**ORIGINAL RESEARCH**

# Histopathological and biochemical impacts of aqueous Carica papaya leaf extract on the liver of streptozotocin-induced diabetic Albino Rats

Idehen I.C.[1], Yibala O.[1], Yakubu B.S.[1], Onyinyechi B.[1], Dic-ijiewere E. O.[3], Chelimo J. J.[2]

[1]Department of Medical Laboratory Science, School of Allied Health Sciences, Kampala International University, Western Campus, Ishaka, Uganda.
[2]Department of Public Health, School of Allied Health Sciences, Kampala International University. Western Campus, Ishaka, Uganda
[3]Department of Chemical Pathology, College of Medical Sciences, Ambrose Alli University, Ekpoma, Edo State, Nigeria.

## ABSTRACT

This study was conducted to examine the effects of an aqueous extract of *Carica papaya* leaf on the liver of a Wistar rat that had been streptozotocin-induced diabetic. For this investigation, one hundred (100) male Wistar rats weighing between 200 and 300g were employed. They were split up into five groups of twenty rats each (I, II, III, IV, and V). Group I was used as a non-diabetic control, whereas Groups II, III, IV, and V received intraperitoneal injections of 60 mg/kg streptozotocin freshly dissolved in 0.1M citrate buffer (pH 4.5) at a volume of 1 ml/kg body weight in order to induce diabetes. Groups III, IV, and V received freshly made aqueous extract of Carica papaya leaves at a rate of 0.75g/kg body weight, 1.5g/kg body weight, and 3g/kg body weight, respectively. Diabetes control was provided by Group II, whereas non-diabetic control was provided by Group I. At baseline and throughout the course of treatment, weight and blood glucose levels were also recorded. The liver histology section of diabetic rats given 1.5 and 3.0 grams per kilogram of body weight. The aqueous extract of *Carica papaya* leaves improved the hepatic morphological disruption caused by induced diabetes, which in turn improved the hepatic histoarchitecture. Liver impairment was also detected by the biochemistry of the liver enzymes. Compared to rats that were not treated, diabetic rats treated with aqueous *Carica papaya* showed a substantial decrease ($p<0.05$) in the biomarkers ALT, AST, and ALP. According to the study's findings, adult Wistar rats with diabetes induced by streptozotocin showed less liver damage when given an aqueous extract of *Carica papaya* leaves.

**Keywords:** *Carica Papaya*, Liver, Streptozotocin, Diabetes, Rats.

*Corresponding Author
Idehen Iyore Charles; Department of Medical Laboratory Science, School of Allied Health Sciences, Kampala International University, Western Campus, Ishaka, Uganda.; charlesidehen@kiu.ac.ug

Citing this article
Idehen I.C., Yibala O., Yakubu B.S., Onyinyechi B., Dic-ijiewere E.O., Chelimo J.J. Histopathological and Biochemical Impacts of Aqueous Carica papaya Leaf Extract on the Liver of Streptozotocin-Induced Diabetic Albino Rats. KIU J. Health Sci, 2024: 4(2);

Conflict of Interest: authors are required to disclose any potential conflict of interest

## INTRODUCTION

The usage of herbal remedies, phytonutrients, or nutraceuticals has grown significantly worldwide, and they are now the final option for treating a variety of illnesses (1). Herbal medications are used for both preventative and therapeutic management of diabetes in various societies (2-4). Normal organs and their cellular tissue—particularly pancreatic beta-cells and liver tissue—as well as their preventative action against diabetes inducers are responsible for the observed prophylactic action (3,5). Curative effects on hepatic and pancreatic tissue, as well as organs associated with diabetes, may be the source of therapeutic advantages (6–8). These plants' actions are caused by the presence of several phytoconstituents. Among the key components of this plant that contribute to its antidiabetic potential are phenols, flavonoids, terpenoids, alkaloids, anthraquinones, tannins, saponins, minerals, and maybe more (9–14).

Diabetes patients often experience morbidity and death as a result of hyperglycemia, which is typically followed by increasing advances in complications of both the macro-vascular and micro-vasular systems (15). Over the past 20 to 30 years, there has been a sharp rise in both the prevalence and the number of cases. The number of persons with diabetes worldwide increased from around 108 million in 1980 to approximately 400 million in 2014 (1, 16). Despite the endocrine nature of the disease, complications can affect the cardiovascular, renal, neurological, immunological, and other systems of the body, making the condition more severe (17, 18).

Several layers of high-volume biochemical reactions, such as the creation and metabolism of small and compound molecules, are present in the liver, an essential vertebrate organ that is required for regular vital processes (19). In summary, the liver performs a number of tasks, such as the metabolism of carbohydrates, amino acids, proteins, fats, detoxification, drug metabolism, bile secretion and excretion, clotting factor synthesis (I, II, V, VII, IX, X), hormone synthesis, phagocytotic activity, glucose storage, vitamin A, D, B12, copper, and iron.

In most tropical and subtropical parts of the world, carica papaya, a member of the Caricaceae family, has been utilized to treat a variety of medical ailments. In traditional medicine, several elements of the *Carica papaya*, such as the seeds, root, leaves, flowers, latex, bark, and fruit, have been used to cure a range of illnesses (20). Additionally, it contains a number of vital components, including minerals like potassium and magnesium, vitamin B pantothenic acid, fiber, folate, and vitamins A, E, and C, which are abundant in antioxidants (21). Papaya's antioxidant activity demonstrates how it helps counteract the production of free radicals and ultimately stops the pathogenesis. On the other hand, fiber, a highly valuable and significant component, is crucial for lowering or crashing cholesterol. Furthermore, the primary source of cysteine, proteinases such as chymopapain, caricain, papain, and glycylendopeptidase, and proteinase levels vary by portion of the plant, including fruit, leaves, and roots, is papaya latex (21).

Because of their accessibility, availability, and affordability, medicinal plants are increasingly being used as supplements or substitutes for conventional medications. Because conventional therapies are costly, prone to side effects, and infrequently available in the majority of developing or underdeveloped nations, the financial implications of managing diabetes and its associated consequences are astounding (22, 23). Diabetes is frequently managed with drugs (chemicals and hormones) (24). Notwithstanding their efficacy, issues with availability, cost, and adverse effects persist, particularly in middle- and low-income nations (25, 26).

Numerous evaluations have been conducted on the use of medicinal plants to treat diabetes (2, 3). These effects and their potential as antidiabetic agents are caused by the existence of several phytochemical constituents in plants, including phenols, flavonoids, terpenoids, alkaloids, anthraquinones, rannins, saponins, minerals, etc. (12–14). The antidiabetic potential of several phytonutrients from medicinal plants, such as tannins, glycosides, minerals, etc., has also been investigated through a variety of mechanisms, including hypoglycemic effect, insulin release activity, hepatoprotective and pancreato-protective action,

glucose uptake and utilization in muscles, inhibition of intestinal glucose absorption, antioxidant and immunomodulatory effect (27). This study aims to investigate the effects of an aqueous extract of Carica papaya leaves on the liver of streptozotocin-induced diabetic wistar rats, as diabetes is associated with hyperglycemia and abnormalities in liver functioning.

## MATERIALS AND METHODS

**Study Design:** The current study used a randomized control trial design and included both observational and experimental research. One hundred (100) of the 130 adult wistar rats that were purchased were employed for this investigation for six weeks (42 days).

### Plant Material & Substance Preparation

Freshly picked carica papaya leaves from a local garden in Emuhi-Ekpoma, Edo State, Nigeria, were botanically identified and verified at the Botany Department's herbarium at Ambrose Alli University in Ekpoma. Voucher number PTBG0000043455 is used. They were ground into a fine powder for extraction after being minced and oven-dried for ten days at 400 degrees Celsius. The aqueous leaf extract was prepared for administration using the aqueous crude extraction procedure. The rats were given dried papaya leaves every day after they had been pulverized and weighed into graded dosages. Each dose was mixed in 1 milliliter of water solution and soaked for two days.

### Experimental Animals

A total of 130 male sex wistar rats weighing between 200 and 300 grams (on average, 250 grams) were obtained from the laboratory animal house at Ambrose Alli University Ekpoma, Edo State's College of Medical Sciences. After that, the animals were brought to the Calvary Medical and Diagnostic Center, where they were given seven days to get used to their new surroundings. They were fed growers mash and given unrestricted access to water.

### ETHICAL CONSIDERATION

All laboratory principles especially the internationally accepted principles for laboratory animal use and care as found in the European community guidelines (EEC Directive of 1986;86/609/EEC) were strictly observed throughout the duration of laboratory animal treatment and conduct of this work.

Approval for the study was obtained from the Research Ethics Committee of the College of Medical Sciences (Ref No: AAU/HREC/23/1024)..

### Diabetes Induction in Wistar Rats

After an overnight fast, 60 mg/kg body weight of a newly prepared streptozotocin solution at a volume of 1 ml/kg body weight was injected into the rats to induce diabetes and hyperglycemia. It was administered as a single, last dose. 1 cc of sterile saline was given to the control animals.

**Formula:**

$$\text{Concentration For Rat} = \frac{\text{Standard Conc(60) X Average Weight of Test Rat(0.25)}}{\text{Standard Weight (1kg)}}$$

Concentration for rat=15mg(0.25ml) Streptozotocin per rat.

After 72 hours, or three days, following the intraperitoneal injection, the hyperglycemia was confirmed. The glucose oxidase enzymatic method was used to estimate blood samples taken from the rats' tails and test the sugar (glucose) concentration in the blood. The animals involved in this study had fasting blood sugar levels of at least 250 mg/dl.

### Experimental Design

Five groups of twenty (20) wistar rats each were randomly selected from the study's sample. Carica papaya has an LD50 of more than 5000 mg/kg (Timothy et al., 2022).

**Group I:** Growers mash and distilled water were the sole treatments given to non-diabetic control rats.

**Group II:** Growers mash and distilled water were the only treatments given to diabetic (untreated) control rats.

**Group III:** One milliliter of an aqueous solution of 0.75 grams/kg body weight of extracted carica papaya leaves and growers mash was administered to each diabetic rat (treated) in this group.

**Group IV:** The treated diabetic rats were given 1 milliliter of an aqueous solution containing 1.5 grams per kilogram of body weight of Carica papaya leaves and growers mash alone (i.e., each rat received 1 milliliter of 0.375 grams of Carica papaya leaf extract).

**Group V:** Only growers' mash and 3g/kg body weight of extracted Carica papaya leaves were administered to diabetic rats (treated) in 1ml aqueous preparation (i.e., 1ml of 0.75g of Carica papaya leaf extract was given to each rat).

**Formula:**

Concentration For Rat =

$$\frac{\text{Standard Conc X Weight Of Test Rat}}{\text{Standard Weight (1)}}$$

**Animal Sacrifice**

Following their sedation with chloroform, the animals were sacrificed. The liver, the organ of interest, was taken out. Before undergoing additional histological procedures and analysis, the removed organs were placed in 10% formol saline to fix for at least 72 hours.

Both at baseline and prior to sacrifice, the animals were weighed. The values of their body weight were noted.

**Biochemical and Histopathological Analyses**

**Biochemical Analysis**

**Estimation of Alanine Amino Transferase (ALT)**

**Principle**: The amino group is transferred from alanine to alpha oxoglutarate by ALT, resulting in the formation of L-glutamate and pyruvate. When pyruvate and 2, 4-dinitrophenyl hydrazine combine in an alkaline media, the result is a reddish brown color that may be detected by spectrophotometry at a wavelength of 546 nm. The enzyme activity is directly correlated with the color's intensity.

**Estimation of Aspartate Amino Transferase (AST).**

**Principle:** When an amino group is transferred from aspartate to alpha oxoglutarate by AST, L-glutamate and oxaloacetate are produced. These react with 2, 4-dinitrophenyl hydrazine to produce a reddish brown color that may be detected by spectrophotometry at a wavelength of 546 nm in an alkaline media. The enzyme activity is directly correlated with the color's intensity.

**Estimation of Alkaline Phosphatase (ALP)**

The ALP activity in the sample was determined using the Deutsche method.

**Principle**: P-nitrophenol and inorganic phosphate are released when ALP hydrolyzes the substrate p-nitrophenol phosphate. Sodium hydroxide (0.5N) is added to stop the reaction, and a spectrophotometer set to 405 nm is used to measure the absorbance of the color complex that is created. The amount of ALP activity in the sample is directly correlated with the color's intensity.

**Histopathological Analyses**

I. General tissue morphology of liver was done using H&E

II. Special Histopathological technique and staining

a) Aldehyde fuchsin technique and staining

b) Periodic acid Schiff (PAS) Method for liver.

**Tissue Processing Schedule**

In accordance with the Standard Processing Schedule, the tissues were processed using an automatic tissue processor in the Histopathology Laboratory of the Irrua Specialist Teaching Hospital in Irrua, Edo State, Nigeria.

**Embedding**

Melted paraffin wax was used to fill a metallic tissue mold, and an embedding center assisted with the process. The blocks were allowed to set before being cut with a knife to remove them from the metallic case. A rotary micro-tome was then used to trim and cut the blocks serially at 3 nm. After floating out in a water bath, the portions were lifted using a sanitized slide.

To ensure that the portions were sufficiently attached to the slide, the frosted end slides with the sections were heated for forty minutes. The sections were prepared for staining by being dewaxed, let to air dry, and then placed in a slide rack.

**Staining Procedure**

**Haematoxylin and Eosin (H&E):** For Demonstration of General Tissue Structure

**Periodic Acid Schiff (PAS):** To Show Carbohydrate in the Liver, Use the PAS Technique (adapted from McManus 1946).

**Data Analysis**

The statistical software program SPSS version 20 was used to examine the collected data. A P-value of less than 0.05 was deemed significant after our obtained findings were statistically examined and presented as Mean± SD. Repeated-measures analysis of variance (ANOVA) was used to determine the significance difference between the groups. The Olympus CX23 light microscope was used to take a photomicrograph of the liver's histology.

## RESULTS

The purpose of this study was to evaluate the effects of

Carica papaya leaf extract in water on rats that had been infected with streptozotocin to induce diabetes. For this study, we employed one hundred (100) adult wistar rats over the course of forty-two days. Weights of animals in groups I (normal control), II (diabetic control), III (diabetic rats receiving 0.75g/kg body weight of aqueous pawpaw or Carica papaya leaf extract and growers mash only), IV (diabetic rats receiving 1.5g/kg body weight of aqueous pawpaw or Carica papaya leaf extract and growers mash only), and V (diabetic rats receiving 3g/kg body weight of aqueous pawpaw or Carica papaya leaf extract and growers mash only) at various weeks of the experiment are displayed in Table 4.1.

At baseline, the weights of the rats in the various groups did not differ significantly ($p>0.05$). However, when compared to the control group (non-diabetic group), we saw a decrease in the weight of the experimental groups (diabetic groups). Additionally, when compared to group 4 and group 5 rats (1.5g/kg body weight Carica Papaya treated rats and 3.0g/kg body weight Carica Papaya treated rats, respectively), we observed a notable/significant weight reduction in group 2 and group 3 rats (diabetic control Rat group and 0.75g/kg body weight Carica papaya treated rats, respectively).

In comparison to group 2 (diabetic control rats), we found an appreciable/significant ($p<0.05$) increase in rat weights in groups 3 (0.75g/kg body weight Carica papaya treated rats), 4 (1.5g/kg body weight Carica papaya treated rats), and 5 (3.0g/kg body weight Carica papaya treated rats) at week 2.

In comparison to group 2 (diabetic control rat), we found that the experimental rats in groups 3 (0.75g/kg body weight Carica papaya treated rats), 4 (1.5g/kg b.w. Carica papaya treated rats), and 5 (3.0g/kg body weight Carica papaya treated rats) had significantly/appreciably gained weight at week 3. The same pattern of results was also observed at weeks 4, 5, and 6.

At different weeks during the experiment, the glucose levels of the animals in groups I (normal control), II (diabetic control), III (diabetic rats receiving 0.75g/kg body weight of extracted carica papaya leaves and growers mash only), IV (diabetic rats receiving 1.5g/kg body weight of extracted carica papaya leaves and growers mash only), and V (diabetic rats receiving 3g/kg body weight of extracted carica papaya leaves and growers mash only) are displayed in Table 2. At baseline, the glucose levels of experimental rats in Groups II, III, IV, and V were significantly higher ($p<0.05$) than those of the normal control rats in Group I. When compared to the experimental diabetic control group (Group II), there was a substantial drop in the sugar (glucose) level of the experimentally treated rats (Groups III, IV, and V) at week one ($P<0.05$). There was no discernible variation ($P>0.05$) in the glucose levels of the experimentally treated rats.

When compared to the experimental diabetic control group (group II), there was a substantial drop in the sugar (glucose) level of the experimentally treated rats (groups III, IV, and V) at week two ($P<0.05$). When compared to group III rats, there was a significant difference ($p<0.05$) in the glucose levels of rats in groups IV and V.

When compared to the experimental diabetic control group (group II), there was a substantial drop in the sugar (glucose) level of the experimentally treated rats (groups III, IV, and V) at week two ($P<0.05$). When compared to group III rats, there was a significant difference ($p<0.05$) in the glucose levels of rats in groups IV and V.

When compared to the experimental diabetic control group (group II), the glucose levels of experimentally treated rats (groups III, IV, and V) were significantly lower ($p<0.05$) at weeks three through six. Additionally, there was a substantial ($p<0.05$) decrease in glucose levels across Groups IV and V in comparison to Group III. Between weeks three and six, Group-IV and Group-V do not differ statistically significantly ($p>0.05$).

Table 3 lists the liver or hepatic enzyme values and, consequently, their functions for the animals in groups I (normal control), II (diabetic control), III (diabetic rats received 0.75g/kg body weight of extracted Carica papaya leaves and growers mash only), IV (diabetic rats received 1.5g/kg body weight of extracted Carica papaya leaves and growers mash only), and V (diabetic

rats received 3g/kg body weight of extracted Carica papaya leaves and growers mash only). Comparison with the control group (group I) at the end of the experiment revealed a marked/significant elevation or rise ($p<0.05$) in the functions of the liver or hepatic enzymes in the experimental groups (group II, III, IV, and IV). Additionally, when comparing the diabetic-treated groups (Group III, Group IV, and Group V) to the diabetic-untreated group (Group II or Diabetic-control), we found a substantial ($P<0.05$) decline in the liver or hepatic enzyme functioning.

## DISCUSSION

The purpose of this study was to examine the effects of an aqueous papaya leaf extract on the liver of wistar rats with diabetes caused by streptozotocin. The current study has shown that experimental rats' blood sugar (glucose) levels significantly increased when Streptozotocin (STZ) was administered intraperitoneally (Table 2).

This study's observations and conclusions supported the findings of Montano et al. (28), Juárez-Rojop et al. (29) and Ajibade et al. (30) by showing that streptozotocin (STZ) was effective in causing severe hyperglycemia in experimental mice. When it comes to inducing diabetes in laboratory animals, particularly insulin-dependent (Type 1) diabetes, streptozotocin (STZ) is typically the best option. This is due to the fact that it damages or poisons the beta-cells in the pancreas (31, 32).

When compared to controls, the diabetic rats in this study exhibit a noticeable decrease in weight (Table 1). The findings of Uárez-Rojop et al. (29), Sonia et al. (33), J, and Afaf-Haniem et al. (34) that documented notable weight loss in rats with diabetes are consistent with this. Weight loss is a common sign and symptom of diabetes, although little is known about the process underlying this phenomenon. It is believed to be complex, involving increased muscle waste, tissue protein loss, and appetite loss (35–37).

According to reports, diabetes has a significant role in the initiation and development of liver injury, which provides an environment that is conducive to the development or accumulation of chronic liver disorders (38, 39). Biomarkers of hepatic injury or damage include the serum activity of alkaline phosphatase (ALP), aspartate amino transferase (AST), and alanine amino transferase (ALT) (40).

Enzymes called aspartate amino transferase and alanine amino transferase aid in the breakdown of amino transfer reactions and play a key role in the synthesis and breakdown of amino acids (41, 42). On the other hand, alkaline phosphatase (hydrolase) aids in the hydrolysis of phosphate sters (43).

The current investigation demonstrated that there were notable changes in liver dysfunction linked to diabetes produced by streptozotocin. Compared to the Control group, we found that the Aspartate Amino Transferase and Alanine Amino Transferase levels and functions were significantly higher in the STZ-induced diabetic rats (Table 3). This is consistent with the findings of Zafar et al. (44), Najla et al. (45), Omonkhua et al. (46), Aja et al. (47), and Hassan et al. (48), who in their different investigations noted notable changes in the levels and capabilities of the liver's enzymes. This is because diabetes causes liver damage.

According to Giacco & Brownlee (49) and Ahmadieh & Azar (50), the primary causes of diabetic complications are the generation of free radicals and an unintentional deficiency in a cell's antioxidant capacity. Diabetes also has a significant impact on a number of endogenous organs, most notably the liver. According to Mohamed et al. (51) the primary causes of hepatic impairment in patients are disturbances in the metabolism of proteins, lipids, and carbohydrates brought on by stress from diabetes. This is consistent with the findings of Okechukwu et al. (52) who concluded that hepatocellular damage leading to the release of ALT and AST from liver cells is responsible for the elevated oxidative stress caused by streptozotocin-induced diabetes. Additionally, we found in this study that streptozotocin-induced diabetes rats had considerably higher alkaline phosphates (ALP) enzyme activity than non-diabetic rats (Table 3). The findings of Omonkhua et al. (46), as well as Zafar et al. (44) are consistent with this. However, nothing is known about how membrane-bound enzymes are released. The sinusoids and the endothelium of the central and periportal veins contain

the largest quantities of the glycoprotein and liver enzyme alkaline phosphatase (ALP); the biliary canaliculi have lower concentrations of this enzyme (44).

The current study has demonstrated that in streptozotocin-induced diabetic rats, aqueous papaya leaf extract can correct hyperglycemia. According to this study, as compared to Group-II (Diabetic Control) rats, the extract from Carica papaya leaves significantly ($p<0.05$) decreased blood glucose levels in Group III, IV, and V rats (Treated Rats) (Table 2). Venkateshwarlu et al. (53), Abiola et al. (54) and Augustine (55), as well as Juárez-Rojop et al. (29), Ajibade et al. (30), and Afaf-Haniem et al. (34), concurred with this conclusion.

Carica papaya's nutritional and therapeutic qualities have been connected to its anti-diabetic effects. Research on Carica papaya leaves by Owoyele et al. (56), Okoko & Ere (57), and Pinnamaneni (58) revealed that the leaves included phenolic compounds, glycosides, alkaloids, and flavonoids in addition to having exceptional antioxidant activity. The hypoglycemic effect of pawpaw (papaya) leaves is believed to be caused by these compounds. One possible explanation for the sugar-lowering effect is a decrease in the intestinal absorption rate of sugar (glucose) (59, 60). An increase in the use of glucose or peripheral sugar may also be the cause (60). According to certain theories, the action of the glucose transporter (GLUT4) in muscle and adipose tissue (35, 61) and the overexpression of muscle protein (35, 62, 63) cause an increase in the breakdown of glucose. The aqueous leaf extract of Carica papaya may also act by stimulating the few remaining β-cells with the subsequent release of more insulin, as suggested by a possible stimulatory mechanism on the few surviving β-cells (64) rather than pointing to the regeneration of β-cells of the islets as the cause of the insulin increase.

The potential for correcting faulty liver enzymes was demonstrated by the effect of an aqueous extract of Carica papaya leaves on hepatic enzyme function. Following treatment of the Stz-induced rats with varying concentrations of aqueous leaf extract of Carica papaya, we noticed a significant/notable drop or reduction in the levels and functions of these enzymes (see Table 3). The findings of Ajibade et al. (30) and Juárez-Rojop et al. (29) are consistent with this.

The extract's preventive action, perhaps through its antioxidant impact in reversing diabetes-induced liver damage, is responsible for the decrease in liver enzyme levels and function in the diabetic rats treated with C. papaya. This may also result in a metabolic recovery, preventing more issues.

The control group's histological analysis of liver tissue revealed normal histoarchitecture. The liver photomicrograph plate (plate 5) shows normal hepatocytes without any bleeding and no inflammatory cell infiltration in the liver parenchyma. Periportal inflammation and other signs of liver damage were seen in the histological analysis of the liver tissue of diabetic wistar rats (plate 6). This is consistent with the results of Noman et al. (65) who documented significant congestion in the portal region of the cell, including necrotic foci, hydropic alterations, and lymphocyte aggregation and infiltration between hepatocytes. Additionally, they noted that streptozotocin-induced diabetic mice had hyperplasia of kupffer cells and a marked, progressive decrease in the glycogen content of their hepatocytes. Similar studies by Guven et al. (2006) showed that strepzotocin-induced hyperglycemia caused liver damage, including hydropic degeneration, periportal swellings, sinusoidal congestion, and necrosis. The chronic nature of these diseases is shown by the necrosis manifested in the form of mitochondrial and chromatin degradation. Additionally, the histological section of diabetic control rats revealed increased sinusoids with fatty infiltration, peri-portal fatty infiltration (PFI) with focal necrosis of hepatocytes, and an enlarged central vein, according to Juárez-Rojop et al., (29) and Ajibade et al., (30).

Hepatic impairment in diabetics has been linked to a number of important pathways (68–70). According to Bugianesi et al. (68), Manna et al. (71) and Palsamy et al. (72): The liver is a multipurpose organ that is particularly vulnerable to oxidative stress brought on by hyperglycemia or diabetes, which can result in hepatic injury. According to Leclercq et al. (70), Manna et al. (71) and Palsamy et al. (72) this hepatic damage causes

elevated oxidative stress and further initiates the inflammatory cascade. A fatty liver is the result of an excessive buildup of fat cells in the liver, which is complicated by inflammation and oxidative stress (67, 73, 74).

The study's findings indicate that papaya (pawpaw) plant aqueous leaf extracts have hepatoprotective qualities that may be used to treat liver damage. The improvement in the histological characteristics of diabetic rats' hepatocytes, which show a normal liver histological section, supports this. According to our findings, the group that received 1.5 g/kg body weight of Carica papaya leaf extract had normal hepatocytes and less periportal inflammation, whereas the group that received 3.0 g/kg body weight had normal hepatocytes and architecture. Congested veins and sinusoids were still present in 0.75g/kg body weight Carica papaya extract, nevertheless, and these findings were in line with those of Juárez-Rojop et al. (29). Therefore, it is evident from this study that aqueous leaf extract of Carica papaya can enhance hepatic functions in diabetic rats at a minimum low dose of 1.5g/kg body weight and a high dose of 3.0g/kg body weight. Thus, we can conclude that a controlled high concentration/dosage of Carica papaya leaf aqueous extract is more hepatoprotective than a low dose.

## CONCLUSION

The results of this study show that the aqueous extract of papaya leaves from carica has an antihyperglycemic or hypoglycemic effect. Furthermore, the extract has the ability to alleviate or improve some of the symptoms related to hyperglycemia and diabetes.

At doses of 1.5g/kg body weight and 3.0g/kg body weight, the aqueous extract of Carica papaya (pawpaw) leaves has been shown to have a hepatoprotective effect by positively reversing liver histology and morphology.

The effect of hyperglycemia on the animals' weight was demonstrated in this investigation. Animals in the diabetic control group lost weight in comparison to those in the non-diabetic control group. Comparing the treated experimental groups (groups 3, 4, and 5) to the diabetic non-treated group 2, however, showed consistent weight gain.

When compared to the experimental diabetic control group (group II), the experimentally treated rats (groups III, IV, and V) showed a significant decrease in their blood glucose levels. Additionally, there was a notable drop in blood glucose levels between Groups IV and V in comparison to Group III, suggesting that the effect of aqueous Carica papaya leaf extract on blood glucose was dose-dependent.

When comparing the diabetic-treated groups (Groups III, IV, and V) to the diabetic-untreated group (Group II or Diabetic-control), we also found a substantial decrease in the liver or hepatic enzyme values.The results of this study show that aqueous papaya leaf extract from carica has hepatoprotective qualities, reducing liver damage, which is a typical side effect of diabetes or hyperglycemia.

The aberrant morphological alterations brought on by hyperglycemia in the experimental animals' livers were positively reversed by the aqueous Carica papaya leaf extract. As shown by the PAS technique, there was also an increase in the liver's glucose (glycogen) store in the treated groups. These modifications were dose-dependent.

According to the current study, papaya leaves from Carica are a strong antidiabetic agent that works similarly to the common diabetes medication glibenclamide. It is advised that herbal medicine investigate the use of Carica papaya leaf extract in the management and treatment of diabetes mellitus in light of the study's findings. Purifying and defining the active ingredients in Carica papaya leaf extract should be the main focus of future research since this could result in the development of novel diabetic treatment agents.

## REFERENCE

1. World Health Organisation (2016). Global Report on Diabetes. WHO Press, Geneva, Switzerland, ISBN: 9789241565257, 86.

2. Perera, P.K. & Li, Y. (2012). Functional herbal food ingredients used in type 2 diabetes mellitus. Pharmacy Review, 6 (1), 37-45.

3. Ezuruike, U.F. & Prieto, J.M. (2014). The use of plants in the traditional management of diabetes in Nigeria: Pharmacological and toxicological considerations. Journal of Ethnopharmacology, 15 (5), 857-924.

4. Yatoo, M.I. (2015). Evaluation and validation of diabetic biomarkers in small ruminants and biomodulatory management of diabetes mellitus. Ph.D. Thesis, Indian Veterinary Research Institute, Izzatnagar Bareilly, U.P. India, 144-150.

5. Yatoo, M.I., Saxena, A. Malik, M.H., Sharma, M.K. & Dimri, U. (2014). Nanotechnology based drug delivery at cellular level: A review Journal of Animal Science, 4 (1), 705-709.

6. Mohamed, E.A.H., Yam, M.F, Ang, L.F., Mohamed, A.J. & Asmawi, M.Z. (2013). Antidiabetic properties and mechanism of action of Orthosiphon stamineus Benth bioactive sub-fraction in streptozotocin-induced diabetic rats. Journal of Acupuncture Meridian Studies, 6 (1), 31-40.

7. Tiwari, N., Thakur, A.K., Kumar, V., Dey, V. & Kumar, V. (2014): Therapeutic targets for diabetes mellitus: An update. Clin. Pharmacol. Biopharm., 3(2), 89 – 94.

8. Asante, D.B., Effah-Yeboah, E., Barnes, P., Abban, H.A. & Ameyaw, E.O. (2016). Antidiabetic effect of young and old ethanolic leaf extracts of Vernonia amygdalina: A comparative study. Journal of Diabetes Research, 82(5), 741-750.

9. Kunyanga, C.N., Imungi, K.J., Okoth, M., Momanyi, C., Biesalski, H.K. & Vadivel, V. (2011). Antioxidant and antidiabetic properties of condensed tannins in acetonic extract of selected raw and processed indigenous food ingredients from Kenya. Journal Food Science, 7 (6), 560-567.

10. Joseph, B. & Jini, D. (2013). Antidiabetic effects of Momordica charantia (bitter melon) and its medicinal potency. Asian Pacific Journal of Tropical Diseases, 3 (1), 93-102.

11. Tiong, S.H., Looi, C.Y., Hazni, H., Arya, A. & Paydar, M. (2013). Antidiabetic and antioxidant properties of alkaloids from Catharanthus roseus (L.) G. Don. Molecules, 18 (2), 9770-9784.

12. Zhao, D.D., Yu, N., Li, X.K., Fang, X. & Mu, Q.Q. (2014). Antidiabetic and antioxidative effect of Jiang Tang Xiao Ke granule in high-fat diet and low-dose streptozotocin induced diabetic rats. Evidence Based Complementary & Alternative Medicine, 10 (1), 5192-5195.

13. Abdirahman, Y.A., Juma, K.K., Mukundi, M.J., Gitahi, S.M. & Agyirifo, D.S. (2015). In-vivo antidiabetic activity and safety of the aqueous stem bark extract of Kleinia squarrosa. Journal of Diabetes & Metabolism, 6 (1), 2155-2161.

14. Lavle, N., Shukla, P. & Panchal, A. (2016). Role of flavonoids and saponins in the treatment of diabetes mellitus. Journal of Pharmaceutical Science, Bioscientific Research, 6 (1), 535-541.

15. Campos, C. (2012). Chronic hyperglycemia and glucose toxicity: pathology and clinical sequelae. Postgraduate Medicine, 12 (4), 90-97.

16. Mohd, I.Y., Archana, S., Arumugam, G., Mahmoud, A. & Kuldeep D. (2017). Promising antidiabetic drugs, medicinal plants and herbs: An update. International Journal of Pharmacology, 13 (1), 732-745.

17. Wild, S., Roglic, G., Green, A. Sicree, S. & King, H. (2004). Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care, 27 (3), 1047-1053.

18. Graves, D.T. & Kayal, R.A. (2008). Diabetic complications and dysregulated innate immunity. Frontier Biosciences, 13 (1), 1227-1239.

19. Garcia-Compean, D., Jaquez-Quintana, J.O., Gonzalez-Gonzalez, J.A. & Maldonado-Garza, H. (2009). Liver cirrhosis and diabetes: Risk factors, pathophysiology, clinical implications and management. World Journal of Gastroenteroloy, 15

(1), 280-288.

20. Jaiswal, P., Kumar, P., Singh, V.K. & Singh, D.K. (2010). Carica papaya linn: a potential source for various health problems. Journal of Pharmaceutical Research, 3 (1), 998–1003.

21. Vij, T. & Prasha, Y. (2015). A review on medicinal properties of Carica papaya Linn. Asian Pacific Journal of Tropical Disease, 5 (1), 1-6.

22. Pandey, A., Tripathi, P., Pandey, R., Srivatava, R. & Goswami, S. (2011). Alternative therapies useful in the management of diabetes: A systematic review. Journal of Pharmacy & Bioallied Science, 3 (1), 504-512.

23. Sun, J. & Buys, N.J. (2016). Glucose-and glycaemic factor-lowering effects of probiotics on diabetes: A meta-analysis of randomised placebo-controlled trials. British Journal of Nutrition, 11 (5), 1167-1177.

24. Kalra, S., Jacob, J.J. & Gupta, Y. (2016). Newer antidiabetic drugs and calorie restriction mimicry. Indian Journal of Endocrinology & Metabolism, 20 (2), 142-146.

25. Hasan, S.S., Clavarino, A.M., Mamun, A.A. & Kairuz, T. (2015). A comparative drug utilisation study of the treatment of diabetes in Malaysia and Australia. Australian Medical Journal, 8 (1), 179-188.

26. Chaudhury, A., Duvoor, C., Dendi, V.S.R. Kraleti, S. & Chada, A. (2017). Clinical review of antidiabetic drugs: Implications for type 2 diabetes mellitus management. Frontier Endocrinology, 8 (10) 338-349.

27. Ahmed, I., Qamar, R., Masroor, M., Sattar, A. & Imran, K. (2005). Effect of glycemic control on lipid profile in Diabetics. Medical Channel, 10 (1), 44-47.

28. Montano, M.E., Molpeceres, V., Mauriz, J.L., Garzo, E., Cruz, I.B., González, P. & Barrio, J.P. (2010). Effect of melatonin supplementation on food and water intake in streptozotocin-diabetic and non-diabetic male Wistar rats. Nutrition & Hospitality, 25 (3), 931–938.

29. Juárez-Rojop, I.E., Díaz-Zagoya, J.C., Ble-Castillo, J.L. & Miranda-Osorio, P.L. (2012). Hypoglycemic effect of Carica papaya leaves in streptozotocin-induced diabetic rats. British Medical Council of Complementary and Alternative Medicine, 12 (236), 1-11.

30. Ajibade, A.J. Fakunle, P.B., Adetunji, T.J. & Kehinde, B.D. (2019). Protective Effects of Aqueous Extract of Carica papaya Leaf on the Liver of Streptozotocin (STZ)-Induced Diabetic Adult Wistar Rats.Asian Journal of Research in Medical and Pharmaceutical Sciences, 7(4), 1-12.

31. Fadillioglu, E., Kurcer, Z., Parlakpinar, H., Iraz, M. & Gursul, C. (2008). Melatonin treatment against remote open injury induced by renal ischemia reperfusion injury in diabetes mellitus. Archive in Pharmaceutical Research, 31(6), 705-712.

32. Punithavathi, V.R., Anuthama, R. & Prince, P.S. (2008). Combined treatment with naringin andvitamin C ameliorates streptozotocin induceddiabetes in male Wistar rats. Journal of Applied Toxicology, 28(6), 806-813.

33. Sonia, R., Leila, M., Ana, B., Grando-Serrano, O.V., Begona, M., Luis, G. and Laura, B. (2008). Hypolipidemic effect on cholesterol- fed rats of soluble fiber rich product obtained from cocoa husks. Journal of Agriculture & Food Chemistry, 56 (4), 6985-6993.

34. Afaf-Haniem, M. R., Hanaa, F. E. & Madiha, M. A. (2015). Effect of Fortified Cake with Papaya (Carica papaya L.) on Hypoglycemia of Streptozotocin (STZ) Induced Diabetic in Experimental Rats. World Applied Sciences Journal, 33 (7), 1142-1153.

35. Adisa, R.A., Choudhary, M.I. & Olorunsogo, O.O. (2011). Hypoglycemic activity of Buchholzia coriacea (Capparaceae) seeds in streptozotocin-induced diabetic rats and mice. Experimental

Toxicology & Pathology, 63(8), 619–625.

36. De, D., Chatterjee, K., Ali, K.M., Bera, T.K. & Ghosh, D. (2011). Antidiabetic potentiality of the aqueous-methanolic extract of seed of Swieteniamahagoni (L.) Jacq.instreptozotocin-induced diabetic male Albino rat: A correlative and evidence-based approach with antioxidative and antihyperlipidemic activities. Evidence Based Complement Alternative Medicine, 15 (5), 892-897.

37. Islam, M.S. (2011). Effects of the aqueous extract of white tea (Camellia sinensis) in a streptozotocin-induced diabetes model of rats. Phytomedicine, 19 (2), 25–31.

38. Harrison, S.A. (2006). Liver disease in patients with diabetes mellitus. Journal of Clinical Gastroenterology, 40 (6), 68-76.

39. Hickman, I.J. & MacDonald, G.A. (2007). Impact of diabetes on the severity of liver disease. American Journal of Medicine, 120 (10), 829-834.

40. Ahmadvand, H., Tavafi, M. & Khalatbary, A.R. (2012). Hepatoprotective and hypolipidemic effects of Satureja Khuzestanica essential oil in alloxan-induced type 1 diabetic rats. Iranian Journal of Pharmacology Research, 11 (1), 1219-1226.

41. Ayepola, O.R., Chegou, N.N., Brooks, N.L. & Oguntibeju, O.O. (2013). Kolaviron, a Garcinia biflavonoid complex ameliorates hyperglycemia-mediated hepatic injury in rats via suppression of inflammatory responses. British Medical Council of Complement & Alternative Medicine, 13(4), 363-370.

42. Mossa, A.T., Refaie, A.A., Ramadan, A. & Bouajila, J. (2013). Amelioration of prallethrin-induced oxidative stress and hepatotoxicity in rat by the administration of Origanum majorana essential oil. Biomedical Research International, 8 (5), 908-915.

43. Kim, E.E. & Wyckoff, H.W. (1991). Reaction mechanism of alkaline phosphatase based on crystal structures. Two-metal ion catalysis. Journal of Molecular Biology, 21 (8), 449-464.

44. Zafar, M., Naeem-Ul-Hassan Naqvi, S., Ahmed, M. & Kaimkhani, Z.A. (2009). Altered liver morphology and enzymes in streptozotocin induced diabetic rats. International Journal of Morphology, 27 (3), 719-725.

45. Najla, O.A., Olfat, A.K., Kholoud, S.R., Enas, N.D. & Hanan, S.A. (2012). Hypoglycemic and Biochemical Effects of Matricaria chamomilla Leave Extract in Streptozotocin-Induced Diabetic Rats. Journal of Health Sciences, 2(5), 43-48.

46. Omonkhua, A.A, Adebayo, E.A, Saliu, J.A., Ogunwa, T.H. & Adeyelu, T.T. (2014). Liver function of Streptozotocin- Induced Diabetic Rats Orally Administered Aqueous Root-Bark Extracts of Tetrapleura tetraptera (Taub). Nigerian Journal of Basic & Applied Science, 22 (3&4), 99-106.

47. Aja, P.M., Ani, O.G., Offor, C.E., Orji, U.O. & Alum, E.U. (2015). Evaluation of Anti-Diabetic Effect and Liver Enzymes Activity of Ethanol Extract of Pterocarpus santalinoides in Alloxan Induced Diabetic Albino Rats. Global Journal of Biotechnology & Biochemistry, 10 (2), 77-83.

48. Hassan, B. Y., Vida, H., Abdolhossein, S., Sara, H., Gholamhassan, V. & Mousa-Al-Reza, H. (2019). Liver Dysfunction and Oxidative Stress in Streptozotocin-Induced Diabetic Rats: Protective Role of Artemisia Turanica. Journal of Pharmacopuncture, 22 (2), 109-114.

49. Giacco, F. & Brownlee, M. (2010). Oxidative stress and diabetic complications. Circulation Research, 107(9), 1058-1070.

50. Ahmadieh, H. & Azar, S.T. (2014). Liver disease and diabetes: association, pathophysiology, and management. Diabetes Research and Clinical Practice, 104(1), 53-62.

51. Mohamed, J., Nafizah, A.N., Zariyantey, A. & Budin, S.B. (2016). Mechanisms of Diabetes-Induced Liver Damage: The role of oxidative stress

and inflammation. Sultan Qaboos University Medical Journal, 16 (2), 132-135.

52. Okechukwu, P.N., Ndyeabura, A.W., Chiang, C.N & Akowuah, G.A. (2013). Effect of Standardized Extract of Cosinium fenestratum Stem Bark on Liver and Kidney Function Parameters in Streptozotocin-Induced Diabetic Rats. Journal of Acute Disease, 2(3), 201-206.

53. Venkateshwarlu, E., Dileep, P., Rakesh Kumar Reddy, P. & Sandhya, P. (2013). Evaluation of anti diabetic activity of carica papaya seeds on streptozotocin- induced type-ii diabetic rats. Journal of Advanced Scientific Research, 4(2), 38-41.

54. Abiola, F. A., Muhibah, F. I., Fatai, O. B. & Mutiu, I. K. (2014). Protective Effect of Ethanol Leaf Extract of Carica papaya Linn (Caricaceae) in Alloxan-induced Diabetic Rats. Tropical Journal of Pharmaceutical Research, 13 (11), 1877-1882.

55. Augustine, I.A. (2019). Antidiabetic Effect of Ethanolic Extract of Carica papaya Leaves in Alloxan-Induced Diabetic Rats. American Journal of Biomedical Sciene & Research, 5(3), 174-180.

56. Owoyele, B.V., Adebukola, O.M., Funmilayo, A.A. & Soladoye, A.O. (2008): Anti-inflammatory activities of ethanolic extract of Carica papaya leaves. Inflammopharmacology, 16 (4), 168-173.

57. Okoko, T. & Ere, D. (2012). Reduction of hydrogen peroxide-induced erythrocyte damage by Carica papaya leaf extract. Asian Pacific Journal of Tropical Biomedicine, 2 (6), 449-453.

58. Pinnamaneni, R. (2017). Nutritional and Medicinal Value of Papaya (Carica papaya Linn). World Journal of Pharmacy and Pharmaceutical Sciences, 6 (8), 2559-2578.

59. Hamden, K., Jaouadi, B., Zara, N., Rebai, T., Carreau, S. & Elfeki, A. (2011). Inhibitory effects of estrogens on digestive enzymes, insulin deficiency, and pancreas toxicity in diabetic rats. Journal of Physiology & Biochemistry, 67 (4), 121–128.

60. Gupta, R., Sharma, A.K., Sharma, M.C. & Gupta, R.S. (2012). Antioxidant activity and protection of pancreatic β-cells by Embelin in streptozotocin-induced diabetes. Journal of Diabetes, 4 (1), 248–256.

61. Shen, Y., Fukushima, M., Ito, Y., Murak, E., Hosono, T., Seki, T. & Ariga, T. (2010). Verification of the antidiabetic effects of cinnamon (Cinnamomum zeylanicum) using insulin uncontrolled type 1 diabetic rats and cultured adipocytes. Biosciences, Biotechnology & Biochemistry, 74 (8), 2418–2425.

62. Adeneye, A.A., Adeyemi, O.O. & Agbaje, E.O. (2010). Anti-obesity and antihyperlipidaemic effect of Hunteria umbellata seed extract in experimental hyperlipidaemia. Journal of Ethnopharmacology, 130(1), 307–314.

63. Abeywickrama, K.R., Ratnasooriya, W.D. & Amarakoon, A.M. (2011). Oral hypoglycaemic, antihyperglycaemic and antidiabetic activities of Sri Lankan broken orange pekoe fannings (BOPF) grade black tea (Camellia sinensis L.) in rats. Journal of Ethnopharmacology, 13(5), 278–286.

64. Cumaoglu, A., Ari, N., Kartal, M. & Karasu, C. (2011). Polyphenolic extracts from Olea europea L. protect against cytokine-induced β-cell damage through maintenance of redox homeostasis. Rejuvenation Research, 14 (1), 325–334.

65. Noman, D.S., Raad, K.M. & Salim R.H. (2009). Histological Liver Changes in Streptozotocin induced Diabetic Mice. International Medical Journal Malaysia, 8 (1), 1-4.

66. Guven, A., Yavuz, O., Cam, M., Ercan, F., Bukan, N., Comunoglu, C., & Gokce, F. (2006). Effects of melatonin on streptozotocininduced diabetic liver injury in rats. Acta Histochemical, 10 (8), 85–93.

67. Romagnoli, M., Gomez-Cabrera, M.C., Perrelli,

M.G., Biasi, F., Pallardo, F.V. & Sastre, J. (2010). Xanthine oxidase-induced oxidative stress causes activation of NF-kappaB and inflammation in the liver of type I diabetic rats. Free Radical in Biology & Medicine, 49 (8), 171–177.

68. Bugianesi, E., McCullough, A.J. & Marchesini, G. (2005). Insulin resistance: A metabolic pathway to chronic liver disease. Hepatology, 42 (8), 987–1000.

69. Larter, C.Z. & Farrell, G.C. (2006). Insulin resistance, adiponectin, cytokines in NASH: Which is the best target to treat? Journal of Hepatology, 44 (5), 253–261.

70. Leclercq, I.A., Da Silva, M.A., Schroyen, B., Van Hul, N. & Geerts, A. (2007). Insulin resistance in hepatocytes and sinusoidal liver cells: Mechanisms and consequences. Journal of Hepatology, 47 (4), 142–156.

71. Manna, P., Das, J., Ghosh, J. & Sil, P.C. (2010). Contribution of type 1 diabetes to rat liver dysfunction and cellular damage via activation of NOS, PARP, IkappaBalpha/NF-kappaB, MAPKs, and mitochondria-dependent pathways: Prophylactic role of arjunolic acid. Free Radical Biology & Medicine, 48 (4), 1465–1484.

72. Palsamy, P., Sivakumar, S. & Subramanian, S. (2010). Resveratrol attenuates hyperglycemia-mediated oxidative stress, proinflammatory cytokines and protects hepatocytes ultrastructure in streptozotocin-nicotinamide-induced experimental diabetic rats. Chemistry & Biology Interaction, 18 (6), 200–210.

73. Porepa, L., Ray, J.G., Sanchez-Romeu, P. & Booth, G.L. (2010). Newly diagnosed diabetes mellitus as a risk factor for serious liver disease. Canadian Medical Assocation Journal, 18 (2), 526–531.

74. Cohen, J.C., Horton, J.D. & Hobbs, H.H. (2011). Human fatty liver disease: Old questions and new insights. Science, 33 (2), 1519–1523.

75. Reid, A.E. (2006). Non-alcoholic fatty liver disease. In: Feldman M, Friedman LS, Brandt LJ, Eds. Sleisenger and Fordtrans Gastrointestinal and Liver Disease: Pathophysiology/diagnosis/management, 8th ed. St. Louis, Missouri, USA: Saunders, 1772–1799.

## TABLES AND FIGURE

Tables

Table 1: Impacts of Different Concentration of Aqueous *Carica papaya* Extract on Body Weight of Wistar Rat

| | Group 1 (N=20) Mean±SD | Group 2 (N=20) Mean±SD | Group 3 (N=20) Mean±SD | Group 4 (N=20) Mean±SD | Group 5 (N=20) Mean±SD | F-value | P-value |
|---|---|---|---|---|---|---|---|
| Baseline | 233.40±7.94$^{a}$ | 233.70±8.12$^{a}$ | 231.80±9.71$^{a}$ | 233.50±9.16$^{a}$ | 233.40±8.77$^{a}$ | 0.088 | 0.986 |
| Week 1 | 236.00±6.38$^{a}$ | 181.10±7.39$^{b}$ | 188.10±8.31$^{b}$ | 213.50±4.86$^{c}$ | 221.30±8.44$^{c}$ | 29.996 | 0.000 |
| Week 2 | 238.80±5.61$^{a}$ | 173.20±8.90$^{b}$ | 197.80±4.65$^{c}$ | 217.00±4.94$^{d}$ | 222.10±9.04$^{d}$ | 72.940 | 0.000 |
| Week 3 | 240.60±4.57$^{a}$ | 167.70±7.57$^{b}$ | 199.50±4.46$^{c}$ | 219.60±5.93$^{d}$ | 223.10±9.02$^{d}$ | 98.330 | 0.000 |
| Week 4 | 241.60±4.81$^{a}$ | 159.90±7.82$^{b}$ | 204.20±4.52$^{c}$ | 219.40±7.99$^{d}$ | 225.10±9.57$^{d}$ | 108.680 | 0.000 |
| Week 5 | 244.00±5.27$^{a}$ | 152.70±7.20$^{b}$ | 206.50±4.64$^{c}$ | 220.70±8.50$^{d}$ | 227.40±8.73$^{d}$ | 137.368 | 0.000 |
| Week 6 | 246.70±5.52$^{a}$ | 142.60±7.73$^{b}$ | 213.60±4.39$^{c}$ | 222.40±8.41$^{d}$ | 228.90±8.20$^{d}$ | 190.362 | 0.000 |

Key: Mean Results/Values of test groups with b,c,d superscripts indicate statistical significance when compared with the control group

Table 2: Impacts of Different Concentration of Aqueous *Carica papaya* Leaf Extract on Blood Glucose of Wistar Rat

| | Group 1 (N=20) Mean±SD | Group 2 (N=20) Mean±SD | Group 3 (N=20) Mean±SD | Group 4 (N=20) Mean±SD | Group 5 (N=20) Mean±SD | F-value | P-value |
|---|---|---|---|---|---|---|---|
| Baseline | 81.00±2.75$^{a}$ | 330.90±9.13$^{b}$ | 334.50±7.10$^{b}$ | 329.70±8.42$^{b}$ | 333.80±7.39$^{b}$ | 2023.193 | 0.000 |
| Week 1 | 79.90±1.60$^{a}$ | 339.00±27.26$^{b}$ | 321.50±6.04$^{c}$ | 311.00±3.43$^{c}$ | 312.80±8.46$^{c}$ | 695.418 | 0.000 |
| Week 2 | 82.00±1.83$^{b}$ | 350.00±10.64$^{b}$ | 266.70±4.83$^{c}$ | 241.90±4.27$^{d}$ | 222.10±9.04$^{e}$ | 261.051 | 0.000 |
| Week 3 | 81.70±1.42$^{a}$ | 385.00±9.26$^{b}$ | 220.40±33.47$^{c}$ | 199.70±2.26$^{d}$ | 192.70±10.60$^{d}$ | 433.962 | 0.000 |
| Week 4 | 81.00±4.90$^{a}$ | 460.90±24.82$^{b}$ | 193.40±20.89$^{c}$ | 173.30±12.80$^{d}$ | 163.60±11.77$^{d}$ | 764.344 | 0.000 |
| Week 5 | 80.20±1.40$^{a}$ | 484.70±15.51$^{b}$ | 167.70±10.32$^{c}$ | 143.00±8.99$^{d}$ | 133.80±11.84$^{d}$ | 2411.764 | 0.000 |
| Week 6 | 81.50±2.59$^{a}$ | 498.60±8.79$^{b}$ | 165.60±10.49$^{c}$ | 139.60±7.47$^{d}$ | 126.50±11.08$^{d}$ | 3639.728 | 0.000 |

Key: Mean Value/Result Having Different Superscript Are significantly different at p≤0.05

Table 3: Impacts of Different Concentration of Aqueous *Carica papaya* Leaf Extract on some Liver Enzymes of Albino Wistar Rat

| Parameters | Group 1 (N=20) Mean±SD | Group 2 (N=20) Mean±SD | Group 3 (N=20) Mean±SD | Group 4 (N=20) Mean±SD | Group 5 (N=20) Mean±SD | F-value | p-value |
|---|---|---|---|---|---|---|---|
| ALP (U/L) | 111.70±13.12$^{a}$ | 244.00±7.33$^{b}$ | 154.40±5.93$^{c}$ | 140.80±6.16$^{d}$ | 134.30±4.05$^{d}$ | 412.454 | 0.000 |
| ALT (U/L) | 48.70±5.31$^{a}$ | 75.70±4.92$^{b}$ | 62.60±2.67$^{c}$ | 60.10±2.96$^{c}$ | 57.50±4.50$^{c}$ | 53.990 | 0.000 |
| AST (U/L) | 106.20±8.19$^{a}$ | 220.20±12.43$^{b}$ | 210.10±2.23$^{c}$ | 195.00±5.56$^{d}$ | 163.10±4.01$^{d}$ | 387.025 | 0.000 |

Key: Mean Results/Values with Different Superscripts are Significantly Different at P≤0.05
GROUP I=NORMAL CONTROL RATS, GROUP II= DIABETIC CONTROL RAT,
GROUP III=Diabetic Rat + 0.75G/KG Body Weight aqueous *Carica Papaya* Extract
GROUP IV= Diabetic Rat + 1.50G/KG Body.Weight aqueous *Carica Papaya* Extract
GROUP V= Diabetic Rat + 3.0G/KG Body Weight aqueous *Carica Papaya* Extract

Figures

Photomicrograph Plates of Histological Evaluations of Liver

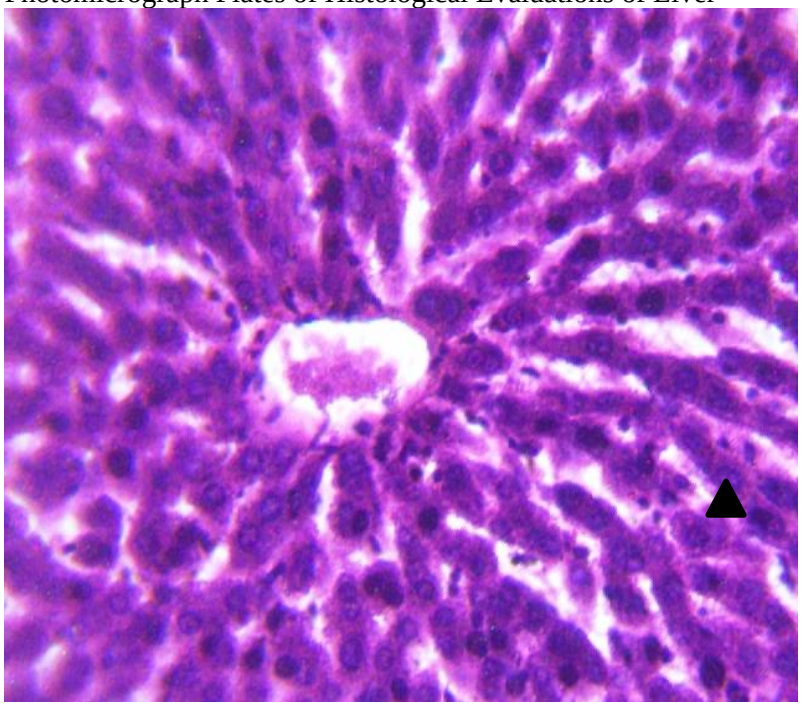

Plate 1: Photomicrograph of Non-Diabetic (Normal) control rat liver received distilled water plus growers mash. Showing normal liver hepatocytes and architecture (H&E x400)

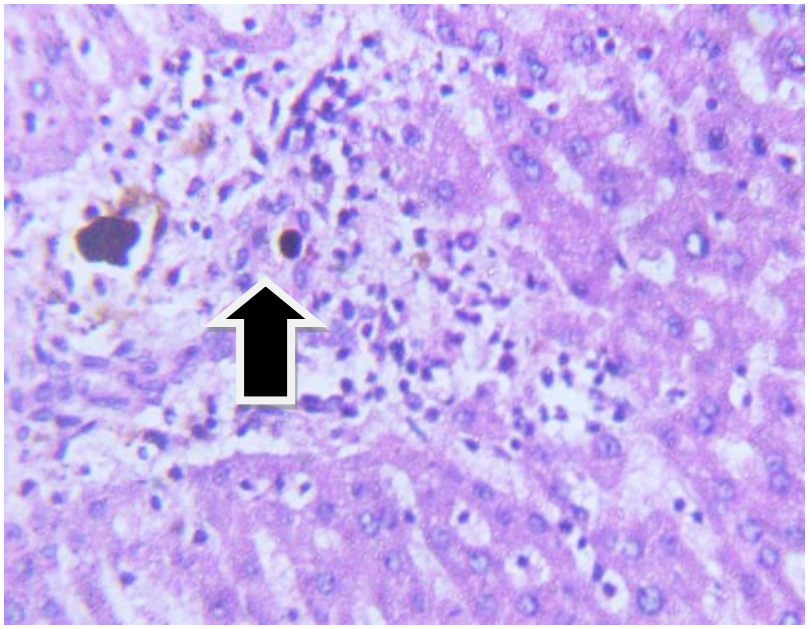

Plate 2: Photomicrograph of Diabetic Control rat liver received distilled water plus growers mash. Showing Periportal inflammation (Black arrow) (H&E x400)


https://kjhs.kiu.ac.ug https://doi.org/10.59568/KJHS-2024-4-2-12 KJHS 4(2); 2024. Pages (152-170)

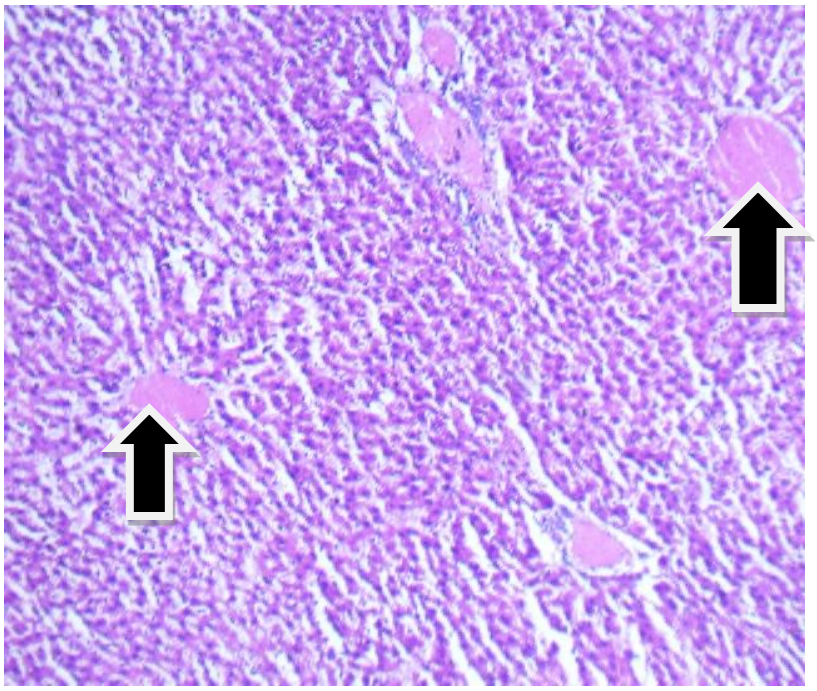

Plate 3: Photomicrograph of Diabetic rat liver received distilled water and 0.75g/kg body weight carica papaya extract.
Showing congested veins and sinusoids (Black arrows) (H&E x400)

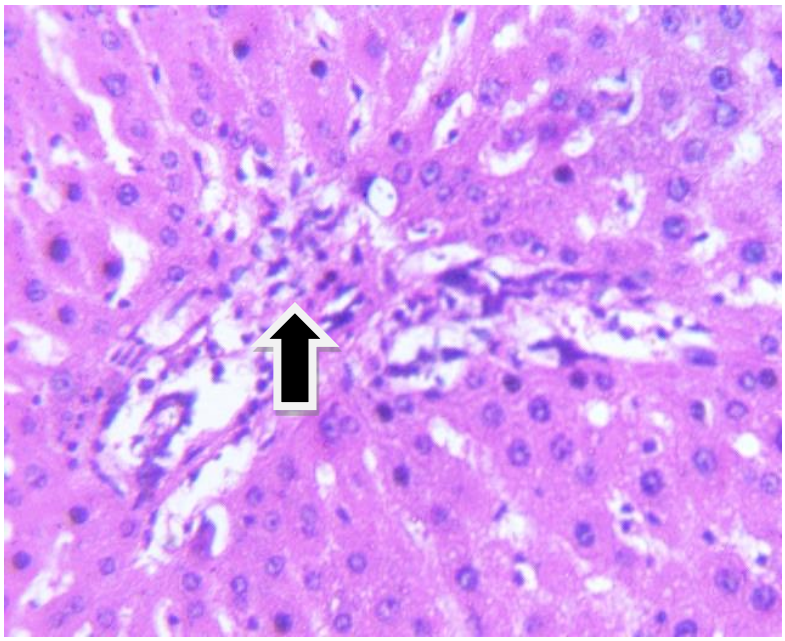

Plate 4: Photomicrograph of Diabetic Rat liver received received distilled water and 1.5g/kg body weight *Carica papaya* extract.
Showing normal hepatocyte with reduced periportal inflammation (Black arrow) (H/E x400)

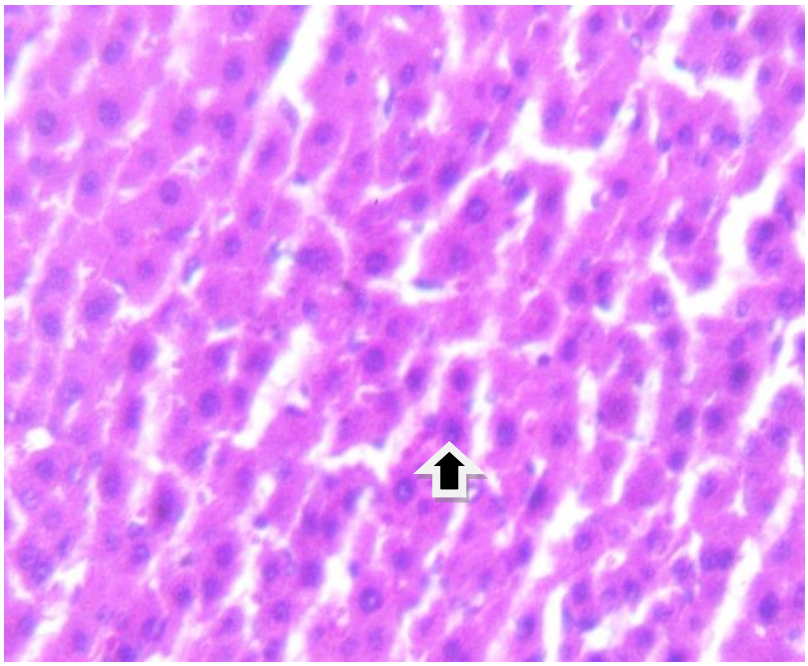

Plate 5: Photomicrograph of Diabetic Rat liver received received distilled water and 3.0g/kg body weight *Carica papaya* extract.
Showing normal hepatocytes (Black arrow) (H/E x400)

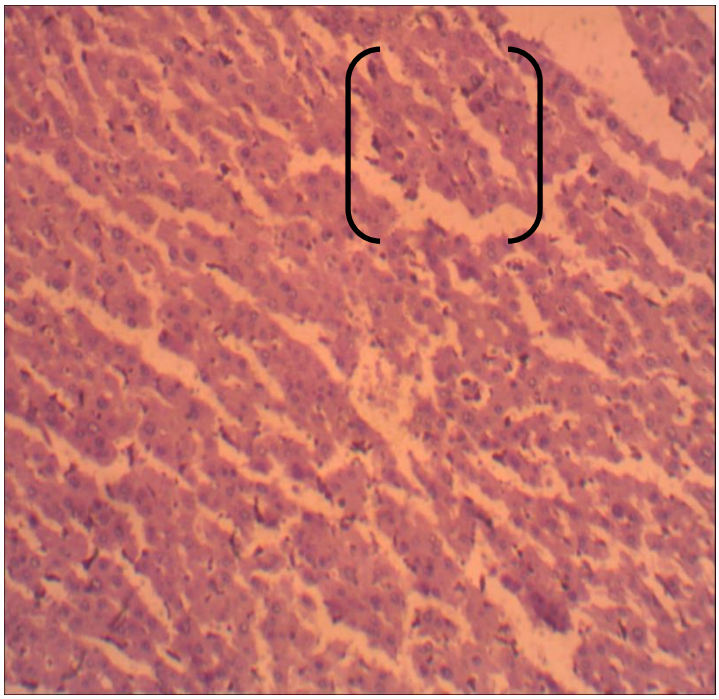

Plate 6: Photomicrograph of Rats in Normal Control group I (Non-Diabetic). Displaying a STRONG PAS-

POSITIVE reaction evidenced by **presence of red granule**s in hepatic tissues (PAS X400)

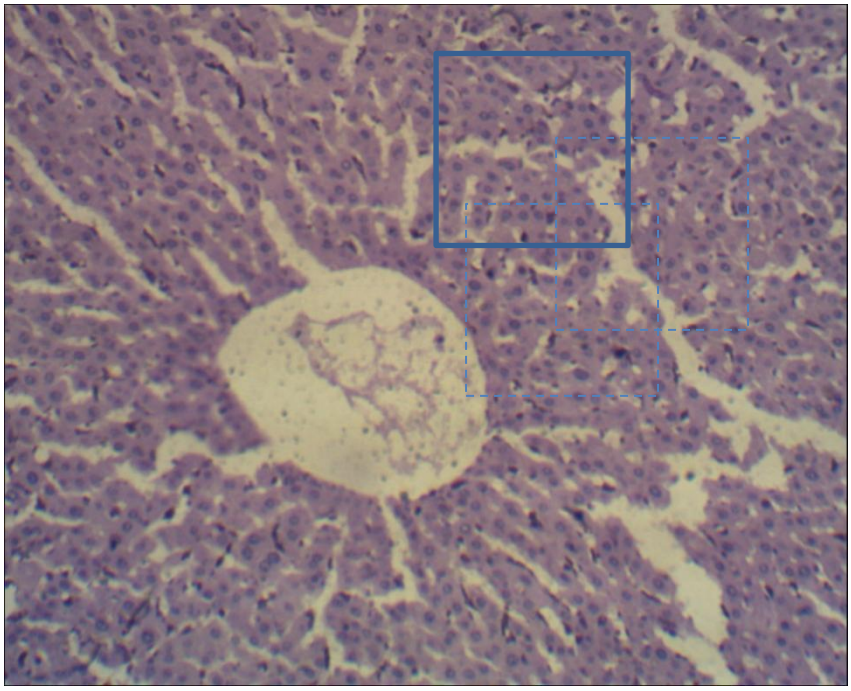

Plate 7: Photomicrograph of Diabetic Control group. Showing NEGATIVE PAS reaction **evidenced by absence of red granules** in hepatic tissues(PAS X400)

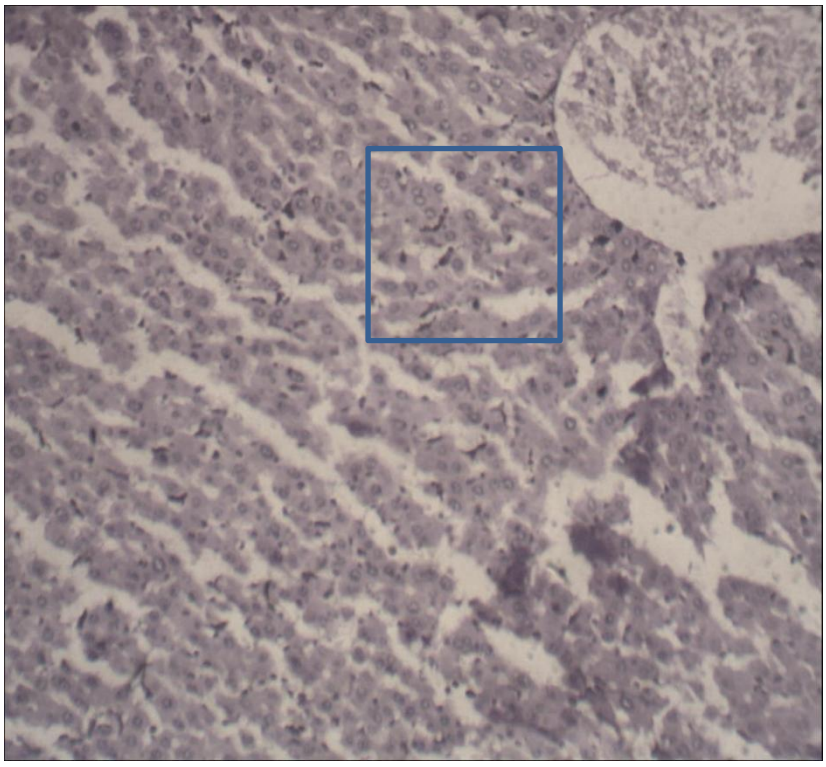

Plate 8: Photomicrograph of Diabetic Test group given 0.75g/kg body weight *Carica papaya* extract. Showing NEGATIVE PAS reaction evidenced by **absence of red granules** in hepatic tissues (PAS X400)

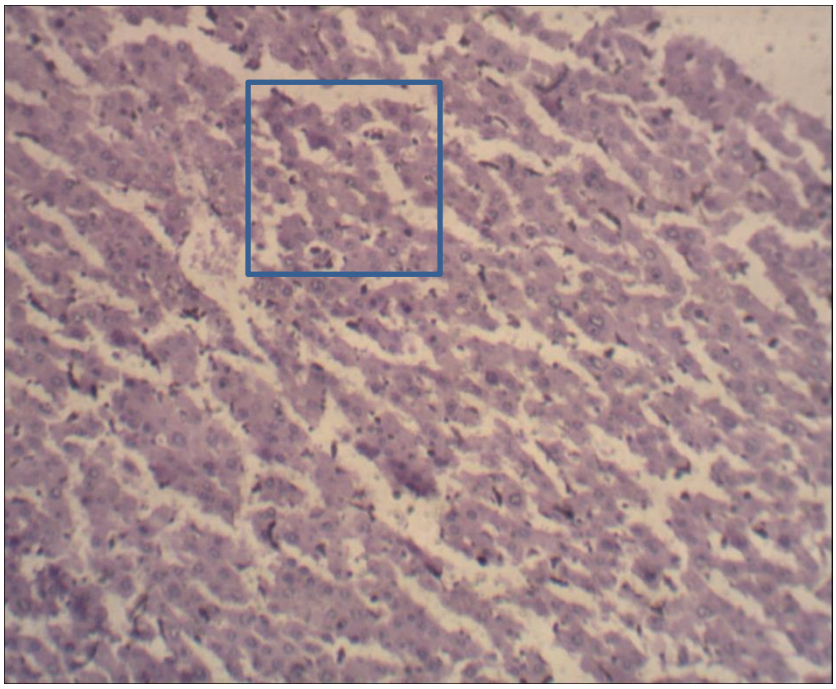

Plate 9: Photomicrograph of Diabetic Test group given 1.5g/kg body weight *Carica papaya* leaves extract. Showing MILD POSITIVE PAS reaction evidenced by **presence of light-red granules** in hepatic tissues (PAS X400)

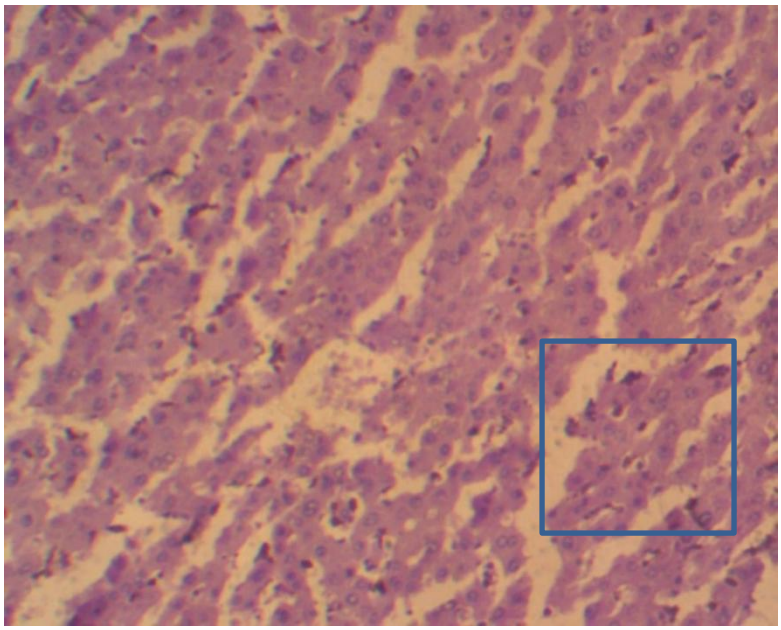

Plate 10: Photomicrograph of Diabetic Test group given 3g/kg body weight *Carica papaya* leaf extract. Showing MODERATELY-POSITIVE PAS reaction evidenced by **presence of red granules** in hepatic tissues (PAS X400)