



ANTIHYPERGLYCAEMIC EFFECT OF ETHANOLIC EXTRACT OF *Carica papaya* SEEDS ON STREPTOZOTOCIN-INDUCED HYPERGLYCAEMIC WISTAR RATS

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ABSTRACT

Diabetes is one of the leading causes of death in the world today. Medicinal plants have been employed as therapeutics before modern medications became prevalent. This research work was aimed at evaluating the antihyperglycaemic effect of the ethanolic extract of *Carica papaya* seeds on streptozotocin-induced hyperglycaemic Wistar rats. The phytochemical properties of ethanolic extract of *Carica papaya* seeds were conducted using the method of Association of Analytical Chemists (AOAC). Twenty-five (25) male Wistar rats weighing between 250 and 296 g were distributed into five groups. Apart from Group 1, Group 2 to Group 5 Wistar rats were induced hyperglycaemia with 45 mg/kg of streptozotocin (STZ). The Group 1 was normal control (distilled water), Group 2: 45 mg/kg STZ, Group 3: 10 mg/kg glibenclamide, Group 4: 50 mg/kg ethanolic extract of *C. papaya* seeds, Group 5: 100 mg/kg ethanolic extract of *C. papaya* seeds. The phytochemical analysis of the ethanolic extract of *Carica papaya* seeds revealed the presence of alkaloids, eugenols, flavonoids, glycoside, phenols, saponins, steroids, tannins and terpenoid. The Effect of ethanolic extract of *Carica papaya* seeds on streptozotocin-induced hyperglycaemia on Wistar rats showed significant decrease in the blood sugar levels for Group 4 (50 mg/kg ethanolic extract) and Group 5 (100 mg/kg ethanolic extract) at day 3 and 7 treatment periods. The ethanolic extract of *C. papaya* also showed ameliorative abilities on biochemical and haematological parameters. In the kidney of hyperglycaemic treated rats, the ethanolic extract of *C. papaya* seeds reduced distortion of the renal corpuscles (glomeruli and Bowman's capsules), as well as accumulation of glycogen and lipids was prevented. Damaged pancreatic islet cells from hyperglycaemic Wistar rats were regeneration as preservation of cells occurred. This research shows the potency of the medicinal nature of the seeds of *Carica papaya*.

**Keywords:** *Carica papaya*, Diabetes, Glibenclamide, Streptozotocin, Wistar rats

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INTRODUCTION

Diabetes is a disorder of carbohydrate, fat and protein metabolism characterized by high blood glucose levels, which could be because of lack of insulin. Diabetes is one of the leading causes of death in the world [1]. The prevalence of diabetes has increased considerably on a global scale. The most significant aspect in lowering the risks of diabetes and its complications is the challenge of controlling hyperglycemia [2]. The number of patients with diabetes is rising quickly, making it difficult to manage their consequences. Medicinal plant extracts have a long history in helping to manage diabetics and these plants can be quite beneficial to modern medicine. Medicinal plants and the phytochemicals they yield have proven to be a remarkable source of compounds with promise for use in medicine and therapy development [3]. These compounds possess unique and intricate structures that can be utilized as lead molecules to create derivatives with reduced side effects and increased specificity [4]. About 65-80% of

the world's population in developing countries due to poverty lack access to modern medicine, therefore depend on traditional medicine which are easily accessible, cheap and with low side effects. Different parts of plants are used such as leaves, flowers, seeds, roots, bulb [5]. *Carica papaya* belongs to the Caricaceae family of herbaceous plants and is native to the tropical regions of Mexico, Central America, and northern South America. It has prominent leaves that range in length from 20 to 60 cm. *C. papaya* is widely farmed and found across the tropics and subtropics. Patients with type 2 diabetes and healthy individuals have considerably lower plasma glucose levels when given a fermented papaya preparation [6]. The fruit and leaves of *Carica papaya* have previously been reported to exhibit hypoglycemic properties [7, 8]. The purpose of this study was to investigate the antihyperglycaemic effect of the ethanol extract of *Carica papaya* seeds on streptozotocin-induced hyperglycaemic Wistar rats.

## MATERIALS AND METHODS

### Collection of plant material

The fruits of *Carica papaya* were purchased from Uselu market in Egor Local Government Area, Benin City, Edo State, Nigeria. It was identified and authenticated by Prof. Timothy Odaro in the Herbarium Unit of the Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin, Edo State, Nigeria with the voucher number UBH-W24190.

### Preparation of plant material

The fruits of *Carica papaya* were rinsed in clean water, sliced into halves, the seeds were removed and then air dried for 7 days in the laboratory. The dried seeds were grinded into powdered using the British milling machine. 800 g of the pulverized *Carica papaya* seeds was weighed into a big bottle and then soaked with 2 litres of ethanol for 72 hrs.

### Phytochemical analysis

The plant extract was subjected to qualitative phytochemical analysis using established techniques with slight modifications [9, 10, 11]. The following tests below were carried out to identify substances:

**Test for saponins:** One gramme (1 g) of powdered pawpaw seed was boiled with 10 ml of distilled water in a water bath for 10 mins. The mixture was filtered while hot and allowed to cool. Two (2) drops of olive oil was mixed with 2.5 ml filtrate and made up to 10 ml with distilled water. It was then shaken vigorously for a few minutes; the formation of a fairly stable emulsion indicated the presence of saponins.

**Test for alkaloids:** One gram (1 g) of ethanolic extract of pawpaw seed was boiled with water and acidified with 5 ml of 1 % HCl on a steam bath. The solution obtained was filtered and 2 ml of the filtrate was treated with few drops of Mayer's reagent (potassium mercuric iodide). The formation of a creamy white precipitate indicated the presence of alkaloids in the extract.

**Test for glycosides:** After dissolving 0.5 mg of the extract in water, an aqueous NaOH solution was added. The presence of glycosides was revealed by the emergence of a yellow tint.

**Test for glycosides:** Five milliliters (5 ml) of the ethanolic extract was treated with 2 ml of glacial acetic acid containing one drop of ferric chloride solution. Then 1 ml of concentrated sulphuric acid was introduced. The formation of a brown ring at the interface indicated the presence of glycosides.

**Test for flavonoids:** One gram (1 g) of powdered pawpaw seed was boiled in 20 ml of water and then filtered. 5 ml of diluted ammonia solution was added to the filtrate, followed by the addition of concentrated H<sub>2</sub>SO<sub>4</sub>. A yellow colouration was indicative of the presence of flavonoids.

**Test for phenol:** A 0.5 g of powdered pawpaw seed was boiled with 10 ml of distilled water for 5 mins and

filtered while hot. Then 1ml of ferric chloride solution was added. The formation of blue-black or brown colouration indicated the presence of phenol.

**Test for Tannins:** One milliliter (1 ml) of sodium chloride-containing gelatin solution was combined with 1.0 ml of ethanolic extract. The formation of white precipitate is indicative of tannins.

**Test for eugenols:** Two milliliters (2 ml) of the ethanolic extract was mixed with 5 ml of potassium hydroxide and the resulting solution was treated with hydrochloric acid. A pale-yellow precipitate indicated the presence of eugenols.

**Test for steroids:** Two milliliters (2 ml) acetic anhydride and sulphuric acid was added to 0.5 g ethanolic extract of pawpaw seed. The colour change from violet to blue or green indicated the presence of steroids.

**Test for terpenoids:** Concentrated H<sub>2</sub>SO<sub>4</sub> and 2 ml of chloroform was combined with 0.2 g ethanolic extract of pawpaw seed. The formation of a reddish-brown colour was indicative of terpenoid.

### Experimental animals

For the hyperglycemic investigation, twenty-five (25) mature male Wistar rats weighing between 250 and 296 g were utilized. The animals were kept in hygienic wooden cages (five per cage), with free access to water and food and were kept at room temperature for two weeks for acclimatization. The experiment was carried out in compliance with Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA) Guidelines and received ethical approval from the Institutional Animal Ethical Committee.

### Preparation/ Induction of diabetes

For diabetic induction, after 24 hours fast, the animals in the diabetic group (n=5) received 60 mg/kg STZ (i.p.) diluted in 0.1 M citrate buffer (pH 4.5). The animals in the normoglycemic group (n=5) received only vehicle (1 ml/kg citrate buffer (i.p.)). After Seventy-two hours (72 hours) of STZ administration, hyperglycaemia was diagnosed using an Accu check glucometer. The Wistar rats were considered diabetic when glycemia was  $\geq 250$  mg/dl [12].

### Treatment protocol

Five groups consisting of five Wistar rats were selected (n = 5). Rats in Group I were non-diabetic rats, while the other four groups had diabetic rats. Group 2 were diabetic Wistar rats that were not given any form of treatment. Group 3 were diabetic Wistar rats that were treated with 50 mg/kg of ethanolic extract of *Carica papaya* seeds. Group 4 were diabetic Wistar rats that were treated with 100 mg/kg of ethanolic extract of *Carica papaya* seeds. Group 5 were diabetic Wistar rats that were treated with 10 mg/kg of Glibenclamide. The treatment protocol was followed, while the sugar levels for day 1, 3 and 7

were recorded. Using a glucometer (Accu-Chek®, Model-GC, Roche, Germany), blood glucose levels (mg/dl) was measured on day 1 (baseline), day 3 and day 7 following an overnight fast for each group. The rats were anesthetized in a chamber that was saturated with isoflurane (1-3 %) and blood was collected from the ocular plexus.

**Biochemical parameters:** Using diagnostic kits from Merck Limited's India Ecoline Range, biochemical estimates of cholesterol, high density lipoprotein (HDL), triglycerides, low density lipoprotein (LDL), bicarbonate, chloride ion, urea, sodium, potassium were performed.

**Haematological parameters:** For the evaluation of haematological parameters, after all the experimental Wistar rats were sacrificed, blood was collected into EDTA bottles and the following haematological parameters were analyzed – white blood cells, lymphocytes, granulocytes, hemoglobin and human colorectal carcinoma.

**Histopathology**

The animals were sacrificed and tissues such as kidney and the pancreas were collected and preserved in 10 % formal-saline for further histopathological analysis. Using the techniques described by Ibeh [13], serial slices of the formalin organs were cut to a thickness of 5 µm, fixed on microscope slides, dewaxed, and stained with haematoxylin and eosin. The pieces were set in Canada balsam and subjected to a light microscope examination to see whether architectural flaws were present or not.

**Data analysis**

The data were analyzed using student ANOVA and the data were expressed as mean and standard error of mean. Values of P <0.05 were considered statistically significant. Version 6 of Graph Pad Prism version 6.0 was also used for the statistical analysis

**RESULTS**

The results in Table 1 shows the qualitative phytochemical screening of ethanolic extract of *Carica papaya* seeds. The result revealed the presence of the phytochemical components such as glycoside, saponins, phenol, eugenols, terpenoid, steroids, alkaloid, flavonoids. Table 2 revealed the quantitative phytochemical components, showing flavonoid as the

highest with 404.90±2.54 mg/kg and tannins having the smallest, 2.00±0.34 mg/kg. Tables 3 and 4 showed the result of 7 days treatment with ethanolic extract of *Carica papaya* on fasting and random blood glucose levels of streptozotocin-induced hyperglycaemic Wistar rats. Table 5 revealed the effect of ethanolic extract of *Carica papaya* seeds on the lipid profile of streptozotocin-induced hyperglycaemic Wistar rats. Tables 6 revealed the effect of the ethanolic extract of *Carica papaya* seeds on the kidney functions of streptozotocin-induced hyperglycaemic Wistar rats. Table 7 revealed the effect of ethanolic extract of *Carica papaya* seeds on the haematological components of streptozotocin induced hyperglycaemic Wistar rats.

**Table 1:** Preliminary qualitative phytochemical screening of Ethanolic extract of *Carica papaya* seed

S/N	Phytochemicals	Test method	Ethanolic extract of <i>Carica papaya</i> seeds
1	Glycosides	General Test	+
2	Saponins	Frothing Test	+
3	Phenols	Ethanol/Ferric Chloride	+
4	Eugenols	Ethanol/Ferric Chloride	+
5	Terpenoids	Salkowski Test	+
6	Steroids	KOH test	+
7	Alkaloids	Picric Acid	+
8	Flavonoids	Lead Acetate	+

Keys: Negative (-), Present (+)

**Table 2** Results of the Quantitative Phytochemical Screening of Ethanolic Extract of *Carica papaya* Seeds

S/N	Parameters	Units	Ethanolic extract of <i>Carica papaya</i> seeds
1	Alkaloids	%	5.82 ± 0.23
2	Total Tannins	mg/kg	2.00 ± 0.34
3	Total Saponin	mg/kg	26.24 ± 3.75
4	Total Phenolics	mg/kg	186.20 ± 3.67
5	Total Flavonoid	mg/kg	404.90 ± 2.54

The values are the Means ± SEM for five rats in each group. Significance at p<0.05, with respect to normal control

**Table 3:** Results of 7 days fasting blood sugar using ethanolic extract of *Carica papaya* seeds on experimental Wistar rats as treatment

S/N	Treatment/dose	Day 1	Day 3	Day 7
1	Control (distilled water)	91.50 ± 4.50	90.00 ± 3.00	80.00 ± 9.00
2	45 mg/kg STZ	527.50 ± 72.50	483.00 ± 117.00	333.00 ± 20.00 <sup>a</sup>
3	10 mg/kg	376.50 ± 55.50	373.00 ± 13.0	100.50 ± 80.00 <sup>a</sup>

	glibenclamide			
4	50 mg/kg ethanolic extract	448.33 ± 31.52	284.00 ± 15.53	87.00 ± 17.38 <sup>a</sup>
5	100 mg/kg ethanolic extract	537.00 ± 63.00	338.00 ± 35.5	82.33 ± 23.21 <sup>a</sup>

The values are the Means ± SEM for five rats in each group. Significance at  $p < 0.05$ , with respect to normal control

**Table 4:** Results of 7 days random blood sugar using ethanolic extract of *Carica papaya* seeds on experimental Wistar rats as treatment

S/N	Treatment/dose	Day1	Day 3	Day 7
1	Control (distilled water)	114.00 ± 19.03	112.33 ± 05.61	103.33 ± 3.93
2	45 mg/kg STZ	583.00 ± 01.53	578.33 ± 00.88	543.00 ± 1.00
3	10 mg/kg glibenclamide	597.00 ± 03.00	300.00 ± 20.00	100.00 ± 1.00 <sup>a</sup>
4	50 mg/kg ethanolic extract	586.00 ± 14.00	489.67 ± 11.68	141.00 ± 51.00 <sup>a</sup>
5	100 mg/kg ethanolic extract	587.67 ± 12.33	534.33 ± 24.77	125.33 ± 26.56 <sup>a</sup>

The values are the Means ± SEM for five rats in each group. Significance at  $p < 0.05$ , with respect to normal control

**Table 5:** Effect of extract of *Carica papaya* seeds on lipid profile of streptozotocin-induced diabetic rats and non-diabetic rats

S/N	Treatment	Cholesterol mg/dL	HDL mg/dL	Triglyceride mg/dL	LDL mg/dL
1	Control (distilled water)	98.33±1.45	31.33 ± 1.33	106.00 ± 1.00	45.67 ± 2.18
2	45 mg/kg STZ	113.0 ± 12.17	21.0 ± 1.53	169.7 ± 4.84	47.67 ± 4.177
3	10 mg/kg glibenclamide	95.33 ± 12.45	38.00±3.06	98.00 ± 1.00	36.00 ± 2.08
4	50 mg/kg ethanolic extract	59.0 ± 1.57	20.20 ± 0.58	79.60 ± 3.326	21.20± 0.8602
5	100 mg/kg ethanolic extract	80.13 ± 2.10	21.29 ± 0.38	87.07 ± 2.91	28.11 ± 0.63

The values are the Means ± SEM for five rats in each group. Significance at  $p < 0.05$ , with respect to normal control.

**Table 6:** Effect of extract of *Carica papaya* seeds on kidney functions of streptozotocin-induced diabetic rats and non-diabetic rats

S/N	Treatment	HCO <sub>3</sub> <sup>-</sup> mmol/L	Cl <sup>-</sup> mmol/L	Creatine mg/dL	Urea mg/dL	Na <sup>+</sup> mmol/L	K <sup>+</sup> <u>mmol/L</u>
1	Control (distilled water)	22.00 ± 2.00	103.70 ± 2.03	0.53 ± 0.03	29.00 ± 0.58	136.7 ± 1.67	4.53 ± 0.15
2	45 mg/kg STZ	25.33 ± 1.33	105.00 ± 1.00	0.83 ± 0.03	43.33 ± 1.86	141.00 ± 1.00	5.37 ± 0.19
3	10 mg/kg glibenclamide	22.67 ± 1.33	101.30 ± 2.96	0.80 ± 0.06	55.00 ± 4.163	136.7 ± 1.20	5.50 ± 0.25
4	50 mg/kg extract	16.80 ± 1.158	95.20 ± 0.8000	0.3800 ± 0.5831	74.00 ± 3.356	138.2 ± 0.5832	8.860 ± 0.1208
5	100 mg/kg extract	19.11 ± 2.07	98.10 ± 2.62	0.77 ± 0.07	74.00 ± 3.356	137.01 ± 1.63	7.19 ± 0.32

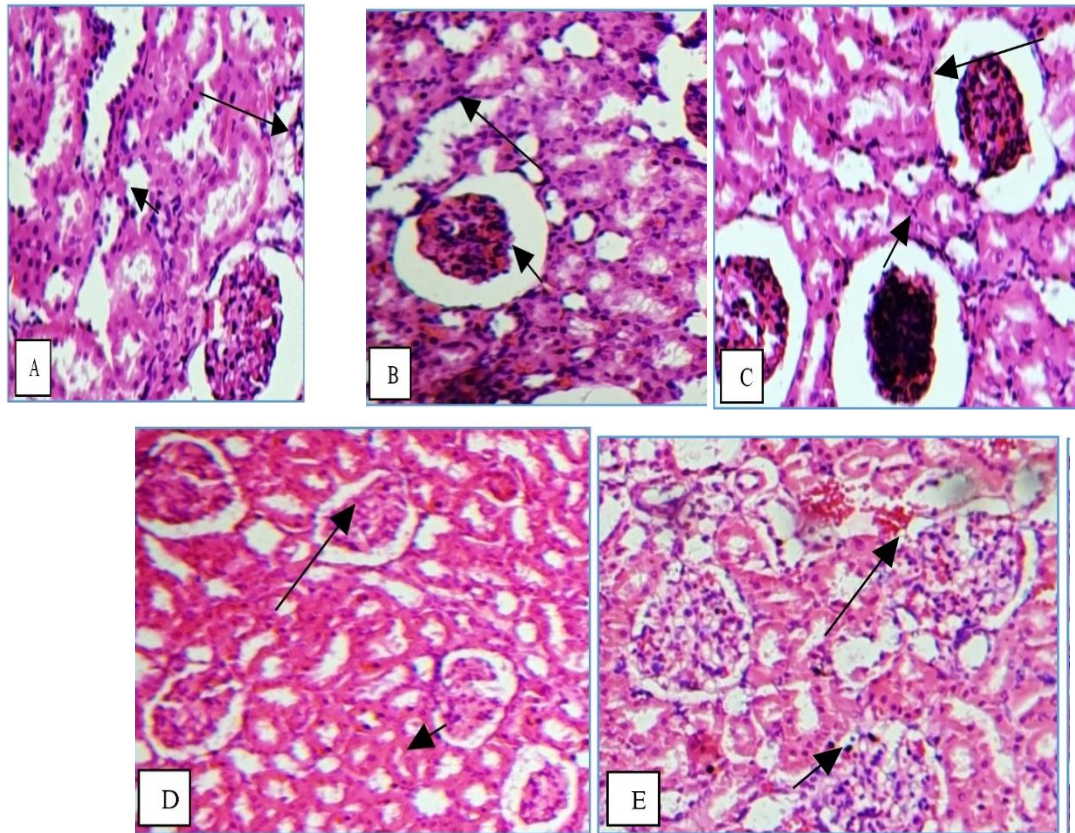
The values are the Means ± SEM for five rats in each group. Significance at p<0.05, with respect to normal control

**Table 7:** Effect of extract of *Carica papaya* seeds on haematological components of streptozotocin-induced diabetic rats and non-diabetic rats

S/N	Treatment	WBC 10 <sup>3</sup> /U1	LYM %	MID %	GRAN %	RBC 10 <sup>6</sup> /uL	HGB g/dL	HCT %
1	Control (distilled water)	4.20 ± 0.15	85.60 ± 0.26	10.97 ± 0.23	3.43 ± 0.15	6.24 ± 0.06	12.14 ± 0.07	35.67 ± 0.35
2	45 mg/kg STZ	7.20 ± 0.12	86.67 ± 1.00	10.53 ± 0.90	2.80 ± 0.12	4.99 ± 0.05	14.17 ± 0.41	40.70 ± 0.99
3	10 mg/kg glibenclamide	3.40 ± 0.26	86.93 ± 1.07	8.967 ± 0.61	4.10 ± 0.46	5.78 ± 0.26	24.57 ± 0.27	38.83 ± 0.99
4	50 mg/kg ethanolic extract	5.860 ± 1.04	91.12 ± 1.1176	6.680 ± 0.9997	2.200 ± 0.1945	7.698 ± 0.1262	15.04 ± 0.3076	40.80 ± 0.6935
5	100 mg/kg ethanolic extract	5.61 ± 0.11	89.00 ± 1.29	9.21 ± 0.71	3.10 ± 0.16	7.51 ± 0.30	19.12 ± 0.41	39.61 ± 1.02

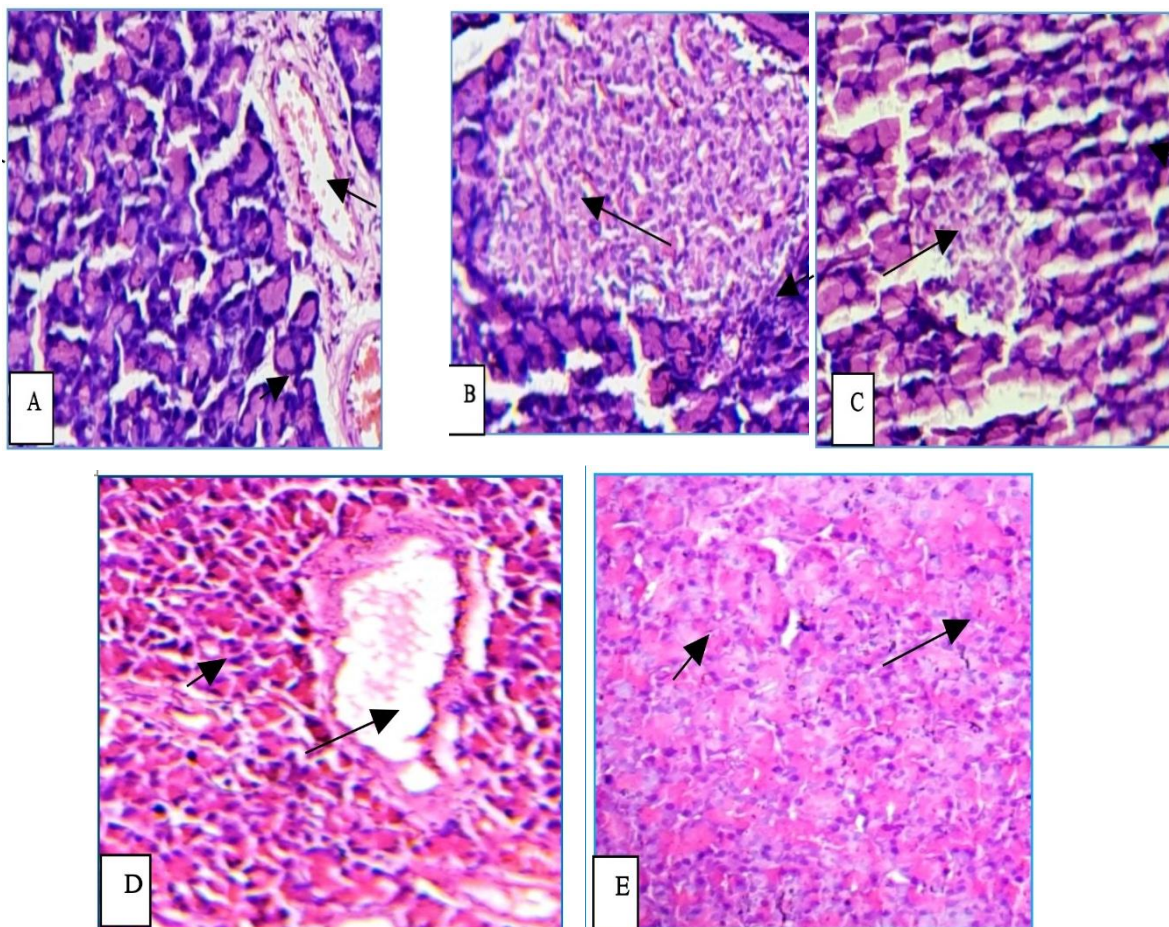
The values are the Means ± SEM for five rats in each group. Significance at p<0.05, with respect to normal control

**Keys:** WBC – White blood cell, LYM – lymphocytes, MID – Mid cell, GRAN – Granulocytes, RBC – Red blood cells, HGB - Hemoglobin, HCT – Human colorectal carcinoma



**Plate 1:** Effects of the ethanolic extract of *Carica papaya* seeds on kidney cells

- A. Normal control (distilled water): Kidney reveals visible renal corpuscle and interstitial space and tubules.
- B. 45 mg/kg STZ: Kidney reveals visible renal corpuscle and interstitial tubules and space necrosis.
- C. 10 mg/kg glibenclamide: Kidney reveals visible renal corpuscle and interstitial space with mononuclear infiltrate
- D. 50 mg/kg ethanolic extract: Kidney reveals visible atrophied renal corpuscle and tubules slight distortion
- E. 100 mg/kg ethanolic extract: Kidney reveals visible atrophied renal corpuscle with distortion tubules having mononuclear infiltrates.



**Plate 2:** Effects of the ethanolic extract of *Carica papaya* seeds on pancreas cells

- A. Normal control (distilled water): Pancreas reveals secretory acini with intralobular duct on low power.
- B. 45 mg/kg STZ: Pancreas features had several acinar cells with mildly despaired pyknotic infiltrates. Nuclei and intralobular duct appeared fatty.
- C. 10 mg/kg glibenclamide: Pancreas reveals features with several acinar cells with mildly despaired pyknotic nuclei.
- D. 50 mg/kg ethanolic extract: Pancreas reveals secretory acini which reveals intralobular duct.
- E. 100 mg/kg ethanolic extract: Pancreas have acinar cells having islet-cells with mildly pyknotic nuclei.

## DISCUSSION

The utilization of medicinal plants has become increasingly important in the treatment and prevention of various diseases [14]. Every plant contains numerous significant constituents that have potential applications in the field of medicine, contributing to the advancement of diverse pharmaceutical formulations [15]. Many underdeveloped or even advanced nations utilize herbal remedies to promote human welfare, uphold personal health, and address several ailments. Some of these medicinal plants include Echinacea, Garlic, Ginger, Ginkgo, Ginseng and various others [14]. Medicinal plants and the phytochemicals present in their various parts have been proven to be beneficial to health in terms of

curing and preventing diseases. However, due to lack of standardized doses for use, they may pose health threats to consumers [16].

The result obtained from the phytochemicals present in the ethanolic extract of the *Carica papaya* seeds are glycosides, saponins, phenols, eugenols, terpenoids, steroids, alkaloids and flavonoids. Similar study carried out by [17] also revealed similar phytochemicals as reported in this study. The research of Kanadi *et al.* [18] shows the presence of similar qualitative phytochemical results reported in this study. The research of Achuwu *et al.* [19] revealed the presence of similar qualitative phytochemical constituents as reported in Table 1 in this study. These results from other research confirms the qualitative phytochemical result of this study. The quantitative phytochemical result in Table 2 revealed that

flavonoids had the highest quantity followed by phenolics in this study. The research of Omidwura *et al.* [20] revealed the quantitative presence of flavonoids ( $50.00 \pm 0.01$  mg/kg) to be higher than other components such as alkaloids ( $47.00 \pm 0.01$  mg/kg) and phenols ( $21.40 \pm 0.01$  mg/kg), This result agrees with the quantitative result of this study in Table 2 where flavonoids had the highest quantity. The results in Table 3 and 4 revealed the result for the fasting and random blood sugar level of the hyperglycaemic Wistar rats. The values indicated the presence of hyperglycaemia in the Wistar rats Muhd *et al.* [21].

The research of Okolafor *et al.* [22] on fasting and random blood sugar on Wistar rats induced by STZ revealed that hyperglycaemic Wistar rats showed similar results like that of this study. The results in Table 3 and 4 revealed that the Wistar rats where hyperglycaemic as reported in this study. The result in Table 3 and 4 showed that the 50 mg/kg and 100 mg/kg of the ethanolic extract of *Carica papaya* seeds reduced the hyperglycaemic state of the Wistar rats in the treatment groups. The ethanolic extract of *Carica papaya* seeds showed encouraging performance indicating its ability of control hyperglycaemic state like the standard drug 10 mg/kg glibenclamide showed in this study. The research of Venkateshwarlu *et al.* [23]. revealed the anti-hyperglycaemic nature of *Carica papaya* seeds just as reported in this study. The result in Table 5 revealed the effect of the ethanolic extract of *Carica papaya* seeds on lowering lipid profile when compared to the normal control and standard drug. The research of Juarez-rojop *et al.* [24] revealed a better amelioration of the lipid profiles by the 50 mg/kg and 100 mg/kg of ethanolic extract of *Carica papaya* seeds, which is like the result reported in this study. A similar result of the ethanolic extract of *Carica papaya* seeds ameliorating the lipid profile of hyperglycaemic Wistar rats as reported in this study was also reported by Juarez-rojop *et al.*, [24]; Venkateshwarlu *et al.* [23]; Okolafor *et al.* [22] and Ugwu [25].

The research of Wala'a *et al.* [26] reported a regulation and readjustment of the lipid profile of the STZ induced hyperglycaemic Wistar rats by the ethanolic extract of *Carica papaya* seeds which was also used in this present study. The results in Table 6 revealed the effect of ethanolic extract of *Carica papaya* seeds on kidney functions. It was observed that treatment with 50 mg/kg and 100 mg/kg ethanolic extracts of *Carica papaya* seeds when compared with normal control 10 mg/kg glibenclamide showed increase in urea and potassium ( $K^+$ ) values which signifies resuscitation of dysfunctional kidney. The research of Abu *et al* [27] reported similar results like that of this study where plant extract in comparison with normal control showed the reduction and regulation of the kidney functions. The effects of the 50 mg/kg and 100 mg/kg of the ethanolic extract of *Carica papaya* seeds showed encouraging reduction of sodium like the standard drug 10 mg/kg

glibenclamide. Table 6 shows the effect of hyperglycaemia on the kidney functions of the Wistar rats and similar result was reported by the research of Asiwe *et al.* [28] on hyperglycaemic Wistar rats. The study of Olawale *et al.* [29] reported the stress caused by hyperglycaemia on the kidney such as increase in creatine, urea and sodium level just like observed in this present study. The result in Table 7 revealed the amelioration effect of 50 mg/kg and 100 mg/kg ethanolic extract of *Carica papaya* seeds in comparison with the normal control.

This result is in agreement with the research carried out by Udinyiwe *et al.* [30] where the haematological parameters of hyperglycaemic Wistar rats were compromised due to STZ induced diabetics, just like reported in this study. The haematological result of this study is also in agreement with the research of Fagbohun *et al.* [31] which showed changes in hematological parameters of STZ induced hyperglycaemic Wistar rats and its amelioration after treatment with ethanolic plant extract. The histopathological study (normal control) of the rat kidney as shown in Plate 1 revealed visible renal corpuscle with interstitial space and tubules which means that the basic structural components of the kidney, including the renal corpuscles (glomeruli and Bowman's capsules), the interstitial space between the tubules, and the tubules themselves, are visible and appear normal. The histopathological study of 45 mg/kg STZ elicited visible renal corpuscle and interstitial tubules and space necrosis and cell death. The histopathological study of 10 mg/kg glibenclamide revealed visible renal corpuscle and interstitial space with mononuclear infiltrate. The histopathological study of 50 mg/kg extract revealed visible atrophied renal corpuscle and tubules slight distortion. The histopathological study of 100 mg/kg extract revealed visible atrophied renal corpuscle with distortion tubules having mononuclear infiltrates. The finding of this research concerning the histopathological distortions were in agreement with the research conducted by Okolafor *et al.* [22]; Udinyiwe *et al.* 30; Heptinstall *et al.* [32].

The histopathological study (normal control) of the rat pancreas as shown in Plate 2 revealed secretory acini islet with intralobular duct on low power which indicates that small cluster of pancreatic acini (secretory units) is seen in close association with an intralobular duct. The histopathological study of 45 mg/kg STZ revealed that pancreas features had several acinar cells with mildly despaired pyknotic. The histopathological study of 50 mg/kg extract revealed secretory acini which indicates intralobular duct. The histopathological study of 100 mg/kg extract revealed that the pancreas has acinar cells having islet-cells with mildly pyknotic nuclei. The histopathological study of 10 mg/kg glibenclamide revealed pancreas features with several acinar cells with mildly despaired pyknotic nuclei which indicates cellular damage but not to the severe extent. The result of this

study was in alignment with the research conducted by Wang *et al.* [33]; Eboh *et al.* [17]. The resuscitation potential of the ethanolic extract of *Carica papaya* seeds in Streptozotocin-induced hyperglycaemic rats was in agreement with the plant extract used for the research conducted by Okolafor *et al.* [22]; Anhwangeet *et al.* [34]; Udinyiwe *et al.* [30]; Kloppel *et al.* [35].

## CONCLUSION

Medicinal plants contain certain natural substances that exert specific functions to the human body. This present study has revealed the presence or absence of certain phytochemicals and their concentrations. This study has also revealed the potentials found in the seeds of *Carica papaya*. These findings highlight the hypoglycemic potential of *Carica papaya* seeds and support its continuous use. However, more research is needed to isolate, purify and identify the specific active compounds responsible for these effects.

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