

Impact of Cinnamon Extract on Hyperlipidemic and Diabetic Rats

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Abstract

The present study was designed to investigate the effects of impact of cinnamon extract on some physiological, biochemical, hematological parameters among normal, hyperlipidemic and diabetic rats. Seventy adult male rats were randomly divided into seven groups each with 10 rats; each group was designed as follows: The first group was used as a control and was fed on standard diet and tap water ad libitum. The second group was treated with alcoholic cinnamon extract (500 mg/kg.bw). Third group was fed on high cholesterol diet (hyperlipidemic) while the fourth group was fed on high cholesterol diet and treated with alcoholic cinnamon extract (500 mg/kg.bw). The fifth group was injected with alloxan as a diabetic group. The sixth group was diabetic rats treated with alcoholic cinnamon extract (500 mg/kg.bw) and the seventh group; diabetic rats were treated with metformin drug (300 mg/kg.bw). After 30 days of experiment, rats were anaesthetized and the blood was taken by cardiac puncture for estimation of hematological, biochemical and immunological parameters. From the obtained results, the mean value of fasting blood glucose level in hyperlipidemic rats (135.5 ± 1.9 mg/dl) and diabetic rats (401.8 ± 3.5 mg/dl) was significantly decreased when hyperlipidemic rats (123.2 ± 1.9 mg/dl) and diabetic rats (221.1 ± 3.5 mg/dl) treated with cinnamon extract and further decreased when diabetic rats treated with metformin drug (161.56 ± 2.2 mg/dl) in comparison with control group (107.2 ± 2.7 mg/dl). The mean values for serum lipid in hyperlipidemic rats were significantly decreased when hyperlipidemic rats treated with cinnamon extract as follows: total cholesterol (120.7 ± 1.9 to 95.10 ± 2.2 mg/dl), triglyceride (138.8 ± 3.1 to 102.8 ± 1.51 mg/dl), low-density lipoprotein (LDL) (56.24 ± 1.9 to 33.14 ± 1.9 mg/dl) and very low-density lipoprotein (VLDL) (27.76 ± 0.62 to 20.56 ± 0.30 mg/dl). In diabetic rats, total cholesterol, triglyceride, LDL, and VLDL were significantly decreased when treated with cinnamon extract and metformin drug. The level of high-density lipoprotein (HDL) was improved when hyperlipidemic and diabetic rats treated with cinnamon extract. In diabetic rats, red blood cells, hemoglobin, packed cell volume, platelets were lower, but after treating of cinnamon extract; these parameters improved to significant level in diabetic rats. Conclusion: From the results of the present study, it can be concluded that extract of cassia cinnamon bark is effective in controlling blood glucose level, serum lipids among hyperlipidemic and diabetic rats.

Keywords

Cinnamon Extract, Hyperlipidemic Rats, Diabetic Rats, Metformin Drug

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1. Introduction

Plants have a long history in the traditional medicine uses that are in a rising demand using their extracts and chemical bioactive compounds for producing drugs and treating many infectious diseases (Nikbakht and Kafi, 2004). Therefore,

despite the active role of modern drugs, medical plants are still forming the basis of traditional or indigenous health systems in which most populations used them for their physiological and physical health care requirements (Najafi, *et al.*, 2010).

Cinnamon plant (family: Lauraceae) is a common additive

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for its flavor and aroma properties. Cassia cinnamon (*Cinnamomum cassia*) is one of the popular species of cinnamon, which is widely distributed in Asia especially in China (Jayaprakasha, *et al.*, 2003). In spite of using its inner bark before many years as a food additive in cooking or to treat digestive system disorders, urinary problems, fight bad breath, stave off common cold and promotion of wound healing (Archer, 1998), but just recently it has become increasingly popular for its benefit in glucose and lipid metabolism (Preuss, *et al.*, 2006). Some study were mentioned that the active compounds of cinnamon (such as cinnamaldehyde, eugenol and other compounds) possess wide ranges of pharmacological effects that seems to be highly bioactive against diabetes by its effect on insulin secretion and stimulate glucose uptake by hepatocytes and adipocytes (Qin, *et al.*, 2003 and Vangalapati, *et al.*, 2012).

2. Materials and Methods

2.1. Animal and Housing

During the present study, adult male albino rats (*Rattus norvegicus*) weighting 170-188g and 9-10 weeks of age were used. Rats were breed in the Animal House of the Department of Biology/ Faculty of Science / University of Duhok and placed in ventilated polypropylene cages (30×25×17cm), four rats per cage with their access to standard diet and tap water ad libitum under standard laboratory conditions (12 h light: 12 h dark photoperiod, at 24 ± 2 °C) and acclimated to the laboratory conditions for 3 weeks then were mixed for breeding then adult males were used for experimental studies.

2.2. Preparation of Alcoholic Extract of Cassia Cinnamon

The stem barks of {*Cinnamomum cassia* (L.) Don.} Was purchased commercially from local markets in Duhok City in April 2013. The barks were authenticated by the Professor Dr. Saleem Esmael Shahbaz, Taxonomist at the Faculty of Agriculture and Forestry, Department of Forestry, University of Duhok.

Extraction of cassia cinnamon was prepared according to other previous studies by adding 100g dried powdered bark of cinnamon into 1000 ml of ethanol 70% (Scharlab S.L-Spain) in a dark bottle and mixed manually (4 times at least in a day) and kept in dark place at a room temperature for 2 days, then the mixture was filtrated with wattman paper no.2 and evaporated to dryness under vacuum at 45°C by Rotary Evaporator (Eyela-United Kingdom) for removing ethanol. The residual extract was dissolved in a tap water whenever it used in the experiments (Soliman, *et al.*, 2012 and Su-Chen, *et al.*, 2013). This was repeated in each week to obtain a fresh

cinnamon extract as a treatment for the experiment.

2.3. Induction of Diabetes

Thirty male albino rats were fasted for overnight and treated with a single subcutaneously injection of alloxan monohydrate (150 mg/kg.bw) (Sigma- Alorich from United Kingdom), which was freshly dissolved in 0.1M citrate buffer (PH = 4.5) and injected immediately to prevent degradation before injection. Alloxan treated animals were allowed to drink 5% of D-Glucose (Scharlab S.L-Spain) for 2-4 h to prevent the potentially fatal hypoglycemia as a result of alloxan injection. Symptoms of diabetes were appeared within 2 days after alloxan injection such as elevated blood glucose, loss of body weight, polyuria, and glycosuria. Diabetes was confirmed in treated rats after 3 days by testing blood glucose from the tail of animals by Acc-glucose check (Roche-Germany) and glucose in urine by using urine strips (Machinary-Nagel/ Germany), animals with fasting blood glucose more than 200mg/dl and glycosuria (glucose in urine) were considered as diabetes rats (Mona, 2011).

2.4. Standard Diet

Standard diet was prepared for 1kg as follows: wheat 665.5g, soya 256.2g, oil sun flower 43.5g, lime stone 14.9g, Ca₂(PO₄) 6.42, salt 6.34g, lysine 2.44g, methionine 1.56g, enzymes 0.8g, choline chloride 0.62g, vitamins 0.58g and trace elements 0.5g (National Research Council, 1995).

2.5. Preparation of High Cholesterol Diet

High fat diet was prepared by adding 5g of cholesterol powder (Griffin-England) + 1g of cholic acid (Rome-Italy) + 10ml of coconut oil (Emad-Iraq) to the 1kg of standard diet (Rachh, *et al.*, 2010).

2.6. Hematological Analysis

After 30 days of experiment, rats were deprived from food overnight, but left free access to water. Animals were anesthetized with diethyl ether (Scharlab S.L-Spain) and 7 ml of blood samples were obtained directly by heart puncture (Sherin, 2011) in which 2 ml of blood were collected in heparinized tubes (Arzer Grande- Italy) for the determination of hematological parameters such as RBC Hb, PCV, MCV, MCH, MCHC, RDW, WBCs and platelets by using automated Hematological analyzer (Sysmex Corporation Kobe, Japan) according to the standard methods by (Sodipo, *et al.*, 2011).

2.7. Estimation Biochemical Parameters

Another 5ml of blood were placed in non-heparinized dry centrifuge tubes and were allowed to clot at room temperature for 30 minutes then centrifuged at 3000 rpm for

15 minutes to obtain serum. Serum samples were placed in Eppendorf tubes for the determination of serum lipids by Cobas Integra-400 plus automated chemistry analyzer (Roche/Germany) in Dr. Amer medical lab in Duhok City. This apparatus estimates cholesterol TG, VLDL, LDL and HDL depending on their measurement principles according to their reagents kits (Roche/Germany) that include: absorbance photometry (enzymes, substrates, specific proteins).

2.8. Statistical Analysis

Data were analyzed statistically by using excel and GraphPad Prism 5 using analysis of variance (ANOVA) followed by Dunnett's test. Firstly all groups were compared with control group (pointed as *), then untreated group feed on high cholesterol diet was compared with treated group with cinnamon extract and feed on high cholesterol diet (pointed as capital letters; A and B). Diabetic groups were compared with each (pointed as small letters; a, b, c). Results were expressed as mean \pm standard error and P-values < 0.05 were considered statistical significant.

3. Results

3.1. Effect of Cinnamon Extract on Serum Glucose Level

As shown in (table 1 and fig 1), blood glucose was significantly ($P < 0.05$) lower in control rats treated with

cinnamon alone in comparison with control group. In hyperlipidemic and diabetic groups, glucose level was significantly ($P < 0.001$) higher in comparison with control group, after they treated with cinnamon extract, glucose level was significantly ($P < 0.001$) lower when compared with untreated hyperlipidemic and diabetic group. In diabetic rats treated with metformin, glucose level was significantly (c) lower in comparison with diabetic group (a) and diabetic rats treated with cinnamon (b).

3.2. Effect of Cinnamon Extract on Serum Lipids

Table (1) represents the effect of cinnamon extract on total cholesterol, TG, VLDL, LDL and HDL levels. In the control rats treated with cinnamon alone, cholesterol and TG levels were significantly ($P < 0.01$) lower when compared with control group. The level of cholesterol and TG were shown to be significantly ($P < 0.001$) higher in untreated hyperlipidemic and diabetic groups in comparison with control group. In hyperlipidemic rats treated with cinnamon extract, cholesterol and TG levels were significantly (B) lower when compared to untreated hyperlipidemic rats (A). In diabetic group treated with cinnamon extract, cholesterol and TG level were significantly lower, but no significant changes found in diabetic group treated with metformin in comparison of these groups with untreated diabetic group (fig. 2 and 3).

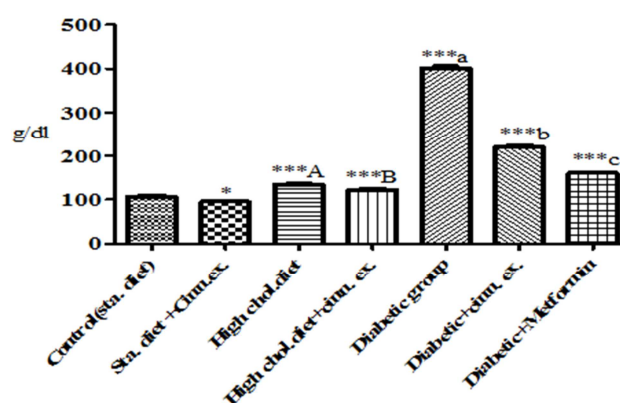


Figure (1). Effect of cinnamon extract on glucose level, in which * = comparison of all groups with control group, capital letters = comparison between high cholesterol diet groups, small letters = comparison among diabetic groups, Cinn. = cinnamon, Sta. = standard, chol. = cholesterol, ex= extract and significance is shown as *** ($P < 0.001$), ** ($P < 0.01$), * ($P < 0.05$).

Table (1). Effect of cinnamon on blood glucose and serum lipids.

Treatments Parameters	(Standard diet) Control	Standard diet+Cinn. extract	High cholesterol diet
Glucose mg/dl	107.2 \pm 2.7	94.56 \pm 2.8*	135.5 \pm 1.9***A
Total Cholesterol mg/dl	66.0 \pm 0.97	58.22 \pm 1.4**	120.7 \pm 1.9***A
TG mg/dl	63.00 \pm 3.1	50.44 \pm 1.3**	138.8 \pm 3.1***A
HDL mg/dl	41.60 \pm 1.7	44.11 \pm 1.3	35.10 \pm 1.9**A
VLDL mg/dl	12.60 \pm 0.29	10.91 \pm 0.65	27.76 \pm 0.62***A
LDL mg/dl	10.75 \pm 0.64	5.09 \pm 0.81*	56.24 \pm 1.9***A

Table (1). Continuous.

Treatments	High cholesterol diet+Cinn. extract	Diabetic group	Diabetic+ Cinn. extract	Diabetic+ Metformin
Parameters				
Glucose mg/dl	123.2±1.9***B	401.8±3.5***a	221.1±3.5***b	161.56±2.2***c
Total Cholesterol mg/dl	95.10±2.2***B	75.58±2.9**a	67.20±1.5b	69.78±1.3a
TG mg/dl	102.8±1.51***B	85.86± 4.85***a	68.11±2.711b	75.86±1.7*a
HDL mg/dl	41.20±1.8B	34.14±1.4**a	36.33±1.1*a	40.44±1.6b
VLDL mg/dl	20.56± 0.30***B	16.95±0.51***a	13.62±0.54b	14.93± 0.30*a
LDL mg/dl	33.14±1.9***B	28.64±1.6***a	14.87±1.2b	13.73± 1.1c

Values are mean \pm SE, * = ($P < 0.05$), ** = ($P < 0.01$), *** = ($P < 0.001$) for comparison all groups with control group. Capital letters (A and B) represent comparison between high cholesterol diet groups and small letters (a, b and c) represent comparison between diabetic groups.

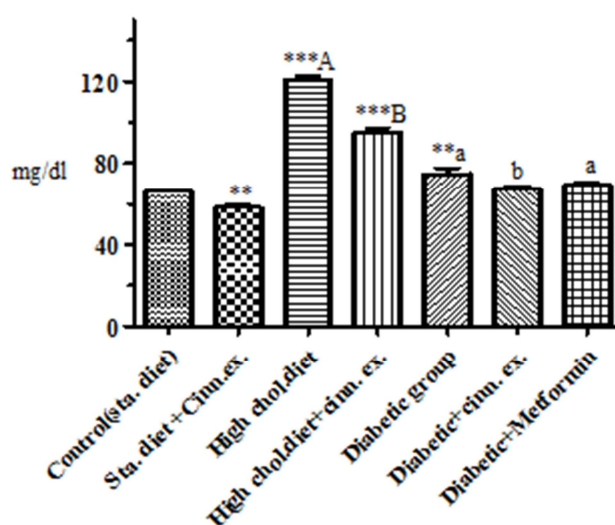


Figure (2). Effect of cinnamon extract on cholesterol level, in which * = comparison of all groups with control group, capital letters = comparison between high cholesterol diet groups, small letters = comparison among diabetic groups, Cinn. = cinnamon, Sta. = standard, chol. = cholesterol, ex = extract and significance is shown as *** ($P < 0.001$), ** ($P < 0.01$), * ($P < 0.05$).

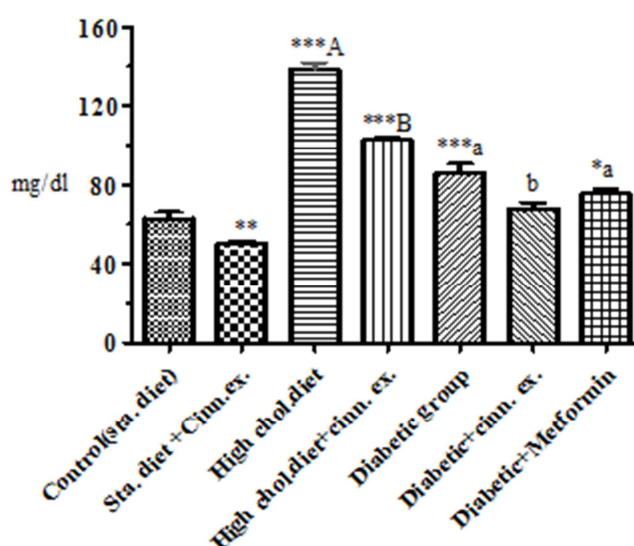


Figure (3). Effect of cinnamon extract on triglycerides level, in which * = comparison of all groups with control group, capital letters = comparison between high cholesterol diet groups, small letters = comparison among diabetic groups, Cinn. = cinnamon, Sta. = standard, chol. = cholesterol, ex = extract and significance is shown as *** ($P < 0.001$), ** ($P < 0.01$), * ($P < 0.05$).

The VLDL level showed no significant change in the group treated with cinnamon alone. In untreated hyperlipidemic and

diabetic groups, VLDL was significantly ($P < 0.001$) higher in comparison with control group. In hyperlipidemic rats treated

with cinnamon, VLDL was significantly (B) lower when compared with untreated hyperlipidemic group (A). In diabetic rats treated with cinnamon, VLDL was significantly (b) lower, but in diabetic group treated with metformin glucose level showed no significance changes (a) in comparison with untreated diabetic group (table 1).

In control rats treated with cinnamon extract, LDL was significantly ($P<0.05$) lower when compared with control group. LDL level was significantly ($P<0.001$) higher in untreated hyperlipidemic and diabetic groups when compared with control group. In hyperlipidemic rats treated with cinnamon, LDL was significantly (B) lower when compared with untreated hyperlipidemic (A). In diabetic rats treated with cinnamon, LDL was significantly (b) lower and further lowered in diabetic group treated with metformin (c) in comparison with untreated diabetic group (a) (table 1).

In contrast to the all above parameters, HDL level was significantly ($P<0.01$) lower in untreated hyperlipidemic and diabetic groups in comparison with control group. In hyperlipidemic group treated with cinnamon, HDL was significantly (B) lower in comparison with untreated hyperlipidemic group (A). In diabetic group treated with metformin, HDL was significantly (b) lower, but no significant change (a) observed in diabetic group treated with cinnamon in comparison with untreated diabetic group (a). In the group treated with cinnamon extract alone, no significant differences observed in HDL level in comparison with control group (table 2).

3.3. Effect of Cinnamon Extract on Hematological Parameters

As shown in the table (2) RBCs and Hb were significantly ($P<0.001$) lower only in the diabetic group

When compared with control group, but after administration of cinnamon and metformin, RBCs became significantly (b)

higher and Hb slightly improved (with no significant changes) when compared with untreated diabetic group (fig. 4). In other groups, RBCs and Hb were showed no significant changes. PCV percentage in untreated diabetic group was significantly ($P<0.01$) lower in comparison with control group. In diabetic rats treated with cinnamon extract, PCV showed slight non-significant changes (a), but when treated with metformin it was significantly improved (b) in comparison with untreated diabetic group (a). In other groups, PCV was showed no significant changes. There were no statistical significant changes in the level of MCV, MCH, MCHC and RDW in all groups when compared with control group (table 3).

Platelets were significantly ($P<0.001$) lower in untreated diabetic rats in comparison with control group, but improved significantly (b) when treated with cinnamon and further improved (c) in diabetic rats treated with metformin in comparison with untreated diabetic rats (a). In other groups, platelets differences were significantly not changed when compared to control group (table 2).

As shown in (fig. 5), WBCs count in control rats treated with cinnamon alone was not changed significantly in comparison with control group. WBCs were significantly (b) in hyperlipidemic group treated with cinnamon in comparison to untreated hyperlipidemic group (A). In diabetic rats WBCs was not found to be statistically significant in comparison with control group. In diabetic group treated with cinnamon, WBCs was not changed significantly, but in diabetic group treated with metformin, WBCs was significantly (b) higher when compared with untreated diabetic rats (a). The percentages of neutrophils, lymphocytes, monocytes and eosinophil were not changed statistically. Basophils not observed in the blood sample of all groups (table 3).

Table (2). Effect of cinnamon on RBC and platelets count.

Treatments	(Standard diet) Control	Standard diet+Cinn. extract	High cholesterol diet
Parameters			
RBC ($\times 10^6/\text{mm}^3$)	7.17 \pm 0.25	7.45 \pm 0.08	7.42 \pm 0.19A
Hb (g/dL)	14.36 \pm 0.16	14.47 \pm 0.23	14.78 \pm 0.14A
PCV (%)	43.02 \pm 0.44	43.41 \pm 0.69	44.33 \pm 0.42A
MCV (fL)	60.50 \pm 1.8	58.30 \pm 1.1	59.99 \pm 1.3A
MCH (pg)	20.20 \pm 0.61	19.43 \pm 0.39	19.40 \pm 0.33A
MCHC (g/dL)	32.07 \pm 0.49	34.39 \pm 0.61	32.32 \pm 0.37A
RDW %	18.63 \pm 0.85	18.37 \pm 0.38	16.57 \pm 0.70A
Platelets/ mm^3	432700 \pm 15317	442667 \pm 8588	419500 \pm 10851A

Table (2). Continuous.

Treatments	High cholesterol diet+Cinn. extract	Diabetic group	Diabetic+Cinn. extract	Diabetic+Metformin
Parameters				
RBC($\times 10^6/\text{mm}^3$)	7.21 \pm 0.16A	5.91 \pm 0.18***a	6.29 \pm 0.18*b	6.67 \pm 0.27b
Hb (g/dL)	14.42 \pm 0.16A	13.06 \pm 0.34***a	13.47 \pm 0.23*a	13.93 \pm 0.26a
PCV (%)	43.27 \pm 0.49A	39.19 \pm 1.034***a	40.40 \pm 0.71*a	42.21 \pm 0.82b
MCV (fL)	60.11 \pm 0.95A	63.30 \pm 1.4a	64.54 \pm 1.9a	63.97 \pm 2.2a
MCH (pg)	20.04 \pm 0.31A	21.10 \pm 0.49a	21.51 \pm 0.64a	21.32 \pm 0.74a
MCHC(g/dL)	32.91 \pm 0.75A	33.05 \pm 0.61a	32.47 \pm 0.53a	33.28 \pm 0.98a
RDW %	16.88 \pm 0.59A	20.53 \pm 0.55a	18.10 \pm 0.76a	19.22 \pm 0.81a
Platelets/ mm^3	427000 \pm 8916A	357625 \pm 10667***a	388444 \pm 10824**b	40311 \pm 5834c

Values are mean \pm SE, * = (P < 0.05), ** = (P < 0.01), *** = (P < 0.001) for comparison all groups with control group. Capital letters (A and B) represent comparison between high cholesterol diet groups and small letters (a, b and c) represent comparison between diabetic groups.

Table (3). Effect of cinnamon on WBCs count.

Treatments	(Standard diet) Control	Standard diet+Cinn. extract	High cholesterol diet
Parameters			
WBC / mm^3	9278 \pm 617	9120 \pm 575	12075 \pm 359**A
Neutrophils%	11.60 \pm 1.1	10.30 \pm 0.5	15.06 \pm 1.2A
Lymphocytes%	83.70 \pm 1.3	85.00 \pm 0.85	82.10 \pm 1.2A
Monocytes%	2.70 \pm 0.33	2.30 \pm 0.26	3.70 \pm 0.30A
Eosinophil%	2.00 \pm 0.21	2.40 \pm 0.34	1.60 \pm 0.16A

Table (3). Continuous.

Treatments	High cholesterol diet+Cinn. extract	Diabetic group	Diabetic+Cinn. extract	Diabetic+Metformin
Parameters				
WBC / mm^3	11478 \pm 470*A	8800 \pm 365a	10686 \pm 719a	11171 \pm 797b
Neutrophils%	11.56 \pm 0.91A	13.30 \pm 1.2a	11.70 \pm 0.67a	11.90 \pm 1.3a
Lymphocytes%	83.67 \pm 1.5B	79.13 \pm 1.3a	82.60 \pm 1.2a	82.80 \pm 1.5a
Monocytes%	3.11 \pm 0.20A	2.30 \pm 0.26a	3.40 \pm 0.30a	3.30 \pm 0.33a
Eosinophil%	1.67 \pm 0.23A	1.80 \pm 0.24a	2.30 \pm 0.37a	2.00 \pm 0.33a

Values are mean \pm SE, * = (P < 0.05), ** = (P < 0.01), *** = (P < 0.001) for comparison all groups with control group. Capital letters (A and B) represent comparison between high cholesterol diet groups and small letters (a, b and c) represent comparison between diabetic groups.

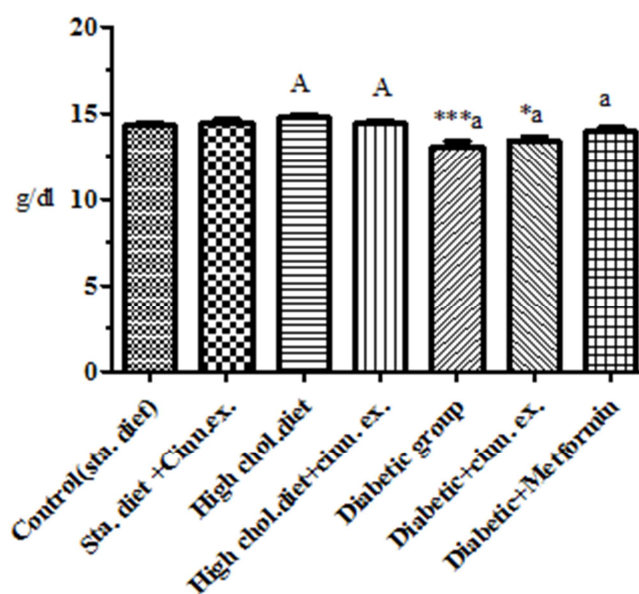


Figure (4). Effect of cinnamon extract on Hb level, in which * = comparison of all groups with control group, capital letters = comparison between high cholesterol diet groups, small letters = comparison among diabetic groups, Cinn. = cinnamon, Sta. = standard, chol. = cholesterol, ex= extract and significance is shown as *** (P<0.001), ** (P<0.01), * (P<0.05).

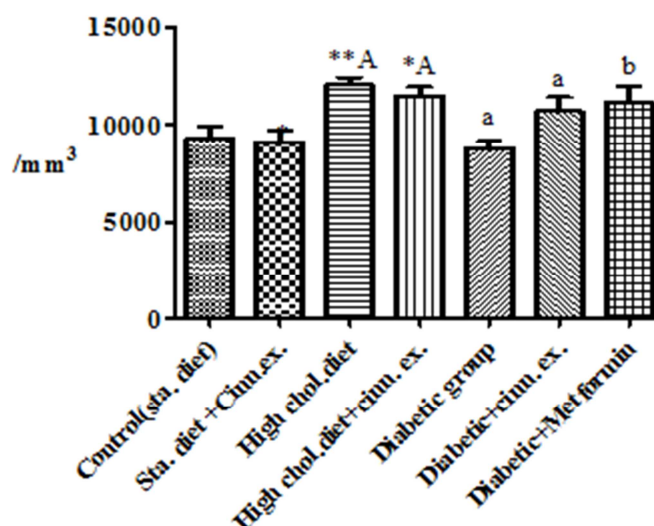


Figure (5). Effect of cinnamon extract on WBCs, comparison of the changes in WBC count of the treated groups' (Cinn. = cinnamon, sta= standard, chol. = cholesterol, ex= extract) with the control and the significance is shown as *** ($P<0.001$), ** ($P<0.01$), * ($P<0.05$).

4. Discussion

4.1. Effect of Cinnamon Extract on Serum Glucose Level

Administration of cinnamon bark extract to control, hyperlipidemic and diabetic rats showed a hypoglycemic effect of this extract on all above groups especially in diabetic rats. The expected interpretation of these effects in treated groups may be due to the enhancement of insulin secretion of the beta cells of the pancreas. These findings were in agreement with (Khan, *et al.*, 1990; Shalaby and Samar, 2010 and Al-Jamal and Rasheed, 2010). The first author of them reported the hypoglycemic effect of cinnamon could be due to insulin potentiating factor (IPF) that was isolated from cinnamon, which increased the activity of insulin 3 folds in glucose metabolism in the epididymal fat cells of rat. Later, this isolated factor (IPF) from cinnamon was termed as methyl hydroxy chalcone polymers (MHCP). They reported that MHCP was increased insulin dependent glucose metabolism many folds (more than 3 folds) when it was examined during *in vitro* studies (Broadhurst, *et al.*, 2000). Others explained that MHCP caused fat cells more responsive to insulin through activating the insulin-receptor-kinase enzyme that causes binding of insulin to the cells and inhibiting insulin-receptor-phosphatase enzyme that blocks this binding process thereby MHCP leads to maximal phosphorylation of the insulin receptor, which is associated with increased insulin sensitivity and enhances glycogen synthase activity (Khan, *et al.*, 2003; Qin, *et al.*, 2003; Anderson, *et al.*, 2006; Kim, *et al.*, 2006 and Nadia, *et al.*, 2011).

Others mentioned that cinnamon increases the production of glucose-6-phosphate dehydrogenase (G-6-PDH) in the liver

in which G-6-PDH leads to reduce glucose transporting by pentose phosphate pathway (pentose shunt) and storage of glucose as a glycogen in the liver (Ugochukwu and Babady, 2003). Cinnamon was mentioned in other study to activate the function glucokinase enzyme which in turn stimulates glucose transporters (GLUT4) for entering of glucose to the hepatic cells (glycogenesis) and adipocytes lead to increase in glycogen storage available for energy production (Cao, *et al.*, 2007). Bugudare, *et al.*, (2011) were found that hydroalcoholic extract of cassia cinnamon reduced blood glucose in alloxan induced diabetic rats when used alone or combined with glibenclamide and metformin drugs. Other concluded that serum glucose of hyperlipidemic rats fed on high fructose diet was significantly reduced with cinnamon treatment, which could be due to the hypolipidemic activity of cinnamon extract that acted an agonist with insulin *in vivo* to increase fat synthesis in adipose tissues and decrease blood glucose level in hyperlipidemic rats (Dugoua, *et al.*, 2007). Other studies were observed that lowering postprandial glucose effect of cinnamon exhibited by suppression of alpha-glycosidase enzyme to enhancing the metabolism of glycogenesis in liver and decrease the circulating glucose (Mohamed, *et al.*, 2011; Hassan, *et al.*, 2012 and Moraveji, *et al.*, 2013).

These effects of cinnamon extract in this study were appeared more prominent during fatal hyperglycemia; the mortality rate was 34% in untreated diabetic rats, 16.5% in diabetic rats treated with cinnamon, but all of the diabetic rats lived for 30 days of the experiment when they were treated with metformin drug. Similar results were obtained in the mortality rate of alloxan induced diabetic rats by (Sherin, 2011). Observing of mortality in diabetic treated rats could be due to that most of the insulin secretory beta cells of the pancreas destructed after induction of diabetes by alloxan, only few cells were survived

to be stimulated by cinnamon to increase insulin secretion. Thus, when blood glucose was highly elevated, cinnamon is able to control specific level of blood glucose (Khan, *et al.*, 2003 and Verspohl, *et al.*, 2005). Solomon and Blannin, (2007) were reported that effects of cinnamon remain mostly for about 12 hours after ingestion whereas others mentioned after cinnamon consumption, postprandial blood glucose was reduced at the same time delaying the gastric emptying without affecting satiety that could be useful to decrease the complications of polyphagia in diabetic patients (Hlebowicz, *et al.*, 2007). Others recommended when blood glucose levels were poorly controlled by diet, weight loss, exercise and oral traditional uses; insulin with other oral hypoglycemic agents (metformin, Glibenclamide, sulphonylureas, biguanides, alpha glucosidase inhibitors and thiazolidenediones) was recommended for the treatment of diabetes patients (Kumar and Clark, 2002). In the present study, when diabetic rats were treated with metformin, serum glucose level was significantly lower, but still higher in the blood glucose of control group. Some of the expected reasons could be due to limited metformin dose (more than 300 mg/kg) and time of the administration. Therefore, daily estimation of glucose level will be best to decide the metformin dose because of the fluctuation in the glycemic level throughout entire of the day. Liliane, *et al.*, (2011) mentioned that a daily estimation of food intake and measurement in variation of glycemic level (at least two times per/day) was needed to find a correct dose of drugs therapy for diabetic animal to maintain normoglycemia until the final day of the experiment.

4.2. Effect of Cinnamon Extract on Serum Lipids

Cinnamon extract lowered the level of total cholesterol, TG, VLDL and LDL and improved the level of HDL in hyperlipidemic and diabetic rats. The observation of higher level of serum lipids in diabetic rats in many studies were found to be resulted from increase in the mobilization of FFAs from the peripheral depots to the circulation thus, excess FAs in alloxan-induced diabetic rats promote the conversion of FAs into phospholipids and cholesterol by lipase enzyme in the liver during the absence of normal insulin level and increment in the activity of lipase enzyme resulted in hypercholesteremia and hypertriglyceridemia. On the other hand, glucagon, catecholamine and other hormones enhance lipolysis in the blood during diabetes (Simsolo, *et al.*, 1992 and Sharma, *et al.*, 1996).

Stimulation of insulin secretion by cinnamon treatment was observed to reduce the elevated level of serum lipids through suppression of endogenous synthesis of lipoproteins lipids (Al-Khazraji and Khalil, 2009), antioxidant properties of polyphenols in cinnamon against tissue damage in organs

that regulated serum lipids (Mancini-Filho, *et al.*, 1998) and the ability of cinnamon to inhibit (or reduce) the activity of HMG CoA reductase in the liver of rats fed on high fructose diet could be another reason for hypolipidemic activity of cinnamon (Kannappan, *et al.*, 2006 and Lee, *et al.*, 2003).

Others mentioned the level of apolipoprotein B-48 that is synthesized by the intestine and liver is increased after feeding rats on fructose rich diet, but with oral administration of cinnamon extract, its level was decreased in enterocytes through ameliorating the intestinal insulin resistance, which could be helpful in the control of lipid metabolism, because insulin has been shown to have acute inhibitory effects on apolipoprotein B-48 in enterocytes (Bolin, *et al.*, 2009). El-Kholy, *et al.*, (2012) mentioned that major compounds of cinnamon (cinnamaldehyde, cinnamyl acetate and cinnamyl alcohol) are converted into cinnamic acid by oxidation and hydrolysis, respectively. In the liver, cinnamic acid oxidized to benzoate that exists as sodium benzoate or benzoyl-CoA. Sodium benzoate was found to reduce the level of cholesterol *in vivo* in mice (Brahmachari, *et al.*, 2009) as an alternative interpretation of cinnamon had the ability to decrease the serum lipids.

Bugudare, *et al.*, (2011) were found that hypolipidemic effect of cinnamon extract was observed to be almost similar to metformin effect among diabetic rats. Other were found that administration of cinnamon extract to STZ induced diabetic rats was resulted in the reduction of TG and total cholesterol (Qin, *et al.*, 2003) and improved serum lipids in people with type 2 diabetes (Cao *et al.*, 2007).

Improving level of HDL and LDL in groups treated with cinnamon may be due to the increase in hepatic HDL binding activity and increase in hepatic LDL receptors activity and increasing in the action of lecithin cholesterol acyl transferase, which has a role in the regulation of serum lipids (Patil, *et al.*, 2004). Others found that flavonoids compounds of cinnamon are responsible for increasing the level of HDL and decreasing in LDL and VLDL concentration in hypercholesterolemic rats (Patel, *et al.*, 2009). Others observed due to hypercholesterolemia serum level of TC, TG, VLDL and LDL decreased while the HDL increased in diabetic rats treated with cinnamon (Mona, 2011 and Mansour and Amira, (2009). Therefore, cinnamon extract has potential ability to reduce the long-term cardiovascular complications related with diabetes (Roussel *et al.*, 2009 and Hassan *et al.*, 2012).

4.3. Effect of Cinnamon Extract on Hematological Parameters

In the diabetic rats treated with cinnamon, lower levels of RBCs and platelets count was improved to significant level and PCV and Hb showed slight improvement, but these

parameters were further improved when diabetic rats treated with metformin. Hypoglycemic effect of cinnamon extract could be the main reasons that prevent the prevalence of diabetic complications for controlling level of above mentioned parameters during diabetes through decreasing the fatal effects of hyperglycemia on the hemopoietic system through reduction of the tissue damage in kidneys and liver resulted in the increasing and regulation of the necessary proteins required for RBCs and Hb synthesis (Hadjadj, *et al.*, 2001). Jarvill-Tavilor, *et al.*, (2001) were found that anti-oxidant glutathione activity of cinnamon extract may have a beneficial role on these hematological indices. Cinnamon was also reported to prevent platelets aggregation during hyperlipidemia and hyperglycemia (Hala, *et al.*, 2011). This effect of cassia cinnamon bark on platelets has been advised that patients can use it without taking anticoagulant (anti-platelet aggregation) drugs for preventing prevalence of heart disease (Aslan and Orhan, 2010). Ayman, (2013) was found that RBCs count and related parameters were increased in the diabetic rats treated with cinnamon. Thus, cinnamon might be capable for improving the hematological abnormalities and pathophysiological effects of diabetes mellitus.

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