AMERICAN JOURNAL OF PHARMTECH RESEARCH
Journal home page: http://www.ajptr.com/

The Effects of Aqueous Extract of Ginger (*Zingiber Officinale*) On Blood Glucose And Lipid Profile In Cholesterol-Fed Male Diabetic Albino Wistar Rats

Maduka Stephen Ozoemena[1], Ugwu Chidiebere Emmanuel[2*],Okonkwo Chukwudi Onyeka[1], Dimkpa Uchechukwu[1], Ezeh Stanley C[1].
1.Department of Human Physiology, Faculty of Basic Medical Sciences Nnamdi Azikiwe University, Nnewi Campus.
2. Department of Human Biochemistry, Faculty of Basic Medical Sciences, Nnamdi Azikiwe University, Nnewi Campus.

ABSTRACT

Diabetic mellitus goes with metabolic disorders involving hyperglycaemia and lipid disorders. The study investigated the activity of aqueous ginger extract on the glucose level and lipid profile of cholesterol-fed diabetic rats. The rats were randomly distributed into four groups of 5 rats per group. Group A (control) were placed on normal rat feed. Diabetes was induced in groups B, C, and D by intraperitoneal administration of one dose of alloxan monohydrate (150mg/kg/bwt) and fed diet mixed with 1% cholesterol. The rats in groups C and D were orally administered with 250 and 500mg/kg/bwt of ginger extract respectively for 14 days. Biochemical parameters were analysed by standard methods. A significant decrease ($P<0.05$) in the blood glucose concentration in the ginger administered groups (C and D) was observed compared to diabetic cholesterol-fed rats (group B). After 14 days of aqueous ginger extract administration (250 and 500mg/kg/bwt), the serum total cholesterol level reduced in the test groups (C and D) relative to the test control group (group B) ($P>0.05$). There was a statistical increase in the serum triacylglycerol level in group B compared to group A ($P<0.05$) but the extract administration at 500mg/kg/bwt significantly led to a reduction of triacylglycerol compared to group B ($P<0.05$). It can be concluded that the extract possess hypoglycaemic and hypolipidaemic properties and confirms its use in the traditional medicine. This result should be taken with caution as the extract did not restore the serum levels of these parameters to the same levels as the non-diabetic control groups.

Key words: alloxan, Ginger, glucose, lipid profile.

*Corresponding Author Email: ugwuchidiksu@yahoo.com
Received 11 April 2016, Accepted 17 April 2016

Please cite this article as: Maduka SO *et al*., The Effects of Aqueous Extract of Ginger (Zingiber Officinale) On Blood Glucose And Lipid Profile In Cholesterol-Fed Male Diabetic Albino Wistar Rats. American Journal of PharmTech Research 2016.

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia emanating from defects in insulin secretion or action that leads to serum lipoprotein disorders usually accompanied with increased morbidity and mortality [1,2]. Ginger (*Zingiber officinal*) belongs to the *Zingiberaceae* family and has been used in traditional medicine for ages. The extract of ginger has been demonstrated to exhibit a number of biological functions[3] Therapies with traditional medicine are taught to be cheaper than synthetic chemical agents [4,5] .

The hypolipidemic effect of ginger extract in vanaspatic rats has been reported [5]. The effect of ginger extract on the levels of blood glucose, lipid profile and kidney functions in alloxan-induced diabetic rats was studied previously[6]. Ginger has been reported to act as a hypolipidemic agent in cholesterol-fed rabbits and to significantly lower serum total cholesterol and triacylglycerols concentrations compared to pathogenic diabetic rats [7] . The report of Afshari *et al.* [8] demonstrates that ginger causes a decrease in lipid peroxidation, an increase of plasma antioxidant capacity and a reduction in renal nephropathy.

It has been suggested that the hypocholesterolemic effects of ginger stems from the inhibition of cellular cholesterol synthesis. Attenuation of cholesterol synthesis results in augmentation of low density lipoprotein cholesterol (LDL-c) from plasma [8]. As part of the on-going efforts to authenticate the folkloric use of ginger in the traditional medicine, the study investigated the activity of aqueous ginger extract on the glucose level and lipid profile of cholesterol-fed diabetic rats.

MATERIALS AND METHOD

Animals and treatment

A total of twenty male laboratory wistar rats weighing between 170-210g were used as experimental animals. They were 7 weeks old. They were kept in animal cages for two weeks to acclimatize in the animal house of the Faculty of Basic Medical Sciences Nnamdi Azikiwe University Nnewi Campus, Nigeria. They were allowed free access to water and food *ad libitum*. The protocol for the experiment was approved by the Faculty of Basic Medical Sciences Experimental Ethics Committee in line with the guideline of the National Institute of Health (NIH). The experimental animals were randomly distributed into four groups of five rats each as shown in Table 1. The rats in group A were fed standard rat diet only (Vital Feed, Nigeria), and served as the control while groups B, C, and D served as test groups. The rats in groups B, C, and D were fed on diets mixed with 1% cholesterol while groups C and D received 250 and

500mg/kg/bwt of extract in addition. To induce diabetes, the rats in groups B, C, and D were fasted for 16 hours and their glucose concentration checked using a glucometer. Diabetes was induced by intraperitoneal injection of alloxan monohydrate (150mg/kg/bwt). After injecting the alloxan,, the rats were given 10g of glucose solution after 6 hours to prevent hypoglycaemic shock. The blood glucose concentration was determined after 72 hours and the rats whose blood glucose concentration was ≥ 200 mg/dl were used for the study. At the end of the experiment all the rats were fasted overnight and blood samples collected.

Table 1: Animals and treatment

Group	Treatment
A	Normal feed (control).
B	1% cholesterol feed + alloxan
C	1% cholesterol feed + alloxan + 250mg/kg/bwt ginger extract.
D	1% cholesterol feed + alloxan + 500mg/kg/bwt ginger extract.

Preparation of extracts.

Fresh bulbs of *Zingiber officinale* were purchased from a local market in Nnewi, Nigeria. The botanical identification and authentication were confirmed at the Department of Botany, Nnamdi Azikiwe University. The seeds were carefully dressed, washed and dried at room temperature. The aqueous extract was prepared as described by Mahesar *et al*. [9] with slight modification. 200g of *Zingiber officinale* sample was blended in a mixing machine with 1 litre of warm distilled water and allowed to stand for 48 hours. The resultant slurry was squeezed in a porcelain cloth and filtered with a Watman number 1 filter paper. The filtrate was concentrated in an oven with extractor fan at 50 ^{o} C. The crude extract was stored in a refrigerator for use.

Collection of samples.

Overnight prior to treatment, the animals were starved of food. Blood samples were collected from the ocular median-cantus vein of the rats with the aid of capillary tubes, transferred to test tubes, allowed to clot and subsequently centrifuged to obtain the serum component used for lipid analysis.

Determination of biochemical parameters.

The blood glucose concentration was determined by the glucose monitoring meter and test strips (Life-Scan Inc- USA) as described by Mark and Dawson [10]. The lipid profiles were determined using kits manufactured by TECO diagnostics Lakeview, Aneheim, CA, USA. Serum total cholesterol (TC) was determined by the method of Alain *et al.*[11], while triacylglycerol was determined as described by Burstein *et al*.[12]. The high density lipoprotein-cholesterol (HDL) fraction was precipitated using phosphotungstic acid and magnesium chloride. After

centrifugation, the supernatant contained the HDL fraction which was assayed for cholesterol[13]. The low density lipoprotein cholesterol (LDL-C) was estimated using the method of Fridewald *et al.*[14] .

Statistical analysis

All results are expressed as mean ± SD. The data were analysed by one-way analysis of variance (ANOVA) followed by Fischers LSD post- hoc test using SPSS version 20 software (SPSS Inc. Chicago, IL, USA). Statistical significance was considered at $P<0.05$.

RESULTS AND DISCUSSION

The results of the biochemical parameters assayed are represented in Table 2. The results show that there was a significant increase on the mean serum glucose values of the groups administered alloxan compared to the control ($P<0.05$). A significant decrease ($P<0.05$) in the blood glucose concentration in the ginger administered groups (C and D) was observed compared to diabetic cholesterol-fed rats (group B). The results show that there was an increased concentrations of the serum cholesterol in the diabetic groups administered cholesterol fed diet compared to the control group ($P<0.05$). Our results show that after 14 days of aqueous ginger extract administration (250 and 500mg/kg/bwt), the serum total cholesterol concentration reduced in the test groups (C and D) relative to the test control group (group B) which was not significant ($P>0.05$). In the study, there was an increase in the serum LDL-cholesterol concentration. The results show that there was a significant decrease in the serum LDL-cholesterol in the group administered 500mg/kg/bwt of extract relative to group B while the group administered 250mg/kg/bwt of extract did not significantly reduce the LDL-cholesterol compared to group B. In terms of the effects of the ginger extract on serum HDL-cholesterol concentration, the results show that at 500mg/kg/bwt administration the extract significantly increased the serum HDL-cholesterol concentration compared to groups A,B, and C. There was a statistical increase in the serum triacylglycerol concentration in group B compared to group A ($P<0.05$) but the extract administration at 500mg/kg/bwt significantly led to a reduction of triacylglycerol compared to group B ($P<0.05$).

Table 2: Effects of aqueous extract of Ginger (*Zingiber officinale*) on blood glucose and lipid profile in cholesterol-fed male diabetic Albino Wistar rats.

Group	Glucose (mg/dl)	Total cholesterol (mg/dl)	Low density lipoprotein (mg/dl)	High density lipoprotein (mg/dl)	Triacylglycero (mg/dl)
A	86.15 ±5.43^{c}	103.54± 8.59^{a}	48.24± 4.99	48.23 ±3.48^{b}	75.03 ±5.53^{a}
B	235.40 ±6.39^{a}	143.19 ±6.55^{b}	63.99± 4.03^{b}	56.58 ±3.25^{b}	102.27± 4.90^{b}
C	192.01± 5.67^{b}	136.36 ±4.89^{b}	58.57 ±4.54	54.57± 2.93^{b}	93.17 ±5.25
D	157.24± 6.47^{b}	126.85 ±6.12^{b}	51.56 ±1.76^{c}	63.79± 3.42^{c}	76.55± 4.19^{a}

Results are mean ± SD. Values with different superscript in a column are statistically significant ($p<0.05$).

DISCUSSION

In the study, the anti-hypoglycaemic properties of aqueous ginger extract on alloxan induced diabetic rat fed cholesterol rich diet was investigated. There was a dose dependent hypoglycaemic effect of the extract which was more pronounced at 500mg/kg/bwt. This observed hypoglycaemic effect was in line with the results of previous studies [15-17]. It should be noted that the observed decrease in the serum glucose concentration in the ginger extract administered groups could not drop to the normal serum levels at the dosages used in the study. A similar trend was reported on the effects of ginger juice in streptozotocin-induced diabetic rats[15]. From the results obtained it can be inferred that the treatment with ginger extract helped to alleviate the nephropathy resulting from alloxan-induced diabetes. Gingerol has been reported to be the major bioactive constituent in ginger taught to confer its anti-hypoglycaemic property [15,18-20]. The report of Al-Noory *et al.* [2] showed that the administration of ginger to diabetic rats reduced plasma glucose levels compared to the diabetic control group but could not reduce it the normal group level. Another report indicated that both pre-treatment and post-treatment with ginger extract reduced plasma glucose levels in diabetic rats [6] but also did not return the glucose levels to the non-diabetic control group levels. There are suggestions that some essential minerals in ginger (Zn, Ca, K, Mn and Cr) can modulate insulin release in animal models and man [21].

The abnormalities of blood lipid profile represented by the rise in triacylglycerol and total cholesterol in the cholesterol-fed diabetic rats were seen in the study. This could be as a result of both endogenous changes of lipid metabolism caused by diabetes and feeding of the rats in cholesterol diet. Also, the results indicated a significant rise ($P<0.05$) in the serum HDL-cholesterol values in the group treated with 500mg/kg/bwt of extract relative to the control and test control group (group B) but not with 250mg/kg/bwt extract ($P>0.05$). In the report of Elshater *et al.* [21], the post-treatment of diabetic rats with ginger extract led to a decrease in the plasma total cholesterol, triacylglycerols, and LDL-c in line with the results from this study. Also, the report of Al-Noory *et al.* [2] showed that treatment with ginger led to a significant decrease in LDL-c and increase in HDL-c compared to the control diabetic groups. The report of Paul *et al.* [5] pointed out that the simultaneous administration of ginger extract caused a significant decrease in serum total cholesterol, LDL-C, and an increase in HDL-c indicating a beneficial modulatory effect on cholesterol metabolism and turnover. These reports are in-line with other findings [4,7,22-24]..

The ability of ginger to lower serum cholesterol in rats and mice can be attributed to a compound in ginger ZT (E-8b,7-epoxylabd-21-ene-15,16-dial) that inhibits HMG-Co-A reductase [25]. There was also another study that reported that oral administration of ginger extract to rabbits reduced cholesterol absorption from the gastrointestinal tract [26]. The presence of niacin in ginger has also been linked to its hypocholesterolenemic property by the reduction in cellular biosynthesis [27] . The reduction in the serum triacylglycerol following treatment with ginger in the diabetic rats as seen in this study may be that ginger extract has a stimulating effect on insulin [28]. Many reports have demonstrated that ginger has antioxidant effects that are anti-atherogenic and hypocholesterolemic[29,30] . Afshari *et al.* [8] demonstrated that ginger caused decreased lipid peroxidation, increased plasma antioxidant capacity and a reduction in renal nephropathy in diabetic rats.

CONCLUSION

Ginger can be said to possess hypoglycaemic and hypolipidaemic properties and confirms its use in the traditional medicine. This result should be taken with caution as the extract did not restore the serum levels of these parameters to the same levels as the non-diabetic control groups.

REFRENCES

1. Zhang J, Huang Y, Hou T, Wang Y. Hypoglycemic effect of *Artemisia sphaerocephala Krasch* seed polysaccharide in alloxan-induced diabetic rats. Swiss Med Wkly 2006; 136: 529-532.
2. Al-Noory AS, Abdul-Nasser A, Hymoor S. Antihyperlipidemic effects of ginger extracts in alloxan-induced diabetes and propylthiouracil-induced hypothyroidism in (rats). Pharmacogn Res 2013; 5(3):157-161.
3. Alizadeh-Navaei R, Roozbeh F, Saravi M, Pouramir M, Jalali F, Moghadamnia AA. Investigation of the effect of ginger on lipid levels. A double blind controlled clinical trial. Saudi Med J 2008; 29:1280-1284.
4. Harini M, Astrin OP. Blood cholesterol levels of hypercholesterolemic rat (*Rattus norvegicus*) after VCO treatment. Nusantara Biosci 2009; 1:53-58.
5. Paul P, Islam MK, Mustari A, Khan MZI. Hypolipidemic effect of ginger extract in vanaspati fed rats. Bangl J Vet Med 2012; 10(1and2):93-96.
6. Elshater AE, Muhammad MAS, Mahrous MAM. Effect of ginger extracts consumption on levels of blood glucose, lipid profile and kidney functions in alloxane induced-diabetic rats. Egypt Acad J Biolog Sci 2009; 2(1):153-162.

7. Bhandari U, Kanojia R, Pillai KK. Effect of ethanolic extract of *Zingiber officinale* on dyslipidemia in diabetic rats. J Ethanopharmacol 2005; 97:227-30.
8. Afshari AT, Shirpoor A, Farshid A, Saadatian R, Rasmi Y, Saboory E et al. The effect of ginger on diabetic nephropathy, plasma antioxidant capacity and lipid peroxidation in rats. Food Chem 2007; 101:148-153.
9. Mahesar H, Bhutto MA, Khand AA, Narejo NT. Garlic used as an alternative medicine to control diabetic mellitus in alloxane-induced male rabbits. Pak J Physiol 2010; 6(1):39-41.
10. Mark SV, Dawson A. Rapid stick methods for determining blood glucose concentration. Brit Med J 1965;1:293.
11. Alain CC, Poon LS Chan CS, Richmond W, Fu PC. Enzymatic determination of total cholesterol. Clin Chem 1974; 20: 470-475.
12. Burstein M, Schnolnic HR, Marlin R. Rapid method for the isolation of lipoprotein from human serum by precipitation with polyanions. Scan J Clin Lab Invest 1980; 40:583-595.
13. Grove TH. Effect of reagent pH on determination of high density lipoprotein cholesterol by precipitation with sodium phosphotungstate-magnesium. Clin Chem 1979; 25:560-564.
14. Fridewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972; 18: 499-502.
15. Akhani SP, Vishwakarma SL, Goyal RK. Anti-diabetic activity of *Zingiber officinale* in streptozotocin-induced type 1 diabetic rats. Journal of Pharmacy and Pharmacology 2004; 56: 101-105.
16. Al-Amin ZM, Thomson M, Al-Qattan KK, Peltonen-Shalaby R, Ali M. Anti-diabetic and hypolipidaemic properties of ginger in streptozotocin-induced diabetic rats. Br J Nutr 2006; 96:660-666.
17. Abdulrazaq NB, Cho MM, Win NN, Zaman R, Rahman MT. Beneficial effects of ginger (*Zingiber officinale*) on carbohydrate metabolism in streptozotocin-induced diabetic rats. Brit J Nutri 2011; 108(7):1194-1201.
18. Yamahara J, Mochizuki M, Rong H, Matsuda H, Fujimura H. The anti-ulcer effect in rats of ginger constituents. J Ethnopharmacol 1988; 23, 299–304.
19. Wohlmuth H, Leach DN, Smith MK, Myers SP. Gingerol content of diploid and tetraploid clones of ginger (*Zingiber officinale Roscoe*). J Agric Food Chem 2005; S3:5772-5778.

20. Singh AB, Akanksha N, Singh N, Maurya R, Srivastava AK. 2009. Antihyperglycaemic, lipid lowering and antioxidant properties of 6-gingerol in db/db mice. Int J Med Med Sci 2009; 1:536-544.
21. Castro VR. Chromium in series of Portugese plants used in the herbal treatment of diabetes. Biologic Trace Element Res 1998; 62(1-2):101-106.
22. Gujaral S, Bhumra H, Swaroop M. Effect of ginger oleoresin on serum and hepatic cholesterol levels in cholesterol-fed rats. Nutri Rep Intern 1978;17:183-187.
23. Sharma I, Gusain D, Dixit VP. Hypolipidemic and antiatherosclerotic effects of Zingiber officinale in cholesterol-fed rabbits. Phyth. Res 1996; 10(6):517-518.
24. Heeba GH, Abd-Elghany MI. Effect of combined administration of ginger (*Zingiber officinale*) and atorvastatin on the liver of rats. Phytomedicine 2010;17:1076-1081.
25. Tanabe M, Chen YD, Saito K, Kano Y. Cholesterol biosynthesis inhibitory component from *Zingiber officinale Roscor*. Chem. Pharm Bull (Tokyo) 1993; 41:710-713.
26. Bhandari U, Sharma JN, Zafar R. The protective action of ethanolic ginger extract in cholesterol-fed rabbits. J Ethnopharmacol 1998; 61:167-71.
27. Ness GC, Zhao Z, Lopez D. Inhibitor of cholesterol biosynthesis increase hepatic low density lipoprotein receptor protein degradation. Arch Biochem Biophy. 1996; 325:242-248.
28. Lopes-Virella MF, Stone P, Ellis S, Colwell JA. Cholesterol determination in high-density lipoproteins separated by three different methods. Clin Chem 1977; 23(5) 882-884.
29. Ahmed RS, Seth V, Banerjee BD. Influence of dietary ginger (*Zingiber officinale*) on the antioxidant defence system in rat: comparison with ascorbic acid. Indian J Exper Biol 2000; 38:604-606.
30. Stoilova I, Krastanov A, Stoyanova A, Denev P, Gargova S. Antioxidant activity of ginger extract (*Zingiber officinale*). Food Chem 2007; 102:764-770.