The International Journal of Biotechnology
2018 Vol. 7, No. 1, pp. 25-30
ISSN(e): 2306-6148
ISSN(p): 2306-9864
DOI: 10.18488/journal.57.2018.71.25.30

ANTIHYPERGLYCEMIC EFFECTS OF AQUEOUS EXTRACTS OF *Zingiber Officinale, Cinnamonum Zeylanicum* AND THEIR COMBINATION IN EXPERIMENTAL RATS

Muhammad Ibrahim Usman[1+]
Adamu Jibrin Alhassan[2]
Hauwa Sa'ad[3]

[1]*Department of Biochemistry, Faculty of Basic Medical Sciences, Yusuf Maitama Sule University, P.M.B. 3220, Kano, Nigeria*
Email: Ibrahimmuhdusman@gmail.com
[2,3]*Department of Biochemistry, Faculty of Basic Medical Sciences, Bayero University, P.M.B. 3011, Kano, Nigeria*
[2]*Email: ibrahimmuhd@yahoo.com*
[3]*Email: ajalhassan@yahoo.com*

(+ Corresponding author)

Article History
Received: 17 July 2018
Revised: 24 August 2018
Accepted: 27 September 2018
Published: 7 November 2018

Keywords
Anti-hyperglycemic
Ginger
Cinnamon
Metformin
Diabetes mellitus and alloxan.

ABSTRACT

This research was conducted to evaluate antihyperglycemic property of aqueous extract of Cinnamon (*Cinnamonum 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 were normal rats and administered with 200mg/kg body weight of ginger aqueous extract, group III were normal rats and administered with 150mg/kg body weight of Cinnamon aqueous extract. Group IV served as diabetic control group, group V were diabetic and administered with 200mg/kg body weight of ginger extract, group VI were diabetic and administered with 150mg/kg body weight of Cinnamon extract. Group VII were diabetic and administered with a combination of Ginger and Cinnamon extract in a ratio of 4:3 respectively. Group VIII were diabetic and administered with metformin at a dose of 500mg/kg body weight. The animals were administered with the extracts for 14 days while monitoring the fasting blood glucose at a 3-day intervals. The fasting blood glucose level was found to be significantly ($p<0.05$) decreased in all groups administered with the extracts, with the highest hypoglycemic activity seen in group VII administered with a combination of the two extract compared to the diabetic control group. The findings of this study suggests that Ginger rhizome, cinnamon bark and their combination may be used in the management of diabetes mellitus, although further studies need to be carried to confirm their potential benefits in diabetes management.

Contribution/Originality: This study contributes in the existing literature by providing basic information for other researchers regarding the antihyperglycemic potential of *Zingiber officinale* rhizome and *Cinnamonum zeylanicum* bark so that they may be considered as alternative medicines in management of hyperglycemia.

1. 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). WHO calculates that over 347 million people around the world suffer from diabetes, which this number will double by 2030, and that 80% of diabetics live in developing countries (WHO, 2012). Diabetes mellitus is a chronic disorder of glucose metabolism resulting from dysfunction of pancreatic beta cells and/or insulin resistance (Abdul, 2009).

Diabetes mellitus is characterized by hyperglycemia due to insufficiency of secretion or action of endogenous insulin. Symptoms include polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger). Plant remedies have been used for centuries for the management of diabetes mellitus but only a few of these plants have been scientifically evaluated (Gwarzo *et al*., 2010). Cinnamon is mainly known as a spice in most western countries, but it has an old history of been used as a 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 *invitro* studies carried out since the early 1990's have indicated that cinnamon may mimic insulin effects, hence improving glucose utilization (Qin *et al*., 2004; Verspohl *et al*., 2005). 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).

2. MATERIALS AND METHODS

2.1. 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.

2.2. 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 was 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.

2.3. Extraction of Plants Materials

Five hundred grams (500g) each of ginger and cinnamon were ground and pulverized respectively, 1litre 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.

2.4. Experimental Design

A total of 32 albino rats placed in eight groups of four 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 Accucheck glucometer. The treatment was withdrawn for a period of 1 week during which the fasting blood glucose was still monitored at 3 day interval.

2.5. Induction of Diabetes Mellitus

1.5g of Alloxan Hydrate was dissolved in 10ml of distilled water and 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 hour 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).

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

2.6. Statistical Analysis

Results were expressed as mean ± 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 Differences of $P < 0.05$ were considered to be significant.

3. RESULTS

Figure 1 showed the fasting blood glucose of diabetic rats administered with the extracts. There was 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 tests groups administered with the extracts compared to the diabetic control group.

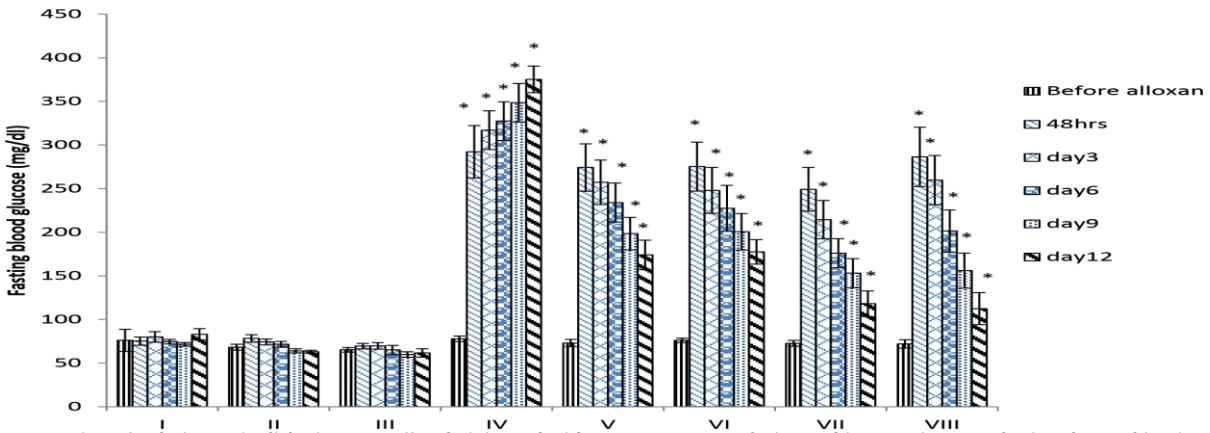

Fig-1. Fasting Blood glucose in diabetic rats orally administered with aqueous extract of Ginger rhizome, Cinnamon bark and a combination of both Ginger and Cinnamon extracts. Bars with * are significantly different from the control at ($p<0.05$). Values are expressed as Mean ±SEM.

Figure 2 summarized the results for the effect of withdrawal of aqueous extract ginger; cinnamon and their combination on fasting blood glucose of alloxan induced diabetic rats. There is significant ($p<0.05$) difference between diabetic control group compared to diabetic groups treated with metformin, ginger extract, cinnamon extract and their combination. However there is no significant difference between the diabetic group treated with metformin and that treated with a combination of ginger and cinnamon extracts.

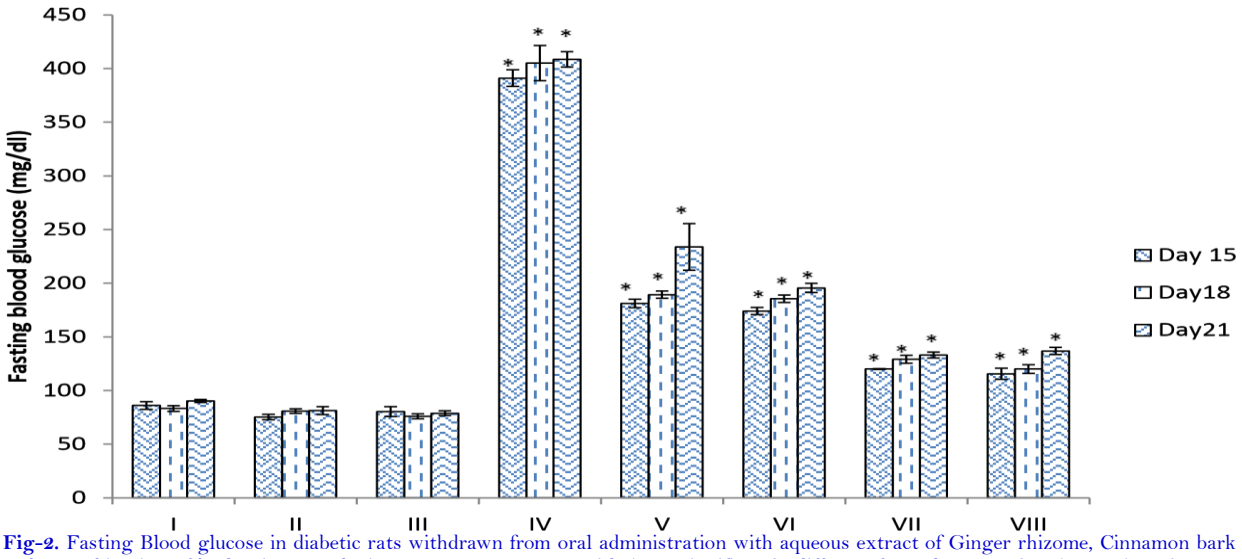

Fig-2. Fasting Blood glucose in diabetic rats withdrawn from oral administration with aqueous extract of Ginger rhizome, Cinnamon bark and a combination of both Ginger and Cinnamon extracts. Bars with * are significantly different from the control at ($p<0.05$). Values are expressed as Mean ±SEM

4. DISCUSSION

The observed blood glucose lowering effect of the ginger rhizome may be due to the presence of phenols in the ginger. These phenols are found in the pungent components of ginger rhizome such as gingerols (Ovesen, 2012). Shagoals are phenolic compounds found in ginger which is dried or semi-dried, they are produced from gingerols upon drying, and this is because gingerols are heat labile. Khulood (2014) showed that a compound in ginger 6-gingerol showed antidiabetic properties. The 6-gingerol is also found to reduce fasting blood sugar significantly and improve glucose tolerance when administered at a dose of 100mg/kg for 12 days (Singh *et al.*, 2009). Two important enzymes associated with carbohydrates metabolism in diabetes are α-amylase and α-glucosidase, ginger extract show very high α-glucosidase and α- amylase inhibitory activities, the action of ginger rhizome extract against these two enzymes found to be correlated with the phenolic contents of gingerol and shogaol in these extracts (Rani *et al.*, 2011). In *vivo* studies on rats showed that after long-term (8 weeks) feeding with ginger rhizome, the activities of pancreatic lipase, amylase, trypsin, and chymotrypsin were significantly increased (Platel and Srinivasan, 2000).

Diabetic group treated with cinnamon bark extract showed a significant reduction in fasting blood sugar compared to the diabetic control. This result is in agreement with studies carried out by Lee *et al.* (2013) which showed that administration of cinnamon at 20mg/kg was found to help glycemic control and improve insulin secretion in diabetic patients. Aqueous extract of cinnamon was shown to decrease alanine absorption hence reducing the blood sugar level because alanine plays a vital role in gluconeogenesis; decrease in alanine suggests alterations in substrate availability such as utilization of available glucose in the blood (Kreydiyyeh *et al.*, 2000). This is one of the possible mechanisms through which cinnamon decreases blood sugar. Cinnamon was also showed to contain flavonoids and saponins as some of its phytochemical constituents. Flavonoids in the extract may have stimulating effect on insulin secretion from the remaining β-cells not completely destroyed by alloxan. However the gradual increase in glucose concentration post withdrawal of treatment with cinnamon suggests that the effect of the extract may not be curative.

The diabetic group administered with a combination of ginger (200mg/kg) and cinnamon (150mg/kg) showed the highest activity in decreasing blood glucose compared to either ginger or cinnamon extract alone. This may be attributed to the presence of flavonoids in both cinnamon and ginger that may inhibit glucose-6-phosphatase activity in the liver thereby suppressing gluconeogenesis and glycogenolysis and consequently reduce hyperglycemia (Chen *et al*., 1998). The hypoglycemic effect of the combination of these two plants is as significant as that of metformin treated group.

Different mechanisms of action of anti-hyperglycemic plants have been proposed such as inhibition of intestinal glucose absorption (Youn *et al*., 2004) correction of insulin resistance (Hu *et al*., 2003) inhibition of hepatic glucose production (Eddouks *et al*., 2003) and potentiation of insulin effect either by increasing the pancreatic secretion of insulin from the β cells (Pari and Amarnath, 2004).

5. CONCLUSION

The study concludes that aqueous extract of Ginger rhizome and Cinnamon bark possess anti-hyperglycemic properties in rats. The highest activity was seen in the group administered with a combination of ginger and cinnamon suggesting that this combination may be very effective in management of diabetes mellitus.

Funding: This study received no specific financial support.
Competing Interests: The authors declare that they have no competing interests.
Contributors/Acknowledgement: All authors contributed equally to the conception and design of the study.

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