

"ANTIDIABETIC AND PANCREATIC PROTECTIVE EFFECTS OF AQUEOUS SEED EXTRACT OF *PERSEA AMERICANA* IN ALLOXAN-INDUCED DIABETIC WISTAR RATS"

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 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 content, and may improve nutrient utilization, as evidenced by weight gain. The seed extract of *Persea americana* may offer therapeutic benefits in managing diabetes mellitus.

Key Words: Avocado pear, *Persea americana*, Alloxan, Diabetes, Serum glucose

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 (Abdel MA, El-Feki M, 2020). DM is a condition that is pathological and results in chronic metabolic imbalances and non-physiologic changes in organic tissues (J. V. Hunt, M. A. Bottoms, 2020). Oxidative stress play 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 heart, kidney, eyes, liver, small and large blood vessels and gastrointestinal system (Evans and Gold fire, 2020).

Increased level of glucose concentration directly increases hydrogen peroxide produced by murine mesangial cells and lipid peroxidation of glomeruli and glomerular mesangial cells (, T. Tuvemo, U. Ewald, 2020). Hyperglycaemia supports glycosylation of circulating cells and cellular protein and may introduce a series of autooxidative reactions in that culminate in accumulation of advanced glycosylation as end-products (AGE) in tissue protein. The AGE has an oxidizing potency and can support tissue destruction by free radicals (J. E. Hall, and A.C Guyton ,2020). Furthermore, increased lipid 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 connected with atherosclerosis and brain destruction, 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. (T. Tuvemo, U. Ewald, 2020). Several experimental studies have demonstrated that alloxan evokes a sudden rise in insulin secretion in the presence or absence of glucose which appeared just after alloxan treatment. This particular alloxan-induced insulin release occurs for short duration followed by the complete suppression of the islet cells, response to glucose even when high concentrations of glucose were used (T. Tuvemo, U. Ewald, 2020). 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 (Evans and Gooldfire, 2020).

The International Diabetes Federation (IDF) reports that the prevalence of diabetes mellitus has reached epidemic levels globally. Recent estimates (Evans and Gooldfire, 2020) 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 year 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, (Evans and Gooldfire, 2020) although the values range from 1–7% of the Nigerian population. Over 30 years, the prevalence of diabetes has steadily increased. Iloh et al. reported a prevalence of 3.9% for Imo state. However, a higher prevalence rates was reported in Port Harcourt (6.8%) by (Nyenwe et al. 2021). According to the estimates in 2020, by 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 (Evans and Gooldfire, 2020).

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 the avocado pear, (J.L.Evans, I.D, Gooldfire, vol 23, 2020). The medicinal relevance of the various parts of this tropical plant is enormous. The effects of aqueous seed extracts of *Persea americana* on the blood pressure, plasma, and tissue lipids of albino rats were investigated by Imafidon and Amaechina, 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. 2020) suggests that *P. americana* can lower blood glucose levels in cases of mild hyperglycemia but not severe hyperglycemia. Edem et al. studied the effects of aqueous alligator pear seed extracts on normal and alloxan-induced diabetic rats, and their results suggested a restorative (protective) (J.L.Evans, I.D, Gooldfire, 2020)effect of the extract on pancreatic islet cells. The work of (Mahadeva et al., 2020) 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.

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, 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 endocrine has a group of cells known as the islets of Langerhans which produce insulin and glucagon that maintain the balance of blood sugars (,,).

METHODOLOGY

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.

MATERIALS AND METHODS

Sixty 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.

COLLECTION AND PREPARATION OF PLANT MATERIAL

The Fruits and seeds of avocado pear were obtained from Ekokaka 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 hrs at temperature within room temperature with occasional and consciously making. It was then filtered through filter paper, and the filtrate was dried and stored in refrigerator for further use. During experiment the crude extract was distilled water diluted before the administration of extract to animals present.

CHEMICALS

Reagents used during research were analytically graded

3.4. MAINTENANING ANIMALS AND PROTOCOL APPROVAL

Sixty adult male Wistar rats, weighing 200–250 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 thier 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 cconsciously marked on the different parts of their hairy bodies, which was used as an identification mark for a particular Rat, this is to enable the response of a particular rat before and after administration.

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 ,(without the treatment).

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).

3.9.PHYTOCHEMICAL ANALYSIS OF THE SAMPLE

During the experiment the 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 of animal treatments, animals 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 underwent cervical dislocation for sacrifice and the pancreas from each animal harvested and fixed in 10% formal saline and used for histological examination using the H&E method.

STATISTICAL ANALYSIS

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

RESULTS AND DISCUSSION

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 of the control and experimental groups were recorded.

Rats in the Control group A had significant increase in 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. Group VII; this experiment involved the combination of induced alloxan, pericarp pear oil, and seed oil. The following observations were taken, 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 extracts. Hypoglycemia levels were noticed. This was followed by a former decreased weight to a significant increased weights of experimental rats. This meant that regeneration of pancreatic tissues of islets of Lange hangs were observed.

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		

The result of rat weight changes presented in Table 1 shows that rats in the control group A showed that rats in the control group 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.

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
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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 instead, it was mg/dL (range values: 190 to 270, and) in alloxanized group. After the treatment of rats with the fruit extract of Avocado oil and it's pericarp seed oil a (100 mg/kg weight of body) the level of glucose decreased down to mg/dL h

with a range value of 156–220 mg/dL and more potential effect at 250 mg/kg dose of weight of body of fruit extract and glucose level also significantly decreased to mg/dL having range of 90–129 mg/dL.. The significant glucose concentration increase 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 III and IV (100 and 250 mg/kg body weight) on the serum glucose levels in alloxan induced rats. Values are the means \pm S.D. for seven animals in each group. Values are significant at; statistical relevance was checked within groups as follows. Normal rats were compared with Diabetic rats. Iv and III groups were treated diabetic rats were compared with non diabetic rats.

HISTOPATHOLOGY STUDY

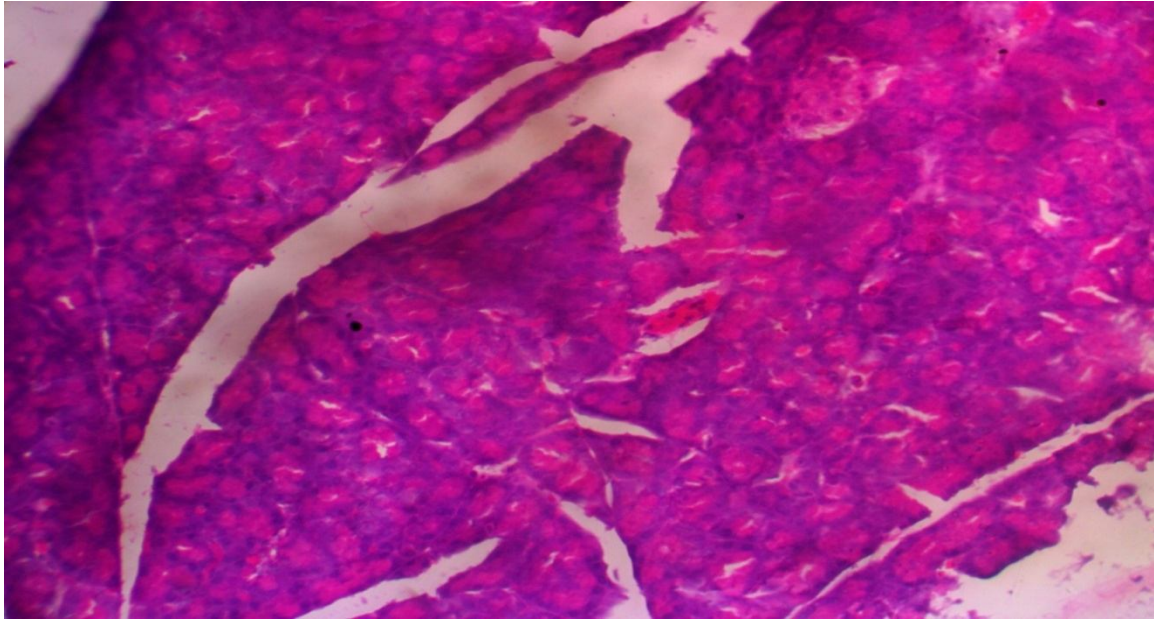


Plate 1: Which indicate normal histological features of endocrine pancreas in control group A (H&E) X 100). Photomicrograph section of pancreas shows well-spaced pancreatic acinar (PA) and Islets of Langerhans (IL) appearing normal.

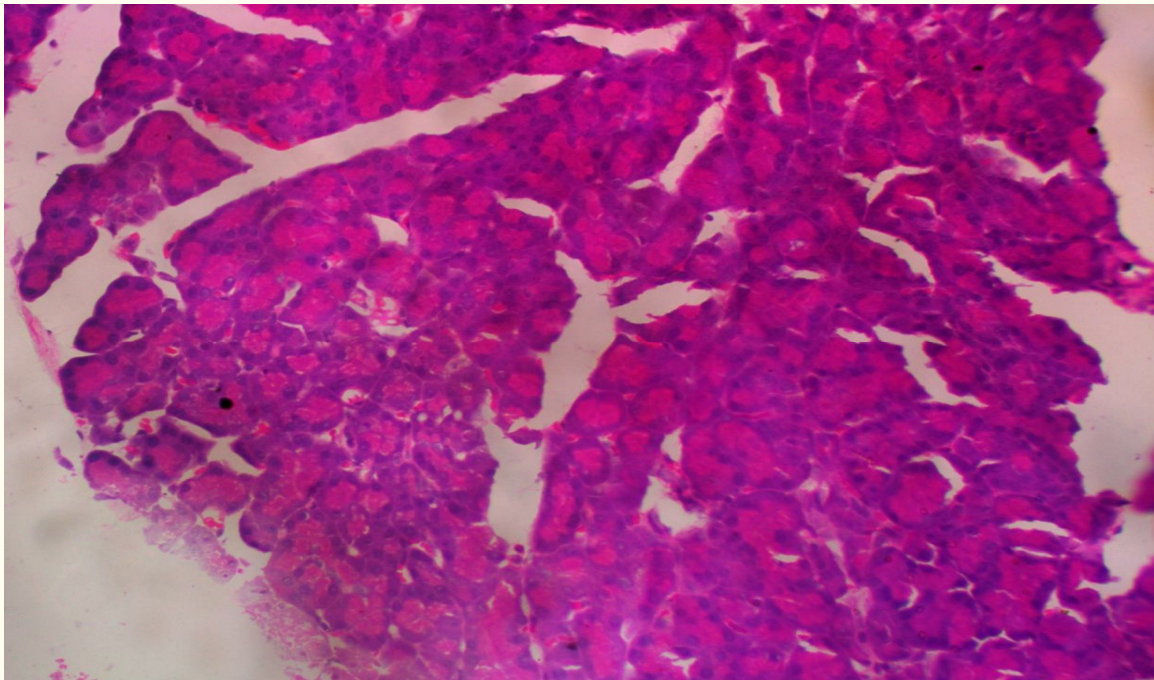


PLATE 2: Shows group B alloxan effect on the pancreatic islets of langerhans shows Photomicrograph section of pancreas degenerated pancreatic acinar (PA) and Islets of Langerhans appearing abnormal.

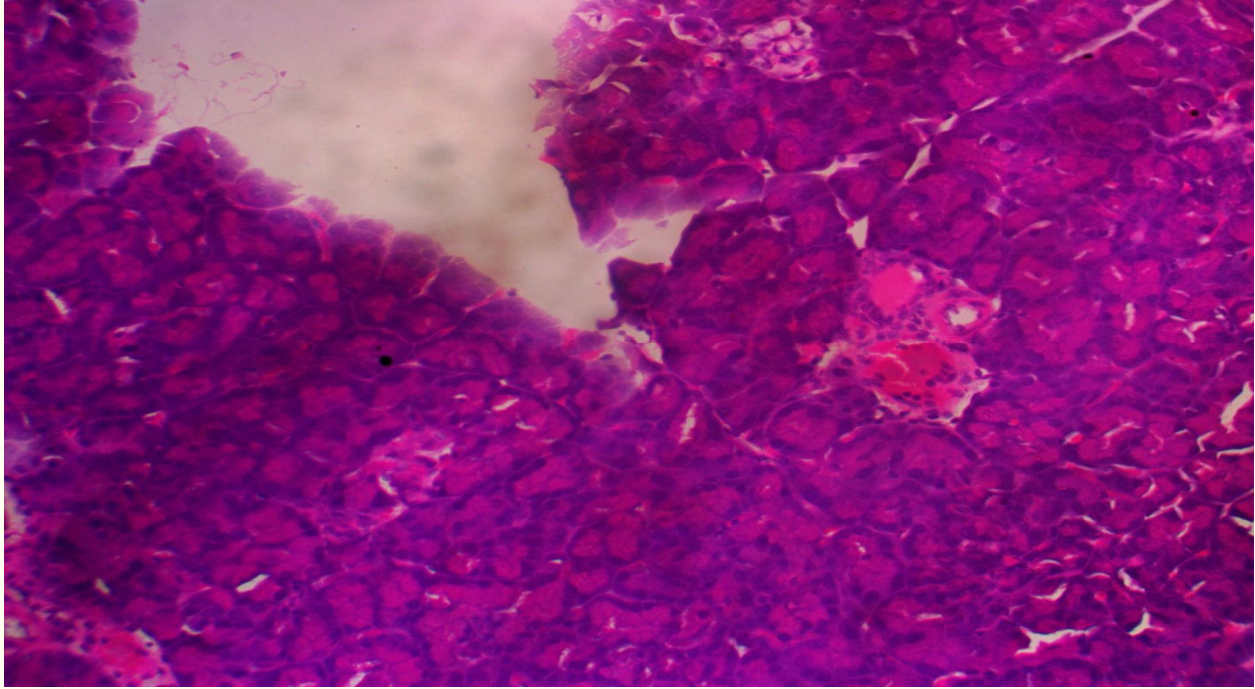


Plate 3: Which indicate normal histological features of endocrine pancreas in GROUP C and D (H&E)* 100). Photomicrograph section of pancreas shows well-spaced pancreatic acinar (PA) and Islets of Langerhans appearing well prominent on treatment of Pear and Seed oil methanoic extracts.

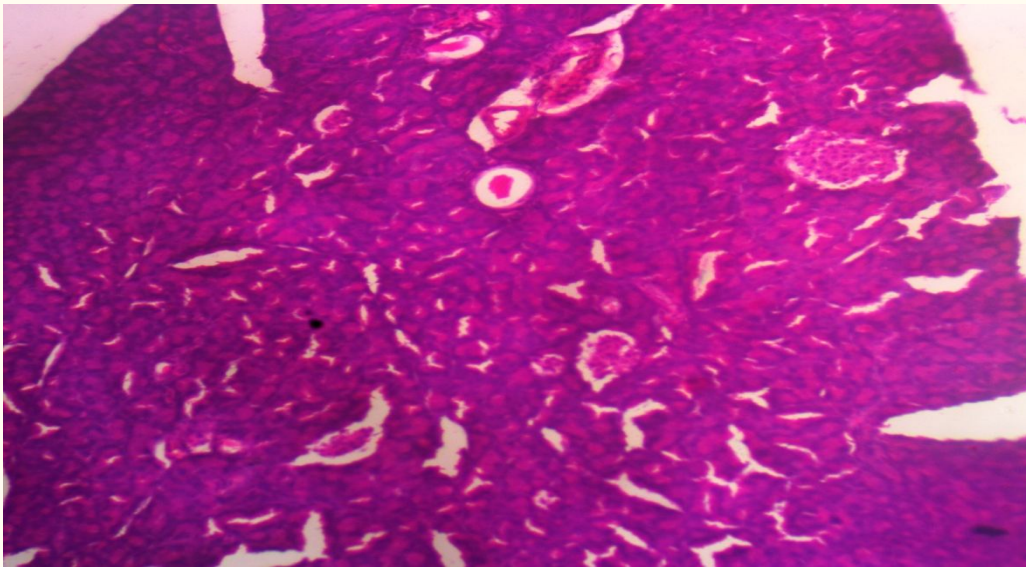
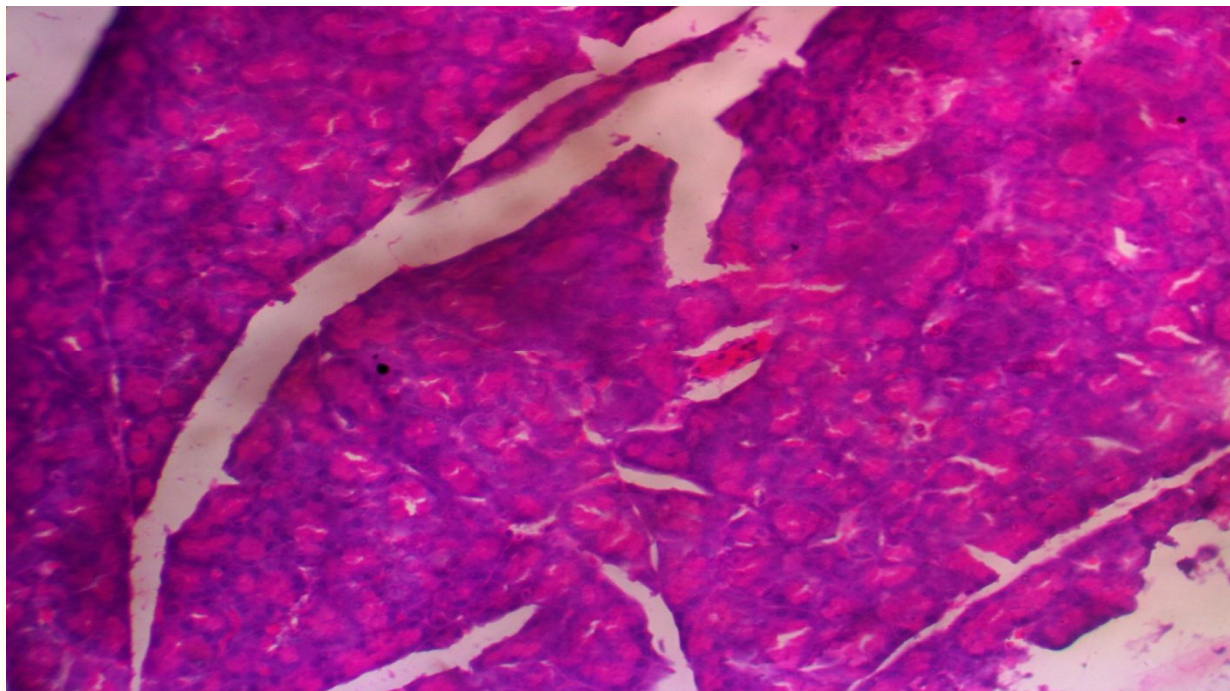


Plate 4: Which indicate slightly abnormal histological features of endocrine pancreas in control group V AND VI (H&E)* 100). Photomicrograph section of pancreas shows abnormal pancreatic acinar (PA) and Islets of Langerhans (IL) appearing a little degenerated on treatment of Alloxan, seed and Pear oil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



SLIDE 5: Which indicate slightly abnormal but rejuvenated histological features of endocrine pancreas in group VIII,(H&E)* 100).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 methanoic extracts.

DISCUSSION, CONCLUSION AND RECOMMENDATION

Plants that are medicinal are nature are the potential sources of bioactive agencies are being accepted worldwide. Studies on ethnomedicinal plants and medicinal herbs have been conducted in through time past and plants have been known for being used for purpose of medicine by tribe men in several nations. The survey on ethnobotanical can bring forth many clues for the production of drugs to cure human diseases like diabetes.(, M. Eidi, A. Midi and M. Sokhteh, "Effect of *Trigonella foenum-graecum* 2020).

In Table 1, before, during and after the acclimatization windows of the rats by treatment of *PERSEA AMERICANA*, (Pear), seed and fruit oil methanoic extracts, and also inducing of alloxan monohydrate, and standard drugs, Metformin. Phytochemicals in *Americana* fruits oil includes: carbohydrates ,alkaloids, saponins, tannins, flavonoids, and resins were found in *PERSEA. AMERICANA*.

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, in Table 3.0, Glucose Levels were also measured for p-value, $p < 0.05$ and f-value, mean and standard deviation of all groups, (A-H), were determined during 1st-2nd week, of acclimatization, Induction and Treatment. During the 1st week of acclimatization of Albino Wistar rats, Blood Glucose Level remain 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, had stabilize, drastically, in all groups induced and treated with alloxan monohydrate, pear oil, seed oil, and standard drug, metformin.

In confirming the levels of Insulin in all groups, in table, 4, insulin levels of group A, (control), being 6.09 ± 0.73 , mean and standard deviation, (Evaluation, measurements), and p-values of $P < 0.05$ or $P > 0.05$ were also determined.

Although, P-value, of $P < 0.05$ value for each groups (A, B, C, D, E, F, G, AND H) were observed for plasma Insulin levels of groups, (A-H),.

Groups, B (Alloxan), Significantly, had a lower insulin value, physiologically, because of the presence of alloxan monohydrate induction, compared to Groups H, C, D, G, H, treated with pear seed, oil, and metformin, (Standard drugs).

Seed with serum normal parameters and streptozotocin- diabetic induced rats," Research Nutrition, vol. 2, 2020. Safe, effective, and cost efficient remedies are gaining grounds among the people of the urban and rural settlements, especially in developing countries such as India.

In this study, B. L. Chaudhary, S.S. Katewa and A. Jain, "Folk herbal medicine India," Journal of Ethnopharmacology, p. 41-46, 2020. PERSEA AMERICANA was selected for diabetic anti study and rejuvenation capacity of the tissues. Therefore, this study was carried out to justify a claimed use. Alloxan is the most commonly used chemical used to induce diabetes in experimental animals.

Alloxan chemical is a β -cytotoxin chemical and (S. S. Katewa, B. L. Chaudhary, pp. 41-46, 2020) induces diabetes by damaging the tissues, secreting insulin beta cells in decreased insulin endogenous release. Administered Alloxan rabbits now get hyperglycemic in brief period of time, this is filled by glucose hepatic overproduction.

High glucose ambience can support apoptosis, by causing cellular destruction as a result of diatic hyperglycemia. 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 g

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 electron chain. Another source (B. L. Chaudhary, S.S Katewa and A. Jain, no. 1, pp. 41–46, 2020) of induced glucose oxidative stress is the pathway where glucose is reduced to sorbitol by reductase aldose in a process that ejects NADPH. This will retard the NADPH-dependent gen of glutathione, an essential antioxidant cell.

In this study significant hyperglycemia was gotten after (150 mg/kg alloxan quantity if body weight) was injected. Alloxan diabetic induced rats with more than 200 mg/dL of glucose blood level were knownto be diabetic and was used for this study. However,(, B. L. Chaudhary,S.S,Katewa and A. Jain, 2020) administed the aqueous extract at the dose of 100 / 250 mg/kg of weight of body which decreased the level of glucose in alloxan induced rats.

These results are in line e with the findings of such an effect may be checked for in part by a decrease in the rats of intestinal glucose level , (, B. L. Chaudhary, pp. 41–46, 2020) absorption was achieved by an pancreatic pump action which include the stimulation of glucose.periphery utilization or glycolytic enhancement and glycogenic process with decrease in gluconeogenesis .

Effective glucose blood control is the option for preventing or reducing diabetic complications and enhancing life quality in patients with diabetes. On this basis, we have seen that glucose induces hyperglycaemic action, (S. S. Katewa, B. L. Chaudhary,2020), model to screen the antihyperglycaemic activity in plant extracts content.

The present study verified the changes in weight of body and weight of organs 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.

These results are in line with the findings that are quit contradictory by (Dans et al., 2020) who revealed Momordica charantia had no revelant effect on weight of body of a diabetic. This, (S. S. Katewa, B. L. Chaudhary, and pp. 41–46, 2020) elevates body weight of diabetic rats because of result of Persea Americana treatment may be directed to the increase in insulin release.

Results gotten from our research showed that alloxanization caused a relevant increase in uric serum acid, and decrease in albumin and protein levels (S. S. Katewa, B. L. Chaudhary, and A. Jain,2020) values gotten in animals that are diabetic when compared with those that are nondiabetic in the control.

This could be due to the glycation of protein in diabetes which could lead to wasting of muscles and elevated release of purine, the original source of uric acid, as well as elevated xanthine oxidase release action.

Results of our research are consistent with the research reported by others who revealed that serum uric acid, and creatinine levels were elevated in diabetic rats. This may be caused based on metabolic unrest in diabetes reflected in high level activities of lipid peroxidation, oxidase oxanthibe and elevated levels of cholesterol

Results were also reported showing the increased urea concentration and creatinine cause based on excessive lipolysis in diabetes mellitus causing ketosis and acidosis. Kidney maintains a chemical composition fluid in the body by acidification in urine and metabolic wastes removals such as urea, uric acid, and creatinine. During diseases of the renals the concentration of these metabolites elevates in blood. On the other wing treatment of extract Aqueous *Persea Americana* for 21 days on rats that are diabetic, the elevated level were now normal.

Based on this results, the serum albumin decrease and protein in animals that are diabetic were restored to rate of control by treatment of insulin, which speeds up amino acid transportation by cells and the protein manufacturing machinery of the cell.

Reduced plasma albumin was observed in induced alloxan rats which may be caused by microproteinuria and albuminuria, which is a sacrosanct clinical marker of diabetes which could also cause increased protein catabolism. Insulin lack also reduces RNA and mRNA, which is a factor for the reduction of total protein. Results also connect with findings above.

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 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 [60]. 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 diabetes rats. This normal state may be achieved by the antioxidant and radicals that are free and thier quenching nature of *Persea Americana*.

However, the Hypoglycemic effect of the avocado fruit and seed extract may be due probable contents of elements such as calcium, magnesium, potassium, sodium, zinc, chromium e.t.c that

play key role in blood glucose homeostasis by regulating the key enzymes involved in gluconeogenesis in the liver e.g. glucose-6-phosphatase, fructose-1, 6-bisphosphatase and phosphoenolpyruvate carboxykinase, thereby blocking gluconeogenesis and enhancing glucose utilization in the body (Abdel MA, El-Feki M, 2020). The seed may in addition to these elements contain certain hypoglycemic agents such as phytochemicals (e.g. flavonoids, saponins, steroids, terpenoids, tannins and alkaloids etc) which contain insulin stimulatory substances such as insulin receptors substrate (IRS), pro-hormone convertase, glycogen synthase, the β_3 adrenergic receptor, glucose dependent insulinotropic polypeptide (GIP) receptor and peroxisome proliferators – activated receptor gamma (Abdel MA, El-Feki M, 2020). However, the mechanism by which the extract lowered the blood glucose level in alloxan induced diabetic rats is still unclear. It could be by (B. T. Dumas, W. Ard Watson, and H. G. Biggs, “Albumin”, 2020), 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. A prolonged (B. T. Dumas, W. Ard Watson, and H. G. Biggs, 2020) administration of the extract shows higher hypoglycemic effects on alloxan induced diabetic rats than are shorter period. And after withdrawal of the treatment for one week the blood glucose gradually rised, however below that of the untreated group, this signifies the management effect of the avocado seed extract. The (B. T. Dumas, W. Ard Watson, and H. G. Biggs, 2020) increase in weight of diabetic rats treated with avocado seed extract (Table) was found to be significant between diabetes groups treated with avocado seed and diabetic non-treated (Group II). This could be due to certain (B. T. Dumas, W. Ard Watson, and H. G. Biggs, 2020), compounds and or mineral elements that may stimulate effective utilization of nutrients. In addition, the seed may contain nutrients such as (B. T. Dumas, W. Ard Watson, and H. G. B, 2020) protein and fat this coupled with their effective utilization, may be responsible for the weight gain.

CONCLUSION

Data results from the research study indicate clearly that the extract of *Persea Americana* fruit at (100,150,200 mg/kg weight of body dose showed significant antihyperglycemic than at low dose (100 mg/kg weight of body) in the diabetic Induced rats, v biochemical parameters like KFT together with kidney tissues regeneration. Therefore, further investigations is a necessity to examine the phytoconstituent which is responsible for the anti-diabetic effect.

The (J. Welihinda, E. H. Karunanayake, M. H. R. Sheriff, 2020,) chemical induction of diabetes appears to be the most popularly used procedure in inducing diabetes mellitus in experimental animals. The foremost drug-induced diabetic model is the alloxan diabetes that is capable of inducing type I diabetes mellitus in experimental animals. The surgical and genetic methods of diabetes induction are associated with a high percentage of animal morbidity and mortality. Hence, alloxan induced diabetes model appears to be the most reliable and easily reproducible method of inducing diabetes mellitus in experimental animals. So, efforts should be made

towards (J. Welihinda, E. H. Karunanayake, M. H. R. Sheriff, and K. S. A. Jaya, 2020), upbringing and uplifting the model of alloxan induced diabetes mellitus in the experimental animals.

Eventually, the plant extract exerted a dose-dependent protective effect on the pancreas, kidneys and liver, like the reference drug Metformin. (B. T. Dumas, W. Ard Watson, and H. G. Biggs, 2020) 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 results show that combination of this seeds and fruits can form good dietary combination of Healthy Meals and Ready to Use Therapeutic Foods. Which could be produced for both Adult and Young Ones to improve their Health States.

RECOMMENDATIONS

I recommend that extensive researches be carried out with other fruit extracts and standard drugs.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

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Author(s) hereby declare that generative AI technologies such as Large Language Models, etc have been used during writing or editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology

Details of the AI usage are given below:

- 1.
- 2.
- 3.

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