ANTI-DIABETIC EFFECT OF CINNAMON POWDER AND CINNAMON AQUEOUS EXTRACT ON SERUM GLUCOSE OF RATS

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Abstract: The anti-diabetic effect of Cinnamon Powder (CP) and Cinnamon Aqueous Extract (CAE) in type II diabetic rats was studied. Cinnamon was administered at different doses (5, 10 and 15 g/100 gm diet of CP and 5, 10 and 15% of CAE at 2 ml/kg rat body weight, P.O.) for five weeks. It was found that blood glucose concentration significantly ($p < 0.05$) decreased compared with the control. Also, serum High Density Lipoprotein Cholesterol (HDL-C) levels were significantly ($p < 0.05$) increased and the concentration of Triglyceride (TGL), Total Cholesterol (TC), Total Lipids (TL), Low-Density Lipoprotein Cholesterol (LDL-C), Alanine Amino Transferase (ALT), Aspartate Amino Transferase (AST), urea and creatinine were significantly decreased after five weeks of the administration. The results obtained indicated that using 10% and 15% from CP and CAE were more beneficial than using 5% for glucose reduction in diabetic rats. These results suggested that CP and CAE have a regulatory role in blood glucose level and lipids and the most effective material used was 15% CAE.

Keywords: cinnamon; chemical composition; anti-diabetic; serum glucose; cholesterol; lipids; transferases; urea; creatinine.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder affecting approximately 4% population worldwide and is expected to increase by 5.4% in 2025 (Kim et al., 2006). It is characterised by abnormalities in carbohydrate, lipid and lipoprotein metabolism, which not only lead to hyperglycemia but

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also cause many complications, such hyperlipidemia, hyperinsulinemia, hypertension and atherosclerosis (Chait and Brunzell, 1996). Diabetes mellitus is classified as: Insulin-Dependent Diabetes Mellitus (IDDM) and Non-Insulin-Dependent Diabetes Mellitus (NIDDM). About 90% of patients are NIDDM with insulin resistance playing a key role in the development of the disease (Fuller et al., 1980). Insulin resistance includes decreased stimulation of muscle glycogen synthesis, defects in glycogen syntheses and hexokinase activity (Muller et al., 1973). Plants have been used for the treatment of diabetes since 1550 BC (Gray and Flatt, 1997). These plants are important for the prevention and control of type 2 DM, especially for people with elevated levels of blood glucose and glucose intolerance who have a greater risk of developing diabetes. Plant seeds, fruits, leaves and bark contain polyphenols. These compounds are the end products of the flavonoid biosynthetic pathway in plants and are used by plants for the protection against predators (Dixon et al., 2005). Plant polyphenols are also widely present in the diet (Prior and Gu, 2005) and are important for human health (Yang et al., 2001). Cinnamon is one of the traditional folk herbs used in Korea, China and Russia for diabetes mellitus (Bailey and Day, 1989; Chung, 1994). Cinnamon is the bark of the *Cinnamomi cassiae* (Lauraceae). Cinnamic aldehyde (Wijesekera, 1978), cinnamic acid (Hiromu et al., 1974), tannin (Inokuchi et al., 1984) and methylhydroxychalcone polymer (MHCP) (Jarvull-Taylor et al., 2001) are its main components. Cinnamon extract decreases blood glucose in Wistar rats (Qin et al., 2003) and cinnamon increases the insulin sensitivity and glucose uptake in adipocytes (Jarvull-Taylor et al., 2001). Cinnamaldehyde was administered at different doses (5, 10 and 20 mg/kg bwt) for 45 days to streptozotocin (STZ) (60 mg/kg bwt)-induced male diabetic Wistar rats. It was found that plasma glucose concentration was significantly ($p < 0.05$) decreased in a dose-dependent manner (63.29%) compared to the control. In addition, oral administration of cinnamaldehyde (20 mg/kg bwt) significantly decreased glycosylated hemoglobin (HbA1C), serum Total Cholesterol (TC), triglyceride levels and at the same time markedly increased plasma insulin, hepatic glycogen and high-density lipoprotein-cholesterol levels. Also cinnamaldehyde restored the altered plasma enzyme (aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, alkaline phosphatase and acid phosphatase) levels to near normal levels (Subash Babu et al., 2007). Cinnamon exhibits the potential to increase the amount of proteins involved in insulin signaling, glucose transport and anti-inflammatory/anti-angiogenesis response (Heping et al., 2007).

A cinnamon extract improves the postprandial overproduction of intestinal apoB48-containing lipoproteins by ameliorating intestinal insulin resistance and may be beneficial in the control of lipid metabolism (Qin et al., 2009). The conventional pharmacological treatments for type II diabetes have a number of limitations, such as adverse effects and high rates of secondary failure. However, medicinal herbs are expected to have a similar degree of efficacy without the troublesome side effects associated with conventional drug treatment. So the aim of this work was to investigate the effect of administration Cinnamon Powder (CP) and oral administration of Cinnamon Aqueous Extract (CAE) on serum glucose, TC, TL, TGL, HDL-C, LDL-C, ALT, AST, urea and creatinine in diabetic rats.

MATERIALS AND METHODS

Sample and chemicals

Commercial cinnamon was obtained from Giza local market – Giza, Egypt. kits of glucose; TC; HDL-C; TGL; TL; ALT; AST; urea and creatinine were obtained from Biodiagnostic Co., 29 El-Tahreer St., Dokki-Giza, Egypt, E-mail Biodiagonstic eka @ Lycos. Com. STZ was obtained from Sigma Chemical Co., Saint Louis, Missouri, USA.

Chemical analysis of cinnamon

Moisture, crude protein, crude fibre, Crude oil and ash contents were determined according to the methods outlined AOAC (2000). Total hydrolysable carbohydrates were determined according to the method described by Montgomry (1961).

Extraction of CAE

The CAE was prepared by heating 5, 10 and 15 g cinnamon in 100 ml boiling water for 5 min.

GC/MS spectrum for cinnamon essential oil

After steam distillation of raw cinnamon essential oil, GC/MS spectrum (Hp. 5890A Hewlett Packard type) was used to identify the components of cinnamon essential oil as Naglaa (1998).

The conditions of GC/MS technique

The conditions of GC/MS technique used were 50 m × 0.2 mm × 0.3 for thickness film of carbowax20M capillary column; 20 cm/sec. for helium carrier gas; 100:1 for split ratio; 150°C for injector temperature; 60°C, prog. 3°C/min up to 200°C for oven temperature; 280°C for transferring temperature; 2 uL for sample volume (1:10 diluted in alcohol); 10 min for initial time and 60 min for final time. The conditions of MS selective detector were 8 min. for scan start delay; 35–350 amu. for scan range(Atom Mass Unit); 2000 for threshold; 3 scan/sec for a/d sampling rate and 2000 for electron multiplier.

Automatic injection

The HP 7673A automatic injector was used to inject 2.0 µl of sample diluted in ethyl alcohol (1:10).

Mass spectrum chemstation

The colour computer 10 MHZ 68,010 processor 30.48 cm monitor, 2 Megabyte RAM with 40 Megabyte Hard disc drive was used to control and compare the spectrum with the other stored in NBS Mass Spectral library containing over 43,000 compounds.

Biological methods

Male albino adult rats (48 animals weighing 120 g ± 2) were obtained from the private market, Helwan, Giza, Egypt, and then transported to Animal House of Ophthalmology Research Institute, Giza, Egypt.

Rats were housed in individual cages with screen bottoms and fed on basal diet (corn starch 70%, casein 10%, corn seed oil 10%, cellulose 5%, salt mixture 4% and vitamins mixture 1%) for seven days. After equilibration, rats were weighted and assigned to one of eight diet groups (normal, diabetic and six diabetic groups given CP and CAE) six animals per group as illustrated in Table 1.

Diabetes was induced in rats as described (Dawson et al., 1986) as follows: over night fasted rates were injected intraperitoneal by streptozotocin (STZ) at dose 60 mg/kg bwt. After four days of injection (zero time), blood samples were taken from each rat for the determination of serum glucose to ensure the occurrence of diabetes. Animals with serum glucose levels of 250–550 mg/100 ml were considered as diabetic rats. Total body weight of the animals was recorded at the beginning and during the experimental period. The extracts (2 ml/kg bwt) were given orally per 48 hr and the rats were weighted weekly. Blood samples were collected from the orbital plexus by mean of heparinized capillary glass tubes according Schermer (1967). Each sample was placed into a dry clean centrifuge tube and centrifuged 1500 × g for 30 min. at 4°C to obtain serum. Serum glucose was determined according to the method described Trinder (1969). TC was determined according to the method described Allain et al. (1974), TL were determined according to the method described Kinght et al. (1972) and TGL were determined according to the method described Fossati and Prencipe (1982).

HDL-C was determined according to the method described Lopez-virella et al. (1977) and LDL-C levels and risk ratio were calculated for serum samples using the formula of Friedewald et al. (1972) using the following equations:

$$\text{LDL-C} = \text{TC} - \frac{\text{T.G}}{5 + \text{HDL-C}}$$

$$\text{Risk ratio} = \frac{\text{LDL-C}}{\text{HDL-C}}$$

Serum transaminases sAST and sALT (Aspartate transferase and Alanine transferase) were measured colorimetrically according to the method described Reitaman and

Table 1 Composition of diets (%) for male rats

Diet	Corn starch	Casein	Oil	Cellu-lose	Salt mixture	Vit. mixture	CP (5 gm/100 gm)	CP (10 gm/100 gm)	CP (15 gm/100 gm)
C	70.00	10.00	10.00	5.00	4.00	1.00	___	___	___
STZD	70.00	10.00	10.00	5.00	4.00	1.00	___	___	___
CP (5%)	66.47	9.80	9.88	3.85	4.00	1.00	5	___	___
CP (10%)	62.92	9.60	9.77	2.71	4.00	1.00	___	10	___
CP (15%)	59.39	9.40	9.65	1.56	4.00	1.00	___	___	15
CAE (5%)	70.00	10.00	10.00	5.00	4.00	1.00	___	___	___
CAE (10%)	70.00	10.00	10.00	5.00	4.00	1.00	___	___	___
CAE (15%)	70.00	10.00	10.00	5.00	4.00	1.00	___	___	___

Note: C = Control (basal diet); STZD = streptozotocin diabetic rat; CAE = cinnamon aqueous extract; CP = cinnamon powder (5, 10 and 15 gm/100 gm diet).

Frankel (1957). Serum urea was determined according to Fawcett and Soctt (1960) and creatinine was determined according to the method of Barthes et al. (1972).

Statistical analysis of data

Data collected from biological evaluation were statistically analysed using one-way ANOVA with post-hoc Newman Keuls, test. $P < 0.05$ was considered significant. All data are expressed as mean ± S.D.

RESULTS AND DISCUSSION

Diabetes mellitus is becoming a major public health problem worldwide, including in the WHO Eastern Mediterranean Region. Due to the lack of physical activity as well as dietary changes, the incidence of diabetes is increasing at an alarming rate. Diabetes affects more than 230 million people worldwide. If the current trend continues, 370 million people worldwide are expected to have diabetes by the year 2030 (WHO, 2006). In Egypt, diabetes mellitus is a major emerging clinical and public health problem. Considering the population distribution of Egypt, in 1993, 5.4% had diagnosed diabetes and 4.0% had previously undiagnosed diabetes and the combined prevalence of diagnosed and undiagnosed diabetes in the Egyptian population[3] 20 years of age was 9.3%. When these age-, sex- and residence-specific diabetes prevalence rates are applied to the projected demographics of the Egyptian population for the years 1995, 2000 and 2025, the total number of persons with diagnosed and undiagnosed diabetes in Egypt will increase from 3.24 million in 1995 to 3.80 million in 2000 and to 8.80 million by the year 2025. Between 1995 and 2025, the number of people with diabetes 65 years of age will increase 3.6 times, from approximately 515,000 to 1.87 million. The number of urban residents with diabetes will increase 3.2 times from approximately 2.28 million to 7.21 million. By the year 2025, 13.3% of the population 20 years of age will have diabetes. The elderly will represent 21% of the total population with diabetes and urban residents will represent 82% (William et al., 1997).

So that, a comprehensive strategies to address the problem of diabetes in Egypt are urgently needed. And thus could be achieved via developing a plan for prevention and control this disorder. For example using some plants for the prevention and control of type 2 DM, especially for people with elevated levels of blood glucose and glucose intolerance who have a greater risk of developing diabetes. In our area of research we tested the anti-diabetic effect of CP (CP) and CAE in type II diabetic rats.

Sample of commercial CP was subjected to chemical analysis with mean of three replicate for every determination. Ash, crude protein, crude oil, crude fiber and hydrolyzable carbohydrates. The results showed that ash; crude protein, crude oil, crude fibre and hydrolyzable carbohydrates amounted to 3.4269%, 4.0217%, 2.3207%, 22.9247% and 69.2911%, respectively.

The chemical composition of cinnamon essential oil was shown in Table 2; it was analysed by using GC/MS spectrum. The results showed that cinnamaldehyde, cinnamic acid and cinnamyle acetate were found to be the highest (75.57, 11.91 and 2.83%). Eugenol, linalool, carbophellene, ρ-cymene and limoncenene amounted to 1.72, 1.61, 1.44, 1.033 and 1.00%. On the other hand, α-pinine, mycene, phenyl ethyl

alcohol, α-terpineol, benzaldehyde and comphene were found to be lowest (0.64, 0.45, 0.35, 0.34, 0.33 and 0.24%).

These results are partially in accordance with those (De Paula et al., 2004). That isolated coumarin, ρ-hydroxybenzoic acid and cinnamic acid from the methanolic extracts from leaves of Cinnamon osmophloeum. Coumarin and its derivatives are known to exhibit photosensitizing properties and find that the application as fragrances, pharmaceuticals and agrochemicals. Cinnamic acid and its derivatives, in particular, are widely found in edible plants produced from the shikimate pathway and their biological

Table 2 Chemical composition of cinnamon essential oil

Chemical constituent	Sub chemical constituents	%
1. Cyclic terpines	α-pinine	0.64
	β-pinine	0.20
	Limoncenene	1.00
	α-Terpineol	0.34
Total		2.18
2. Aliphatic hydro carbons	Mycene	0.45
3. Aromatic hydro carbons	ρ-cymene	1.033
4. Aromatic aldehydes	Benzaldehyde	0.33
	Cinnamaldehyde	75.57
Total		75.90
5. Aromatic terpine alcohol	Phenyl ethyl alcohol	0.35
	Eugenol	1.72
Total		2.07
6. Terpine Ester	Cinnamyle acetate	2.83
7. Aliphatic terpine alcohol	Linalool	1.61
8. Sesquterpine	Caryophellene	1.44
	Comphene	0.24
Total		1.68
9. Aromatic acid	Cinnamic acid	11.91

Table 3 Effect of CP and CAE on serum glucose level (mg/dl) in normal and streptozotocin- induced diabetic rats

Treatments	Zero time	After 1 week	After 2 weeks	After 3 weeks	After 4 weeks	After 5 weeks
C	89.31 ± 3.70	87.32 ± 3.60	89.00 ± 4.24	88.35 ± 3.05	90.70 ± 4.04	89.38 ± 3.47
STZD	370.81 ± 17.54	370.79 ± 17.54	373.20 ± 18.64	382.01 ± 19.10	393.20 ± 19.69	399.01 ± 21.17
5% CP	378.21 ± 18.91	303.21 ± 15.85	299.01 ± 12.74	258.82 ± 14.19	221.31 ± 10.07	198.32 ± 9.44
10% CP	372.71 ± 17.63	302.01 ± 14.89	263.01 ± 13.61	221.30 ± 10.65	199.91 ± 10.11	168.01 ± 7.89
15% CP	369.31 ± 18.44	299.00 ± 13.95	237.31 ± 11.49	200.01 ± 9.53	173.08 ± 7.65	130.82 ± 5.89
5% CAE	369.32 ± 18.44	308.71 ± 17.16	287.03 ± 13.35	243.81 ± 12.55	208.71 ± 9.44	188.31 ± 8.42
10% CAE	368.10 ± 19.45	299.11 ± 16.59	249.93 ± 13.70	211.00 ± 10.72	187.31 ± 8.86	139.91 ± 6.36
15% CAE	375.21 ± 18.75	293.09 ± 15.98	229.81 ± 11.77	198.31 ± 11.67	169.21 ± 7.91	121.81 ± 5.37

Note: C = Control (basal diet); STZD = streptozotocin diabetic rat; CP = cinnamon powder (5, 10 and 15 gm/100 gm diet); CAE = cinnamon aqueous extract. Each value is mean ± SD for six rats in each group.

Table 4 Effect of CP and CAE on TC, TL and TGL levels (mg/ dl) in normal and streptozotocin- induced diabetic rats

Treatments	TC mg /dl	TL mg /dl	TGL mg /dl
C	107.83 ± 4.39	247.32 ± 12.74	87.31 ± 3.85
STZD	268.03 ± 13.89	482.01 ± 25.78	228.31 ± 10.42
5% CP	181.11 ± 9.65	288.35 ± 15.96	119.38 ± 4.97
10% CP	150.03 ± 7.73	260.70 ± 12.04	108.81 ± 4.41
15% CP	121.31 ± 5.07	252.37 ± 12.28	100.00 ± 4.03
5% CAE	163.23 ± 7.59	273.91 ± 12.69	111.39 ± 4.86
10% CAE	139.81 ± 6.36	253.82 ± 13.10	101.31 ± 4.96
15% CAE	119.32 ± 6.02	251.45 ± 12.97	99.91 ± 4.55

Note: C = Control (basal diet); STZD = streptozotocin diabetic rat; CP = cinnamon powder (5, 10 and 15 gm/100 gm diet); CAE = cinnamon aqueous extract. Each value is mean ± SD for six rats in each group.

Table 5 Effect of CP and CAE on HDL-C and LDL-C level (mg/dl) in normal and streptozotocin- induced diabetic rats

Treatments	HDL-C mg/dl	LDL-C mg/dl	Risk ratio
C	66.80 ± 2.34	30.01 ± 0.58	1.61 ± 0.085
STZD	36.71 ± 0.93	211.97 ± 10.16	7.30 ± 0.365
5% CP	46.21 ± 1.31	120.31 ± 5.33	3.92 ± 0.196
10% CP	53.01 ± 1.96	100.71 ± 6.92	2.83 ± 0.149
15% CP	63.21 ± 2.33	61.37 ± 2.07	1.92 ± 0.101
5% CAE	49.32 ± 1.47	115.81 ± 5.43	3.32 ± 0.184
10% CAE	60.21 ± 2.01	75.20 ± 2.95	2.32 ± 0.912
15% CAE	65.99 ± 2.67	55.31 ± 1.77	1.81 ± 0.091

Note: C = Control (basal diet); STZD = streptozotocin diabetic rat; CP = cinnamon powder (5, 10 and 15 gm/100 gm diet); CAE = cinnamon aqueous extract. Each value is mean ± SD for six rats in each group.

Table 6 Effect of CP and CAE on ALT and AST levels (U/dl) in normal and streptozotocin-induced diabetic rats

Treatments	ALT U/dl	AST U/dl
C	16.03 ± 0.79	28.18 ± 1.31
STZD	65.81 ± 3.07	83.71 ± 4.01
5% CP	38.21 ± 1.98	35.80 ± 1.89
10% CP	28.31 ± 1.29	31.08 ± 1.54
15% CP	26.13 ± 1.28	30.12 ± 1.59
5% CAE	30.01 ± 1.57	33.07 ± 1.74
10% CAE	27.31 ± 1.32	30.11 ± 1.67
15% CAE	25.51 ± 1.04	30.00 ± 1.07

Note: C = Control (basal diet); STZD = streptozotocin diabetic rat; CP = cinnamon powder (5, 10 and 15 gm/100 gm diet); CAE = cinnamon aqueous extract. Each value is mean ± SD for six rats in each group.

Table 7 Effect of CP and CAE on urea and creatinine levels (mg/dl) in normal and streptozotocin-induced diabetic rats

Treatments	Urea mg/dl	Creatinine mg/dl
C	18.99 ± 0.85	0.65 ± 0.024
STZD	69.81 ± 2.67	4.83 ± 0.170
5% CP	25.31 ± 1.31	1.01 ± 0.041
10% CP	22.10 ± 1.01	1.00 ± 0.040
15% CP	20.99 ± 1.07	0.91 ± 0.038
5% CAE	22.81 ± 1.10	1.00 ± 0.046
10% CAE	21.13 ± 0.96	0.99 ± 0.042
15% CAE	20.81 ± 1.06	0.89 ± 0.037

Note: C = Control (basal diet); STZD = streptozotocin diabetic rat; CP = cinnamon powder (5, 10 and 15 gm/100 gm diet); CAE = cinnamon aqueous extract. Each value is mean ± SD for six rats in each group.

activities are well described in the literature (Castelli et al., 1999). Also, Adisakwattana et al. (2005) investigated the antihyperglycemic effect of ρ-methoxycinnamic acid (ρ-MCA), a cinnamic acid derivative, on plasma glucose and insulin concentrations, activities of hepatic glucose-regulating enzymes and hepatic glycogen content in normal and streptozotocin (STZ)-induced diabetic rats. They found that, p-MCA administration increased glycogen storage in diabetic rats by 80%. P-MCA also increased hepatic G6-P and increased the glucokinase activity and inhibiting gluconeogenesis in the liver in diabetic rats. While, McCarty (2005) reported that Cinnamon contains hydroxychalcone compounds which inhibit a tyrosine phosphatase that targets the insulin receptor; thus, these compounds have the potential to potentiate insulin signaling. Wang et al. (2009) extracted essential oils from five types of cinnamon leaves and identified of their volatile compound compositions. However, there were significant difference of volatile compound composition between species but, trans-Cinnamaldehyde was detected to exist in all the species tested as an important volatile component.

The effect of various doses of CP and CAE are reported in Table 3 which shows a comparison between levels of serum glucose in normal and diabetic rats fed for five weeks. On the starting day (zero time) of the experiment (after streptozotocin induced diabetes in rats), the data showed that CP at 5%, 10% and 15% significantly ($p < 0.05$) decreased serum glucose after five weeks from 378.21, 372.71 and 369.31 to 198.32, 168.01 and 130.82 mg/dl, respectively, compared with diabetic group (370.81 to 399.01 mg/dl) of the same groups at the start of the experiment. Administration of CAE at 5, 10 and 15% significantly ($p < 0.05$) lowered serum glucose from 369. 32, 368.10 and 375.21 to 188.31, 139.91 and 121.81 mg/dl, respectively.

The data indicated that using 10% and 15% from CP and CAE were more beneficial than using 5% for glucose reduction in diabetic rats.

This hypoglycemic effect may be due to the content of CP and CAE from cinnamaldehyde (75.57%).

McCarty (2005) mentioned that doses of 1–6 g daily, whole cinnamon decreases the fasting glucose of diabetics by about 20%. And, the suggested mechanisms of action reported by Villasenor et al. (2004) whom mentioned that insulin producing cells are functioning and the stimulation of insulin release could be responsible for most of the metabolic effects (Sheehan and Zemaitis, 1983). It may be suggested that the mechanism of action of cinnamaldehyde is similar to glibenclamide. Although a number of active principles have also been observed with antidiabetic activity.

Identified polyphenolic polymers from an aqueous extract of commercial cinnamon that increase glucose metabolism several fold in an epididymal fat cell assay (Anderson et al., 2004). Strong evidence suggests that cinnamon polyphenols exhibit insulin-like activity in cells, animals and people with type II diabetes. Firstly, a water-soluble Cinnamon Extract (CE), like insulin, increases the activity of autophosphorylation of the insulin receptor β (IRβ) and decreases the activity of tyrosine phosphatase in vitro (Imparl-Radosevich et al., 1998). Secondly, cinnamon polyphenols, like insulin, stimulate glucose uptake inhibit glycogen synthase kinase-3β (Jarvull-Taylor et al., 2001). Thirdly, CE potentates in vitro insulin-regulated glucose utilisation via increasing glucose uptake, and prevents insulin resistance induced by a high-fructose diet in rats (Qin et al., 2003, 2004). It also decreases glucose and increases insulin in blood of

rats fed diets containing CE (Verspohl et al., 2005) and decreases blood pressure (Preuss et al., 2006). While, Rudkowska (2009) reported that not all studies have reported beneficial effects of cinnamon. More research is needed before cinnamon can be recommended for treatment of type 2 diabetes. Therefore, studies should be conducted to determine how specific variables, such as diet, population type, Body Mass Index (BMI), glucose levels, cinnamon type/dose and concurrent medication affect cinnamon responsiveness.

Lipids play a vital role in the pathogenesis of diabetes mellitus. The most common lipid abnormalities in diabetes are hypercholesterolemia, hyperlipidemia and hypertriglyceridemia. In our study, we have noticed elevated levels of serum lipids such as cholesterol, total lipid and triglycerides in diabetic rats to evaluate the role of CP and CAE on metabolism of TC, TL and TGL.

The effect of CP and CAE oral administration during five weeks on lipid pattern is recorded in Table 4.

The present results indicated that the levels of serum TL and TGL were highly significantly decreased to (288.35, 260.70, 252.37, 273.91, 253.82, 251.45 mg/dl) and (119.38, 108.81, 100.00, 111.39, 101.31, 99.19 mg/dl) at 5%, 10% and 15% CP and CAE, respectively. Also, a significant decrease occurred in TC to (181.11, 150.03, 121.31, 163.23, 139.81 , 119.32 mg/dl) at 5%, 10% and 15% CP and CAE, respectively, was observed relatively to STZD. This indicates that CAE has lasting hypocholesterolemic, hypolipidemic and hypotriglycerdemic effects in diabetic rats.

Spices and natural products have an effect on cholesterol in humans. Cinnamon bark has also shown strong lipolytic (ability to hydrolyze fats) action (Leung and Foster, 1996). Spices–Murraya Koenigii and Brassica juncea reduce the concentrations of cholesterol, TGL and phospholipids in serum (Khan et al., 1998).

The changes in HDL-C, LDL-C and the ratio of LDL-C and HDL-C (risk ratio) of hyperglycemic rats fed on CP and CAE (5%, 10% and 15%) were investigated. The results are summarised in Table 5.

The data revealed that HDL-C value close to the C (66.80 mg/dl) in all treatments even in STZD (36.71 mg/dl) except those administrations CP and CAE (46.21, 53.01, 63.21 and 49.32, 60.21, 65.99 mg/dl) at 5%, 10% and 15%, respectively. These values were near that observed for C. LDL-C increased from 30.01 in C to 211.97 mg/dl in STZD.

It could be said that in hyperglycemic rats LDL-C significantly ($p < 0.05$) high compared with C. In addition, administration of CP and CAE significantly decreased LDL-C in rats. It was increased to 211.97 mg/dl in STZD and decreased to 120.31, 100.71, 61.37 and 115.81, 75.20, 55.31 mg/dl in rats taken 5%, 10% and 15% CP and CAE respectively.

These values are close to the C. The risk ratio was increased to 7.30 in STZD as compared with C (1.61). It decreased to 3.92, 2.83, 1.92 and 3.32, 2.32, 1.81 in rats taken 5%, 10% and 15% CP and CAE, respectively. The increase in HDL-C and decrease in LDL-C may be due to the increase in hepatic HDL-C binding activity and significant increase in hepatic LDL-C receptor activity. HDL-C is an antiatherogenic lipoprotein. It transports cholesterol from peripheral tissues into the liver and thereby acts as a protective factor against coronary heart disease. The level of HDL-C, which increased after cinnamaldehyde administration, might be due to the increase in the activity of lecithin cholesterol acyl transferase (LCAT), which may contribute to the

regulation of blood lipids (Patil et al., 2004). Cinnamon was shown to decrease the level of glucose, triglycerides and LDL cholesterol in people with type II diabetes (Khan et al., 2003). Administration of CP and CAE lowers serum LDL-C, and also increases the serum HDL-C level in diabetic rats.

The activities of ALT and AST were determined in serum to evaluate the role of CP and CAE on liver functions. The results are shown in Table 6. The increase in the activities of serum ALT and AST indicated that diabetes may be induced due to liver dysfunction.

Data of ALT activity showed that it increased in serum of hypoglycemic rats from 16.03 in C to 65.81 U/dl in STZD. On the other hand, serum AST activity was also increased from 28.18 in C to 83.71 U/dl in STZD; all these values are highly significant. The effect of CP and CAE administration during five weeks on ALT and AST are recorded in the same Table. The results showed that the activity of serum ALT and AST highly significantly decreased from 65.81 and 83.71U/dl in STZD to 38.21, 28.31, 26.13U/ dl and 35.80, 31.08, 30.12U/dl after administration of CP at 5%, 10% and 15% to hyperglycemic rats for five weeks, respectively.

The activity of serum ALT and AST highly significantly decreased to (30.10, 27.31, 25.51 U/dl) and (33.07, 30.11, 30.00 U/dl) after oral administration of CAE at 5%, 10% and 15%, respectively, compared with STZD (65.81 and 83.71 U/dl). The present findings are in agreement with those obtained by Subash Babu et al. (2007) whom said that the activities of plasma enzymes AST, ALT, LDH, ALP and ACP significantly ($p < 0.05$) increased in diabetic rats compared to controls. Oral administration of cinnamaldehyde for 45 days significantly restores the enzyme levels to near normal in diabetic rats.

Urea and creatinine values in serum of streptozotocin-induced diabetic rats after five weeks (mg/dl) are presented in Table 7.

Data showed that the level of urea and creatinine in rats as administration and oral administration different levels of CP and CAE. C showed the lowest levels, while STZD gave the highest levels of these parameters. Data of urea and creatinine, showed that they increased in STZD from 18.99 and 0.65 to 69.81 and 4.83 mg/dl, respectively compared with C.

Also, the results showed that the level of serum urea highly significantly decreased from 69.81 in STZD to 25.31, 22.10, 20.99 mg/dl after administration of CP (5%, 10% and 15%), respectively, and to 22.81, 21.13, 20.81 mg/dl after oral administration of CAE (5%, 10% and 15%), respectively. In the same table, the effect of CP and CAE at 5%, 10% and 15% on serum creatinine showed a significant decrease from 4.83 in STZD to 1.01, 1.00, 0.91, 1.00, 0.99 and 0.89 mg/dl after administration of CP and oral administration of CAE at 5%, 10% and 15%, respectively. Administration of CP and oral administration of CAE for five weeks significantly restores urea and creatinine levels to near normal in diabetic rats.

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REFERENCES

Adisakwattana, S., Roengsamran, S., Hsu, W.H. and Yibchok-anun, S. (2005) 'Mechanisms of antihyperglycemic effect of ρ-methoxycinnamic acid in normal and streptozotocin-induced diabetic rats', *Life Science*, Vol. 78, pp.406–412.

Allain, C.C., Poon, L.S., Chan, C.S., Richamand, W. and Fu, P. (1974) 'Enzymatic determination of total serum cholesterol', *Journal of Clinical Chemistry*, Vol. 20, p.470.

Anderson, R.A., Broadhurst, C.L., Polansky, M.M., Schmidt, W.F., Khan, A., Flanagan, V.P., Schoene, N.W. and Graves, D.J. (2004) 'Cinnamon supplementations in patients with type 2 diabetes', *Journal of Agriculture and Food Chemistry*, Vol. 52, pp.65–70.

AOAC (2000) *Association of Official Agriculture Chemists, Official Methods of Analysis*, 17th edition, DC, USA. p.350, Longmans, Green & Co. Ltd.

Bailey, C.J. and Day, C. (1989) 'Traditional plant medicines as treatment for diabetes', *Diabetes Care,* Vol. 12, pp.553–564.

Barthes, H., Bohemer, M. and Heirli, C. (1972) 'Colorimetric kinetic method of creatinine', *Clinical Chemistry Acta*, Vol. 37, p.193.

Castelli, F., Ucella, N., Trombetta, D. and Saija, A (1999) 'Using experimental studies and theoretical calculations to analyze the molecular mechanism of coumarin, p-hydroxybenzoic acid, and cinnamic acid', *Journal of Molecular Structure*, Vol. 741, pp.193–199.

Chait, A. and Brunzell, J.D. (1996) 'Diabetes, lipid and atherosclerosis', in D. Le Roith, S.I. Taylor and J.M. Olefsky (Eds). *Diabetes Mellitus*, pp.467–469, Philadelphia: Lippincott-Raven Publisher.

Chung, T.H. (1994) 'Korean Flora' (Herb Part), p.283 In: Anti-diabetic effect of cinnamon extract on blood glucose in db/db mice. *Journal of Ethnopharmacology*, Vol. 104 (2006), pp. 119–123.

Dawson, R.M.C., Elliott, D.C., Elliott, W.H. and Jones, K.M. (1986) *Data for Biochemical Research*, 3rd edition, Oxford: Calderon Press.

De Paula, R., Da Hora Machado, A.E. and De Miranda, J.A. (2004) '3-Benzoxazol-2-yl-7-(N,N-diethylamino)-chromen-2-one as a fluorescence probe for the investigation of micellar microenvironments', *Journal of Photochemistry and Photobiology A: Chemistry*, Vol. 165, pp.109–114.

Dixon, R.A., Xie, D.Y. and Sharma, S.B. (2005) 'Proanthocyanidins–a final frontier in flavonoid research?' *New Phytology*, January, Vol. 165, No. 1, pp.9–28.

Fawcett, J.K. and Soctt, J.E. (1960) 'Enzymatic colorimetric method of urea', *Journal of Clinical Pathology*, Vol. 13, p.156.

Fossati, P. and Prencipe, L. (1982) 'The determination of triglycerides using enzymatic methods', *Journal of Clinical Chemistry*, Vol. 28, p.2077.

Friedewald, W.I., Stewart, S.W. and Arnold, T.F. (1972) 'Estimated calculation of low – density lipoprotein', *Clinical Chemistry*, Vol. 18, p.499.

Fuller, J.H., Shipley, M.J., Rose, G.J., Jarrett, R.J. and Keen, H. (1980) 'Coronary-heart-disease risk and impaired glucose tolerance: the Whitelall Study', *Lancet*, Vol. 1, pp.373–1376.

Gray, A.M. and Flatt, P.R. (1997) 'Pancreatic and extra-pancreatic effects of the traditional anti-diabetic plant, Medicago sativa (lucerne)', *British Journal of Nutrition*, Vol. 78, pp.325–334.

Heping, C., Marilyn, M.P. and Richard, A.A. (2007) 'Cinnamon extract and polyphenols affect the expression of tristetraprolin, insulin receptor and glucose transporter 4 in mouse 3T3-L1 adipocytes', *Archive of Biochemistry and Biophysics*, Vol. 459, pp.214–222.

Hiromu, K., Katudi, O. and Nenokichi, H. (1974) 'Constituent of the essential oil from cinnamomum loureirri Nees', *Reports of the Scientific Research Institute*, Vol. 10, pp.47–50.

Imparl-Radosevich, J., Deas, S., Polansky, M.M., Baedke, D.A., Ingebritsen, T.S., Anderson, R.A. and Graves, D.J. (1998) 'Regulation of PTP-1 and insulin receptor kinase by fractions from cinnamon: implications for cinnamon regulation of insulin signalling', *Hormone Research*, Vol. 50, No. 3, pp.177–182.

Inokuchi, J., Okabe, H., Yamauch, T. and Nagamatsu, A. (1984) 'Inhibitors of agiotensin converting enzyme in crude drugs', *Chemical and Pharmacological Bulletin*, Vol. 32, pp.361–3619.

Jarvull-Taylor, K.J., Anderson, R.A. and Graves, D.J. (2001) 'Functions as a mimetic for insulin in 3T3 – L1 adjpocytes', *Journal of American College of Nutrition*, Vol. 20, pp.327–336.

Khan, B.A., Abraham, A. and Leelanma, S. (1998) 'Influence of spices-Murraya koenigii and Brassica juncea on rats fed atherogenic diet', *The Journal of the Foundation for Science and Technology*, Vol.35, pp. 66- 68.

Khan, A., Safdar, M., li Khan, M.M., Khattak, K.N. and Anderson, R.A. (2003). ' Cinnamonimproves glucose and lipids of people with type II diabetes.', *Diabetes Care*, Vol. 26, No.12, pp. 3215–3218.

Kim, S.H., Hyun, S.H. and Choung, S.Y. (2006) 'Anti-diabetic effect of cinnamon extract on blood glucose in db/db mice', *Journal of Ethnopharmacology*, Vol.104, pp.119–123.

Kinght, J.A., Anderson, S. and Rowler, J.M. (1972) 'Chemical bases of the sulfophosphovanillin reaction for estimating total serum lipid', *Journal of Clinical Chemistry*, Vol. 18, p.199.

Leung, A.Y. and Foster, S. (1996) *Encyclopedia of Common Natural Ingredients used in Food, Drugs, and Cosmetics*, 2nd edition, New York: John Wiley and Sons, Limited liability Company.

Lopez-virella, M.F., Stone, S., Ellis, S. and Collwel, J.A. (1977) 'Cholesterol determination in high density lipoproteins separated by three different methods', *Clinical Chemistry*, Vol. 23, p.882.

McCarty, M.F. (2005) 'Nutraceutical resources for diabetes prevention- an update', *Medical Hypotheses*, Vol. 64, pp.151–158.

Montgomry, R. (1961) 'Further studies of the phenol sulfuric acid reagent for carbohydrates', *Biophysics Acta*, Vol. 48, p.591.

Muller, W.A., Faloona, G.R. and Unger, R.H. (1973) 'Hyperglucagonemi in diabetic ketoacidosis. Its prevalence and significance', *American Journal of Clinical Medicine*, Vol. 54, pp.52–57.

Naglaa, H. (1998) 'Utilization of some spices and their essential oils as flavoring and preservative agents in biscuit', MSc thesis, Food Science and Technology Department, Faculty of Agriculture, Cairo University, Egypt.

Patil, U.K., Saraf, S. and Dixit, V.K. (2004) 'Hypolipidemic activity of seeds of Cassia tora Linn', *Journal of Ethnopharmacology*, Vol. 90, pp.249–252.

Preuss, H.G., Echard, B., Polansky, M.M. and Anderson, R. (2006) 'Whole cinnamon and aqueous extracts ameliorate sucrose-induced blood pressure elevations in spontaneously hypertensive rats', *Journal of American College of Nutrition*, Vol. 25, No. 2, pp.144–150.

Prior, R.L. and Gu, L. (2005) 'Occurrence and biological significance of proanthocyanidins in the American diet', *Phytochemistry*, Vol. 66, pp.2264–2280.

Qin, B., Nugasaki, M., Ren, M., Bajotto, G., Oshida, Y. and Sato, Y. (2003) 'Cinnamon extract (traditional herb) potentates in vivo insulin-regulated glucose utilization via enhancing insulin signaling in rats', *Diabetes Research and Clinical Practices*, Vol. 62, pp.139–148.

Qin, B., Nugasaki, M., Ren, M., Bajotto, G., Oshida, Y. and Sato, Y. (2004) 'Cinnamon extract prevents the insulin resistance induced by a high-fructose diet', *Hormone and Metabolic Research*, Vol. 36, No. 2, pp.119–125.

Qin, B., Polansky, M.M., Sato, Y., Adeli, K. and Anderson, A.R. (2009) 'Cinnamon extract inhibits the postprandial overproduction of apolipoprotein B48-containing lipoproteins in fructose-fed animals', *The Journal of Nutritional Biochemistry*, Vol. 20, No.11, pp. 901–908.

Reitaman, S. and Frankel, S. (1957) 'A colorimetric method for the determination of serum glutamic oxaloacetic and glutamic pyruvic transaminases', *American Journal of Clinical Pathology*, Vol. 28, p.56.

Rudkowska, I. (2009) 'Review: functional foods for health: focus on diabetes', *Maturitas*, Vol. 62, pp.263–269.

Schermer, S. ed., (1967) *The Blood Morphology of Laboratory Animals*, (p. 350), Longmans, Green & Co. Ltd.,

Sheehan, E. W. and Zemaitis, M. A. (1983) 'A constituent of Pterocarpus marsupium, (-)-Epicatechin, as a potential antidiabetic agent', *Journal of Natural Products*, Vol. 46, No. 2, pp. 232- 234.

Subash Babu, P., Prabuseenivasan, S. and Ignacimuthu, S. (2007) 'Cinnamaldehyde-A potential antidiabetic agent', *Phytomedicine*, Vol. 14, pp.15–22.

Trinder, P. (1969) 'Enzymatic colorimetric method of glucose', *Annual of Clinical Biochemistry*, Vol. 6, p. 24.

Verspohl, E.J., Bauer, K. and Neddermann, E. (2005) 'Antidiabetic effect of Cinnamomum cassia and Cinnamomum zeylanicum in vivo and in vitro.', *Phytotherapy Research*, Vol. 19, No.3, pp. 203–206.

Villasenor, I.M., Canlas, A.P., Faustino, K.M. and Plana, K.G. (2004) 'Evaluation of the bioactivity of triterpene mixture isolation from Carmona retusa (Vahl.) Masam leaves', *Journal of Ethnopharmacology*, Vol. 92, pp.53–56.

Wang, R., Wang, R. and Yang, B. (2009) 'Extraction of essential oils from 'five cinnamon leaves and identification of their volatile compound compositions', *Innovative Food Science and Emerging Technologies*, Vol. 10, pp.289–292.

WHO (2006) 'A joint workshop aimed at reducing blindness due to diabetes in the Eastern Mediterranean Region', *Regional Office for the Eastern Mediterranean Region Press Release. No. 21 Emro*, 20–22 November, Cairo.

Wijesekera, R.O. (1978) 'Historical overview of the cinnamon industry', *CRC Critical Reviews in Food Science and Nutrition*, Vol. 10, pp.1–30.

William, H.H., Ronald E. A., Mohammad A. A., Edward S. S. and Ahmed B.(1997) 'Diabetes mellitus in Egypt: risk factors, prevalence and future burden', Eastern *Mediterranean Health Journal*, Vol. 3, No. 1, pp. 144–148.

Yang, C.S., Landau, J.M., Huang, M.T. and Newmark, H.L. (2001) 'Inhibition of carcinogenesis by dietary polyphenolic compounds', *Annual Review of Nutrition*, Vol. 21, pp. 381– 406.