Effects of the Aqueous Extract of the of Cinnamonum zeylanicum Barks (Cinnamon) on Glucose, Haemoglobin and Lipid Profile in Alloxan – Induced Diabetic Rats

Shahbaa M. Al-Khazraji **Zena K. Khalil**
Medical Technical Institute

Abstract

Cinnamonum zeylanicum (cinnamon) bark is considered extensively in the endogenous system of medicine as a drug for diabetes in many countries .

The current investigations focuses attention on the glucose and lipid lowering effect of the aqueous extract of Cinnamonum zeylanicum (cinnamon) barks on experimentally induced diabetes in rats . The biochemical parameters studied were plasma glucose, insulin , total cholesterol, triglycerides, phospholipids, mhaemoglobin, and glycosylated haemoglobin. In addition to measuring body weight , renal glucose reassertion were notified. Aqueous extract of cinnamon barks were orally administered daily for 30 days in a dose of 100 mg / kg body weight to alloxan– diabetic rats, and a significant reduction in the parameters measured was investigated compared to diabetic rats, meanwhile , Glibinclamise was used as standard reference drug. In conclusion cinnamon barks posses a hypoglycaemic with concurrent hypolipidemic effect in diabetic states , and may further suggests that cinnamon parks may be useful in the therapy and managements of diabetic hyperlipidemia through reducing lipids levels.

Keywords

Alloxan, diabetes mellitus, hyperlipidemia, Cinnamonum zeylanicum (cinnamon)

الخلاصة

يعد نبات الدارسين من الاعشاب الطبية المستخدمة كعامل مضاد لداء السكري في الكثير من دول العالم. لقد ركز البحث على تاثير المستخلص المائي لسيقان نبات الدارسين على نسبة السكر والدهون فى دم الجرذان المختبرية المخلقة بداء السكري.

تمت دراسة المؤشرات البايوكيميائية والمتمثلة بالجلوكوز، الانسولين، الهيموكلوبين والهيموكلوبين الـسكري، الكوليـسترول، الفوسفولبدز والترايكليسرايد وكذلك وزن الجسم واعادة امتصاص الكلوكوز من البول. استخدمت الطريقة الفموية فى البحث لاعطاء المستخلص المائي لسيقان نبات الدارسين للجرذان المخلقة بداء السكر لمدة 30 يوم وبجرعة 100 ملغم لكل كغم وزن، واعتمادا على نتائج البحث فقد لوحظ انخفاض معدلات المؤشرات البايوكيميائية المدروسة ولذلك يمكن اعتبار الدارسين من الاعشاب الفعالة لتخفيض معدلات السكري ويجب تواصل الدراسات لايجاد علاجات اخرى فعالة لتخفيض معدلات الدهون بالدم.

Introduction

Diabetes mellitus is a syndrome resulting from variable interactions of heridatory and environmental factors, and characterized by depleted insulin secretion, hyperglycaemia, and altered metabolism of lipids, carbohydrates, and proteins , in addition to damage of Beta–cells of pancreas, with increased risk of complication of vascular disease (Davis and Grammer 1996). A number of pharmacological and chemical agents act as diabetogenic and produce variety of diabetic complication.

Alloxan induced diabetes in experimental models widely used to study glycaemic and lipidemic changes in plasma. Many species of plants and herbs are known to act as anti–diabetic agents, but only few of them have been investigated (Jarvill-Travilor *et al* 2001) .

Cinnamonum zeylanicum (cinnamon) is widely used in traditional system of medicine to treat diabetes (Subosh Babu *et al* 2007). Methylhydroxychalcone polymer (MHCP) found in cinnamon reported to increase insulin dependant glucose metabolism roughly

20 folds in vitro studies, MHCP makes fat cells more responsive to insulin by activating the enzyme that causes insulin binding to the cells (insulin receptor kinase), and inhibiting the enzymes that blocks this process (insulin receptor phosphotase) leading to maximal phosphorylation of the insulin receptor which is associated with increased insulin sensitivity (Khan *et al* 2003, Jarvill- Travilor *et al* 2001 , and Roffey *et a*l 2006). The first in vivo study on cinnamon on human was published recently and gained numerous media attention, and it represent a subsantial reduction in fasting serum glucose concentration (18–29%) and improved blood lipid profile after 40 days of daily supplementation with only 1, 3 , or 6 gm of cinnamon in patient with type II (non– insulin dependent) diabetes . They concluded that inclusion of relatively small amount of cinnamon in the diet of patients with type 2 diabetes likely represents a safe and effective way of reducing the risk factor for the developement of co-morbidities associated with type 2 diabetes and cardiovascular disease (Roffey *et a*l 2006). Studies shows that there was no significant differences in blood glucose level, and cinnamon is not effective in improving glycaemic control in adolescents with type 1 diabetes (Verspohl and Bauer 2005) .

Cinnamaldehyde was isolated and identified as a putative anti-diabetic compound, since it decrease the plasma glucose level, and the LD 50 value of cinnamaldehyde was determined as 1850 mg/kg bw. Oral administration of cinnamaldehyde (20 mg/kg bw) for 30 days significantly decreased glycosylated haemoglobin (HbA ic, total serum cholesterol, triglyceride level, and at the same time markedly increase plasma insulin, hepatic glycogen, and high density lipoprotein-cholesterol level (HDL-Ch). Generally cinnamalehyde possesses hypoglycaemic and hypolipidemic effect in streptosotocin –induced diabetic rats (Subosh Babu 2007) .

The present study was undertaken to investigate the effect of aqueous extract of Cinnamonum zeylanicum (cinnamon) of on serum glucose, insulin, lipid profile haemoglobin, glycosylated haemoglobin, body weight and glucose reabsorption in alloxan induced diabetes in rats .

Materials and Methods

Dried barks of Cinnamonum zeylanicam obtained from commercial source and was identified at the National Herbarum of Iraq Botany Directorate in Abu-Ghraib. Aquous extract of cinnamon was prepared by decoction process of 100 gm powdered material in 200 ml distilled water and stirred magnetically overnight (16 hours) at room temperature, and this was repeated three consecuative times. The residue was removed by filtration and the extract was evaporated to dryness at low pressure in rotating evaporator, and the residual extract were dissolved in normal saline whenever used in the experiments (Al-Khazraji *et al* 1993).

Male wister rats (250 -300 g weight) from a colony bred at college of Pharmacy , Baghdad University animal house were used in this study. Animals were housed in an air conditioned room and water and food supplied ad libetum .

Collection of blood samples from rats was maintained by cardiac puncture technique. The rats were slightly anaesthetized with sodium pentobarbitone administered intraperitoneally at room temperature at a dose of 30 mg/kg bw thirty minutes prior to the experiments (Vinuthan *et al* 2007) .

Diabetes was induced in rats by intraperitoneal injection of 100 mg/ kg body weight of alloxan monohydrate (5 %w/v), freshly dissolved in physiological saline immediately before use (Vinuthan *et al* 2007). The diabetic state was confirmed 48 h after alloxan injection by body weight loss, glucosurea (Jarvill_travilor *et al* 2001), and hyperglycaemia, and the animals which presented blood glucose level above 200

mg /00 ml, as well as with the clinical signs of polydypsia, polyuria, and polyphagia were selected for the experiments (Foster and Dunn 1973). Animals were devided in to following four groups 6 of each :

Group I : normal rats received only physiological saline .

Group II : control diabetic rats received physiological saline .

Group III : diabetic rats received aqueous extract of cinnamon barks (100 mg/kg body weight)/ orally /daily for 30 days .

Group IV: diabetic rats received glibinclamide 600 microgram/kg body weight orally/daily for 30 days .

At the end of the 30 days, the animals were deprived of food overnight and sacrificed by decapitation. Blood was collected in two different tubes (i.e.) one with anticoagulant (potassium oxalate and sodium floride) for plasma, and another without anticoagulant for serum which is separated by centrifugation .

Fasting blood glucose level was estimated by O- toluidine method by Sasaki *et al* 1972. Plasma insulin level was assayed by Enzymetic Linked Immunosorbant Assay (ELISA) kit using human insulin as standard . Haemoglobin was estimated by method of Drabkin and Austin 1932, and glycosylated haemoglobin by method of Sudhakar Nayak and Pattabiraman 1981.

Total cholesterol and triglyceride were estimated by method of Zlatkis *et al* 1953 and Foster and Dunn 1973 respectively. Phospholipids were analyzed by method of Zilversmit *et al* 1950 .

The results were expressed as Mean ±S EM statistically significance of the differences in parameters before and after treatment was calculated using Students - paired –t – test (Siegal 1956) .

Results

Table 1-shows the levels of blood glucose, plasma insulin, haemoglobin, and glycosylated haemoglobin. There was s significant elevation in blood glucose and glycosylated haemoglobin levels ($P<0.005$), while the plasma insulin and haemoglobin levels decreased significantly in alloxan diabetic rats compared with normal rats ($P<0.005$) . Administration of cinnamon barks and glibiclamide tends tobring the parameters significantly towards the normal ($P<0.0005$).

In diabetic rats , there is significant changes in body weight, and the urine sugar, since urine containing sugar were noticed (+++) , but upon treatment with 100 mg/ kg body weight of aqueous extract of cinnamon barks showed decreased urine sugar (+) , these effects were compared to glibinclamide ($P<0.005$) , see Table 1.

Table 2- shows the level of cholesterol , triglycerides , and phospholipids in the plasma of control and experimental rats , Diabetic rats showed significantly increase levels of cholesterol , triglycerides , and phospholipids when compared with normal rats ($P<0.0005$). In rats treated with aqueous extract of cinnamon barks and glibinclamide, there was a significant decrease in the levels of cholesterol, triglycerides, and phospholipids when compared with diabetic control rats ($P<0.0025$).

Discussion

Diabetes mellitus is one of the most common chronic disease associated with hyperlipidemia and co-morbidities such as obesity, hypertension. Hyperlipidemia is a metabolic complications of both clinical and experimental diabetes (Bierman *et al* 1975).

Alloxan , a Beta cytotoxin induces "chemical diabetes" (alloxan diabetes) in a wide variety of animals species by damaging the insulin secreting pancreatic Beta

cells resulting in a decrease in endogenous insulin release which paves the ways for the decreased utilization of glucose by the tissues (Omamoto *et al* 1981) .

In this study, aqueous extract of cinnamon barks decreases blood glucose level in alloxan–diabetic rats could be correlated with the reminiscent effect to hypoglycaemic sulphonylureas that promotes insulin secretion by closure of K^+ ATPase channels , membrane depolarization and stimulation of Ca^{+2} influx , an initial key step in insulin secretion . The results in this study was similar to the results obtained by other studies (Roffey *et al* 2006 , Verspol *et al* 2005) .

In this study, a decrease in l haemoglobin during diabetes was notified, and this may be due to the formation of glycosylated haemoglobin. Increase in the levels of haemoglobins in animals given aqueous extract of cinnamon barks may be due to the decreased level of blood glucose and glycosylated haemoglobin .

Cinnamon barks administration to alloxan–induced diabetic animals reversed the weight loss, this ability of cinnamon barks to recover the body weight loss seems to be due to its hypoglycaemic effect .

Excess of fatty acids in serum produced by alloxan– induced diabetes promote conversion of excess fatty acids into phospholipids and cholesterol in the liver .

These two substances along with excess triglycerides formed at the same time in the liver may be discharged into the blood in the forms of lipoproteins (Bapanna *et al* 1997) .

The abnormal high concentration of serum lipids in the diabetic subject is due, mainly to the increase in the metabolism of free fatty acids from the peripheral fatty depots, since insulin inhibits the hormone sensitive lipase . Hypercholesteremia and hypertriglyceridemia have been reported to occurs in alloxan diabetic rats (Sharma *et al* 1996), and a significant increases observed in our experiment was in accordance of thesestudies. The marked hyperlipdemia that characterize the diabetic state may therefore, be regarded as a consequence of the uninhibited actions of lipolytic hormones on fat depots. Activation of enzymes suggests that enhanced lipid metabolism during diabetes is shifted towards carbohydrates metabolism, and it enhances the utilization of glucose at peripheral sites .

One of the possible action of cinnamon barks may be its inhibition of endogenous synthesis of lipids . Metabolic aberration in alloxan induced diabetes in rats suggests a high turnover of triglycerides and phospholipids. cinnamon barks was antagonizing the metabolic aberration, and thereby restore the normal metabolism by tilting the balance from high lipids to high carbohydrate metabolism decreases blood glucose level in alloxan– diabetic rats (Goodman and Gilman 1985).

It could be concluded that cinnamon exert a significant hypoglycaemic and hypolipidemic effects, since both diabetes and hyperlipidemia are considered to be major risk factors for the premature atherosclerosis and essentially all cholesterol in atherosclerotic plaques is derived from that of circulating cholesterol. The actual mechanism for the hypoglycaemic and hypolipidemic effects of cinnamon barks is not clear, and further biochemical and pharmacological investigations needed to isolate and identify the active ingredient(s) in the composite extract .

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Table 1- The changes in body weight , blood glucose , serum insulin , haemoglobin glycosylated aemoglobin level after treatment of diabetic rats with aqueous extract of cinnamon barks .

Groups	Body weight gm		Blood glucose level mg / 100ml	Plasma insulin milliunit / ml	Haemoglobin g/ 100ml	Glycosylated Haemoglobin mg/ g Hb
	initial	Final				
Group I	198±9.4	206± 8.9	96.5 ± 7.04	15083±1.02	12.65 ± 0.7	0.24 ± 0.01
Group II	202±14.2	150±-14.6++	236± 13.8 ++	4.85±0.96++	5.49±0.42++	0.81±0.07++
Group III	193±-14.8	196±15.3**	158.6±14.9***	13.05 ± 0.48***	9.54 ±- 0.93***	0.49 ± 0.03***
Group IV	194 ±14.8	205 ± 13.1**	133.9 ± 10.1***	12.53 ±0.65***	10.31 ± 1.05***	0.42 ± 0.04***

++ represent $P < 0.005$ of significancy compared to control group
** represent $P < 0.005$ of significancy compared to diabetic group
*** represent $P < 0.0005$ of significancy compared to diabetic group

Table 2- The changes in serum ckolesterol , triglyceride , and phospholipids after treatment of diabetic rats with the aqueous extract of cinnamon barks

Groups	Cholesterol mg / 100 ml	Triglyceride mg / 100 ml	Phospholipids mg / 100 ml
Group I	73 +- 1.49	44.13 +- 3.76	80.15 +- 1.37
Group II	99.33 +- 4.03 +++	+++ 62.43 +- 1.5	97.95 +- 2.28 +++
Group III	92.28 +- 2.98 **	56.19 +- 3.9 **	90.01 +- 2.86 **
Group IV	93.01 +- 3.36 **	60.89 +- 1.96 **	91.19 +- 3.33 **

+++ represents $P< 0.0005$ of significancy compared to control group
** represents $P< 0.0025$ of significancy compared to diabetic group