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Anti-diabetic effect of *Ceylon cinnamon* aqueous extract against blood glucose, lipid profile and hematological parameters in male diabetic rats

Asia Parveen[1*], Khan Arbaz Ali[1], Muhammad Maisam[1], Nureen Zahra[1], Rabail Alam[1], Modasrah Mazhar[2], Ayesha shaukat[3]

[1]*Institute of Molecular Biology and Biotechnology, The University Of Lahore, Lahore Pakistan*
[2]*Biochemistry Department of Eastern Medicine and Surgery-Qarshi University, Lahore Pakistan*
[3]*University Institute of Radiological Sciences and Medical Imaging Technology,The University Of Lahore, Lahore Pakistan*

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Abstract

Diabetes mellitus is a multifactorial endocrine pathology appears mainly with hyperglycemia and disturbed lipid profile. Cinnamon is well known in Asian and Middle East countries for their antidiabetic activity. Main objective was the evaluation of antidiabetic spice cinnamon on diabetes mellitus in terms of blood glucose, lipid profile and hematological parameters. Male albino rats (*Rattus norvegicus*) ageing 10 – 12 weeks and weighting 163-170g were made diabetic with alloxan via intra-peritoneal injection.Rats were divided into four groups each group consist of three rats. Group A is control group, Group B served as negative or diabetic group. Group C Served as cinnamon treated group with 500 mg/kg body of weight of cinnamon extract, Group D served as positive group treated with secretagogue glimepiride. During 14 days of research rats were daily medicated via orally. At the end of study starved rats were anesthetized and dissected for the collection of blood samples. Blood glucose significantly ($P<0.005$) reduced in cinnamon extract treated rats after 7 and 14 days of treatment as compare to diabetic rats. Total cholesterol, triglycerides and low density lipoproteins also significantly ($P<0.05$) reduced in cinnamon extract treated group. While hematological parameters total erythrocyte count (TLC) and hemoglobin (HB) were only improved insignificantly in Group C. Cinnamon has significant hypoglycemic and antilipidemic effects to cure diabetes and diabetes induced dyslipidemia. Cinnamon extract has no toxic effects on hematological parameters. Further studies are required to evaluate the mode of action and longtime toxicity effects of extract on kidney and liver.

* **Corresponding Author:** Ms. Asia Parveen ✉ asia.parveen@imbb.uol.edu.pk

Introduction

Diabetes mellitus is a chronic disease and endocrine disorder of carbohydrate, lipid and protein metabolism in which either insulin action or insulin secretion are get affected and sometimes their co-existence becomes challenge for physician to find out the primary cause of diabetes. Some major causes of diabetes are genetic predisposition, gluco-toxicity, lipo-toxicity and other promotion factors are lack of exercise, dietary habits, sedentary life style, over nutrition and gestational abnormalities. Diabetes is one of the earliest time disease described by Egyptians about 3000 years ago (1). The prevalence of diabetes was globally estimated it was 2.8% in 2000 and according to anticipation it will be 4.4% in near 2030. In 1994 a survey was conducted to figure out the correct sketch of metabolic disorder in Pakistan, In Punjab males are more diabetic 12.14% in comparison of females 9.83% (2). Although various advancements have been achieved in medical sciences but the permanent cure of diabetes is still under the development. Coronary artery diseases and dyslipidemia are significantly more prevalent in diabetic patients in comparison of non-diabetics (3). Hypertension enhances the risk of microangiopathy in diabetics usually nephropathy and retinopathy are more prevalent (4). Diabetes is complex metabolic disorders produces many complication in the body various medicines are being widely used for diabetes including insulin therapy, sulfonyl urea's, biguanides and sitagliptin but often unable to re-establish the homeostasis of blood glucose (5). Many complications are associated with these treatments but studies of medicinal plants have initiated a new spark of excitement in traditional medicines. Traditional antidiabetic plants are might be substitute of present hypoglycemic compounds and valuable oral adjuncts to existing medications (6). Various plants are used for the treatments of diabetes and hyper-lipidemia but only few ones scientifically studied (6). Cinnamon is a medicinal plant its bark uses as antidiabetic spice and consider as treatment for all types of diabetes, but trials show contrasting effects when used as supplement (7). Cinnamon (Cinnamon cassia) contains many active ingredients such as tannin, cinnamic acid, cinnamic aldehyde and methyhydroxychalcone polymer (MCHP) that is mimetic to insulin (8). Therapeutic plants contain potentially helpful agents that can use as basis for the developing of modern medicines (9). In this study we tried to evaluate whether cinnamon extract can be used as a single sole treatment for diabetes, diabetic dyslipidemia and toxic effects of cinnamon extract on hematological parameters

Materials and methods

Animal model

Twelve healthy male albino rats (*Rattus norvegicus*) collected and acclimatized in animal house of the Institute of Molecular Biology and Biotechnology (IMBB), The University of Lahore. Only male albino rats used, their age was 10-12 weeks and body weight (b.wt) was 164g ± 3.80.There was no prominent difference in weight and age of individual rats. During experiment the animals were supplied with laboratory food, water and *ad libitum*.

Grouping of animals

Animals were equally divided into four groups of three animals per group.

Group A- Control (non-diabetic or normal rats)
Group B- Negative (diabetic rats without treatment)
Group C- Treated (diabetic + 500 mg/kg b.wt of cinnamon aqueous extract)
Group D- Positive control (diabetic + glimepiride 5mg/kg b.wt)

Extraction and dosage of cinnamon extract

Cinnamon extract prepared by studying previous cinnamon extraction protocols. Cinnamon ground until to become powder. 100 grams of powdered cinnamon dissolved in 700 ml of distilled water. Mixture placed at dark location for three day at 37°C with daily shaking, as a result dark chocolate color crude extract was observed. This crude filtered and their filtrate was collected. The collected extract was further evaporated for six days under air by putting in half covered petri dishes. Then dried extract collected with surgical blade and saved at 4°C in Eppendorf

tube till further use. Cinnamon extract was given at dose of 500 mg/kg b.wt of rats for fourteen days to cinnamon group. Route of administration was oral by using gavage to deliver extract direct delivered into stomach.

Alloxanisation (induction of diabetes)

Alloxan monohydrate is diabetogenic agent prepared in saline solution of 0.3M Nacl. Required rats were made diabetic via alloxanisation. Rats were fasted for overnight prior to the injection of alloxan, experimental diabetes was induced by injecting intraperitoneal (150 mg/kg b.wt) of alloxan monohydrate in rats except for control group. After one hour of alloxan administration, 5% percent of dextrose solution was given to alloxanized rats and fasting blood glucose level was measured before and after 72 hours of alloxan administration With CERTEZA GL-110 Glucometer with dedicated blood glucose strips.

Blood collection and biochemical analysis

All animals deep anesthetized with chloroform in closed vessel prior to dissection. Their blood samples collected from inferior vena cava with 5ml syringe and immediately transferred into two different vacutainers one with EDTA used for complete blood count analysis and other with clot activator vacutainer. The blood clot activator vacutainers were later centrifuged for 10 mins at 3000 rpm by using a centrifugation machine. The clear supernatant used for the estimation of serum lipid profile parameters. The total erythrocyte count (TEC), total leucocyte count (TLC), haemoglobin concentration (HGB), platelet count and other hematological indices determined in the blood by using Sysmex XP-100 automatic hematology analyser in diagnostic lab of University of Lahore, Pakistan.The plasma total cholesterol, triglyceride and HDL-Cholesterol were determined by using Roche Cobas C-3111 automatic chemistry analyser. Low density Lipoprotein-Cholesterol (LDL-C) was calculated by using formula from (8).Blood sugar tests were performed with CERTEZA GL-110 Glucometer and their dedicated blood glucose strips during two week of treatment their required blood samples were obtained by pricking the tail of the rats with injection syringes.

Statistical analysis

Data was collected, and preceded on computer software SPSS version 16 for statistical analysis. Significance of means were analyzed by using one way ANOVA and significant group differences were analyzed by using post hoc Tukey test.

The benchmark of significance was at least P-value <0.05. The graphs were plotted with Microsoft excel.

Results and discussion

At the end of study high blood sugar level significantly (P <0.05) reduced in diabetic rats those treated with 500mg/kg b.wt of cinnamon extract concern Table 1 and figure 1for more details. Disturbed lipid profile parameters such as total cholesterol, triglycerides and low density lipoproteins reduced significantly (P <0.05) concern Table 2 and figure 2. Hematological indices hemoglobin (HB) and total erythrocyte count (TLC) improved insignificantly (P <0.05) in cinnamon treated group as compare to diabetic rats concern Table 3 for more details.

Table 1. Comparison of fasting blood glucose changes after 7 and 14 days of treatment.

Variables Mean ± S.E.M	Group A (n=3) Control	Group B (n=3) Negative	Group C (n=3) Cinnamon	Group D (n=3) Glimepiride
FBG before Diabetes mg/dl	95 ± 5.4	85.7 ± 5.8	84.7 ± 7.7	102 ± 12.6
FBG after Diabetes mg/dl	99 ± 2.1	519 ± 91.8	470 ± 53.2	583 ± 17.0
FBG after 7 days of Treatment mg/dl	97 ± 2.3***	574 ± 14.7	286 ± 48.3*	517 ± 40.2
FBG After 14 days of Treatment mg/dl	86 ± 2.7***	596 ± 6.9	165 ± 37.4**	438 ± 46.4*

Table 1 shows the hypoglycemic effects of cinnamon extract and standard drug glimepiride on fasting blood glucose of male albino rats when induced with alloxan.Fasting blood glucose (FBG) significantly reduced in cinnamon group after one and two week of study at **(**P <0.05) and (p<0.005) respectively Values in the table are given as mean ± S.E.M standard error of means: one way variances of analysis (ANOVA and post hoc Tukey tests were performed for statisticalanalysis.

Table 2. Comparison of diabetic changes and improvement in lipid profile parameters induced by cinnamon extract.

parameters	Group A Control	Group B Alloxan	Group C Cinnamon	Group D Glimepiride
T. Cholesterol (mg/dl)	55 ± 1.00**	78 ± 5.29	60 ± 3.78*	60 ± 2.51*
Triglycerides (mg/dl)	73.3 ± 1.20*	253 ± 69.5	83 ± 3.60*	84.6 ± 2.60*
HDL (mg/dl)	34.3 ± 1.45	41 ± 7.81	41 ± 1.52	50 ± 0.57
LDL (mg/dl	6 ± 0.52*	13.6 ± 1.67	6.1 ± 2.09*	6.9 ± 1.73

The results of fasting blood glucose in cinnamon treated rats show significant (P <0.05) drop of elevated blood glucose level after 7 and 14 days of treatment**.** Present Study indicates that aqueous extract of Ceylon cinnamon owns significant hypoglycemic activity in male albino diabetic rats. The Hypoglycemic outcomes of cinnamon in diabetic rats were also agreed with previous hypoglycemic work (11).

According to their findings Cassia cinnamon at dose 0.16 g/ kg for 28 days significantly decreased blood sugar 26% percent in diabetic group while it did not show any significant change in normal rats Table 2.

Shows the outcomes of Cinnamon extract on serum lipid profile parameters in alloxan induced diabetic male rats. And asterisk * indicate Significant difference (P <0.05) when control and treated groups (Group C and D) compare with negative (group B).

These values mean ± SEM standard error of means. Serum lipid parameter significantly reduced in cinnamon group at (p<0.05) including total cholesterol (TC), triglycerides (TG) and LDL. Chol as compare to Group B and D.

Table 3. Comparison of hematological parameters among diabetic and treated groups.

parameters	Group A (n=3) Control	Group B (n=3) Alloxan	Group C (n=3) Cinnamon	Group D (n=3) Glimepiride
TEC (× 10^6/ µL)	7.67 ± 0.27	6.81 ± 0.08	7.23 ± 0.31	7.18 ± 0.46
HGB (g/dl)	13.6 ± 0.40*	12.1 ± 0.20	12.5 ± 0.32	12.3 ± 0.40
HCT (%)	46.5 ± 0.78*	35.6 ± 0.88	38.5 ± 0.90	41.0 ± 2.33
PLT (×10^3/ µl)	909 ± 102	729 ± 116	704 ± 113	832 ± 167
MCV (fL)	60.8 ± 2.76*	52.0 ± 1.15	55.0 ± 0.17	57.1 ± 1.63
MCH (pg)	17.83 ± 0.52	17.23 ± 0.62	17.80 ± 0.55	18.06 ± 0.44
MCHC (g/dl)	29.4 ± 0.75*	34.0 ± 0.43	32.1 ± 1.01	31.7 ± 0.92
TLC (×103/µl)	18.26 ± 2.35	10.43 ± 1.47	10.6 ± 1.51	9.3 ± 3.55
Lymphocytes (%)	88.66 ± 1.45	70.5 ± 3.81	72.4 ± 6.16	68.1 ± 14.1

Cholesterol (TC), Triglycerides (TG) and low density lipo- proteins (LDL-Chol) were significantly (P <0.05) reduced in cinnamon treated rats and have tremendous difference when compared with diabetic (Group B) rats. The results of present study indicate that crude extract of Ceylon cinnamon has blood glucose lowering and antilipedmic potential against the alloxan induce experimental diabetic rats. Previous studies proved that increase of blood serum parameters like TC, TG and LDL- Chol are co-related with elevated risk of cardiovascular diseases and diabetic dyslipidemia due to atherosclerosis.

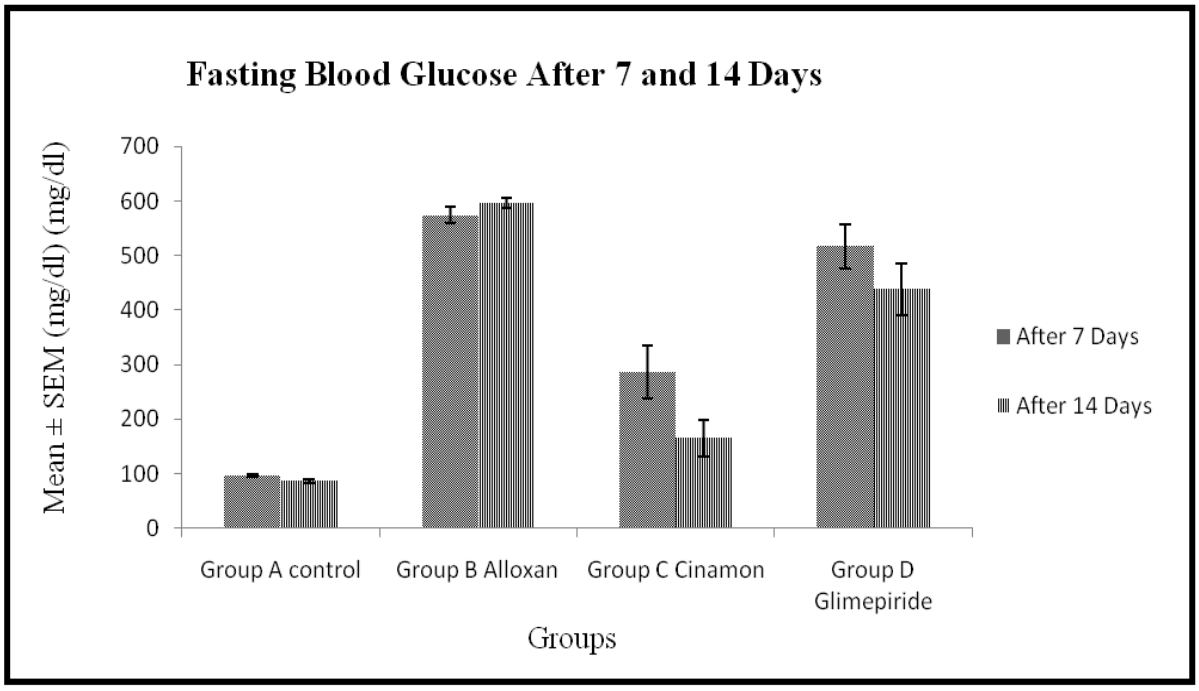

Fig. 1. Graphical illustration of fasting blood glucose (FBG) among all groups and FBG after 7and14daysoftreatment.

An experimental study of (12) on streptozotocin induced diabetes concluded that cinnamaldehyde component of cinnamon possess hypoglycaemic activity. While HDL-Chol non- significantly was raised in all groups in comparison of control group and slightly decreased in diabetic and treated group Table 3. shows the outcomes of Cinnamon extract and glimepiride on haematological parameters of male albino alloxanized rats.

The given values are means ± SEM standard error means, and asterisk * represents significance(P <0.05) differences when control and treated groups (Group C and D) compared with negative (group B).Abbreviation used Total erythrocyte count (TEC), Haemoglobin (HGB), Hematocrit (HCT), Platelets (PLT), Mean cell volume (MCV), Mean corpuscular haemoglobin (MCH), Mean corpuscular haemoglobin concentration (MCHC), Total leucocyte count (TLC), and Lymphocytes (LYM). Hematological parameters total erythrocyte count (TLC) and hemoglobin (HB) improved non-significantly in Group C.

There were non– significant changes (P <0.05) observed in hematology parameters, the results of Cinnamon (Group C) indicate insignificant (P <0.05) elevation in total erythrocyte count (TEC) and haemoglobin (HGB) when compared with (Group B and D).

Deficiency of TEC and HGB is common in diabetes (13). The improvement in these parameters suggests that cinnamon may have direct effect on kidney to variate the erythropoietin secretion.

The decrease of these parameters in diabetic group also suggests that may it happen as a result of glycosylation process. Non- significant decrease in

hematocrit (HCT) was observed in all groups as compare to control (Group A) but more decline in HCT was observed in Alloxan (Group B) may be due to hemolyticanemia , an increased HCT determineshigh blood viscosity, low blood flow to myocytes and decrease insulin sensitivity(14,15).

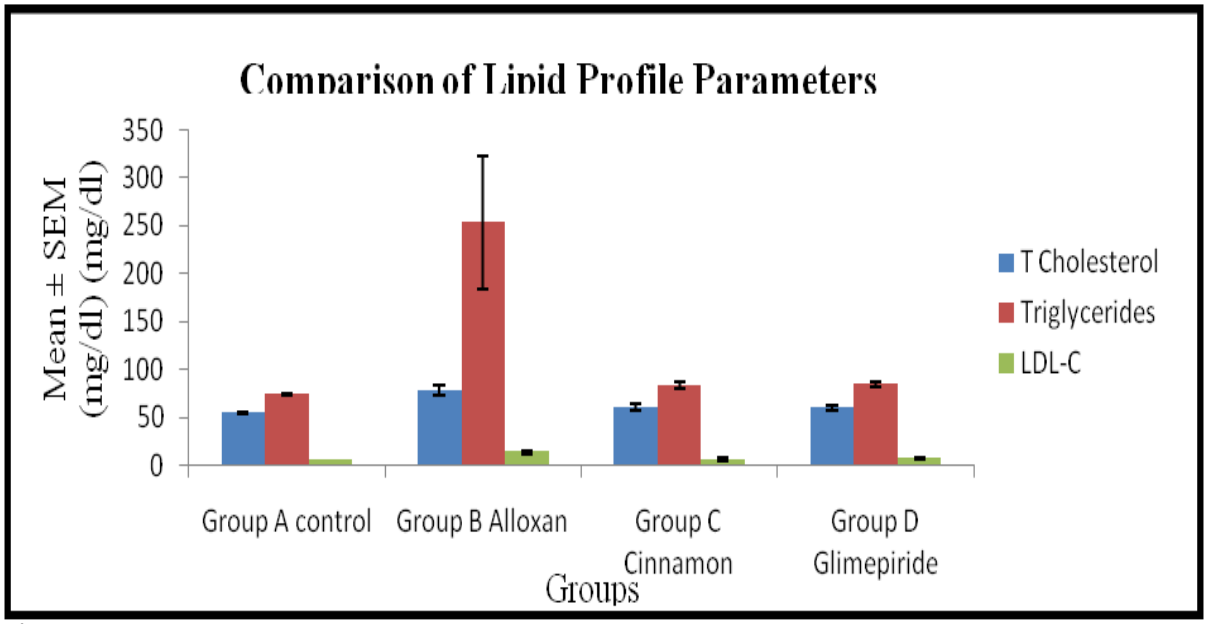

Fig. 2. Graphical illustration of change in lipid profile parameters TC, TG and LDL-C after 14 days of treatment.

Conclusion

The findings of present study concluded that cinnamon extract has significant hypoglycemic and antilipidemic effects on diabetesinduced hyperglycemia and dyslipidemia. Cinnamon extract is not hematotoxicity potential to ameliorate erythrocyte count and hemoglobin level.

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