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Antidiabetic, Antilipidaemic and *Nephrocurative* Studies of the Aqueous Extracts of Ginger (*Zingiber officinale*) and Cinnamon (*Cinnamomum zeylanicum*) and their Combination in Experimental Rats

Alhassan, A. J.*¹, Mohammad, A.², Muhammad, I.U.³, Idi, A.¹, Nasir, A.⁴, Yaradua, A.I.⁴ and Ahmad, S.M.⁵
¹ Department of Biochemistry, Faculty of Basic Medical Sciences, Bayero University, P.M.B. 3011, Kano, Nigeria
¹, Department of Biochemistry, College of Medical Sciences, Abubakar Tafawa Balewa University, P.M.B 0248, Bauchi, Nigeria
², Department of Biochemistry, Faculty of Basic Medical Sciences, Yusuf Maitama Sule University, P.M.B. 3220, Kano, Nigeria
³, Department of Biochemistry, Faculty of Natural and Applied Sciences, Umaru Musa Yaradua University, Katsina, Nigeria
⁴, Department of Biochemistry, Faculty of Sciences, Kano State University of Science and Technology Wudil, Kano
⁵.

Author for Correspondence*: ajalhassan@yahoo.com / +234-703-825-7683

Abstract

Previous researches have reported that Cinnamon (*Cinnamomum zeylanicum*) bark and Ginger (*Zingiber officinale*) rhizome possess strong antihyperglycemic activity. This research was conducted to evaluate the Antidiabetic, hypolipidaemic and nephrocurative properties of aqueous extract of Cinnamon (*Cinnamomum zeylanicum*) bark; Ginger (*Zingiber officinale*) rhizome and a combination of the two on Alloxan- induced diabetic rats. Thirty- two rats were grouped into eight groups of four rats each. Group I served as normal control, Group II was administered 200mg/kg aqueous extract of ginger, group III was administered 150mg/kg aqueous extract of Cinnamon. Group IV served as diabetic control group, group V was diabetic and administered 200mg/kg aqueous extract of ginger, group VI was diabetic; administered 150mg/kg aqueous extract of Cinnamon, group VII was diabetic and administered with a combination of Ginger and Cinnamon aqueous extract in the ratio 4:3 respectively. Group VIII were diabetic treated with metformin 500mg/kg. The animals were administered with the extracts for a period of 14 days while monitoring the fasting blood glucose at 3-day intervals. The animals were then sacrificed after and blood collected was used for analysis of lipid profile and renal function indices. The fasting blood glucose level was found to be significantly ($p < 0.05$) decreased in all groups administered with the extracts, with highest hypoglycemic activity observed in group VII compared to the diabetic group. Hypolipidaemic activities were also seen in groups V, VI, and VII with significant ($p < 0.05$) decrease in these groups

treated with the aqueous extracts of ginger, cinnamon and a combination of both compared to the diabetic control. The electrolytes, urea and creatinine levels were found to be unaffected by the treatment in all the groups, a comparison between the treated groups and untreated one showed no significant difference ($p > 0.05$). The findings of this study suggest that Ginger rhizome, cinnamon bark and their combination may be used in the management of diabetes mellitus and its complications, although further human studies needs to be carried to confirm their potential benefits in diabetes management.

Keywords: Cinnamon, Diabetes, Ginger, Hypolipidemic and Nephrocurative.

Introduction

Diabetes mellitus is the most common metabolic and endocrine disorder worldwide. It is linked to disturbances in carbohydrates, fats and proteins metabolism and is especially important because the global prevalence of diabetes is projected to rise in coming years (Chen *et al.*, 2011). Diabetes mellitus is a serious global health problem. The disease affects both genders and all age groups, so there is a serious concern about its control and treatment. (Abdul Rahim, 2009). According to Sobnigwe *et al.* (2001), the prevalence of diabetes mellitus is on the increase in African communities due to ageing of the population and drastic lifestyle changes accompanying urbanization and westernization.

The goal of management of diabetes is to avoid or minimize chronic diabetic complications, as well as to avoid acute problems of

hyperglycemia (Itelima *et al.*, 2014). Over the last 30 years, Type 2 diabetes has changed from a relatively mild ailment associated with aging to one of a major cause of premature mortality and morbidity in most countries. The biggest populations of diabetics worldwide are to be found in India (51 million), China (43 million), and the USA (27 million). Nevertheless, there is a worsening global epidemic of diabetes, with almost every country showing a rise in prevalence of diabetes (CDCP, 2011). Several types of drugs such as sulfonylurea, thiazolidinedione, Incretin, and Dipeptidyl-peptidase 4 inhibitors have been prescribed for managing hyperglycemia in Type 2 diabetic patients. These drugs work by reducing insulin resistance and improving insulin secretion capacity (Kahn *et al.*, 2014). However, the adverse side effects and high cost of purchase of these drugs still remains a major problem to people living with diabetes. Hence there is need to explore natural products that are speculated to have anti-diabetic activities, so as to establish a scientific basis for recommending these natural products. This work focused on the use of Ginger and Cinnamon which is widely used spices as potential hypoglycaemic agents. This study could add knowledge about the effects of ginger and cinnamon on diabetes that might be useful in encouraging its possible use in management of diabetes mellitus.

Cinnamon is mainly known as a spice in most western countries, but it has an old history of been used as herbal medicine in Asia. It is obtained from the inner bark of trees known as *Cinnamomum zeylanicum*, a tropical evergreen plant (Ranasinghe *et al.*, 2013). Animal and *in vitro* studies carried out since the early 1990's have indicated that cinnamon may mimic insulin effects, hence improving glucose utilization (Qin *et al.*, 2004). Hwa *et al.* (2011) reported cinnamon as one of the spices used in the early treatment of chronic bronchitis. Furthermore, cinnamon is used in other traditional practices for the treatment of impotence, frigidity, dyspnea, eye inflammation, rheumatism, vaginitis as well as wounds and toothaches (Khan *et al.*, 2003).

Ginger (*Zingiber officinale*) is one of the most widely consumed spices used for the flavoring of food worldwide (Li *et al.*, 2012). It is used for cooking and treating a host of ailments throughout Asia, especially in India and China. It can be consumed as a fresh or dried root and is often prepared in teas, soft drinks, and breads (Khulood, 2014).

Materials and Methods

Study animals

Male and female albino rats weighing between 100 - 200 g were purchased from animal house of Biological Science Department; Bayero University, Kano. The animals were housed in well-ventilated cages in the animal house of Biological Science Department of Bayero University, Kano. The rats were allowed to acclimatize for one week prior to the experiment and had free access to food and clean water.

Plant material

Fresh ginger rhizome and dried cinnamon bark were bought from Yan Kaba market. They were respectively identified by a Botanist at Biological Science Department of Bayero University, Kano with accession number BUKHAN0368 and BUKHAN369. The fresh ginger rhizomes were ground and kept at room temperature in a sealed labeled plastic container, also the cinnamon bark was pulverized to powder and kept at room temperature in a sealed labeled container. Both plant materials were then used immediately for extraction.

Extraction of plants materials

Five hundred grams (500g) each of ginger and cinnamon were ground and pulverized respectively, one litre of distilled water was used to soak each of them separately, it was stirred properly and left to stand for 24 hours. After 24 hours the mixtures were then filtered separately using fine cheese cloth of 44×36 threads per inch twice. The extract was then stored at 25°C in a container labeled aqueous ginger extract. The concentration of the clear debris free filtrate was determined using Total Dissolved Solute method (TDS). Four petri-dishes were weighed separately and the initial weight noted, 10ml of both ginger and cinnamon extracts were taken and placed into two petri-dishes each; the petri-

dishes were properly labeled as ginger and cinnamon. The petri dishes were then placed in an oven at 80°C for 1 hour to completely dry, they were then brought out and cooled. The final weight of both petri-dishes was taken. The difference in the weight was used to determine the amount of the extracts in 10ml of distilled water. On this basis the concentration of the ginger extract was found to be 19mg/ml while that of cinnamon was 20.5mg/ml.

Experimental design

A total of 32 albino rats placed in eight groups of 4 rats each were used for the study.

Group I: Normal Control

Group II: Diabetes was not induced, ginger extract given at a dose of 200mg/kg

Group III: Diabetes was not induced, cinnamon extract given at a dose of 150mg/kg

Group IV: Diabetic control

Group V: Diabetic administered with aqueous Ginger extract (200mg/kg)

Group VI: Diabetic administered with aqueous cinnamon extract (150mg/kg)

Group VII: Diabetic administered with Ginger (200mg/kg) and cinnamon (150mg/kg)

Group VIII: Diabetic administered with metformin (500mg/kg)

The animals were administered with the extracts for 2 weeks while monitoring the fasting blood glucose level at 3-days interval using Accu-Check glucometer. The treatment was withdrawn for a period of 1 week during which the fasting blood glucose was still monitored at 3-days interval.

Induction of Diabetes mellitus

Alloxan Hydrate (1.5g) was dissolved in 10ml of

distilled water to give a concentration of 150mg/ml. Diabetes mellitus was induced in the rats by a single intra-peritoneal injection of alloxan at a dose of 150mg/kg body weight after 12 hours of fasting. After 48 hours, fasting blood glucose levels of the rats was measured using glucometer, and rats with fasting blood glucose levels of 11.1mmol/L or above are considered diabetic. The volume of the solution given to each experimental albino rat was determined by the following relationship (Muhammad *et al.*, 2016).

$$Volume(ml) = \frac{Dose(mg/kg) \times weight\ of\ rat\ (kg)}{Concentration\ of\ extract(mg/ml)}$$

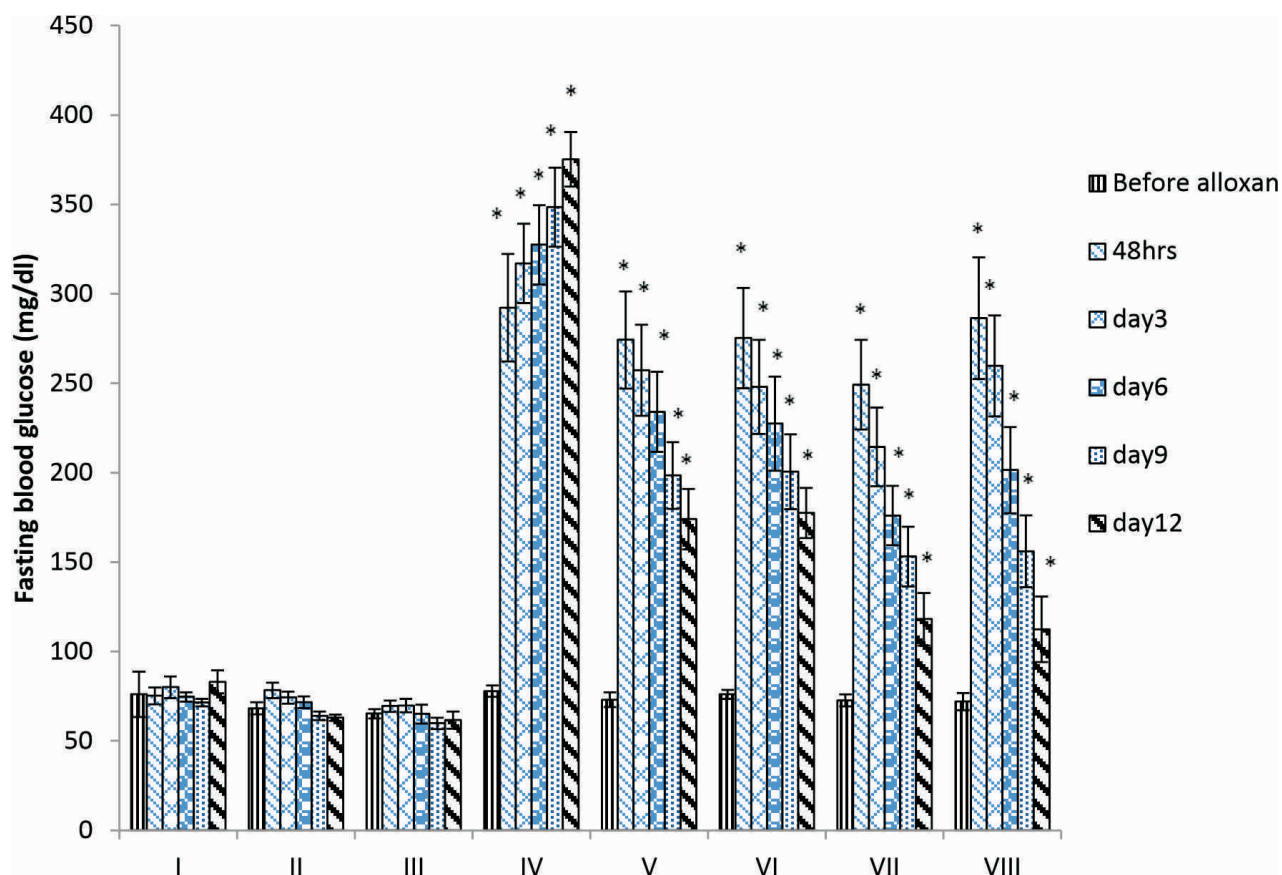
Statistical analysis

Results were expressed as mean \pm standard deviation. Statistical differences between groups were analyzed by one-way analysis of variance (ANOVA) followed by Tukey's test after investigating the data for normality using Shapiro-Wilk test and for variances homogeneity to be sure that the data are normally distributed and variances would be homogenous using GraphPad Instat3 Software version 3.05. A p-value < 0.05 was considered significant.

Results and Discussion

Results

Figure 1 shows the fasting blood glucose of diabetic rats administered with the extracts. There was a significant ($p < 0.01$) elevation in fasting blood glucose of diabetic control compared to the normal control and the non-diabetic groups administered with ginger and cinnamon extracts. A significant ($p < 0.01$) fall in their fasting blood glucose was observed in all the test groups administered with the extracts compared to the diabetic control group.



Key: Bars with * are significantly different from the control at ($p < 0.05$). Values are expressed as Mean \pm SEM.

Figure 1: Fasting Blood glucose in diabetic rats orally administered with aqueous extract of Ginger rhizome, Cinnamon bark and a combination of both Ginger and Cinnamon extracts.

Table 1 shows the effect of administration of ginger, cinnamon and their combination on lipid profile to alloxan induced diabetic rats with. There was a significant ($p < 0.05$) increase in serum total cholesterol, LDL-cholesterol and triglyceride in diabetic control group compared to normal control. A significant ($p < 0.05$) decrease in serum total cholesterol, LDL-cholesterol and triglyceride was observed in extracts administered groups compared to diabetic control with group administered with combination of ginger, cinnamon having the highest decrease.

Table 1: Effect of aqueous extract of cinnamon, ginger and a combination of both on lipid profile of alloxan induced diabetic rats.

Groups	T. CHOL (mmol/L)	LDL (mmol/L)	HDL (mmol/L)	TRIG (mmol/L)
G I	29.82±0.04 ^a	20.26±0.52 ^a	8.72±0.11	6.23±1.77 ^a
G II	34.30±2.90	26.35±2.43	7.99±0.53	5.32±1.81
G III	33.73±1.29	24.50±1.52	7.53±0.13	8.48±0.48
G IV	60.04±2.39 ^{a,b,c,d,e}	51.09±2.49 ^{a,b,c,d,e}	6.12±0.12	17.19±1.09 ^{a,b,c,d,e}
G V	39.33±0.40 ^b	29.21±0.41 ^b	7.90±0.18	11.1±0.86 ^b
G VI	38.14±0.63 ^c	28.19±0.98 ^c	8.14±0.12	8.99±1.15 ^c
G VII	31.06±0.17 ^d	20.08±0.98 ^d	8.63±0.39	9.39±0.97 ^d
G VIII	34.17±2.55 ^c	24.96±2.77 ^c	8.15±0.09	5.25±0.61 ^c

Key: Results are presented as Mean ± SEM (n=4). Value with the same superscripts in a column are significantly different compared to each other (p<0.05).

Table 2 shows the effect of administration of diabetic rats with ginger, cinnamon and their combination on kidney function parameters. No significant (p>0.05) difference in mean sodium, potassium, chloride, urea and creatinine were observed between diabetic control group and extract administered groups.

Table 2: Effect of aqueous extract of Ginger, Cinnamon, and a combination of both on Electrolytes, Urea and Creatinine in alloxan induced diabetic rats.

Groups	Na ⁺ (mEq/L)	K ⁺ (mEq/L)	Cl ⁻ (mEq/L)	Urea(mmol/L)	Cr(mmol/L)
G I	139.75±1.93	5.07±0.27	97.75±2.78	46.79±3.09	0.35±0.13
G II	141.25±1.75	4.62±0.39	100.75±1.03	50.85±0.48	0.45±0.11
G III	139.50±1.71	4.55±0.38	99.75±1.38	55.96±8.46	0.35±0.03
G VI	142.75±2.39	4.32±0.34	98.50±1.55	38.59±0.05	0.43±0.08
G V	141.50±4.69	4.80±0.29	96.00±2.16	57.05±1.52	0.52±0.09
G VI	143.00±1.78	5.30±0.33	94.00±4.50	57.14±10.17	0.42±0.05
G VII	141.25±0.89	5.42±0.29	93.75±2.65	53.15±0.18	0.60±0.04

Key: Values are expressed as mean ±SEM, n=4



Discussion

Diabetic dyslipidaemia as a metabolic abnormality occurs in diabetes mellitus frequently and is associated with high triglycerides, low HDL cholesterol and high LDL cholesterol level (Mooradian, 2009). This is consistent with this study, where triglyceride and LDL cholesterol were significantly increased, and HDL-cholesterol significantly decreased, after induction of diabetes in rats using alloxan. He *et al.* (2015) also reported high triglyceride, very low HDL cholesterol and high LDL cholesterol in Streptozotocin induced diabetic rats.

Administration of diabetic rats with the extract lead to a fall in level of LDL-cholesterol, total cholesterol and triglyceride. This observation is consistent with previous finding by Bhandari *et al.* (2005) which indicated that ethanol extract of ginger produced significant decrease in serum total cholesterol, LDL- cholesterol and triglycerides levels and increased HDL-cholesterol level in diabetic rats, and the extract protected the tissues from lipid peroxidation.

Flavonoids are some of the phytochemical constituents reported in both ginger rhizome and cinnamon bark. These flavonoids were reported to protect the cells through attenuation of lipid peroxidation and decreased production of free radicals thereby offering protection against oxidative stress by scavenging of free radicals. (Nwanjo, 2007). Hayashi *et al.* (2002) showed that the presence of polyphenols in plant extracts have numerous protective health benefits which include lowering of blood lipids, also methoxylated flavonoids have the ability to suppress Apo B containing lipoprotein secretion, this in turn helps in modulating liver lipid metabolism. Apo lipoprotein B is the primary transport protein for LDL, and high levels of this apo protein are found to be related to heart disease.

The exact mechanism of action of the extracts was yet to be elucidated. However, Srinivasan and Sambaiah (1991) reported that hypolipidaemic activities of ginger may be through stimulating the conversion of cholesterol to bile acids, an important pathway of

elimination of cholesterol from the body. Han *et al.* (2005) found that *Z. officinale* increased the faecal excretion of cholesterol, suggesting that ginger may block absorption of cholesterol in the gut. Moreover, previous reports (Ramudu *et al.*, 2011; Nammi *et al.*, 2009; Afshari *et al.*, 2007) mentioned that the hypocholesterolaemic effect of ginger may be attributed to inhibition of cellular cholesterol synthesis which results in augmenting the LDL receptor activity, leading to the elimination of LDL from plasma thus modifying lipoprotein metabolism.

Electrolytes play an important role in many body processes, such as controlling fluid levels, acid-base balance, nerve conduction, blood clotting and muscle contraction. Electrolyte imbalance resulting from kidney failure, dehydration, fever, and vomiting has been suggested as one of the contributing factors toward complications observed in diabetes and other endocrine disorders. (Husain *et al.*, 2009). From this study it can be seen that there is no significant difference seen in the levels of the sodium, potassium and chloride between groups. This shows that neither diabetes mellitus nor the administration of the ginger and cinnamon extracts caused any significant alteration on the reabsorption capacity of the kidneys.

The established markers of Glomerular Filtration Rate (GFR) are plasma urea and creatinine, however plasma creatinine is a more sensitive index of kidney function compared to plasma urea. This is because creatinine fulfills most of the requirement for a perfect filtration marker (Perrone *et al.*, 1992). It was observed from this study that the levels of urea and creatinine were found to be unaffected by neither diabetes nor the treatment. This finding is however at variance with the study carried out by Idonije *et al.* (2011). This may be due to the difference in the specie or duration of the study, because our study was carried out over a short period of time while that of the study carried out by Idonije *et al.* (2011) was on human subjects who might have had the disease for a very long period of time.

Conclusion

The study shows that aqueous extract of Ginger



rhizome and Cinnamon bark possesses anti-hyperlipidaemic properties against diabetes induced hyperlipidaemia. The highest hypoglycaemic activity was seen in the group administered with a combination of ginger and cinnamon. This finding supports the traditional claim of the usage of ginger and cinnamon in the management of diabetes mellitus.

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