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Antidiabetic and Protective Effects of Aqueous Seed Extract of *Persea americana* in the Pancreas of Alloxan-Induced Diabetic Wistar Rats

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The global rise in diabetes mellitus poses a significant challenge to primary healthcare, especially in developing countries. This study aimed to evaluate the effects of aqueous seed extract and pericarp oil of *Persea americana* on the pancreas of alloxan-induced diabetic male Wistar rats. Fifty-six adult male Wistar rats were divided into eight groups of seven rats each. Group A served as the control, receiving only food and water. Groups B to H were made diabetic by intraperitoneal injection of alloxan at 200 mg/kg body weight. Group B received no further treatment. Group C was treated with pericarp oil at 100 mg/kg body weight. Groups D and E received pericarp oil and seed extract respectively, at 200 mg/kg body weight. Group F received both pericarp oil and seed extract, each at 200 mg/kg body weight. Group G received a combination of pericarp oil, seed extract, and the

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standard drug metformin. Group H received only metformin. Blood glucose levels and body weight were recorded at two and four weeks. Significant decreases in blood glucose levels ($P<0.05$) were observed in all treatment groups compared to Group B. Significant body weight increases were noted in Groups C, D, and E compared to Group B ($P<0.05$). These findings suggest that *Persea americana* extracts possess antidiabetic properties, possibly due to their phytochemical contents, and may improve nutrient utilization, as evidenced by weight gain. The seed extract of *Persea americana* may offer therapeutic benefits in managing diabetes mellitus.

Keywords: Avocado pear; Persea americana; alloxan; diabetes; serum glucose.

1. INTRODUCTION

"Diabetes mellitus (DM) is incredibly the world's quickest growing metabolic disorder and as the heterogeneity knowledge of this disorder becomes obvious so does the need for more appropriate and good therapies" [1]. "DM is a condition that is pathological and results in chronic metabolic imbalances and non-physiologic changes in organic tissues" [2]. "Oxidative stress plays important roles in the aetiology of several terminal diseases including DM. Diabetes is linked with building up of reactive oxygen species (ROS) which can cause oxidative damage in the heart, kidney, eyes, liver, small and large blood vessels and gastrointestinal system" [3].

"Increased level of glucose concentration directly increases hydrogen peroxide production by murine mesangial cells and lipid peroxidation of glomeruli and glomerular mesangial cells" [4]. "Hyperglycaemia supports glycosylation of circulating cells and cellular protein and may introduce a series of auto-oxidative reactions that culminate in accumulation of advanced glycosylation as end-products (AGE) in tissue proteins. The AGE has an oxidizing potency and can support tissue destruction by free radicals" [5]. Furthermore, increased peroxidation of lipids retards a membrane's function by reducing membrane fluidity nature and changing the activity of bound-membrane enzymes and receptors alike. Its end-products (lipid radicals and peroxides), are harmful to the cells in the body and are connected with atherosclerosis and destruction of the brain, kidney, liver and other tissues alike.

"Alloxan-induced diabetes has been commonly employed as an experimental model of insulin dependent diabetes mellitus. The mechanism of alloxan action has been studied and can be properly characterized" [4]. "Several experimental studies have demonstrated that alloxan evokes a sudden rise in insulin secretion in the presence or absence of glucose which appears just after alloxan treatment. This alloxan-induced insulin release occurs for short duration followed by the complete suppression of the islet cells" [4]. "Furthermore, the alloxan action in the pancreas is preceded by its rapid uptake by pancreatic beta cells that have been proposed to be one of the important features determining alloxan diabetogenicity. Moreover, in pancreatic beta cells, the reduction process occurs in the presence of different reducing agents like reduced glutathione (GSH), cysteine, ascorbate and protein-bound sulfhydryl (-SH) groups" [3].

"The International Diabetes Federation (IDF) reports that the prevalence of diabetes mellitus has reached epidemic levels globally. Recent estimates" [3] indicate that there were 366 million diabetics worldwide in 2020, and this number is expected to increase to 552 million by 2030. Impaired glucose tolerance in sub-Saharan Africa is expected to rise by 75.8%, from 26.9 million in 2010 to 47.3 million in 2030, which is more than double the predicted global increase of 37%. Mortality that was attributable to diabetes in sub-Saharan Africa was estimated in 2010 to be 6% of the total mortality, and this value had increased from 2.2–2.5% in 2000. The absolute and relative mortality rates are highest in the 20–39 years age-group, i.e., the most economically productive population. In Nigeria, which has over 250 tribes and different culture and food values, the prevalence values of diabetes have not been uniform, [3] although the values range from 1–7% of the Nigerian population. Over 30 years, the prevalence of diabetes has steadily increased. Iloh et al. [6] reported a prevalence of 3.9% for Imo state. However, a higher prevalence rate was reported in Port Harcourt (6.8%) by [7]. "The Diabetes Association of Nigeria (DAN) estimates the diabetic population in Nigeria to be approximately 10 million, and approximately half of that number resides in the Lagos State because of its cosmopolitan nature. These findings indicate that diabetes has become a major public health issue" [3].

"Plants and plant products have been utilized in folkloric medicine in the treatment and management of disease conditions. Plants may act on blood glucose through different mechanisms. Some plants may contain insulin-like substances, inhibit insulinase activity or increase beta β-cells in the pancreas by activating the regeneration of these cells or some may serve as antioxidants by reducing the oxidative stress due to free radicals in the pancreas. *Persea americana* (avocado) is a tree that belongs to the laurel family, *Lauraceae*, and is one of the 150 varieties of avocado pear. This plant is indigenous to Central and South America, but it is now cultivated in the United States of America, Asia, parts of Europe, and Tropical Africa and is commonly known as avocado pear" [3]. "The medicinal relevance of the various parts of this tropical plant is enormous. The effects of aqueous seed extracts of *Persea americana* on blood pressure, plasma and tissue lipids of albino rats were investigated by Imafidon and Amaechina [8], and their results suggested that the use of the aqueous seed extract of this plant in the treatment of hypertension might produce a favourable lipid profile. Alhassan and colleagues also evaluated the hypoglycaemic activity of *P. americana* aqueous seed extracts on alloxan-induced diabetic rats and concluded that the anti-diabetic effects of the extract might be due to certain mineral elements and phytochemicals". However, the work by Okonta et al. [9] suggests that "*P. americana* can lower blood glucose levels in cases of mild hyperglycemia but not severe hyperglycemia". Edem et al. [10] studied "the effects of aqueous alligator pear seed extracts on normal and alloxan-induced diabetic rats, and their results suggested a restorative (protective)" [3] effect of the extract on pancreatic islet cells. The work of Mahadeva et al. [11] concentrated on the mechanism of the antidiabetic activity of *P. americana*. "The insulin-stimulative and antioxidative effects of *Persea americana* were evaluated in streptozotocin (STZ)-treated rats. They found that the activities of pathophysiological enzymes such as serum aspartate transaminase (AST), serum alanine transaminase (ALT), and serum alkaline phosphatase (ALP) were altered in the serum of rats that had been treated with glyclazide, which was used as the standard reference drug, but not control rats. These results revealed the tissue protective nature of *Persea americana* fruits" [12].

The pancreas is a long, soft organ in the upper left abdominal region. It sits below the liver, behind the stomach, and extends from the upper part of the small intestine to the spleen. The main function of the pancreas is to produce chemicals in the correct quantities to help people digest and process the foods they consume. It has both exocrine and endocrine functions.

As an exocrine gland, the pancreas produces enzymes, such as trypsin, chymotrypsin, amylase, and lipase in the pancreatic juice, which help break down food. These pancreatic juices are released into the pancreatic duct and join the common bile duct, which originates in the liver. The juices then enter the first part of the small intestine, where they begin digesting food. As an endocrine gland the pancreas has a group of cells known as the islets of Langerhans which produce insulin and glucagon that maintain the balance of blood sugars.

2. MATERIALS AND METHODS

2.1 Location and Ethical Approval

This research was carried out using adult Wistar rats. The materials used were standard and were used within the University where the research was conducted. Ethical Approval for this study was gotten from the Research ethics committee of the Faculty of Basic Medical Sciences, College of Health Sciences, Nnamdi Azikiwe University, Nnewi campus with Ref: NAU/AREC/ TEMP/2024/00001.

Fifty-six adult Male Wistar rats, 20 pieces of pear fruits, 20 pear seeds, laboratory pipettes, a glucometer (accu check glucometer), insulin test kits, alloxan monohydrate, digital weighing balance, heparinized capillary tube, rat standard pellets meal, EDTA bottles for blood sample serum collection, metformin standard drug, hand gloves, chloroform, enclosed suitable cages, alcohol, cotton, preservative beakers, microscopes, hematoxylin and eosin, histological slides.

3. COLLECTION AND PREPARATION OF PLANT MATERIALS

The Fruits and seeds of avocado pear were obtained from Ekeoka market, Awka, Anambra State. The fruits were cut and dried through several shifting, then powdered with grinder before being sieved. 400g of the powdered fruit was soaked in 1000ml of distilled water for 24 hours at room temperature with occasional vigorous shaking. It was then filtered with Whatman filter paper, and the filtrate was dried in

water bath and stored in refrigerator for further use. During experiment the crude extract was diluted with distilled water to make the stock solution before administration of extract to animals.

3.1 Chemicals

Reagents used during research were of analytical grade.

3.2 Maintaining Animals

Fifty-six adult male Wistar rats, weighing 150–220 g were used in this study. They were housed in clean metal cages and maintained in the animal house at a 12-hour light to dark present cycles. The animals were permitted to acclimatize to condition of laboratory for one week before the administration. Standard Pellets meals were given to animals and used as their diet during the period of the experiment. The control and experimental animals were provided with clean tap water ad libitum. The animals were maintained in accordance with the "CPCSEA guidelines for laboratory animal facility". Before, the experiment began, the animals were consciously marked on different parts of their hairy bodies for identification.

3.3 Induction of Diabetes in Experimental Animals

Diabetes was induced in overnight fasted male Wistar rats by a single intraperitoneal injection of alloxan monohydrates at 200 mg/kg body weight. Blood glucose level of the rats was taken 72 hrs after alloxan administration, and diabetes was confirmed using a blood glucometer (Accu Check Sure, Taiwan). Blood samples were collected from the tip of the tail. Animals with blood glucose level equal to or more than 200 mg/dL were assigned diabetic and were used for the experiments.

Eight groups of Rats, 7 rats in each group received treatment schedules as follows

Group A: Control without alloxan treatment

Group B: Alloxan induced at 200 mg/kg of weight.

Group C: Alloxan induced at 200mg/kg body weight i.p. + pericarp pear oil, (extract of fruit at the dose, 100 mg/kg of body weight);

Group D: Alloxan induced at a dose 200 mg/kg of weight of body i.p. + pericarp pear oil (extract of fruit at 200 mg/kg body weight dose)

Group E: Seed oil only (extract of fruit at 200 mg/kg dose of body weight).

Group F: 150 mg/kg alloxan induction of body weight + pericarp pear oil (fruit extract at the dose of 200 mg/kg body weight) + seed oil (fruit extract at the dose of 200 mg/kg body weight).

Group G; Pear oil + Seed oil + Control drugs metformin

Group H; Alloxan 200mg/kg induction + metformin, (standard drug).

3.4 Termination and Sample collection

Whole blood was used for glucose test and Plasma was used for insulin assay using Radio Immune Assay (RIA) kit for rats. Superoxide Dismutase (SOD), catalase (CAT), Glutathione Peroxide (GPx), Glutathione (GSH) and Glutathione-S-transferase (GST) were determined. After the last doses, animals were fasted 12 hours and sacrificed by cervical dislocation. Blood samples were collected by ocular puncture before sacrifice. Serum was separated from the clot by centrifuging at 3000 rpm for 15 min. Serum check analysis of blood glucose concentration of fasted animal was measured by available glucose kit (coral clinical system, Goa, India) on basis of Trinder.

After blood collection, rats were sacrificed by cervical dislocation and the pancreas from each animal harvested and fixed in 10% formal saline and used for histological examination using the H&E method.

3.5 Statistical Analysis

Data were presented as Mean ± Standard deviation per group. Statistical analysis was done using SPSS version 25. Data was analyzed using one way analysis of variance (ANOVA) followed by least significant difference (LSD) test and Paired Student's t-test to see any difference between the paired groups. Values were considered statistically significant at $P<0.05$.

4. RESULTS

4.1 Physical and Weight Observations

At the beginning of the experiment, all animals were apparently healthy and agile. During the period of inducing diabetes with alloxan, animals showed signs of heavy breathing, weakness, fatigue and loss of appetite. The body weights of the control and experimental groups were recorded.

Table 1. Result of changes in rat weight

Groups	Weights(g)	MEAN ± SEM	t-Value	p-value
A	Initial	170.08±3.74	-5.027	0.015
	Final	196 ± 0.12		
B	Initial	170.58±2.95	-3.534	0.039
	Final	143.75±12.79		
C	Initial	178.63±8.89	-3.759	0.064
	Final	218.90±6.52		
D	Initial	152.54±0.58	-1.679	0.235
	Final	198.80±6.42		
E	Initial	168.63±8.89	-3.742	0.65
	Final	218.90±6.52		
F	Initial	153.53±0.58	-3.679	0.39
	Final	199.80±26.76		
G	Initial	153.56±0.56	-3.756	0.64
	Final	200±6.53		
H	Initial	153.53±0.53	-3.759	0.235
	Final	199.90±27.79		

Table 2. Shows glucose level of rats for 4 weeks

Week	Groups	Mean+_SEM	P-Value
Week 2	A	106.667+_4.48	0
	B	350.65+_5.91	0.857
	C	261.000+_10.94	0.109
	D	251.000+_10.92	0.112
	E	93.33+_4.41	0.085
	F	106.667+_4.41	0.089
	G	262.000+_63.18	0.075
	H	212.000+_62.18	0.085
Week 3	A	112.3321+_4.40	0.214
	B	351.3333+_4.40	0.010
	C	119.500+_5.79	0.269
	D	260.000+_10.94	0.112
	E	251.000+_10.92	0.085
	F	241.000+_13.5332	0.089
	G	105.657+_3.3000	0.085
	H	200.651+_3.30	0.081
Week 4	A	119.533+_6.23	0.231
	B	360.667+_6.56	0.461
	C	173.3333+_49.69	0.174
	D	129.133+_6.43	0.798
	E	188.672+_58.86	0.269
	F	106.867+_4.40	0.269
	G	234.333+_4.40	0.797
	H	229.133+_6.43	0.785
Week 6	A	129.133+_6.43	0.087
	B	230.672+_58.86	0.085
	C	106.867+_4.40	0.089
	D	241.000+_13.5332	0.085
	E	105.657+_3.3000	0.085
	F	200.651+_3.30	0.089
	G	106.667+_4.41	0.075
	H	262.000+_63.18	0.798

Table 3. Result of Antioxidant Expression of Persea Americana in Male Wistar Rats

Groups	SOD (µm/mg protein)	CAT (µm/mg protein)	GPX (µm/mg protein)	GSH (µm/mg protein)	GST (µm/mg protein)
Group I(Control)	13.44+_0.34	73.09+_3.78	14.74+_0.43	49.17+_4.56	7.13+_0.23
Group II (Alloxan)	3.78+_0.08	32.13+_1.43	4.63+_0.07	22.56+_1.34	3.27+_0.97
Group III (Pear Oil)	13.40+_0.35	75.09+_4.72	13.40+_0.45	35.23+_2.78	6.98+_0.35
Group IV (Seed Oil)	8.64+_0.68	62.34+_4.28	8.72+_0.37	22.56+_3.23	6.95+_0.37
Group V (Alloxan +Pear Oil)	8.63+_0.65	63.86+_2.37	8.70+_0.37	23.56+_3.23	5.96+_0.15
Group VI (Alloxan +Seed Oil)	8.64+_0.55	64.82+_2.32	8.14+_0.23	23.54+_3.21	6.98+_0.35
Group VII (Alloxan+Seed Oil+Pear Oil	8.92+_0.52	62.83+_2.38	8.15+_0.26	22.56+_3.25	3.23+_0.32
Group VIII (Alloxan +Metformin)	8.97+_0.44	63.85+_2.36	8.14+_0.25	23.96+_3.23	3.25+_0.31

Rats in the Control group A had significant increase in body weight. Group B that received alloxan without treatment alloxan had significant weight reductions. Group C that received alloxan 200mg/kg body weight had significantly increased body weight. Group D and E also has significant body weight gain (Table 1).

The result of rat weight changes presented in Table 1 showed that rats in the control group A had a significant weight gain at the end of the experimenting period compared to the initial weight. Rats in group B however had a significant weight loss following diabetes induction compared to the initial weight. Following treatment, there were no significant weight differences for rats in groups C to H, although they all show some form of weight gain at final compared to initial.

5. RESULT OF RAT GLUCOSE LEVEL

After induction of diabetes by alloxan, diabetes was confirmed by the presence of hyperglycemia in animals and the mean level of glucose in the control group of rats was evaluated to be (range: 60–95) mg/dl, but 190 to 270 mg/dL in alloxan only group B. After the treatment of rats with the fruit extract of Avocado oil and its pericarp seed oil, the level of glucose decreased down to mg/dL with a range value of 156–220 mg/dL. The significant glucose concentration increases in the animals that are diabetic in comparison to that of the controlled rats is shown on the induction of alloxan. However, the oral administration of aqueous extract of Avocado fruit significantly reduced the glucose level in serum when compared with alloxan induced diabetic rats.

Effect of aqueous extract of *persea americana* on the serum glucose levels in alloxan induced rats. Values are the means ± S.D for seven animals in each group. Normal rats were compared with Diabetic rats. There was increased level of glucose at the initiating stages causing hyperglycemia, diabetes caused destruction of pancreatic islets of Langerhans cells. But at the addition of pericarp pear oil and seed oil fruits extract, serum glucose levels reduced.

Result of Histopathological Examination:

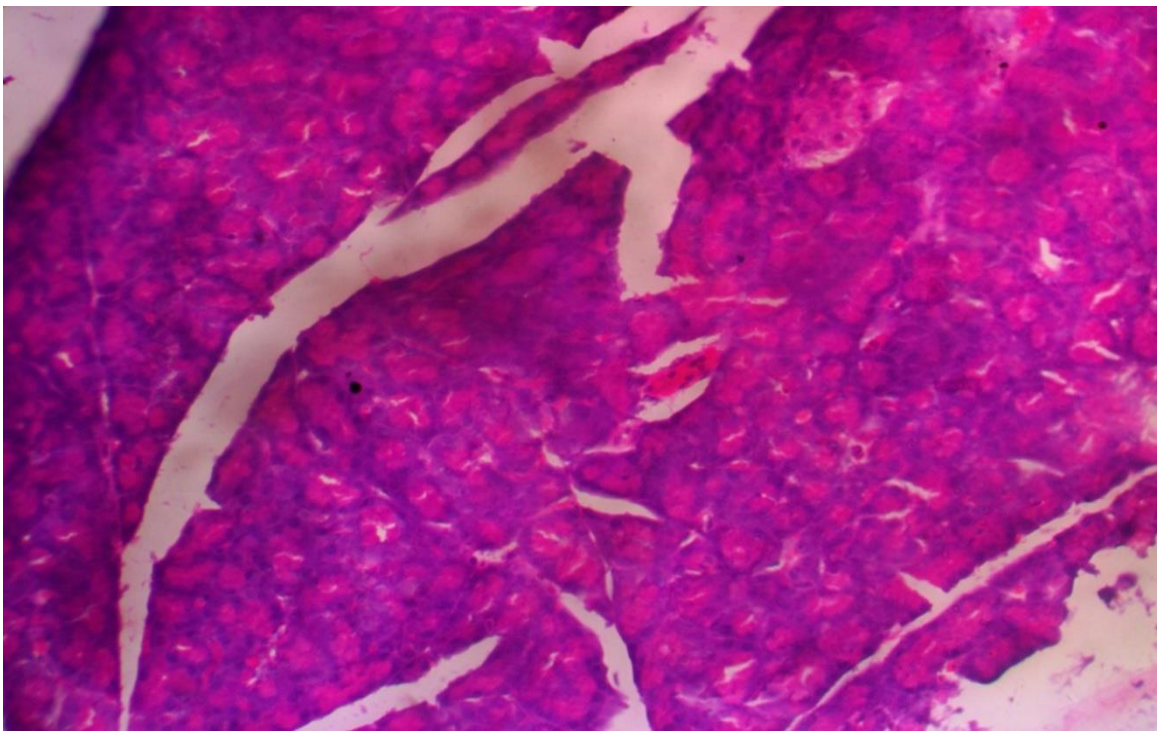

Plate 1. Control Rat pancreas which indicate normal histological features of endocrine pancreas in control group A (H&E) X 100). Photomicrograph section of pancreas shows well-spaced pancreatic acinar (PA) and Islets of Langerhans (IL) appearing normal.

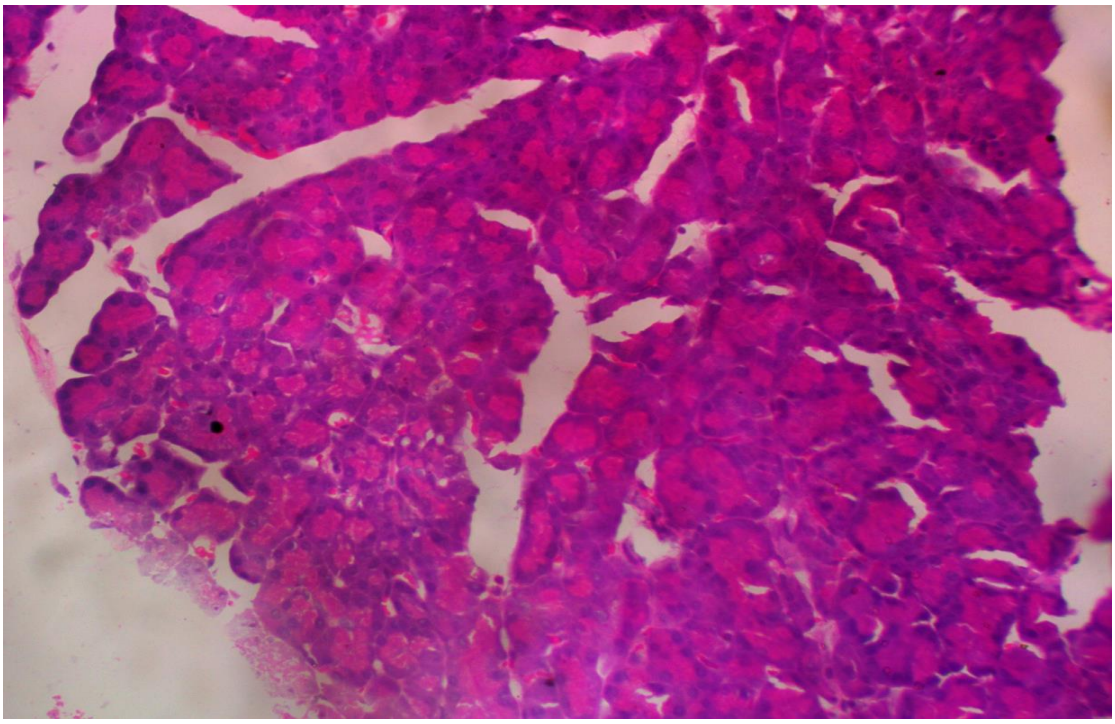

Plate 2. Shows group B alloxan effect on the pancreatic islets of langerhans shows Photomicrograph section of pancreas degenerated pancreatic acinar (PA) and Islets of Langerhans appearing abnormal

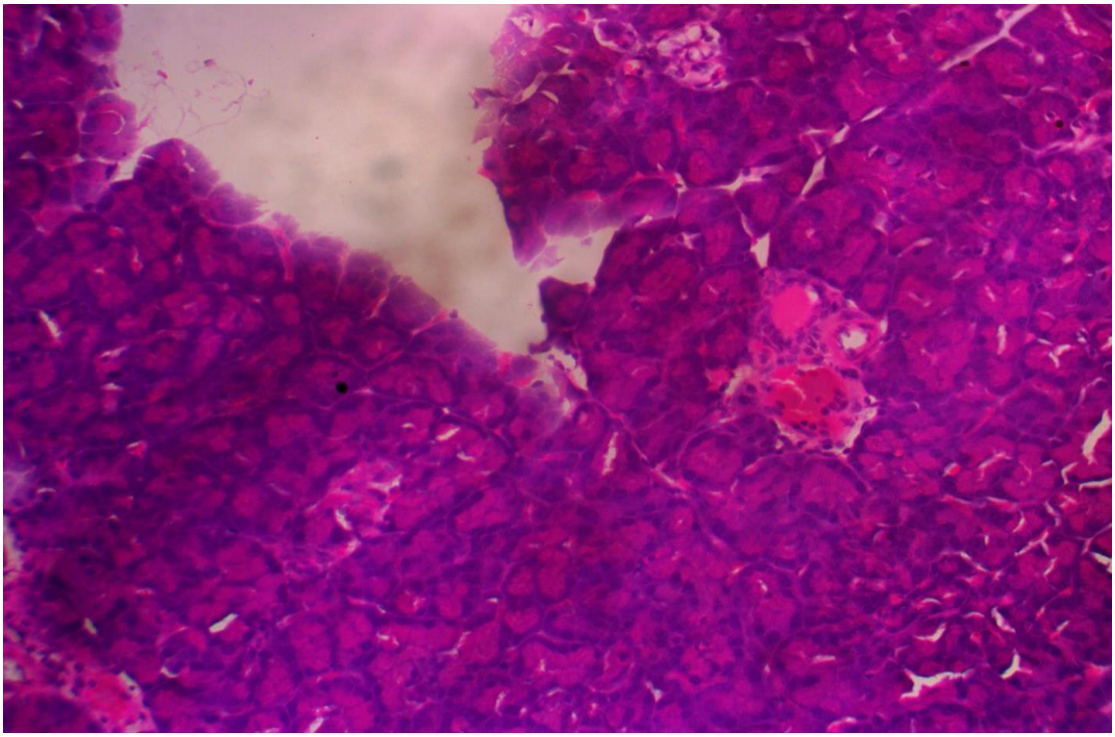

Plate 3. Which indicate normal histological features of endocrine pancreas in group c (H&E) X100). Photomicrograph section of pancreas shows well-spaced pancreatic acinar (PA) and Islets of Langerhans appearing well prominent on treatment of Pear and Seed oil extracts.

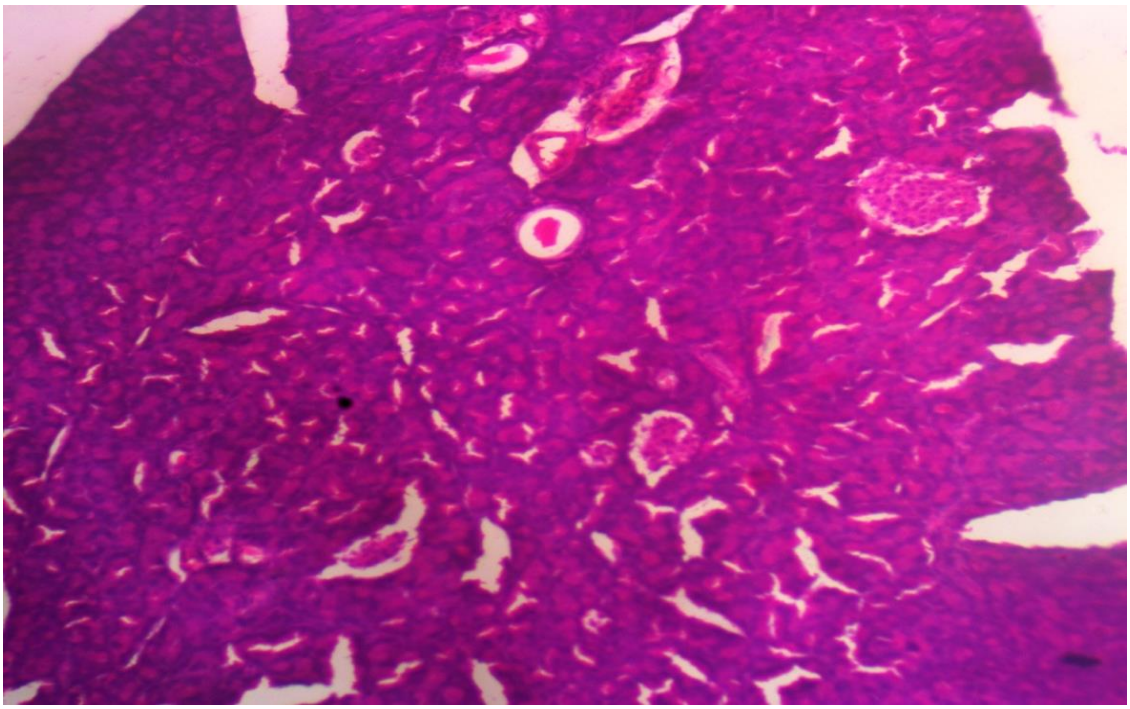

Plate 4. Indicate slightly abnormal histological features of endocrine pancreas in group V AND VI (H&E) *100). Photomicrograph section of pancreas shows abnormal pancreatic acinar(PA) and Islets of Langerhans(IL) appearing a little degenerated on treatment of Alloxan ,seed and Pear oil extracts

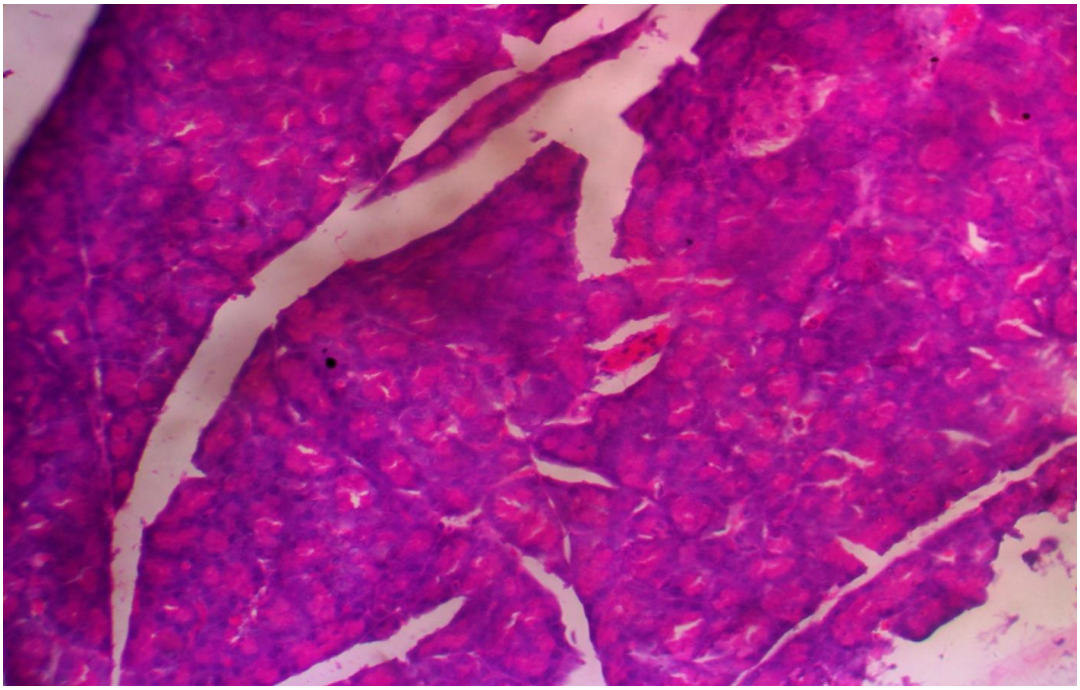

Plate 5. Which indicate slightly abnormal but rejuvenated histological features of endocrine pancreas in group VIII (H&E) X100).Photomicrograph section of pancreas shows abnormal pancreatic acinar (PA) and Islets of Langerhans appearing a little degenerated on treatment of Alloxan ,and Metformin standard drug

6. DISCUSSION, CONCLUSION AND RECOMMENDATION

6.1 Discussion

Plants are medicinal in nature and are the potential sources of bioactive agencies accepted and used worldwide. Studies on ethnomedicinal plants and medicinal herbals have been conducted in through time past and plants have been known for being used for purposes of medicine by tribe men in several nations [13].

In Table 1, before, during and after the acclimatization windows of the rats by treatment of *persea Americana* (Pear), seed and fruit oil extracts, and also inducing of alloxan monohydrate, and standard drugs, Metformin [14].

In Table 2 there was a significant increase in Anti-oxidant levels of SOD, CAT, GPx, GST. Group (A), Groups B, C, and D, seed oil in comparison to Groups, (B), (Alloxan group), Group E (Alloxan +Seed oil), Group, G, (Alloxan +Seed+ Pear Oil), Group H, (Alloxan+ Metformin). Groups, A, C, D, F, G had a relevant increase in weight of body in comparison to Groups B.E.F at p-value and t-value $p<0.05$.

For the Glucose level, during the 1st week of acclimatization blood Glucose Level remained normal, not until the second week and 4th week. During the second- fourth week (2-4) mortalities were observed especially, in Groups B (Alloxan Groups), as well as elevated blood glucose of all groups in 3rd & 4th week. Blood glucose levels began to stabilize in all groups following treatment with pear oil, seed oil, and standard drug and metformin. Alloxan is the most commonly used chemical to induce diabetes in experimental animals. High glucose ambience can support apoptosis by causing cellular destruction as a result of diabetic hyperglycemia [15] The Reactive oxygen species (ROS) are sacrosanct mediators of death of Beta cells during DM onset and development. High level of glucose has been stipulated to create ROS and species of nitrogen in cell types.

Superoxide Generation by high level of glucose is described and principally arise via the mitochondrial transport election chain [14].

The present study verified the changes in weight of body in control induced diabetic and treated animals for the period of the study as decrease in weight of the body is considered as a marker for diabetes development due to continuous glucose excretion and decrease in uptake periphery of glucose and synthesis of glycogen.

Results of our research are consistent with the research reported by others who revealed high level activities of lipid peroxidation in diabetic rats. Lipid which are peroxides are Known to be secondary by products of stress oxidation and are released as a result of the effect of toxic reactive oxygen species produced in lipid during peroxidation period of diabetes.. Peroxidation of Lipids (LPO) is one of the c features of cellular chronic diabetes. Diabetes is thought that hypoinsulinemia elevates the activities of enzyme, fatty acyl coenzyme-A oxidase, which introduces beta fatty acids oxidation, resulting in LPO. Elevated LP retards membrane activity by membrane fluidity and changing the activity of bound membrane-enzymes and receptors. LPO later on result in elevated production of radicals that are free harmful to cells of the body.

However, peroxide lipid mediated tissue destruction has been examined in the development of types I and II diabetes mellitus together with insulin secretion which is close associated with lipoxygenase-derived peroxides. Moreover, elevated LPO levels leads to cellular infiltration and islet cell destruction in diabetes. During this study, increased levels of lipid peroxidation were observed in alloxan rat treatment. There are many reports in literature that expresses the increased levels of lipid peroxides in the induced alloxan diabetic rats. However, “the hypoglycemic effect of the avocado fruit and seed extract may be due contents of elements such as calcium, magnesium, potassium, sodium, zinc, chromium etc. that play key role in blood glucose homeostasis by regulating the key enzymes involved in gluconeogenesis in the liver e.g. glucose-6- phosphatase, fruitcose-1, 6-bisphosphatatase and phosphoenolpyruvate carboxykinase, thereby blocking gluconeogenesis and enhancing glucose utilization in the body” [1],

“The seed may in addition to these elements contains certain hypoglycemic agents such as flavonoids, saponins, steroids, terpenoids, tannins and alkaloids etc which contain insulin stimulatory substances such as insulin receptors substrate (IRS), prohormone convertase, glycogen synthase, the b3 adrenergic receptor, glucose dependent insulinotrophic polypeptide

(GIP) receptor and peroxisome proliferators – activated receptor gamma [1,16]. However, the mechanism by which the extract lowered the blood glucose level in alloxan induced diabetic rats is still unclear. It could be by stimulating peripheral utilization of glucose by inhibiting absorption in the gastrointestinal tract (GIT), increasing glucose metabolism, or regenerating the pancreatic tissue or potentiating the insulin secretion by the surviving B- cells [17].

A prolonged administration of the extract shows higher hypoglycemic effects on alloxan induced diabetic rats than are shorter administration periods, and after withdrawal of the treatment for one week the blood glucose gradually raised, however below that of the untreated group. This signifies the management effect of the avocado seed extract. “The increase in weight of diabetic rats treated with avocado seed extract was found to be significant between diabetes groups treated with avocado seed and diabetic non-treated (Group II)” [17]. “This could be due to certain compounds and or mineral elements that may stimulate effective utilization of nutrients. In addition, the seed may contain nutrients such as protein and fat this coupled with their effective utilization, may be responsible for the weight gain” [17].

6.2 Conclusion

Data from this study indicate that the extract of *Persea Americana* fruit at (100,150,200 mg/kg body weight showed significant antihyperglycemic effect in diabetes induced rats. The plant extract exerted a dose-dependent protective effect on the pancreas like the reference drug Metformin. Taken together, the results of present study provide a pharmacological basis for the folkloric use of the hot-water extract of *Persea americana* seeds and Pericarp Pear oil in the management of diabetes mellitus. Furthermore, this study shows that the combination of the seeds and fruits can form good dietary combination for healthy meals and ready to use therapeutic foods.

6.3 Recommendations

I recommend that extensive researches be carried out with other doses and extraction methods and compare with standard drugs.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Authors hereby declare that NO generative AI technologies were used during the writing and editing of this manuscript.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical Approval was gotten from the Research ethics committee of the Faculty of Basic Medical Sciences, College of Medicine and Health Sciences, Nnamdi Azikiwe University, Nnewi campus. Ref: NAU/AREC/TEMP/2024/00001.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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