Journal of Applied Life Sciences International
4(2): 1-10, 2016; Article no.JALSI.20781
ISSN: 2394-1103

SCIENCEDOMAIN *international*
www.sciencedomain.org

The Antihyperglycemic, Hepatoprotective and Renoprotective Potentials of the Aqueous Extract of *Costus lucanusianus* on Streptozotocin-induced Diabetic Rats

Jamiyu Ayodeji Saliu[1*] and Oluwaseun Fapohunda[1]

[1]Department of Biochemistry, Adekunle Ajasin University, P.M.B. 001, Akungba Akoko, Ondo State, Nigeria.

Authors' contributions

This work was carried out by both authors. Author JAS designed the research, conducted animal experiment and wrote the manuscript. Author OF supported animal experiment, sampling and analyzed the data. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JALSI/2016/20781
Editor(s):
(1) Martin Koller, University of Graz, Research Management and Service, c/o Institute of Chemistry, Austria.
Reviewers:
(1) Ndomou Mathieu, University of Douala, Cameroon.
(2) Anonymous, G. R. Medical College, Gwalir, India.
(3) N. De Kimpe, Ghent University, Belgium.
Complete Peer review History: http://sciencedomain.org/review-history/12658

Original Research Article

Received 8th August 2015
Accepted 19th November 2015
Published 14th December 2015

ABSTRACT

Aim: This study sought to evaluate the effect of *Costus lucanusianus* on streptozotocin-induced diabetic rats.
Methodology: The effect of daily oral administration of aqueous extract of this plant on streptozotocin-induced diabetic rats was monitored for four weeks. Fasting blood glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) activities were determined. In addition, total protein, creatinine and urea levels were also measured.
Results: The result showed that there was a significant increase ($P<0.05$) in the blood glucose level in diabetic rats when compared to the normal rats. However, the administration of the extract normalized the blood glucose. There was a significant increase ($P<0.05$) in the levels of serum ALT, AST, ALP, LDH, creatinine and urea when compared to the normal rats. Nevertheless, the

**Corresponding author: Email: saliujohn@yahoo.com;*

administration of aqueous extract of *Costus lucanusianus* decreased the activities of these marker enzymes.
Conclusion: These findings suggest the antihyperglycemic, hepatoprotective and renoprotective potentials of this plant which can make it suitable candidate in the management of diabetes mellitus.

Keywords: Costus lucanusianus; antihyperglycemic; hepatoprotective; renoprotective; diabetic rats.

1. INTRODUCTION

Diabetes mellitus (DM) has been distinguished with persistently elevated blood glucose leading to acute or long term complications [1]. Globally, DM presents increased public health issue.The prevalence of DM in all age groups rate is expected to rise 8% to (170 million) in 2000 and the 4.4% (366 million) in 2030 [2]. The therapeutic agents currently used for treatment of diabetes have undesirable effects and fail to significantly alter diabetic complications [3]. Attention is now being shifted to traditional practices and herbal remedies with more efficacious and minimal side effects than the currently used oral hypoglycemic agents for the treatment of diabetes [4,5]. *Costus lucanusianus* is a common species in the forest zone of tropical Africa. It is widely used as a medicinal plant in tropical Africa but little is known about the constituents and their pharmacological activities [6]. This merits further research. In fact, saponins as the key ingredients in Chinese medicines responsible for both antiglycation and antioxidant activities had also been addressed in few studies [7-9].

2. MATERIALS AND METHODS

2.1 Materials

Costus lucanusianus leaves were obtained from an open forest in Akungba Akoko, Ondo state and were identified by Dr. Obembe O.A, a taxonomist from the department of Plant Science and Biotechnology, Adekunle Ajasin University Akungba Akoko. Assay kits for AST, ALT, ALP, LDH, creatinine, urea and total protein were products of Randox Laboratory Ltd, Ardmore, Diamond Road, Crumlin, Co. Anrtim, United Kingdom. Streptozotocin (Sigma, Brazil) and other analytical grade chemicals were used for this study.

2.2 Plant Extract Preparation

C. lucanusianus leaves were collected from a farm in Akungba-Akoko, Ondo State, Nigeria. A modification of [10] method was used to prepare the extract. Briefly, the shade dried leaves were crushed and then soaked in distilled water for 72 hours in a plastic container and covered with cheesecloth. The contents were stirred several times a day and at the end of the third day the contents were filtered through two layers of cheesecloth. The extract was quantified by drying 1 mL of the homogeneous filtrate (by controlled heating i.e. in an oven kept at 40℃) in a pre-weighed watch glass; this was done in triplicates and the average determined. The extract was kept in the freezer until use, when it was allowed to thaw at room temperature.

2.3 Experimental Animals and Protocols

Thirty-five (35) adult male and Wistar rats (average weight 228 g) were obtained from the Animal Unit of the University of Ibadan Teaching Hospital (UCH), Ibadan, Nigeria. The rats were kept in a well-ventilated room, with 12 h light and 12 h dark cycles. They were given free access to food (standard pelleted feed) and water and allowed to acclimatize for three weeks before the commencement of the study. Treatment of the animals conformed to the guidelines in the Principles of Laboratory Animal Care (NIH Publication 85-23, revised 1985) and was approved by the local Institutional Review Board (IRB).

Seven groups of five rats each were used for this study, namely:

- **Group 1:** normal control rats given distilled water;
- **Group 2:** diabetic control rats given distilled water;
- **Group 3:** Metformin treated diabetic rats, orally given 200 mg/kg;
- **Group 4:** *C. lucanusianus* treated diabetic rats orally given 100 mg/kg;
- **Group 5:** *C. lucanusianus* treated diabetic rats orally given 200 mg/kg body weight of *C. lucanusianus* aqueous leaf extract;

Group 6: normal control rats orally given 100 mg/kg body weight of *C. lucanusianus* aqueous leaf extract;

Group 7: normal rats orally given 200 mg/kg body weight of *C. lucanusianus* aqueous extract.

2.4 Biochemical Assays

Serum glucose (Reddy's laboratories, Hyderabad, India), Assay kits for AST, ALT, ALP, LDH, creatinine, urea and total protein were products of Randox Laboratory Ltd, Ardmore, Diamond Road, Crumlin, Co. Anrtim, United Kingdom. They were estimated using a commercial diagnostic kit. Serum protein and urea were estimated by the method described by [11,12].

2.5 Statistical Analysis

All the grouped data was statistically evaluated via the statistical package for social sciences version 15. Hypothesis testing method included one-way analysis of various (ANOVA) followed by least significant difference test. P-values of less than 0.05 were considered to indicate statistical significance. All the results were expressed as mean ± SD for 5 animals in each group.

3. RESULTS

3.1 Effect of *Costus lucanusianus* Leaves on Fasting Blood Sugar of Diabetic Rats

The result obtained in Figure 1 showed that there was a significant increase ($P<0.05$) in the fasting blood sugar of the diabetic rats when compared to the normal rats. However, the treatment with aqueous extract of *Costus lucanusianus* leaf on the diabetic rats showed a significant reduction of fasting blood sugar ($P<0.05$) in the treatment groups when compared to the diabetic rats. It is worthy of note that the reduction in the fasting blood sugar is also concentration dependent.

3.2 Effect of *Costus Lucanusianus* on Body Weight of the Diabetic Rats

It was observed that there was a significant decrease in the diabetic control when compared to the normal rats. However, on administration of metformin and *Costus lucanusinus*, there was an increase in body weight of metformin treated group and *Costus lucanusianus* treated group respectively throughout the period of monitoring.

The general increase in body weight observed in *Costus lucanusianus* treated rats as compared with water control rats indicates that *Costus lucanusianus* has an increasing effect on body weight.

3.3 Effect of *Costus lucanusianus* Leaf on Aspartate Aminotransferase (AST) Activity

The result obtained above showed that there was a significant increase ($P<0.05$) in the serum AST activity of the diabetic control when compared to the normal control rats. In contrast, the cardiac and hepatic AST activities were significantly reduced in the diabetic control when compared to the normal control. Furthermore, there was a significant reduction ($P<0.05$) in the serum AST activities of the *Costus lucanusianus* treated groups when compared to the diabetic control.

3.4 Effect of *Costus lucanusianus* Leaf on Alanine Aminotransferase (ALT) Activity

The result in Figure 4 showed that there was a significant increase ($P<0.05$) in the serum ALT activity of the diabetic control when compared to the normal control rats. In contrast, the cardiac and hepatic ALT activities were significantly reduced in the diabetic control when compared to the normal control. Furthermore, there was a significant reduction ($P<0.05$) in the serum ALT activities of the *Costus lucanusianus* treated groups when compared to the diabetic control.

3.5 Effect of *Costus lucanusianus* Leaf on Alkaline Phosphatase (ALP) Activity

The result obtained in Figure 5 revealed that there was a significant increase in the activity of ALP in diabetic rats when compared to the normal control. However, in the liver ALP activity there was a significant reduction in diabetic control when compared to the normal control.

3.6 Effect of *Costus lucanusianus* Leaf on Lactate Dehydrogenase (LDH) Activity

The result obtained in Figure 6 revealed that there was a significant increase in the activity of LDH in diabetic rats when compared to the normal control. However, in the liver LDH

activity there was a significant reduction in diabetic control when compared to the normal control.

3.7 Effect of *Costus lucanusianus* Leaf on Urea Level

The result obtained in Figure 7 revealed that there was a significant increase in the level of urea in diabetic rats when compared to the normal control. However, in the kidney urea level there was a significant reduction in diabetic control when compared to the normal control.

3.8 Effect of *Costus lucanusianus* Leaf on Creatinine Level

The result obtained in Figure 8 revealed that there was a significant increase in the level of creatinine in diabetic rats when compared to the normal control. However, in the kidney creatinine level there was a significant reduction in diabetic control when compared to the normal control.

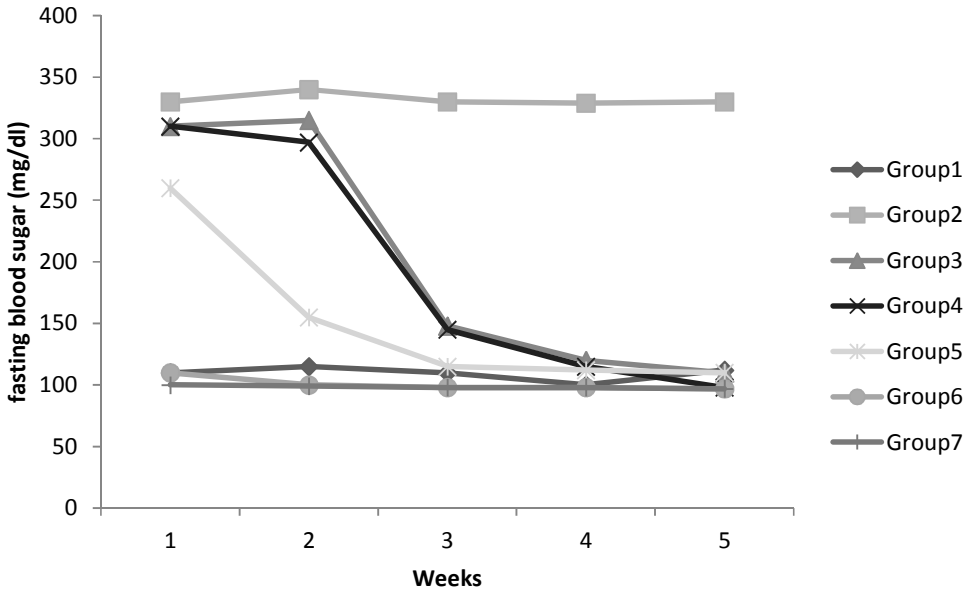

Figure 1. The effect of *Costus lucanusianus* leaves on fasting blood sugar of diabetic rats

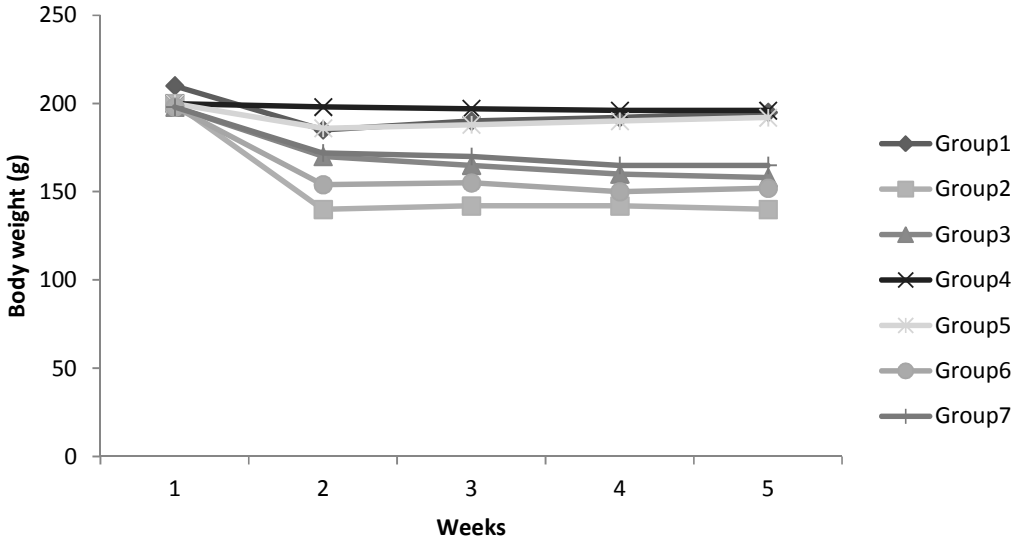

Figure 2. The effect of *Costus lucanusianus* on body weight of the diabetic rats

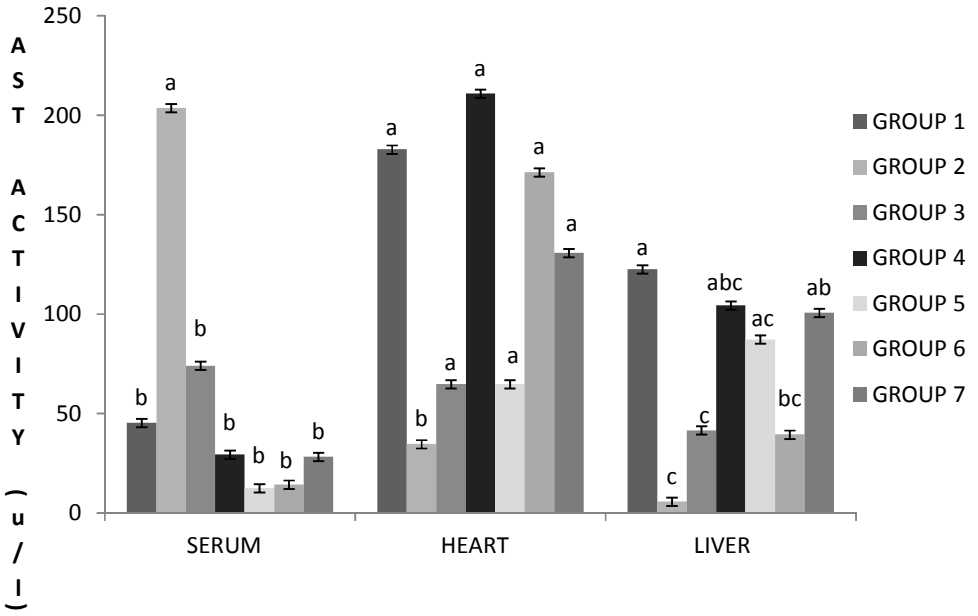

Figure 3. The effect of *Costus lucanusianus* leaf on Aspartate aminotransferase (AST) activity

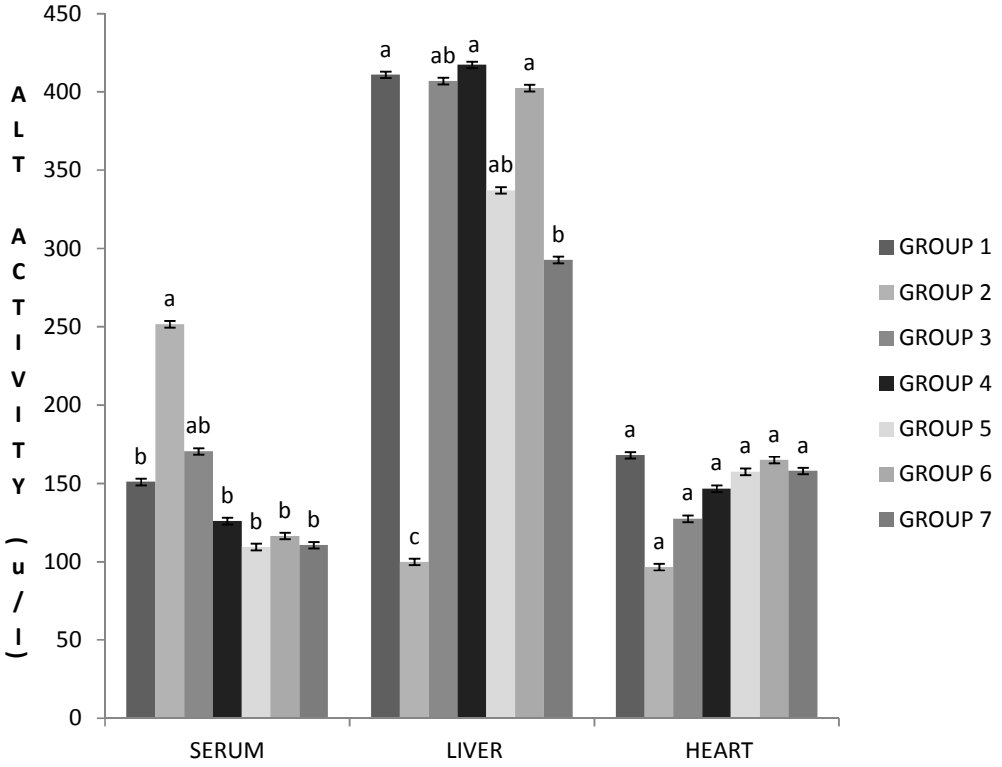

Figure 4. The effect of *Costus lucanusianus* leaf on Alanine aminotransferase (ALT) activity

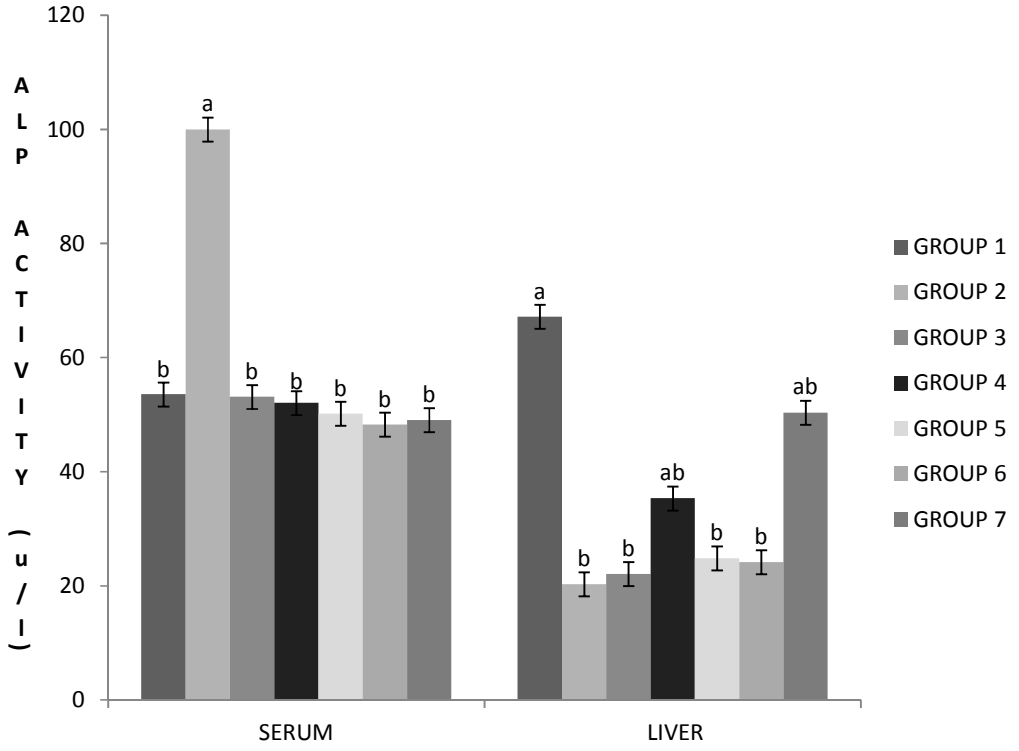

Figure 5. The effect of *Costus lucanusianus* leaf on Alkaline phosphatase (ALP) activity

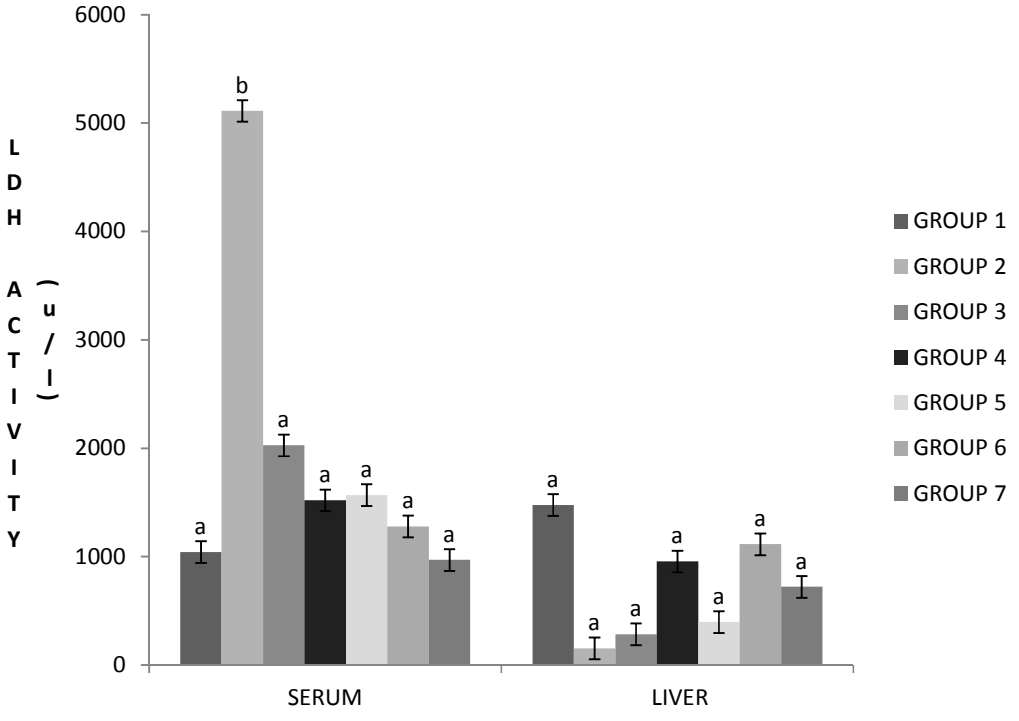

Figure 6. The effect of *Costus lucanusianus* leaf on Lactate dehydrogenase (LDH) activity

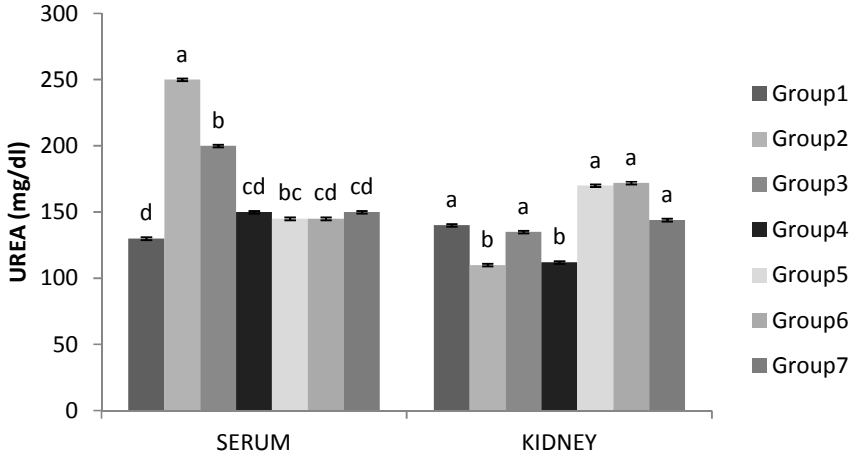

Figure 7. The effect of *Costus lucanusianus* leaf on urea level

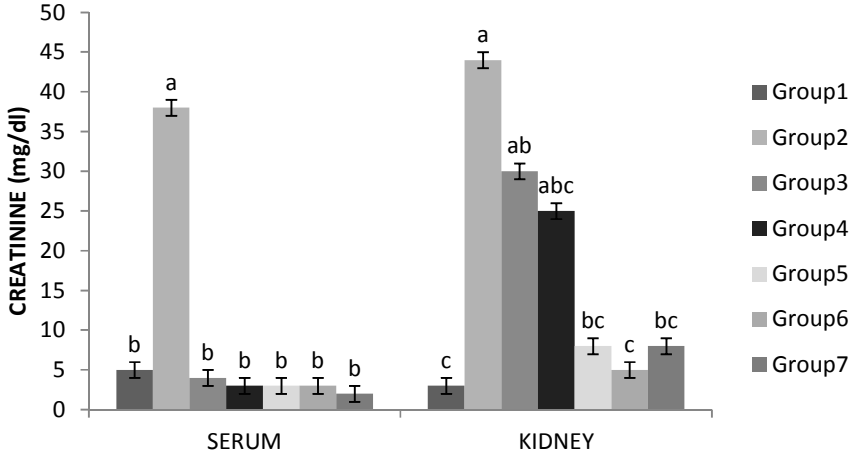

Figure 8. The effect of *Costus lucanusianus* leaf on creatinine

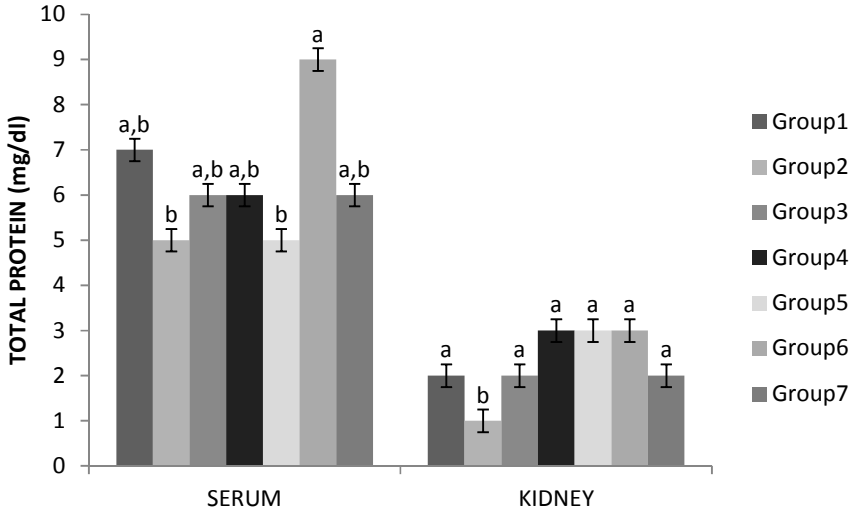

Figure 9. The effect of *Costus lucanusianus* leaf on total protein

3.9 Effect of *Costus lucanusianus* Leaf on Total Protein Level

The result obtained in Figure 9 revealed that there was a significant decrease in the level of total protein in diabetic rats when compared to the normal control. However, in the kidney total protein level there was a significant reduction in diabetic control when compared to the normal control.

4. DISCUSSION

The reduction in the fasting blood glucose observed in the *Costus lucanusianus* treated diabetic groups agrees with the report of [13] which showed that some medicinal plants exhibited antidiabetic activity against the streptozotocin induced diabetic rats. The possible mechanism by which *Costus lucanusianus* extract bring about its hypoglycaemic action in diabetic rats may be improving glycemic control mechanism and insulin secretion from remnant pancreatic beta cells in diabetic rats [14]. Previous work on the phytochemical screening of this plant revealed that it contains saponins which have been known to possess antidiabetic property and are promising compounds with potential to be developed into new drugs for antidiabetes [5].

Aminotransferases (AST and ALT) mediate the catalysis of amino-transfer reactions and they are markers for clinical diagnosis of liver injury [15] while ALP is responsible for removing phosphate group from nucleotides and proteins. This enzyme is primarily produced in the liver and brain [16], and also used as marker of hepatic functions [17]. As revealed in this present study, the significant increase in the activities of serum AST, ALT and ALP observed in diabetic control group as compared to normal control group was mainly due to the leakage of these enzymes from liver cytosol into the blood stream which is an indication of hepatoxic effect of STZ [15] and consistent with previous studies which described increased liver oxidative stress in this model of experimental diabetes mellitus [18]. Moreover, it was suggested that the elevation in serum AST and ALT activities in diabetic rats could be related to excessive accumulation of glutamate and alanine in the serum of diabetic animals, as a result of amino acids mobilization from protein stores [19]. However, *Costus lucanusianus* treated groups exhibited significant decrease in serum AST, ALT and ALP activities which could be attributed to their ability to protect/repair liver tissue damage. Plant foods are rich in saponins and antioxidant polyphenol phytochemicals with hepatoprotective properties [20].

Indeed, elevated LDH levels observed in the experimental diabetic animals are associated with impaired glucose-stimulated insulin secretion [21]. Thus, increased activity of LDH interferes with normal glucose metabolism and insulin secretion in the *β*-cells of pancreas and it may therefore be directly responsible for insulin secretory defects in diabetes. However, treatment with *Costus lucanusianus* to diabetic rats reversed the LDH activity to near normalcy. Similarly treatment with resveratrol to diabetic rats decreased the activity of LDH [22] most probably by regulating the proportion of pyruvate and NADH thereby promoting the mitochondrial oxidation of (pyruvate) glucose. The protective effects due to treatment with *Costus lucanusianus* strongly indicate the possibility of the extract being able to prevent any leakages of marker enzymes. There are some reports on reversal of LDH in diabetic rats with treatment with *Murray koenigii, Ocimum sanctum* [23].

Renal disease is one of the most common and severe complications of diabetes. Insulin is a physiological factor, which plays an important role in the maintenance of protein balance, since it not only stimulates the uptake of amino acids and protein synthesis, but also inhibits protein degradation [24]. In addition, significant elevations in serum creatinine and urea levels indicate impaired renal function of diabetic animals. Aqueous extract of *Costus lucanusianus* leaf increased the total protein and lowered the serum urea and creatinine levels by enhancing the renal function that is generally impaired in diabetic rats. This result is in agreement with a previous study [25].

Reduction in serum protein level observed in diabetic control group may be due to microproteinuria which are clinical important markers of diabetic nephropathy and may be due to increased protein catabolism [26]. Also formation of protein- MDA adducts may have contributed to the decrease in serum protein level due to increased lipid peroxidation [27]. However, the marked increase in the serum total protein of *Costus lucanusianus* treated group may be due to the hepatoprotective properties of their phytochemical constituents and also availability of amino acids. Myricetin is the active principle detected in this plant [28].

5. CONCLUSION

In the present study, the findings may suggest the antihyperglycemic, hepatoprotective and renoprotective potentials of this plant which can make it suitable candidate in the management of diabetes mellitus.

ACKNOWLEDGEMENTS

The authors wish to acknowledge Dr. Obembe for his professional advice in identifying the plant.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Greenbaum CJ, Harrison LC, editors. Diabetes: Translating research into practice. London: Informa Healthcare. 2008;1-2.
2. Fonseca VA. Clinical diabetes: Translating research into practice. Philadelphia: Saunders Elsevier. 2006;2-3.
3. Chandramohan G, Ignacimuthu S, Pugalendi KV. A novel compound from *Casearia esculenta* (Roxb.) root and its effect on carbohydrate metabolism in streptozotocin-diabetic rats. European Journal of Pharmacology. 2008;590(1-3): 437-443.
4. Kim SH, Hyun SH, Choung SY. Antidiabetic effect of cinnamon extract on blood glucose in db/db mice. Journal of Ethnopharmacology. 2006;104(1-2):119-123.
5. Li W, Zheng H, Bukuru J, De Kimpe N. Natural medicines used in the traditional Chinese medical system for therapy of diabetes mellitus. Journal of. Ethnopharmacology. 2004;92:1-21.
6. Aweke G. *Costus lucanusianus* J. Braun and K. SchaumIn: Schmelzer, G.H. and Gurib-Fakim, A. Prota 11(1): Medicinal plants/Plantes Medicina; 2007.
7. He L, Zhou G, Zhang H, He Y. Chemical constituents and biological activities of saponin from the seed of *Camellia oleifera.* Sci. Res. Essays. 2010;5(25):4088-4092.
8. Xi M, Hai C, Tang H, Wen A, Chen H, Liu R, Liang X, Chen M. Antioxidant and antiglycation properties of triterpenoid saponins from *Aralia taibaiensis* traditionally used for treating diabetes mellitus. Redox. Rep. 2010;15(1):20-28.
9. Rodrigues HG, Diniz YS, Faine LA, Galhardi CM, Burneiko RC, Almeida JA, Ribas BO, Novelli EL. Antioxidant effect of saponin: Potential action of a soybean flavonoid on glucose tolerance and risk factors for atherosclerosis. Int. J. Food Sci. Nutr. 2005;56:79-85.
10. Onoagbe IO, Ebhota AO, Udegbe HC, Omondia M, Edeni D, Ebengho SO. Assessment of some medicinal plants for hypoglycemic activities in rats and rabbits. Klobex Academic. 1999;2:159-160.
11. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. Journal of Biological Chemistry. 1951;193(1):265-75.
12. Fawcett JK, Scott JE. A rapid and precise method for the determination of urea. Journal of Clinical Pathology. 1960;13:156-9.
13. Vasi S, Austin A. Effect of herbal hypoglycemic on oxidative stress and antioxidant status in diabetic rats. The Open Diabetes Journal. 2009;2:48-52.
14. Punitha R, Manohara S. Antihyperglycemic and antilipidperoxidative effects of *Pongamia pinnata* (Linn.) Pierre flowers in alloxan induced diabetic rats. Journal of Ethnopharmacology. 2006;105:39-46.
15. Li XM. Protective effect of *Lycium barbarum* polysaccharides on streptozotocin- induced oxidative stress in rats. International Journal of Biological Macromolecule. 2007;40:461-465.
16. Han KH, Hashimoto N, Shimada K, Sekikawa M, Noda T, Yamauchi H. Hepatoprotective effects of purple potato extract against D-galactosamine-induced liver injury in rats. Bioscience, Biotechnology and Biochemistry. 2006;70: 1432-1437.
17. Yoo YM, Nam JH, Kim MY, Choi J, Park HJ. Pectolinarin and pectolinarigenin of *Cirsiumsetidens* prevent the hepatic injury in rats caused by D-galactosamine via an oxidant mechanism. Biology and Pharmacy Bulletin. 2008;31(4):760-764.
18. Maiti R, Jana D, Das UK, Ghosh D. Antidiabetic effect of aqueous extract of seed of *Tamarindus indica* in streptozotocin-induced diabetic rats. Journal of Ethnopharmacology. 2004;92: 85-91.
19. Dias AS, Porawski M, Marroni N, Collado PS, Gonzalez-Gallego J. Quercetin

decreases oxidative stress, NF-KB activation, and iNOS overexpression in liver of Journal of Nutrition. 2005;135(10): 2299-2304.

20. Khan MRL, Islam MA, Hossain MS, Asadujjaman M, Wahed MII, Rahman BM. Antidiabetic effects of the different fractions of ethanolic extract of *Ocimum sanctum* in normal and alloxan induced diabetic rats. Journal of Science Research. 2010;2(1): 158-168.
21. Shimoda H, Tanaka J, Kikuchi M, Fukuda T, Ito H, Hatano T. Walnut polyphenols prevent liver damage induced by carbon tetrachloride and D-galactosamine: Hepatoprotective hydrolysable tannins in the kernel pellicles of Walnut. Journal of Agriculture and Food Chemistry. 2008;56(12):4444-4449.
22. Ainscow EK, Zhao C, Rutter GA. Acute overexpression of lactate dehydrogenase-A perturbs beta-cell mitochondrial metabolism and insulin secretion. Diabetes. 2000;49:1149-1155.
23. Palsamy P, Subramanian S. Modulatory effects of resveratrol on attenuating the key enzymes activities of carbohydrate metabolism in streptozotocin–nicotinamide-induced diabetic rats. Chemico-Biological Interaction. 2009;179: 356-362.
24. Narendhirakannan RT, Subramanian S, Kandaswamy M. Biochemical evaluation of antidiabetogenic properties of some commonly used Indian plants on Streptozotocin-induced diabetes in experimental rats. Clinical and Experimental Pharmacological Physiology. 2006;33:1150-1157.
25. Pathak A, Dhawan D. Effects of lithium on the levels of blood urea and creatinine in diabetic rats. Medicine and Scientific Research. 1988;26:855-859.
26. Daisy P, Nirmala AR, Rajathi M. Hypoglycemic and other related effects of *Elephanto pusscaber* extracts on alloxan-induced diabetic rats. Journal of Biological Science. 2007;7:433-437.
27. Kaleem M, Medha P, Ahmed QU, Asif M, Bano B. Beneficial effects of *Annonas quamosal* extract in streptozotocin-induced diabetic rats. Singapore Medicinal Journal. 2008;49(10):800-804.
28. Obute GC, Adubor GO. Chemicals detected in plants used for folk medicine in South Eastern Nigeria. Ethnobotanical Leaflets. 2007;11:173-194.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/12658