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# Hypoglycemic Effect of Methanol Extract of *Carica Papaya* (Pawpaw) Leaves in Alloxan-Induced Diabetic Rats

Prince O. ALAEBO., Chinwe E. ORIAKU., Chiemeziem A. OBIKE.,
Chimaraoke ONYEABO., George C. NJOKU.
Department of Biochemistry, College of Natural Sciences,
Michael Okpara University of Agriculture,
Umudike, Abia State, Nigeria.

Peter O. EKWUNOH
Department of Biochemistry, Faculty of Natural Sciences,
Chukwuemeka Odumegwu Ojukwu University,
Uli, Anambra State, Nigeria

**Abstract:- This experiment evaluatedthe hypoglycemic effect of methanol extract of *Carica papaya* leaves in alloxan-induced diabetic rats. Forty (40) male albino rats were grouped into eight: Group A (normal control), Group B (positive control) were induced and treated with glibenclamide, group C (negative control) were induced and not treated, group Dwas induced and treated with *Carica papaya* leave extract at doses of 200, group E induced and treated with *Carica papaya* leave extract at doses of 400, group F induced and treated with *Carica papaya* leave extract at doses of 600, group G induced and treated with *Carica papaya* leave extract at doses of 800 and group G induced and treated with *Carica papaya*leave extract at doses of 1000 mg/kg body weight. The blood glucose levels were determined before and after alloxan induction for 28 days. At the end of the experiment, the animals were sacrificed through ocular puncture for the biochemical parameters activity was compared with a reference standard of Acetylcholine esterase, trypsin and pepsin (2mg/kg) negative control of physiological saline. Alloxan-induced diabetic rats treated with methanol extract showed relatively no significant ($p<0.05$) difference in acetylcholine esterase, pepsin and trypsin concentration compared with the controls. The study suggests that alloxan-induced diabetic rats treated with *Carica papaya*leaves extract possess a hypoglycemic effect,contributing to its antioxidant property.**

***Keywords:-*** *Diabetes,Carica papaya leaves, physiological saline, acetylcholine esterase, diabetic rats.*

## I. INTRODUCTION

Metabolic diseases result from disruptions in intricate biochemical processes of the body.For example, diabetes mellitus occurs due to the body tissues' inability to produce or respond to insulin(Olefasky, 1985; Ayber*et al.,* 2001), making it a global health trend (WHO, 2020). Currently, diabetes affects more than 40 million people worldwide (IDF, 2019), and the number of patients is increasing tremendously. Approximately one in every adult worldwide has diabetes, and many are yet to be diagnosed, thus accounting for a large part of the public health expenses. As this menace tends to affect the community and the world, intensified diabetic research is required to improve the knowledge and ability to prevent and treat diabetes.

Although researchers have made it known that oral medications such as metformin, sulfonylurea and some exogenous insulin serve as a therapy for the treatment of diabetes (Fowler, 2007), a recent finding has it that this oral medication has various adverse effects when taken, including gastrointestinal adverse, body fluid accumulation, heart disease. Therefore, there is a need to search for highly efficacious safe and harmless sugar level oral drugs that will be free from side effects of the previous recorded oral medications when used for the treatment of diabetes Pitocco*et al.,* 2012).

Medicinal plants such as *Carica papaya* Linn (family: *Caricaceae*) is promising plant when profiled and isolated, and it could producethe desired therapeutic properties by using high-throughput analytical techniques in which bioactive compounds from medicinal plants could have some pharmaceutical properties which can serve as a therapy for the treatment of many degenerative diseases. Some researchers recently found that *Carica papaya* Linn treats wounds, diarrhoea, and high blood pressure (Kurian, 2001; Mohamed and Riffin, 2006). As of 1992, Asolkarand his research fellow researched the juicy form of *Carica papaya* Linn on some degenerative diseases, of which they came out with a positive outcome detailing that the juicy form of *Carica papaya* Linn can serve as a therapy for the treatment of warts, cancer, and tumours. Moreover, as time went on, various researchers began to see the pharmaceutical properties possessed by *Carica papaya* Linn when profiled. Lohiyaet al.(1999) reported the antifertility, anthelminthic (Satriji*et al.,* 1995). Oladumoye and Osho

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(2007) reported the anti-inflammatory properties also the seeds and fruits possess antibacterial properties against gram-positive and gram-negative bacteria (*Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, and *Pseudomonas aeuroginosa*) according to Emeruwa (1982).

## II. MATERIALS AND METHODS

### A. Collection and Extraction of Plant Material

*Papaya* collected from the Lodu Ndume market in Umuahia North Local Government Area of Abia State, Nigeria, were used for this study.A renowned plant scientist authenticated them in the Department of Plant Science Biotechnology of Michael Okpara University of Agriculture Umudike, Nigeria. The leaves underwent thoroughly washing using running tap water in the biochemistry laboratory to remove the toxin and air-dried for three weeks under room temperature. After three weeks of air-drying, the leaves were ground into a powdered form using an electronic blender (Molineux).The method described by Airaodion et al. (2019) in solvent extraction was used in this study, of which the process could take 18 hours to complete.

### B. ANIMAL

For this study, 40 albino rats weighing 150-200g purchased from Dr Onoja in Veterinary Medicine, Michael Okpara University of Agriculture Umudike, Abia State, Nigeria, were used.They were acclimatized for two weeks, under normal conditions, with free access to food and water till the end of the experiment.

### C. INDUCTION OF EXPERIMENTAL DIABETES

In the experiment induction, a freshly prepared dose of alloxan monohydrate (Sigma Ltd., USA) equivalent to 120mg/kg was used.The blood was collected after 72 hours to establish its diabetic condition.

### D. EXPERIMENTAL DESIGN

- **Grouping of Animals**

There were six groups of five animals each.They were grouped as follows.:

Group A (Normal control): received distilled water only

Group B (Negative control): were diabetic but not treated

Group C (Positive control) were diabetic and treated with glibenclamide

Group D: were diabetic and treated with 200mg/Kg B. WT of *C. papaya* leaves

Group E: were diabetic and treated with 400mg/Kg B. WT of *C. papaya* leaves

Group F: were diabetic and treated with 600mg/Kg B. WT of *C. papaya* leaves

Group G: were diabetic and treated with 800mg/Kg B. WT of *C. papaya* leaves

Group H: were diabetic and treated with 1000mg/Kg B. WT of *C. papaya* leaves

### E. DETERMINATION OF FASTING BLOOD SUGAR

The method used to measure blood sugar was following Airaodionet al. (2019) description of which the measurement occurred in three consecutive stages. Before inducing with alloxan, followed by after the alloxan induction and finally, after twenty-eight (28) days of treatment.

### F. STATISTICAL ANALYSIS

The data obtained were representedas the Mean ± Standard Error of the Mean (SEM). One-way analysis of variance (ANOVA) was used to compare the means. Differences between means were significant at $p<0.05$.

## III. RESULTS

| Groups/Days | DAY 0 | DAY 7 | DAY 14 | DAY 21 | DAY 28 |
|---|---|---|---|---|---|
| Group A (Normal control): received distilled water only | 65.0±1.02 | 64.3±0.02 | 66.0±0.12 | 63.0±1.11 | 62.2±0.05 |
| Group B (Negative control): were diabetic but not treated | 356.2±0.12 | 350.1±0.10 | 352.3±0.12 | 364.0±0.12 | 378.0±1.05 |
| Group C (Positive control) were diabetic and treated with Glibenclamide | 325.1±0.01 | 269.2±0.13* | 240.6±1.11* | 190.3±0.14* | 174.2±1.13* |
| Group D: were diabetic and treated with 200mg/Kg B. WT of *C. papaya* leaves | 303.5±1.00 | 232.4±1.05* | 211.2±1.01* | 179.1±0.10* | 149.0±0.13* |
| Group E: were diabetic and treated with 400mg/Kg B. WT of *C. papaya* leaves | 307.2±1.04 | 265.2±2.02* | 256.2±1.03* | 160.2±1.11* | 100.2±0.02* |
| Group F: were diabetic and treated with 600mg/Kg B. WT of *C. papaya* leaves | 302.5±1.11 | 270.4±1.02* | 243.1±1.14* | 136.2±1.15* | 94.2±1.11* |
| Group G: were diabetic and treated with 800mg/Kg B. WT of *C. papaya* leaves | 315.2±0.15 | 250.3±0.10* | 232.1±1.10* | 112.2±1.05* | 94.2±0.14* |
| Group H: were diabetic and treated with 1000mg/Kg B. WT of *C. papaya* leaves | 306.2±1.12 | 262.1±1.11* | 226.2±1.13* | 100.1±1.02* | 85.0±1.03* |

Table 1: Comparison of mean glucose level in the *C. papaya* leaves extract in normal control, negative and positive (Glibenclamide) for 28 days.

Values are mean ± SD; n=5, values are statistically significant *($p<0.05$). Group A (Normal control): received distilled water only, Group B (Negative control): were diabetic but not treated, Group C (Positive control) were diabetic and treated with Glibenclamide, Group D: were diabetic and treated with 200mg of *C. papaya* leaves, Group

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E: were diabetic and treated with 400mg of *C. papaya* leaves, Group F: were diabetic and treated with 600mg of *C. papaya* leaves, Group G: were diabetic and treated with 800mg of *C. papaya* leaves, Group H: were diabetic and treated with 1000mg of *C. papaya* leaves. The highest activity resides at 28 days of administration when compared to control.

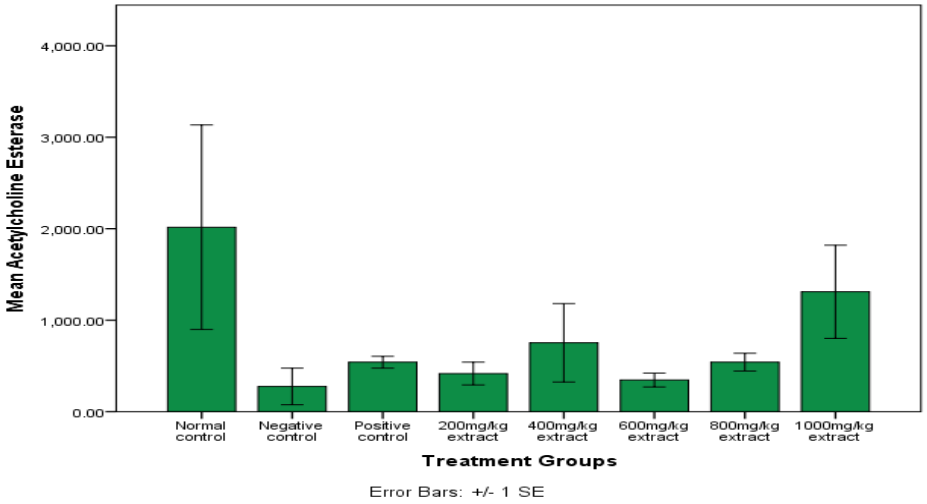


Fig. 1: The effect of *Carica papaya* extract on acetylcholine esterase concentration of treatment groups.

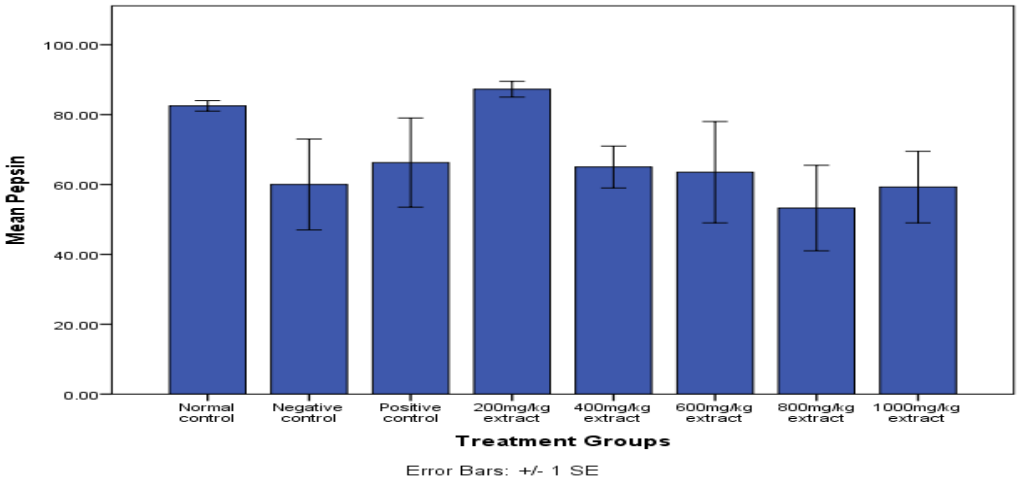


Fig. 2: The effect of *Carica papaya* extract on pepsin concentration of treatment groups.

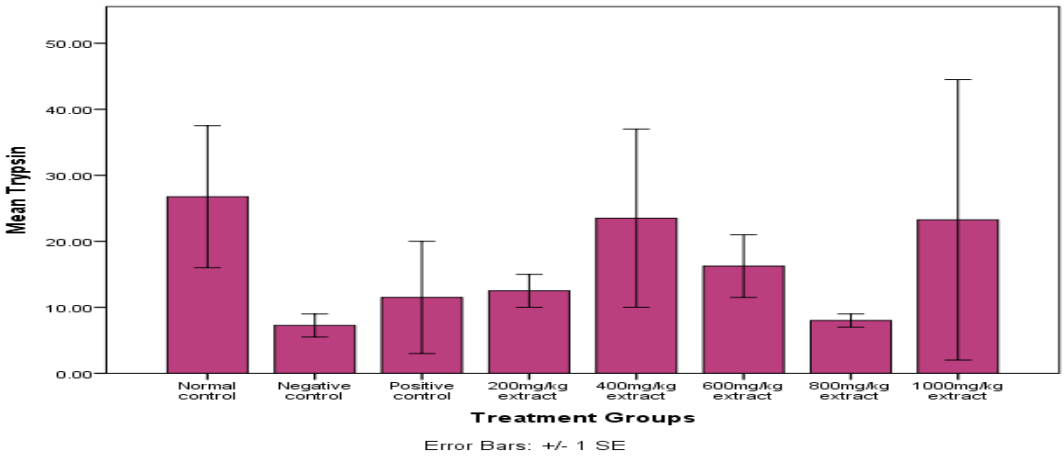


Fig 3: The effect of *Carica papaya* extract on trypsin concentration of treatment groups.

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## IV. DISCUSSION

*Carica papaya* is a promising medicinal plant enrichedwith phytochemicals constituting glycosides, saponins, flavonoids, and phytosterols, of which this bioactive component has various essential roles they play in one's life due to their pharmacological potency. Interestingly, *Carica papaya* has demonstrated digestion remedies excellently for breaking gluten, which is the metabolic factor responsible for the development of celiac disease.

Conducting acute toxicity on plant extract is necessary to determine the correct range of doses for subsequent use and assess the materials' potential adverse effects.*Carica papaya* leave extracts were found to be safe with a broad therapeutic range, as the acute toxicity result revealed no sign of toxicity, as there was no incidence of mortality up to a very high dose.Hence, this study aimed at the hypoglycemic effects of *Carica papaya* leaves and the digestive enzymes (Acetylcholine esterase, Trypsin and Pepsin) in alloxan-induced diabetic rats.

The aqueous extract of *C. papaya* leaves significantly reduced fasting blood glucose levels ($p<0.05$). Comparing our result, the extracts on doses of 200, 400, 600, 800, and 1000 mg/kg body weight of *C. papaya* leave reduced blood glucose as more than glibenclamide, the standard drug used to treat diabetes.This result showed how effective *C. papaya*leaves could serve as a remedy for the treatment of diabetes. Knowing that glibenclamide is a drug with adverse health effects,it is encouraged to use *C. papaya* to prevent and manage diabetes because it has little or no side effects compared to standard drugs. Moreover, the extract was able to reduce the incidence of alloxan-induced diabetes.This study is in line with the previous report by Airaodionet al.(2019). Aside from this, the extract was able to reduce the side effects of alloxan-induced diabetes because no significant differences were observed between the fasting blood sugar of animals treated with 200, 400, 600, 800, and 1000 mg/kg body weight of crude extract of *C.papaya* leaves when compared with non-diabetic animals (normal control) after 28 days at $p<0.05$.

Acetylcholine esterase is a cholinergic enzyme mainly present at postsynaptic neuromuscular junctions, particularly in muscles and nerves that yield acetic and choline upon hydrolysis (Marlos, 1995).From the data obtained in our result, *C.papaya* leaves extract at 400 and 1000 mg/kg significantly increased the Acetylcholine esterase concentration compared to the negative controlindicating a protective effect on the acetylcholine (neurotransmitter) and the primary neuron.Nevertheless, the doses of 200, 600, and 800 mg/kg body weight of *C. papaya* leaves extract significantly reduced the Acetylcholine esterase concentration compared to the negative, normal, and positive control, which prevents the activity of Acetylcholine esterase in Alzheimer's disease treatment.

The most inhibited activity of *C. papaya* leaves extractsdetectedoccurred at 600mg/kg, which could be because of the high content of flavonoids with biochemical and antioxidant effects and anti-cancer anti-genotoxic activity (Patel*et al.*, 2006). According to reports, flavonoids' acetyl-cholinesterase inhibitory activity has been linked to the primary approach to treating Alzheimer's disease. Flavonoids, such as polyphenolic compounds, are also known for their potent phytochemical properties, reducing the incidence of specific age-related neurological disorders.(Pierre, 1997).

The results demonstrated the effect of *C. papaya* leaves extracts to have a positive effect on pepsin levels in treated animals. Pepsin concentrations significantly increased in the group treated with 200 mg/kg compared to the negative control and other treatment groups of 400, 600, 800, and 1000 mg/kg, respectively.However, the *C.papaya* leaves extract reduced pepsin concentration in treatment groups of 400, 600, 800, and 1000 mg/kg doses, indicating the crude extract's inhibitory effect on pepsin's ulceration activity.

Trypsin is a pancreatic serine protease with substrate specificity based upon positively charged lysine and arginine side chains. The enzyme is excreted by the pancreas and takes part in the digestion of food proteins and other biological processes. Trypsin is a medium-sized globular protein produced as an inactive proenzyme; trypsinogenTrypsin cleaves peptides on the C-terminal side of lysine and arginine amino acid residues. If a proline residue is on the carboxyl side of the cleavage site, the cleavage will not occur. Suppose an acidic residue is on either side of the cleavage site. In that case, the rate of hydrolysis is slower, of which the pancreas breakdownminute amounts of pancreatic secretory trypsin inhibitors (PSTI) in whichamounts of the active trypsin and chymotrypsin in the gut areinhibited bydigestiveprotein(Oladumoye and Osho, 2007). Many factors includethe animal species, the animal's age, other ANFs present in the diet, and the type and level of protein.Thisstudy showed that the *C. papaya*leaves extract in the treated groups 200, 400, 600, 800, and 1000mg/kg,respectively,significantly reduced trypsin protein digestion activity. This could be attributed to the extract containing trypsin inhibitors which inhibit its activity in the pancreas (Satrij*et al.*, 1995).

## V. CONCLUSION

The findings indicated that *C. papaya* leaves extract effectively treats and manages diabetes. The *C. papaya* leaves extract inhibitory agents to digestive enzymes, andit also demonstrates a protective effect of the extract on the acetylcholine and neuron (neurotransmitter) at high doses.

## CONFLICTS OF INTEREST

There was no conflict of interest by the authors.

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