 ± 0.12 ^c

Means ± SE with different letters superscripts (a, b, c, d) in the same column are significant at $P < 0.05$ using one way ANOVA test.

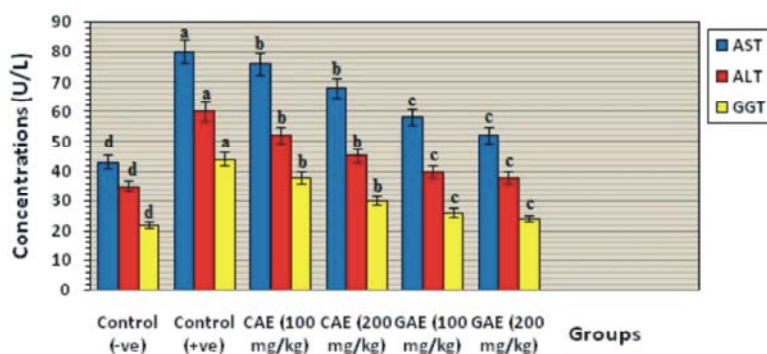


Fig. 1: Effects of cinnamon aqueous extract (CAE) and ginger aqueous extract (GAE) on serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyl transpeptidase (GGT) liver enzymes in obese diabetic rats.

Columns with different superscript letters are significant at $P < 0.05$.

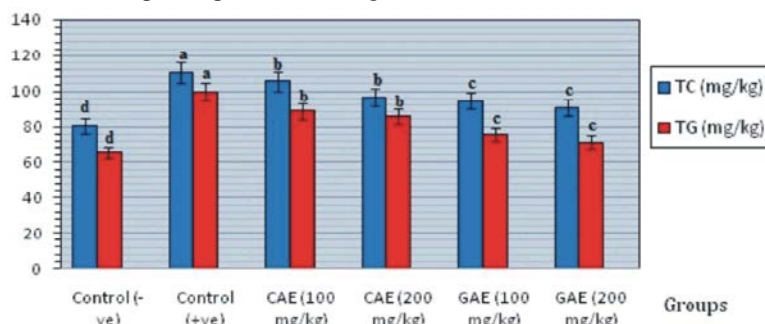


Fig. 2: Effects of cinnamon aqueous extract (CAE) and ginger aqueous extract (GAE) on serum total cholesterol (TC) and triglycerides (TG) in obese diabetic rats.

Columns with different superscript letters are significant at $P < 0.05$.

Table 2: Effects of cinnamon aqueous extract (CAE) and ginger aqueous extract (GAE) on serum levels of high density lipoprotein (HDL-c), low density lipoprotein (LDL-c) cholesterol and atherogenic index (AI) in obese diabetic rats. (n= 9 rats)

Parameters			
Groups	HDL-c (mg/dl)	LDL-c (mg/dl)	AI LDL-c/HDL-c
Group (1) Negative control	69.40 ± 3.11 ^a	12.50 ± 2.41 ^d	0.180
Group (2) Negative control	54.34 ± 2.55 ^c	60.50 ± 4.15 ^a	1.113
Group (3) CAE (100 mg/kg)	60.66 ± 3.22 ^b	44.80 ± 3.25 ^b	0.738
Group (4) CAE (200 mg/kg)	62.45 ± 4.12 ^b	33.20 ± 2.27 ^c	0.531
Group (5) GAE (100 mg/kg)	66.50 ± 3.16 ^c	31.45 ± 3.19 ^c	0.472
Group (6) GAE (200 mg/kg)	68.50 ± 4.16 ^c	25.22 ± 3.16 ^c	0.368

Means ± SE with different letters superscripts (a, b, c, d) in the same column are significant at $P < 0.05$ using one way ANOVA test

Table 3: Effects of Cinnamon aqueous extract (CAE) and Ginger aqueous extract (GAE) on blood glucose (BG) and leptin and insulin hormones levels in obese diabetic rats. (n= 9 rats)

Parameters	BG (mg/dl)	Leptin (ng/ml)	Insulin (ng/ml)
Group (1) Negative control	220 ± 8.0 ^d	2.50 ± 0.15 ^d	2.95 ± 0.15 ^a
Group (2) Negative control	285 ± 7.0 ^a	4.90 ± 0.11 ^a	0.89 ± 0.13 ^d
Group (3) CAE (100 mg/kg)	266 ± 5.0 ^b	4.10 ± 0.18 ^b	1.82 ± 0.14 ^b
Group (4) CAE (200 mg/kg)	255 ± 6.0 ^b	3.35 ± 0.17 ^b	2.43 ± 0.12 ^b
Group (5) GAE (100 mg/kg)	277 ± 7.0 ^c	2.35 ± 0.11 ^c	2.52 ± 0.13 ^c
Group (6) GAE (200 mg/kg)	237 ± 5.0 ^c	2.40 ± 0.12 ^c	2.55 ± 0.11 ^c

Means ± SE with different letters superscripts (a, b, c, d) in the same column are significant at $P < 0.05$ using one way ANOVA test. (n= 9 rats/group)

Table 4: Effects of Cinnamon aqueous extract (CAE) and Ginger aqueous extract (GAE) on activities of tissue superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) antioxidant enzymes in obese diabetic rats. (n= 9 rats)

	SOD (U/mg protein)	GPx (nmol/min /mg protein)	CAT (nmol/min/mg protein)
Group (1) Negative control	58.70 ± 2.24 ^a	0.69 ± 0.01 ^a	0.185 ± 0.001 ^a
Group (2) Negative control	38.50 ± 2.88 ^d	0.18 ± 0.04 ^d	0.138 ± 0.002 ^d
Group (3) CAE (100 mg/kg)	44.74 ± 3.46 ^c	0.22 ± 0.03 ^b	0.145 ± 0.001 ^b
Group (4) CAE (200 mg/kg)	48.95 ± 2.58 ^c	0.24 ± 0.01 ^b	0.158 ± 0.001 ^b
Group (5) GAE (100 g/kg)	50.25 ± 2.73 ^b	0.49 ± 0.02 ^c	0.180 ± 0.002 ^c
Group (6) GAE (200 g/kg)	53.15 ± 2.83 ^b	0.53 ± 0.01 ^c	0.182 ± 0.001 ^c

Means ± SE with different letters superscripts (a, b, c, d) in the same column are significant at $P < 0.05$ using one way ANOVA test.

Unit of GPx= nmol of GSH utilized/min/mg protein

Unit of CAT= nmol of H₂O₂ utilized/min/mg protein

Data in Table 3 showed that rats fed on HFD for 6 weeks had significantly ($P < 0.05$) increased blood glucose and leptin hormone and decreased insulin hormone levels when compared to rats fed on basal diet (negative control group). Cinnamon and ginger aqueous extracts when orally given in doses 100 and 200 mg/kg to obese diabetic rats for 6 weeks significantly ($P < 0.05$) decreased serum glucose and leptin hormone and increased insulin levels when compared with positive control rats, in a dose dependent manner. Feeding HFD to rats for 6 weeks significantly ($P < 0.05$) decreased renal tissue levels of superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) antioxidant enzymes when compared to rats fed on basal diet. Oral administration of aqueous extracts of cinnamon and ginger in doses of 100 and 200 mg/kg to obese diabetic rats for 6 weeks normalized the elevated renal tissue levels of SOD, GPx and CAT enzymes when compared with the positive control group, in a dose-dependent manner, as depicted in Table 4.

DISCUSSION

The primary goal of this study was to evaluate the effects of aqueous extracts of cinnamon and ginger herbs on body weight and fats, serum levels of liver enzymes, blood lipids, glucose, leptin and insulin hormones as well as the activity of renal tissue antioxidant enzymes in

obese diabetic rats. The medicinal plants and culinary herbs which possess antihyperlipidemic and antidiabetic activities have gained much attention, especially those with little toxicity properties. The biological value of plants depends on their bioactive constituents such as saponins, anthocyanins, flavonoids, polyphenols, diterpenes, triterpenes and other phytochemicals [41, 42]. Obesity, especially the abdominal type, is a health problem that constitutes metabolic syndrome and increases the incidence of various diseases, including diabetes, hypertension, dyslipidemia and atherosclerosis. The increased levels of systemic oxidative stress that occur in obesity may contribute to the obesity-associated development of these diseases [43]. Oxidative stress, which is increased in obesity, plays an important role in the development of diabetes and cardiovascular diseases in people who are obese. Increased oxidative stress together with the decreased antioxidative defense seems to contribute to decreased insulin sensitivity and impaired insulin secretory response in obese diabetics and favours the development of diabetes during obesity [44]. In the current study, obesity was induced by feeding rats on high-fat diet (HFD) for 6 weeks according to the method described by Bhatt *et al.* [27]. This model of obesity in rats closely resembles the reality of obesity in humans. However, experimental obesity could be also induced in rats and mice by other methods such as feeding on high-fructose diet, damage in the anterior hypothalamus

and genetically induced-obesity. In the present study, the used rat model was obese diabetic where the obese rats were rendered diabetic by intraperitoneal injection of alloxan for 5 days [28].

Results of the present study showed that the cinnamon aqueous extract (CAE) when given orally to obese diabetic rats for 6 weeks produced anti-obesity effect. This effect was similar to that previously reported by Couturier *et al.* [15] and Boque *et al.* [45], who found that cinnamon extracts and polyphenols of cinnamon induced anti-obesity effect in rats fed on high-fat diet. Moreover, Amin and Nagy [46] reported that feeding rats on high-fat diet significantly increased the body weight, fat weight and serum levels of triglycerides, total cholesterol and low density lipoprotein cholesterol as compared with the rats fed on normal diet. Similarly, the aqueous extract of ginger (GAE) produced anti-obesity effect in obese diabetic rats. This effect was in accordance with that reported by Nammi *et al.* [23] and Mahmoud and El-Nour [24] who concluded that ginger has a great ability to reduce body weight in rats fed high-fat diet. The mechanism(s) underlying the anti-obesity effect of cinnamon aqueous extract (CAE) could be possibly explained by its hyperinsulinemic effect evident in the present study in obese diabetic rats. It was reported that hyperinsulinemia and insulin resistance are common features of obesity in humans [47] and experimental animals [46]. The anti-obesity activity of CAE could also be due to the high level of leptin hormone that reported the current study. In this concern, Friedman [48] mentioned that leptin is a peptide hormone secreted by adipose tissue in proportion to its mass. When leptin circulates in blood and acts on the brain to regulate food intake (appetite) and energy expenditure. When body fat mass decreases, the plasma leptin levels decreases so stimulating appetite and suppressing energy expenditure till fat mass is restored. On this basis, the reduced adiposity index in obese diabetic rats given CAE could be attributed to the reported low serum leptin level in this study.

The hepatoprotective effect of cinnamon and ginger aqueous extracts reported in this study was evident from the significant decreases in the elevated serum levels of liver enzymes (AST, ALT and GGT) in obese diabetic rats. This effect agreed with that reported by Moselhy and Ali, [12] for cinnamon and by Abdel-Azeem *et al.* [20] for ginger extracts. The hepatoprotective effect of cinnamon and ginger could be attributed to the antioxidant activity of cinnamon [13] and of ginger [20]. The decreases in serum levels of total cholesterol, triglyceride and LDL-c

caused by cinnamon and ginger extracts, in this study, were similar to those recorded by Vafa *et al.* [16] and Shatwan *et al.* [17] for cinnamon and by El-Rokh *et al.* [22] for ginger. The authors concluded that cinnamon and ginger extracts lower the elevated levels of total cholesterol, triglycerides and LDLc in man and rats. They attributed the hypolipidemic effects of cinnamon and ginger due to their contents of polyphenols in cinnamon and contents of gingerols and shogaols in ginger which inhibit the intestinal absorption of cholesterol and reduce serum cholesterol levels in experimental animal models. Rats fed on high fat-diet for 6 weeks, in this study, had significantly lower serum insulin level than those fed on basal diet. This finding agreed with that reported by Huang *et al.* [49], who found that feeding high-fat diet to normal rats resulted in impaired pancreatic function and decreased insulin secretion (hypoinsulinemia). Oral administration of cinnamon and ginger to obese diabetic rats caused hyperinsulinemia, in a dose dependant manner. The hyperinsulinemic effects of cinnamon and ginger were similar to that reported by Lee *et al.* [18] and by El-Rokh *et al.* [22] in rats, respectively. Some previous studies revealed that hyperinsulinemia and insulin resistance are common features of obesity in humans [47] and experimental animals [46].

Concerning leptin hormone, the present results revealed that rats fed on high fat-diet (HFD) had high serum leptin hormone level when compared with those fed on basal diet. This finding agreed with that reported by Huang *et al.* [49] who found that HFD increased serum leptin level in rats. Leptin plays a key role in regulating energy intake and energy expenditure and the level of circulating leptin is proportional to the total amount of body fats. Cinnamon and ginger extracts significantly decreased serum leptin levels in obese diabetic rats. This result agreed with that of Shatwan *et al.* [17], who reported that cinnamon extract reduced body weight, decreased serum leptin level and depressed appetite in obese rats fed on HFD. The authors concluded that cinnamon may be useful in the treatment of obesity and related disorders as anti-obesity agent. Concerning ginger, Wadikar and Premavalli [50] reported that ginger decreased (6-16%) in plasma leptin levels in human volunteers. In obese diabetic rats, the activity of antioxidant enzymes (SOD, GPx and CAT) decreased in renal tissues. This finding can be explained by hyperglycemia due to alloxan injection that causes renal oxidative stress. It is known that oxidative stress plays a key role in the onset and development of diabetes

complications, notably diabetic nephropathy [8]. Cinnamon and ginger extracts when given to obese diabetic rats induced antioxidant effect that evident by the increased activity of tissue SOD, GPx and CAT antioxidant enzymes in renal tissue. The antioxidant effect of cinnamon and ginger extracts may be attributed to their hypoglycemic activity that reported in this study and previously demonstrated by Mang *et al.* [11] for cinnamon and by Sanjay *et al.* [21] for ginger.

CONCLUSION

Oral administration of cinnamon and ginger aqueous extracts exhibit good anti-obesity, antidiabetic, hepatoprotective, antihyperlipidemic and antioxidant activities in obese diabetic rats. The obese diabetic rat model is a novel animal model in nutrition researches. The results pointed to the potential possibility of using cinnamon and ginger as a drink for the treatment of obese diabetic patients. The present results provide a scientific evidence to substantiate the traditional use of cinnamon and ginger herbs by public as a drink for the treatment of obesity, hyperlipidemia and diabetes.

REFERENCES

1. Archer, Z.A., J. Corneloup, D.V. Rayner, P. Barrett, K.M. Moar and J.G. Mercer, 2007. Solid and liquid obesogenic diets induce obesity and counter-regulatory changes in hypothalamic gene expression in juvenile Sprague Dawley rats. *Journal of Nutrition*, 137(6): 1483-1490.
2. Power, M.L. and J. Schulkin, 2008. Sex differences in fat storage, fat metabolism and the health risks from obesity: possible evolutionary origins. *British Journal of Nutrition*, 99(5): 931-940.
3. Afolayan, H.J. and B.O. Mbaebie, 2010. Ethnobotanical study of medicinal plants in Nkonkobe Municipality in South Africa. *Pharmacognosy Journal*, 2(11): 368-374.
4. Hotamisligil, G.S. and E. Erbay, 2008. Nutrient sensing and inflammation in metabolic diseases. *Natural Review of Immunology*, 8: 923-934.
5. Raza, H., A. John and F.C. Howarth, 2013. Increased metabolic stress in Zucker diabetic fatty rat kidney and pancreas. *Cell Physiology and Biochemistry*, 32(6): 1610-1620.
6. Luis-Rodríguez, D., A. Martínez-Castelao, J.L. Gorriz, F. De-Alvaro and J.F. Navarro-Gonzalez, 2012. Pathophysiological role and therapeutic implications of inflammation in diabetic nephropathy. *World Journal of Diabetes*, 15: 7-18.
7. Lucchesi, A.N., N.T. Freitas, L.L. Cassettari, S.E. Marques and C.T. Spadella, 2013. Diabetes mellitus triggers oxidative stress in the liver of alloxan-treated rats: A mechanism for diabetic chronic liver disease. *Acta Circular Brassily*, 28(7): 502-508.
8. Wang, G.G., X.H. Lu, W. Li, X. Zhao and C. Zhang, 2011. Protective effects of Luteolin on diabetic nephropathy in STZ-induced diabetic rats. *Evident Based Complementary Alternative Medicine* 2011, 32317 doi: 10.1155/2011/323171. Epub 2011 Apr 28.
9. Qin, B., M. Nagasaki, M. Ren, G. Bajotto, Y. Oshida and Y. Sato, 2003. Cinnamon extract (traditional herb) potentiates in vivo insulin regulated glucose utilization via enhancing insulin signaling in rats. *Diabetes Research and Clinical Practice*, 62: 139-148.
10. Qin, B., M. Nagasaki, M. Ren, G. Bajotto, Y. Oshida and Y. Sato, 2004. Cinnamon extract prevents the insulin resistance induced by a high-fructose diet. *Hormone and Metabolism Research*, 36: 119-125.
11. Mang, B., M. Wolters, B. Schmitt, K. Kelb and R. Lichtinghagen, 2006. Effects of cinnamon extract on plasma glucose, HbA and serum lipids in diabetes mellitus type2. *European Journal of Clinical Investigation*, 36: 340-344.
12. Moselhy, S.S. and H.K. Ali, 2009. Hepatoprotective effect of cinnamon extracts against carbon tetrachloride induced oxidative stress and liver injury in rats. *Biology Research*, 2(1): 93-98.
13. Roussel, A.M., H. Isabelle, B. Rachida, N. Tim and A.A. Richard, 2009. Antioxidant effects of a Cinnamon extract in people with impaired fasting glucose who are overweight or obese. *Journal of American College of Nutrition*, 28: 16-21.
14. Azab, K.S., A.H. Mostafa, E.M. Ali and M.A. Abdel-Aziz, 2011. Cinnamon extract ameliorates ionizing radiation-induced cellular injury in rats. *Ecotoxicology and Environmental Safety*, 74(8): 2324-2329.
15. Couturier, K., C. Batandier, M. Awada, F. Canini and A.M. Roussel, 2010. Cinnamon improves insulin sensitivity and alters the body composition in an animal model of the metabolic syndrome. *Archive of Biochemistry and Biophysics*, 501(1): 158-161.

16. Vafa, M., F. Mohammadi, F. Shidfar, M.S. Sormaghi and F. Amiri, 2012. Effects of cinnamon consumption on glycemic status, lipid profile and body composition in type 2 diabetic patients. *International Journal of Preventative Medicine*, 3(8): 531-536.
17. Shatwan, I.A., L.A. Ahmed and M.M. Badkook, 2013. Effect of barley flour, crude cinnamon and their combination on glycemia, dyslipidemia and adipose tissue hormones in type 2 diabetic rats. *Journal of Medicinal Food*, 16(7): 656-662.
18. Lee, S.C., W.X. Xu, L.Y. Lin, J.J. Yang and C.T. Liu, 2013. Chemical composition and hypoglycemic and pancreas-protective effect of leaf essential oil from indigenous cinnamon. *Journal of Agricultural Food and Chemistry*, 61(20): 4905-4913.
19. Li, R., T. Liang, L. Xu, Y. Li, S. Zhang and X. Duan, 2013. Protective effect of cinnamon polyphenols against STZ-diabetic mice fed high-sugar, high-fat diet and its underlying mechanism. *Food Chemistry and Toxicology*, 51: 419-425.
20. Abdel-Azeem, A.S., A.M. Hegazy, K.S. Ibrahim, A.R. Farrag and E.M. El-Sayed, 2013. Hepatoprotective, antioxidant and ameliorative effects of ginger (*Zingiber officinale* Roscoe) and vitamin E in acetaminophen treated rats. *Journal of Diet Supplements*, 10(3): 195-209.
21. Sanjay, P., S. Akhiani, L. Vishwakarma and R.K. Goyal, 2004. Anti-diabetic activity of *Zingiber officinale* in streptozotocin-induced type I diabetic rats. *Journal of Pharmacy and Pharmacology*, 56(1): 101-106.
22. El-Rokh, S.M., N.A. Yassin, S.M. El-Shennawy and B.M. Ibrahim, 2010. Antihypercholesterolemic effect of ginger rhizome (*Zingiber officinale*) in rats. *Inflammopharmacology*, 18(6): 309-315.
23. Nammi, S., S. Sreemantula and B.D. Roufogalis, 2009. Protective effects of ethanol extract of *Zingiber officinale* rhizome on the development of metabolic syndrome in rats fed high-fat diet. *Basic Clinical Pharmacology and Toxicology*, 104: 366-373.
24. Mahmoud, R.H. and W.A. Elnour, 2013. Comparative evaluation of the efficacy of ginger and orlistat on obesity management, pancreatic lipase and liver peroxisomal catalase enzyme in male albino rats. *European Review of Medicinal and Pharmacological Sciences*, 17: 75-83.
25. Reeves, P.G., F.H. Nielson and G.C. Fahmy, 1993. Reports of the American Institute of Nutrition, adhoc Willing Committee on Reformulation of the AIN 93, Rodent diet. *Journal of Nutrition*, 123: 1939-1951.
26. Shalaby, M.A. and A.R. Hamowieh, 2010. Safety and efficacy of *Zingiber officinale* roots on fertility of male diabetic rats. *Food and Chemical Toxicology*, 48: 2920-2924.
27. Bhatt, B.A., J.J. Dube, N. Dedousis, J.A. Reider and R.M. O'Doherty, 2006. Diet-induced obesity and acute hyperlipidemia reduce I kappa B alpha levels in rat skeletal muscle in a fiber-type dependent manner. *American Journal of Physiology*, 290: 233-240.
28. Ashok, D.C., N.P. Shrimant, M.G. Panadeep and U.A. Akalpita, 2007. Optimization of alloxan dose is essential to induce stable diabetes mellitus for long period. *Asian Journal of Biochemistry*, 2(6): 402-408.
29. Pichon, L., J.F. Huneau, G. Fromentin and D. Tome, 2006. A high - protein, high- fat, carbohydrate - free diet reduces energy intake, hepatic lipogenesis and adiposity. *Journal of Nutrition*, 136: 1256-1260.
30. Bergmeyer, H.U., P. Schreiber and A.W. Wahlefeld, 1978. Optimization of methods for aspartate and alanine aminotransferase. *Clinical Chemistry*, 24: 58-61.
31. Persijin, J.P. and W. Van-der Silk 1976. A new method for the determination of gamma-glutamyl transpeptidase in serum. *Journal of Clinical Chemistry and Clinical Biochemistry*, 14(9): 421-427.
32. Richmond, N., 1973. Colorimetric determination of total cholesterol and high density lipoprotein cholesterol (HDL-c). *Clinical Chemistry*, 19: 1350-1356.
33. Friedewald, W.T., R.I. Levy and D.S. Frederickson, 1972. Estimation of plasma or serum low density lipoprotein cholesterol concentration without use of ultracentrifuge. *Clinical Chemistry*, 18: 499-502.
34. Siest, G., F. Henny and F. Schiele, 1981. Enzymatic determination of glucose. *Interpretation Examination Laboratory*, 2: 206-213.
35. Yallow, R. and W.A. Bauman, 1983. Plasma insulin in health and disease. In: *Diabetes Mellitus: Theory and Practice*. Edrs: Ellenberg, M. and Rifkin, H. *Excerpta Medica*, 15: 119-120.
36. Xiong, Y., L. Shen, K.J. Liu, P. Tso, Y. Xiong, G. Wang, S.C. Woods and K. Liu, 2005. Anti-obesity and antihyperglycemic effects of ginsenoside Rb1 in rats. *Diabetes*, 9: 2505-2512.
37. Paglia, D.F. and W.N. Valentine, 1979. Studies on glutathione and glutathione characterization of erythrocytes glutathione peroxidase. *Journal of Laboratory Clinical Medicine*, 70: 158-169.

38. Spitz, D.R. and L.W. Oberley, 1989. An assay for superoxide dismutase activity in mammalian tissue homogenates. *Anal. Biochemistry*, 179: 8-18.
39. Sinha, K.A., 1972. Colorimetric assay of catalase enzyme. *Anal. Biochemistry*, 47: 328-330.
40. Snedecor, G.W. and W.G Cochran, 1986. *Statistical Methods*. 7th Edition, Iowa State University Press, Ames, USA, pp: 90-99.
41. Veermuthu, D., A. Muniappan and I. Savarimuthu, 2006. Antimicrobial activity of some ethnomedicinal plants used by Paliyar tribe from Tamilnadu. *Indian Journal of Complementary and Alternative Medicine*, 6(35): 1472-1482.
42. Patel, D., S. Prasad, R. Kumar and S. Hemalatha, 2012. An overview on antidiabetic medicinal plants having insulin mimetic property. *Asian Pacific Journal of Tropical Biomedicine*, 2(4): 320-330.
43. Matsuda, M. and I. Shimomura, 2013. Increased oxidative stress in obesity: implications for metabolic syndrome, diabetes, hypertension, dyslipidemia, atherosclerosis and cancer. *Obstetrics Research and Clinical Practice*, 7(5): 330-341.
44. Kocic, R., D. Pavlovic, G. Kocic and M. Pesic, 2007. Susceptibility to oxidative stress, insulin resistance and insulin secretory response in the development of diabetes from obesity. *Vojnosanti. Pregl.*, 64(6): 391-397.
45. Boque, N.J., J. Campion, R. de la Iglesia, A.G. de la Garza and F.I. Milagro, 2013. Screening of polyphenolic plant extracts for anti-obesity properties in Wister rats. *Journal of Science and Food Agriculture*, 93(5): 1226-1232.
46. Amin, K.A. and M.A. Nagy, 2009. Effect of L-Carnitine and herbal mixture extract on obesity induced by high fat diet in rats. *Diabetes Metabolic Syndrome*, 1: 1-17.
47. Kay, J.P., R. Alemzadeh, G. Langley, L. D'Angelo, P. Smith and S. Holshouser, 2001. Beneficial effects of metformin in normoglycemic morbidly obese adolescents. *Metabolism*, 50(12): 1457-1461.
48. Friedman, J.M., 2011. Leptin and the regulation of body weight. *The Keio Journal of Medicine*, 60: 1-9.
49. Huang, B.W., M.T. Chiang, H.T. Yao and W. Chiang, 2004. The effect of high- fat and high-fructose diets on glucose tolerance, plasma lipid and leptin levels in rats. *Diabetes Obesity and Metabolism*, 6(2): 120-126.
50. Wadikar, D.D. and K.S. Premavalli, 2011. Effect of appetizer administration on plasma leptin level in human volunteers. *International Journal of Food Sciences and Nutrition*, 62(2): 148-151.