



Effect of Methanol Extract of Unripe *Carica papaya* Pulp on Lipid Profile and Liver Function of Alloxan-Induced Diabetic Rats

Henry N. Ogbonna^{1*}, Ugonna D. Nwankpa¹, Godwin S. Aloh¹
and Raymond C. Ibeh²

¹Department of Biochemistry, College of Natural Sciences, Michael Okpara University of Agriculture Umudike, P.M.B. 7267, Umuahia, Abia State, Nigeria.

²Department of Biochemistry, School of Biological Sciences, Federal University of Technology Owerri, P.M.B. 1526, Owerri, Imo State, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Author HNO designed the study and wrote the protocol and first draft of the manuscript. Author UDN carried out the literature searches of the work. Author GSA supervised and performed the analyses of the work. Author RCI performed the statistical analysis of the work.

Article Information

DOI: 10.9734/IJBCRR/2020/v29i430180

Editor(s):

(1) Dr. K. V. Ramanath, Dayanand Sagar University, India.

Reviewers:

(1) Dennis Amaechi, Veritas University Abuja, Nigeria.

(2) Bekkouch Oussama, Mohamed First University, Morocco.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/56663>

Received 24 February 2020

Accepted 29 April 2020

Published 07 May 2020

Original Research Article

ABSTRACT

Background: *Carica papaya* is commonly used in the treatment of various diseases like constipation, piles, hypertension and malaria. The ameliorative effect of *Carica papaya* on alloxan-induced diabetic rats has been suggested by several studies.

Aim: The present study aims to investigate the effect of methanolic extract of unripe *Carica papaya* pulp on the lipid profile and liver biomarkers of a diabetic rat.

Materials and Methods: After acclimatization, thirty-two (32) animals were randomly classified into 8 groups (4 rats per group). The different test (extract) groups received in addition to normal diet ad libitum, dosages of 200, 400, 600 and 1000 mg/kg/day of the *Carica papaya* extract. The normal and negative control groups received a normal diet, while the positive control was given oral treatment with 6 mg/65 kg/day of glibenclamide as well as the normal diet. After 28 successive days

*Corresponding author: E-mail: contactogbonnahenry@gmail.com;

of treatment, all the experimental rats were sacrificed by ocular puncture and the serum used in the evaluation of body lipids, liver function parameters and biochemical indexes.

Results: The administration of the unripe *Carica papaya* extract resulted in a dose-dependent and significant decrease ($p < 0.05$) in serum albumin, aspartate aminotransferase (AST), total protein, and in alanine aminotransferase (ALT) level. There was, however, a significant increase in High-density lipoprotein (HDL) level for 400-1000 mg/kg extract groups. The result also showed a reduced cholesterol level at an extract dose of 1000 mg/kg/day.

Conclusion: The ameliorative properties of the unripe pulp of *Carica Papaya* on biochemical parameters of a diabetic rat, as shown from the result could be indicative that unripe *Carica papaya* can be valuable in the management of diabetes mellitus and other complications that may arise.

Keywords: Alloxan; *Carica papaya*; glibenclamide; liver function; hyperlipidemia; bilirubin.

1. INTRODUCTION

Diabetes mellitus is a well-known metabolic disease that has proven to be a serious challenge in the 21st century. It affects protein, lipid and carbohydrate metabolism which are essential biochemical pathways of the body. The prevalence of diabetes is rising globally, mostly in Africa [1]. It is characterized by a deficiency in insulin secretion or insulin action or both [2]. The diabetic state may result in the development of further metabolic disturbances and complications among which are dyslipidemia, hepatomegaly, liver enzyme abnormalities, weight loss, renal disease, and coma [3]. Liver diseases noticed in diabetic patients may be due to excess glycogen in the hepatic tissue, accumulated from an impaired glycogen synthesis. Patients showing only excessive glycogen deposition may suffer from hepatomegaly and liver enzyme abnormalities which can be improved with sustained glucose control [4]. Alloxan induces diabetes mellitus by the destruction of the beta-cells of the pancreas which produces insulin thereby causing cell necrosis [5]. There are so many therapeutic strategies that are being used to treat diabetes, much of which are modern therapies. But since the cost of modern therapies are enormous on the economy of developing countries and has not successfully controlled the pathophysiology of the disorder, other strategies are therefore needed. This trend has prompted an analysis of current dietary and lifestyle behaviors, even to functional foods and nutraceuticals [6]. Because of the poor accessibility of health facilities to rural people, especially in developing countries, traditional management of this disease by the use of medicinal plants could potentially be used [7]. Also, because of the cost of conventional drugs, herbal remedies now represent the first line of treatment available to a large population of the world [8]. Different studies have shown *Carica*

papaya to contain different phytochemicals that have different pharmacological properties, enabling *Carica papaya* to be used in traditional treatment of several ailments including malaria, hypertension, piles and yaws [9]. The antidiabetic potential of its seeds and aqueous extract of its leaves [10,11] and its hypolipidaemic properties [12] have been reported. Some of the reported phytochemicals are alkaloids, carpain, nicotine, flavonols, tannins, terpinenes, saponins, cardiac glycosides, anthraquinones, phlobatins, anthocyanosides and phenols [9,13]. The quantity of these chemicals depends on the solvent used for extraction. There, however, is a dearth of the report on the effect of methanolic extract of *Carica papaya* on these parameters. Hence, this study is evaluating the antidiabetic properties of methanol extract of the unripe pulp of *Carica papaya* on rats induced with diabetes mellitus.

2. MATERIALS AND METHODS

2.1 Plant Material and the Methanol Extraction Method

Unripe fruits of *Carica papaya* (pawpaw) were collected from Umudike in Ikwuano Local Government Area of Abia State, Nigeria. The unripe fruits were washed and pilled and the pulp was chopped into pieces and weighed. Then it was ground using an electric grinder. It was subsequently soaked in methanol, and allowed to stand overnight and sieved, after which rotary evaporator was used to evaporate the methanol.

2.2 Animals and Induction of Experimental Diabetes

40 Wistar rats weighing 110-115 g were used for this study. The experimental animals were kept in the laboratory to acclimatize for two weeks, under standard conditions with free access to

food and water throughout the experiment. After acclimatization, 32 rats were selected for further study. These animals were tested diabetic using a fasting blood sugar method and were now selected and prepared for further studies. The rats were induced with diabetes by intraperitoneal injection of 120mg/kg of alloxan monohydrate dissolved in distilled water after fasting.

2.3 Treatment

The animals were distributed into 8 groups with 4 rats per group. All groups were fed with normal feed and distilled water ad libitum, Groups 2-8 were induced with diabetes. Group 1 and group 2 are the normal and negative controls respectively. Group 3 (positive control) was given daily oral treatment with 6 mg/65 kg/day of glibenclamide (standard drug). Groups 4-8 (treatment groups) were given oral treatment of the *papaya* extract, 200 mg/kg/day, 400 mg/kg/day, 600 mg/kg/day, 800 mg/kg/day and 1000 mg/kg/day respectively. All treatments lasted 28 consecutive days.

2.4 Blood Collection and Bioassays

The experiment was terminated by the overnight fast of the animals with the availability of distilled water ad libitum. All rats were sacrificed and the blood collected by ocular puncture under halothane anesthesia. FBS (Fasting Blood Sugar) was determined by the use of One Touch Basic Blood Glucose Monitoring System (LifeScan Inc., Milpitas, California, U.S.A.). Total plasma cholesterol, triglycerides (TG), high-density lipoprotein-cholesterol (HDL-c) and low-density lipoprotein-cholesterol (LDL-c) concentrations were determined through enzymatic assay method with the use of the analytical kits (Biolabo SA, Maizy, France). TP, albumin and globulin were determined using Agepe diagnostic test kit while AST and ALT were determined using Randox test kit.

3. RESULTS AND OBSERVATIONS

From our observations, the blood sugar decreased significantly ($p < 0.05$) and dose-dependently across treatment groups which were all significantly lower than the negative control (443.5 ± 1.7). There was a non-significant difference between the normal control (72.5 ± 0.6) and treatment group 1000 mg/kg (77.0 ± 0.6). Serum cholesterol showed a dose-dependent significant decrease across treatment groups with a non-significant difference between group

200 mg/kg (4.90 ± 0.12) and negative control (4.20 ± 0.06), while normal control (4.17 ± 0.03), positive control (4.22 ± 0.01) and group 1000 mg/kg (4.10 ± 0.01) showed no significant difference. For TAG, the positive control (1.13 ± 0.01) along with group 400 mg/kg (1.14 ± 0.01) were significantly higher ($p < 0.05$) than groups 1000 mg/kg (0.97 ± 0.01), normal control (1.01 ± 0.12), 800 mg/kg (1.04 ± 0.07) and 200 mg/kg (1.06 ± 0.04), while group 600 mg/kg (1.18 ± 0.04) and negative control (1.18 ± 0.03) were non-significantly different but both significantly higher than the rest. Treatment groups showed a dose-dependent decrease in LDL-C levels without any significant difference between normal control (2.27 ± 0.08), positive control (2.11 ± 0.05) and group 1000mg/kg (2.15 ± 0.01) and between negative control (3.58 ± 0.20) and group 200mg/kg (3.53 ± 0.01). There was a dose-dependent increase in HDL-C across treatment groups. No significant difference was noticed between normal control (1.70 ± 0.06), positive control (1.88 ± 0.04) and group 1000 mg/kg (1.76 ± 0.02) and between negative control (1.12 ± 0.14), group 400 (1.01 ± 0.04) and group 200 mg/kg (1.15 ± 0.13). There was a dose-dependent significant ($p < 0.05$) decrease in AST levels of the unripe *Carica papaya* extracts as compared to a positive control (154.9 ± 1.70) and negative group (137.3 ± 1.00). Also, the mean value for AST levels for the negative group (137.3 ± 1.00) significantly ($p < 0.05$) increased when in comparison to the normal control (127.1 ± 1.65). Extracts groups of 200 mg/kg (35.0 ± 0.35), 400 mg/kg (32.1 ± 0.35), 600 mg/kg (42.6 ± 0.05), 800 mg/kg (39.1 ± 1.25), 1000 mg/kg (40.7 ± 0.90) showed a significant ($p < 0.05$) decrease for ALT levels in comparison to the negative (43.4 ± 1.75) and positive control (3.95 ± 0.11) groups. The mean value of the normal group for total protein level (5.67 ± 0.33) showed significant ($p < 0.05$) increase when in comparison to the positive group (3.95 ± 0.11) and to extract groups of 400 mg/kg (4.91 ± 0.24), 600 mg/kg (5.00 ± 0.25), 800 mg/kg (4.83 ± 0.24) and 1000 mg/kg (4.97 ± 0.11). Also, the 200 mg/kg (5.89 ± 0.08) extract group significantly ($p < 0.05$) increased when compared to other extract groups. The bilirubin levels of the extract groups decrease non-significantly ($p < 0.05$) when compared to each other and the negative (2.00 ± 0.05) and the positive control (2.19 ± 0.05). The positive control (2.19 ± 0.05) showed a non-significant ($p < 0.05$) increase when in comparison to the negative group (2.00 ± 0.05), normal group (1.95 ± 0.14) and the various extract groups of 200 mg/kg (1.92 ± 0.16), 400 mg/kg

(1.87±0.19), 600 mg/kg (1.90±0.18) 800 mg/kg (1.79±0.04), 1000 mg/kg (1.79±0.20). The mean value of the treatment group 200 mg/kg for albumin levels showed a significant ($p < 0.05$) increase when the negative group is compared (2.98±0.20), normal control (2.96±0.12), positive control group (3.16±0.19) and other extracts group. The normal (2.96±0.12) group showed a non-significant difference ($p < 0.05$) when in comparison to the negative (2.98±0.20) and a significant difference ($p < 0.05$) when in comparison to the positive group.

Table 1. Treatment groups, type and amount of treatment given to the experimental rats

Groups	Type of Treatment
Group 1 - Normal Control	Normal feed and distilled water.
Group 2- Positive Control	Normal feed, distilled water and 6 mg/65 kg/day of glibenclamide (standard drug).
Group 3 -Negative Control	Normal feed, distilled water and treatment with 120 mg/kg of alloxan monohydrate.
Group 4 – Extract Group 1	Normal feed, distilled water, alloxan monohydrate and 200 mg/kg/day of unripe <i>Carica Papaya pulp extract</i>
Group 5 – Extract Group 2	Normal feed, distilled water, alloxan monohydrate and 400 mg/kg/day of unripe <i>Carica Papaya pulp extract</i>
Group 6 – Extract Group 3	Normal feed, distilled water, alloxan monohydrate and 600 mg/kg/day of unripe <i>Carica Papaya pulp extract</i>
Group 7 – Extract Group 4	Normal feed, distilled water, alloxan monohydrate and 800 mg/kg/day of unripe <i>Carica Papaya pulp extract</i>
Group 8 – Extract Group 5	Normal feed, distilled water, alloxan monohydrate and 1000 mg/kg/day of unripe <i>Carica Papaya pulp extract</i>

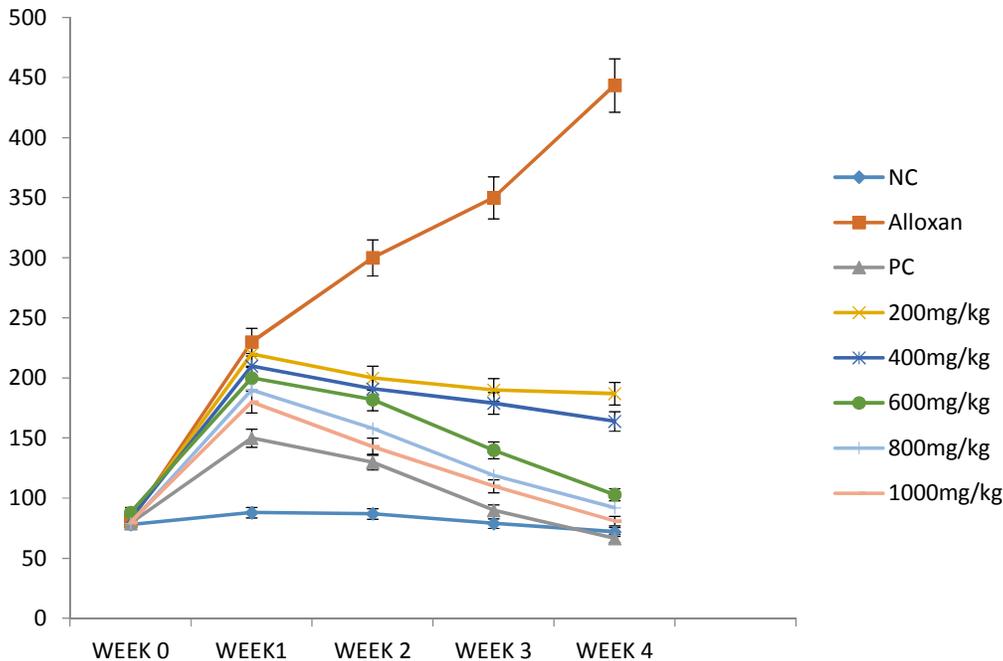


Fig. 1. Shows effects of *Carica papaya* on glucose level of diabetic rats
 Data are expressed as mean ± S.E.M.; n = 5. One-way analysis of variance (ANOVA) followed by POSTHOC test ($p < 0.05$). NC= Negative Control, PC= Positive Control

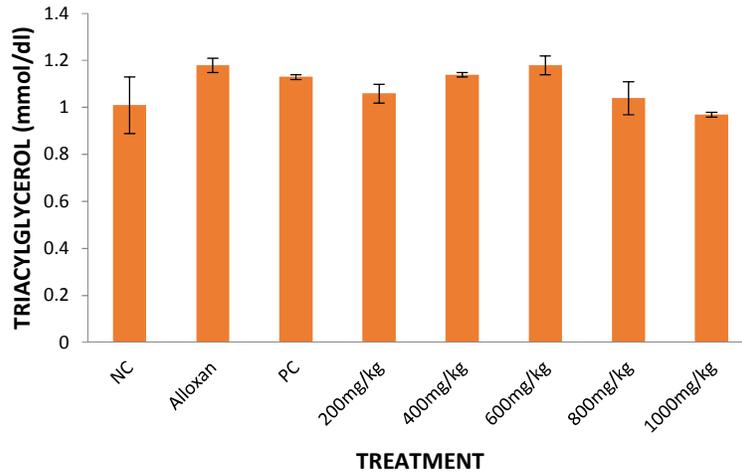


Fig. 2. Shows effects of *Carica papaya* on TAG of diabetic rats
 Data are expressed as mean \pm SD.; n = 5. One-way analysis of variance (ANOVA) followed by POSTHOC test ($p < 0.05$). The result showed no significant difference between the treatment groups. NC= Negative Control, PC= Positive Control

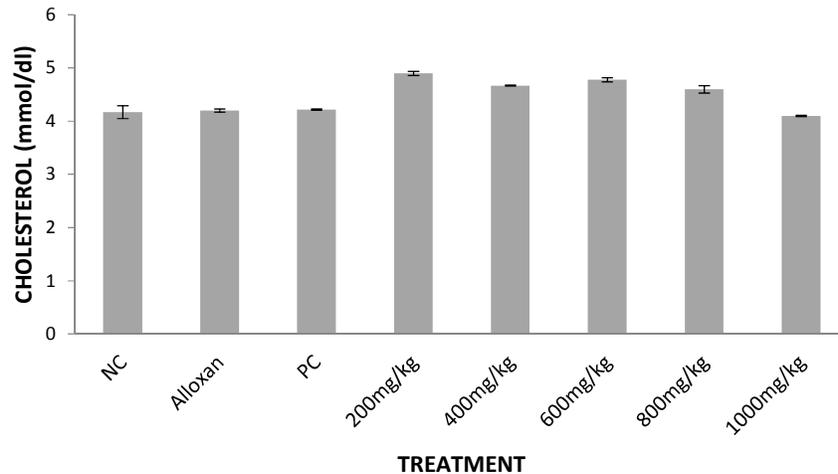


Fig. 3. This figure shows effects of *Carica papaya* on cholesterol of diabetic rats
 Data are expressed as mean \pm SD.; n = 5. One-way analysis of variance (ANOVA) followed by POSTHOC test ($p < 0.05$). The result showed significant increase ($p < 0.05$) in treatment 4 (200 mg/kg extract) when compared to treatment 2 (alloxan) while no significant difference when compared to treatment 5,6,7 and 8 (400 mg/kg, 600 mg/kg, 800 mg/kg and 1000 mg/kg respectively) NC= Negative Control, PC= Positive Control

4. DISCUSSION

Diabetes is a common disorder that is associated with chronic hyperglycemia, dyslipidemia, neuropathy and degenerative vascular changes. This has led to an increase in interest in finding natural remedies to manage the disease. The standard drug used, glibenclamide, belongs to the second generation of sulfonylurea, a type of

oral hypoglycemic agents. Sulfonylureas are known to mediate their hypoglycemic effect by the stimulation of insulin from the pancreatic β cells, reducing hepatic insulin clearance, stimulating the release of somatostatin, suppressing glucagon secretion and by suppressing hepatic gluconeogenesis [14]. The unripe *Carica papaya* may be eliciting its anti-hyperglycemic properties through a similar

mechanism with glibenclamide, namely, induction of hyperinsulinemia or by enhancing utilization of peripheral glucose. It could also be acting by stimulating the regeneration process as well as the revitalization of the viable beta cells [15]. Diabetes mellitus is known to manifest hyperlipidemia which is a result of acceleration in de novo hepatic biosynthesis of VLDL (Very Low-Density Lipoprotein). Since the action of lipoprotein lipase is dependent on high insulin: glucagon ratio, the increased release of VLDL is accompanied by reducing clearance from the bloodstream [16]. The dose-dependent decrease observed in serum cholesterol may have been due to the presence of sterols in *Carica papaya* as reported by Zetina-Esquivel et al. [17]. Phytosterols are known to displace cholesterol in bile salt thereby competing for intestinal absorption and leading to increment in fecal excretion of cholesterol. This reduction in the serum total cholesterol levels may as well be attributed to reduced biosynthesis of cholesterol. This can be due to a decrease in fatty acids β -oxidation, which leads to a reduction in the concentration of acetyl CoA since acetyl CoA is the key substrate in the biosynthesis of cholesterol [18]. The observed reduction in the serum triglyceride level may be attributed to the inhibition of lipolysis [19], to depression in hepatic gluconeogenesis as with glibenclamide or to saponins whose antioxidant activities may have interfered with fatty acid oxidation [18]. A reduction in the level of total cholesterol is

normally followed by a concurrent reduction in LDL level, hence the observed reduction in LDL level is understandable. Liver dysfunctions in diabetes mellitus are caused by overworking of the liver whose work is to maintain normal glucose levels by storing excess glucose as glycogen [20]. Since the cells are resistant to insulin, the liver gets overworked by producing more glucose. Liver dysfunction could also arise due to the toxic effect of alloxan on the liver, which distorts of the membranes of the hepatocyte, thereby leading to enzyme leakage [21]. From the study, the levels of AST and ALT were greatly reduced in the extract fed groups when in comparison to both negative and positive control groups. This harmonizes with previous works who reported that flavonoids, saponin, anthraquinones, alkaloids, tannin, and anthacyanosides in medicinal plants like *Carica papaya* possesses hepatoprotective actions [22]. This shows that *Carica papaya* has an ameliorative effect on the liver. The catabolism of erythrocytes produces bilirubin, which goes through the liver for processing before being excreted through stool. An abnormal increase in blood bilirubin level is an indication of liver damage since it cannot process bilirubin properly. The elevated level of serum total bilirubin in the negative group confirms hepatic lesion [23] indicating the compromised capacity of hepatocytes ability to conjugate bilirubin. The reduced bilirubin level in the extract groups was maybe unconnected with

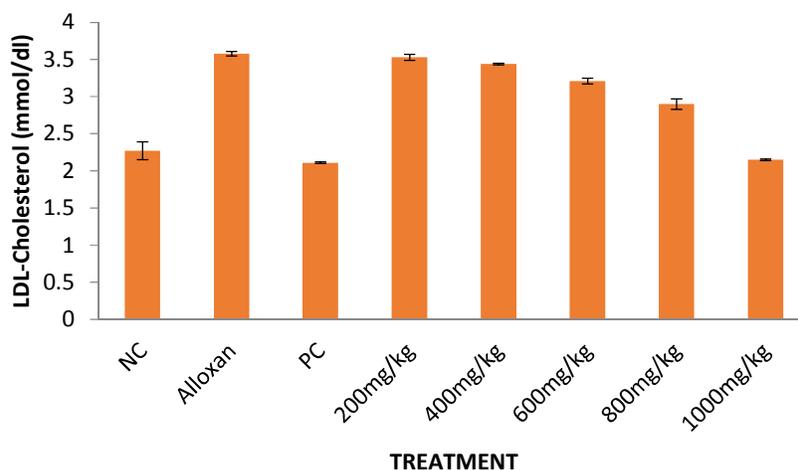


Fig. 4. Effects of *Carica papaya* on LDL-Cholesterol of diabetic rats

Data are expressed as mean \pm SD.; n = 5. One-way analysis of variance (ANOVA) followed by POSTHOC test ($p < 0.05$). The result showed a significant decrease ($p < 0.05$) in 1000 mg/kg extract when compared to alloxan treated group while no significant difference was recorded when compared to positive control (PC).

NC= Negative Control, PC= Positive Control

hepatoprotective and membrane stabilization potentials of the antioxidants present in *Carica papaya* extract. It has been reported that amino acid intake or protein synthesis in the liver is suppressed in cases of hepatic disorders [24]. Hypoinsulinemia increases protein catabolism which may have caused a straight and unexpected adverse effect on the synthesis and secretion of albumin and globulin. Also, the

elevated levels of serum total proteins in diabetic rats treated with methanol extract of the unripe pulp of *Carica papaya* may be related to the recovery of serum insulin levels which agreed with results obtained by Sivajothi (2008). Extract treatments from the study showed an increase of total protein, globulin and albumin which shows the ameliorative action of *Carica papaya*.

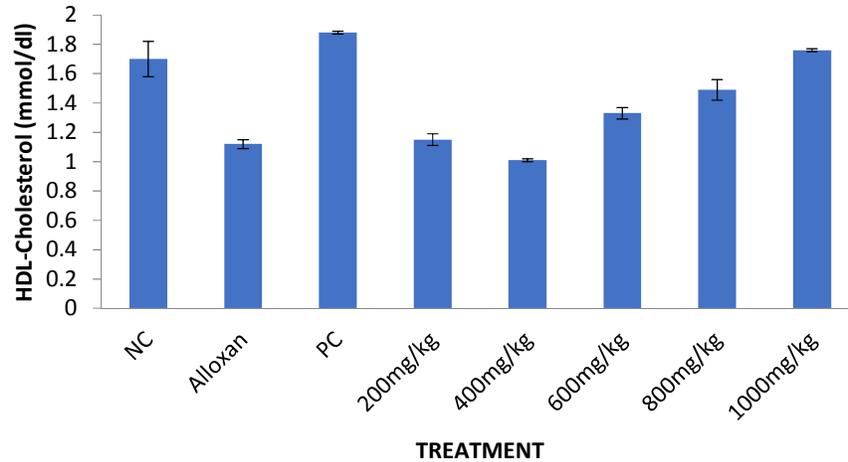


Fig. 5. Effects of *Carica papaya* on HDL-Cholesterol of diabetic rats
 Data are expressed as mean \pm SD.; n = 5. One-way analysis of variance (ANOVA) followed by POSTHOC test ($p < 0.05$). The result showed a significant increase ($p < 0.05$) in 1000 mg/kg extract when compared to alloxan treated group while no significant difference was recorded when compared to positive control (PC).
 NC= Negative Control, PC= Positive Control

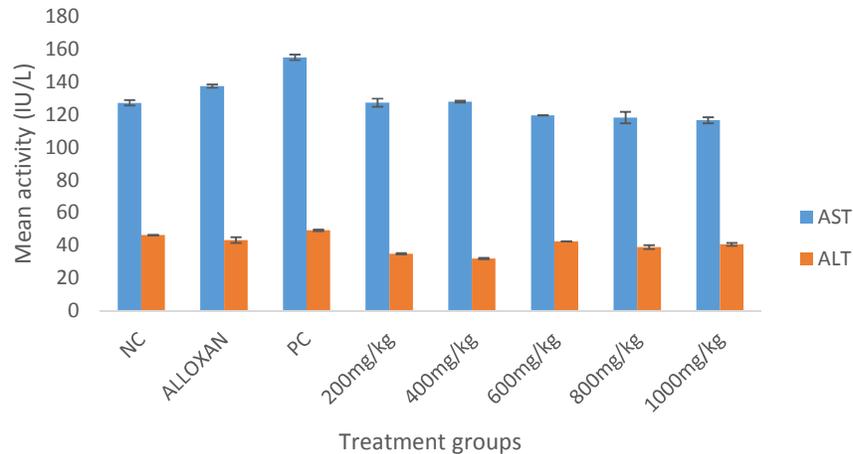


Fig. 6. Effects of *Carica papaya* on AST and ALT levels of diabetic rats
 Data are expressed as mean \pm SD.; n = 5. One-way analysis of variance (ANOVA) followed by POSTHOC test ($p < 0.05$). The result showed a significant decrease ($p < 0.05$) in all the extract-treated groups when compared to alloxan and positive control (PC) treated group while no significant difference was recorded between the extract-treated group. NC= Negative Control, PC= Positive Control

Table 2. This shows the mean and standard error of the mean of the lipid profile and liver function parameters of all groups of the research project

Treatment (mg/kg)	NC	Alloxan	PC	200 mg/kg	400 mg/kg	600 mg/kg	800 mg/kg	1000 mg/kg
Glu (mg/dL)	72.5±0.6	443.5±1.7	66.5±1.2	187.5±2.9	164.0±2.3	103.5±2.0	92.0±2.3	77.0±0.6 ^a
Chol (mmol/L)	4.17±0.03	4.20±0.06	4.22±0.01 ^a	4.90±0.12 ^b	4.67±0.01	4.78±0.03 ^b	4.60±0.01	4.10±0.01 ^a
TAG (mmol/dL)	1.01±0.12 ^a	1.18±0.03	1.13±0.01	1.06±0.04 ^a	1.14±0.01 ^b	1.18±0.04 ^b	1.04±0.07 ^a	0.97±0.01 ^a
LDL-C(mmol/dL)	2.27±0.08	3.58±0.20	2.11±0.05 ^a	3.53±0.01 ^b	3.44±0.03 ^b	3.21±0.08	2.90±0.08	2.15±0.01 ^a
HDL-C(mmol/dL)	1.70±0.06	1.12±0.14	1.88±0.04 ^a	1.15±0.13 ^b	1.01±0.04 ^b	1.33±0.06 ^b	1.49±0.10 ^a	1.76±0.02 ^a
AST (IU/L)	127.1±1.65	137.3±1.00	154.9±1.70	127.2±2.50 ^a	127.9±0.55 ^a	119.5±0.80	118.1±3.50	116.5±1.85
ALT (IU/L)	46.4±0.10	43.4±1.75	49.3±0.45	35.0±0.35	32.1±0.35	42.6±0.05	39.1±1.25	40.7±0.90
TP (g/dL)	5.67±0.33 ^b	5.58± 0.05	3.95± 0.11	5.89± 0.08 ^a	4.91± 0.24	5.00± 0.25	4.83± 0.24	4.97± 0.11
ALB (g/dL)	2.96±0.12	2.98±0.20 ^a	3.16±0.19	3.50±0.06	1.87±0.19	1.90±0.18	2.94±0.13 ^a	2.89±0.17
BL (Mg/dL)	1.95±0.14	2.00±0.05	2.19±0.05 ^b	1.92±0.16 ^b	1.87±0.19 ^b	1.90±0.18 ^b	1.79±0.04 ^b	1.79±0.20 ^b

Data are expressed as mean ± S.E.M.; n = 4. One-way analysis of variance (ANOVA) followed by POSTHOC test ($p < 0.05$). ^aNon-significantly different from normal control (NC); ^bNon-significantly different from negative control (alloxan) ($p > 0.05$). Glu (Glucose), Chol (Cholesterol), TAG (Tryacylglycerols), LDL-C (Low-density lipoprotein cholesterol), HDL-C (High-density lipoprotein cholesterol), AST (aspartate aminotransferase), ALT (alanine aminotransferase), TP (total protein), ALB (albumin), and BL (bilirubin)

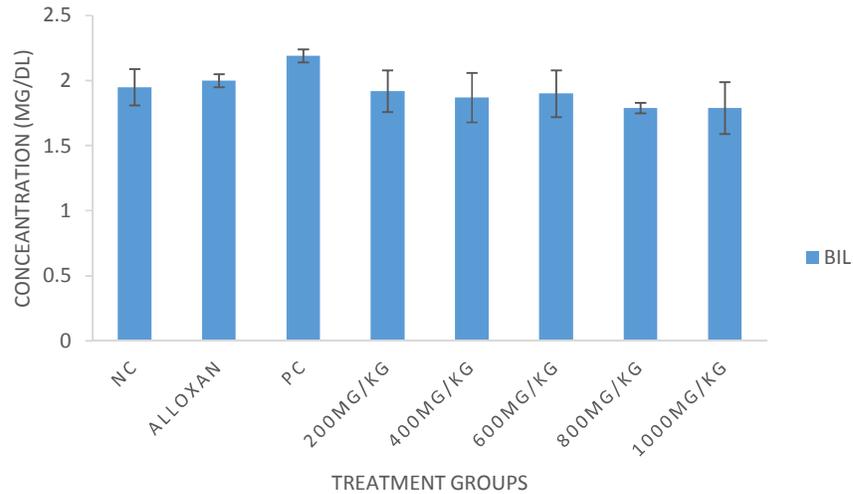


Fig. 7. Effects of *Carica papaya* on Bilirubin level of diabetic rats
 Data are expressed as mean \pm SD.; n = 5. One-way analysis of variance (ANOVA) followed by POSTHOC test ($p < 0.05$). The result showed no significant difference between the treatment groups. NC= Negative Control, PC= Positive Control

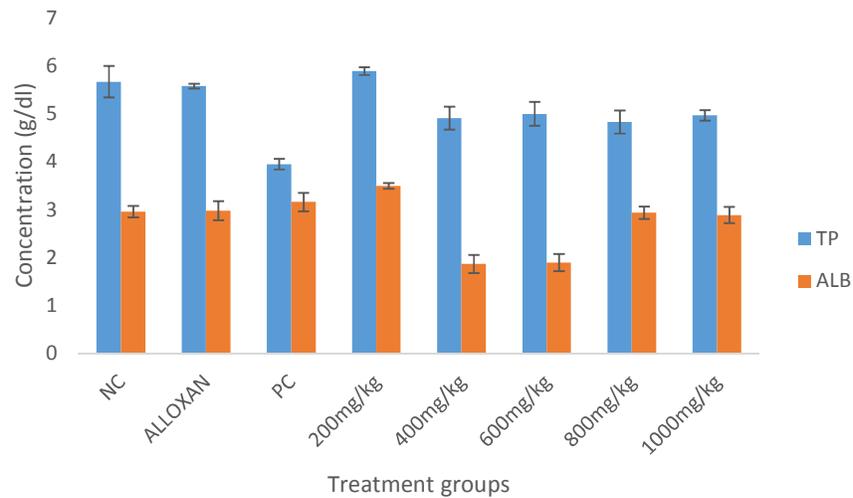


Fig. 8. Effects of *Carica papaya* on total protein and Albumin of diabetic rats
 Data are expressed as mean \pm S.E.M.; n = 5. One-way analysis of variance (ANOVA) followed by POSTHOC test ($p < 0.05$). NC= Negative Control, PC= Positive Control

5. CONCLUSION

The administration of *Carica papaya* methanol extract to diabetic rats showed hypoglycemic, hypolipidemic and ameliorative effects on liver function parameters. This further suggests that the extract may be working in the same mechanism as the standard drug, glibenclamide. However, we recommend that further studies be carried out to characterize the biomolecules

eliciting this effect and determine their mechanism of action.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not

intend to use these products as an avenue for any litigation but the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by the personal efforts of the authors

ETHICAL APPROVAL

The Ethics Board of Michael Okpara University of Agriculture approved and evaluated the procedures of this study. The study was also in accordance with the policies of the Animal Care and Use Committee of the Faculty of Biochemistry, Michael Okpara University of Agriculture.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ime FA, Atangwho IJ, Regina I et al. Hypoglycemic effect and proximate composition of some selected Nigerian traditional diets used in management of diabetes mellitus. *Eur J Food Res Rev.* 2011;1(2):94–101.
2. Anuradha G, Malini S, Jyoti S. A role of insulin in different types of diabetes. *Int J Curr Microbiol App Sci.* 2015;4(1):58-57.
3. Scott AR, Clarke BE, Healy H et al. Microvascular complications in cystic fibrosis – related diabetes mellitus; a case report. *Pancreas.* 2000;1(4):208-210.
4. Chatila R, West AB. Hepatomegaly and abnormal liver tests due to glycogenesis in adults with diabetes. *Medicine.* 1996;75: 327–333.
5. Lenzen S, Panle V. Alloxan; history and mechanism of action. *Diabetologia.* 1988; 31:337- 342.
6. Aloulou A, Hamden K, Elloumi D et al. Hypoglycemic and anti-lipidemic properties of kombucha tea in alloxan-induced diabetic rats. *BMC Complement Altern Med.* 2012;12:63.
7. Abayomi S, Eytape O, Adedeji O. The role and place of medicinal plants in the strategies for disease prevention. *Afr J Tradit Complement Altern Med.* 2013;10(5): 210–229.
8. Okpe O, Ibrahim S, Njoku GC, et al. Pancreatic islet regeneration and some liver biochemical parameters of leaf extracts of *Vitex doniana* in normal and streptozotocin-induced diabetic albino rats. *Asian Pac J Trop Biomed.* 2014;4(2):124-130.
9. Adeneye AA, Olagunju JA. Preliminary hypoglycemic and hypolipidemic activities of the aqueous seed extract of *Carica papaya* Linn. in Wistar rats. *MOJ Biology and Medicine.* 2009;1(1):1-10.
10. Venkateshwarlu E, Dileep P, Rakesh KR, et al. Evaluation of antidiabetic activity of *Carica papaya* seeds on streptozotocin-induced type-II diabetic rats. *Journal of Advanced Applied Scientific Research.* 2013;4(2):38–41.
11. Juárez-Rojop IE, Díaz-Zagoya JC, Ble-Castillo JL, et al. Hypoglycemic effect of *Carica papaya* leaves in streptozotocin-induced diabetic rats. *BMC Complement Altern Med.* 2012;12:236.
12. Nwangwa EK, Ekhoye EI. Anti-hyperlipidemic activity of aqueous extract of *Carica papaya* seed in albino rats fed with high fat diet. *Curr Trends Tech Sci.* 2013;2(3):262-6.
13. Arun KS, Vinay KS. *Carica papaya*- A herbal medicine. *Int J Res Stud Biosci.* 2016;4(11):19-25.
14. Daniele S, Luca R, Gian P, et al. Sulfonyleureas and their use in clinical practice. *Arch Med Sci.* 2015;11(4):840-848.
15. Bolkent S, Yamardag R, Tabakogluoguz A et al. Effects of chord (*Beta vulgaris* L. Var. cicla) extract on pancreatic β -cells in Streptozotocin-diabetic rats: A morphologic and biochemical study. *J. Ethnopharmacol.* 2000;73:251–259.
16. Changting X, Mirjana Pavlic, Linda S, et al. Effects of acute hyperglucagonemia on hepatic and intestinal lipoprotein production and clearance in healthy humans. *Diabetes Care.* 2012;60(2):383-390.
17. Zetina-Esquivel AM, Carlos AT, Crystell GG, et al. Effect of *Carica papaya* leaf extract on serum lipids and liver metabolic parameters of rats fed a high cholesterol diet. *SCIRP.* 2015;7:1196-205.
18. Rao AV. Role of dietary sources of saponins in chemotherapy strategy of lowering the risk of human cancers. *Univ. Tor.* 1993;219-225.
19. Owoyele BV, Yakubu MT, Alonge F et al. Effects of folic acid intake on serum lipid profile on apparently healthy young adult male Nigerians. *Afr. J. Biomed. Res.* 2005; 8:139-142.

20. Brain J, Welch MD, Ivana Z. Diabetic ketoacidosis in Type 2 Diabetes. *J Diabetes Res.* 2004;22(4):198–200.
21. El-Demerdash FM, Yousef MI, Abou-El-Naga NI. Biochemical study on the hypoglycemic effects of onion and garlic in alloxan-induced diabetic rats. *Food Chem. Toxicol.* 2005;43:57–63.
22. Recknagel RO, Glende EA, Dolak JA, Waller RL. Mechanisms of carbon tetrachloride toxicity. *Pharmacol. Ther.* 1989;43(1):139-154.
23. Emang E, Helal NA, ALSayed MK, Mohammad AZ. Anti-diabetic effect of artemisia annua (Kaysom) in alloxan-induced diabetic rats. *Egypt. J. Hosp. Med.* 2014;57:422-430.
24. Sivajothi V, Dey AB, Jayakar BR. Antihyperglycemic, antihyperlipidemic and antioxidant effect of *Phyllanthus rheedii* on streptozotocin induced diabetic rats. *Iran J Pharm Res.* 2008;7(1): 53-59.

© 2020 Ogbonna et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

*The peer review history for this paper can be accessed here:
<http://www.sdiarticle4.com/review-history/56663>*