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HEPATO-PROTECTIVE EFFECTS OF AQUEOUS EXTRACT OF *CARICA PAPAYA* SEED ON LIVER FUNCTION ENZYMES

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ABSTRACT

The effect of aqueous extract of ripe Carica papaya seed on liver function enzymes was studied. Thirty-two adult Wister rats were randomly divided into four (4) experimental groups. (n=8). Group A, were fed with rat chow and water ad labium and Groups B,C and D where fed 100mg/kg, 200mg/kg and 300mg/kg of the extract respectively for 4 weeks. After an overnight fast, the rats were sacrificed and blood collected for assay of liver function enzyme levels. The results showed a statistically significant ($p < 0.05$) dose- dependent decrease in the levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP)and bilirubin. Therefore Carica papaya has a hepatoprotective effect and could be used as an adjunct in management of liver damage/injury.

K**eywords: Carica Papaya, Hepato-Protective Effects, Liver Enzyme Parameters**

INTRODUCTION

Despite tremendous development in the field of medical science, liver diseases are still the threatening problems to our health **[1]**. The absence of an effective treatment in modern medicine has made it urgent to search for suitable herbal drugs for treating hepatic disorders. The hepatoprotective activity of *Moringa oleifera* **[2]**, *Cocculus hirsutus* **[3]**, *Caseria ecsulenta* **[4]** *Trianthema decandra* **[5]** and *Phyllanthus niruri* **[6]** have been

reported. Some liver function parameters (eg, bilirubin or albumin) measure identifiable physiologic functions. Most parameters however, indicate injury to the liver (eg, aminotransferases and alkaline phosphatase [ALP]) or the reaction to that injury, to determine the choice of test **[7]**. It has been estimated roughly, that presently more than half of the total population of the world use herbal drugs **[8]**.

Carica papaya Linn is a short, fast growing large herb. The green fruit contains papain similar to pepsin, pulp of the fresh fruit contain a soft yellow resin, fat, albuminoid sugar and pectin. Leaves contain an alkaloid called carpaine and a glucoside named carposide **[9]**. *C. papaya* is commonly cultivated and planted in Nigeria for its edible fruits, also grows naturally in wastelands. The seed is used to expel worm, the flower may be taken in an infusion to induce menstruation **[10, 11, 12]**. *Annonaceous acetogenins* derived from the ext-racts of the twigs of the pawpaw tree may be good chemotherapeutic agents for cancer as these compounds inhibit enzymes necessary for metabolism in tumour cells **[13-18]**. The aqueous extract of unripe *C. papaya* was reported to possess both antisickling and reversal of sickling properties **[19].** The present study was chosen to investigate the effect of aqueous extract of *C. papaya* seed on the liver function enzymes and serum protein.

MATERIALS AND METHODS

Permission was granted by the ethical committee of College of Health Sciences, Delta State University, to carry out this study for the required period of time and the provisions of the declaration of Helsinki 1995 was complied with **[20]**.

Plant authentication and extract preparation

Matured fresh C. papaya fruit was bought from a local market in Abraka, and was authenticated at the Botany Department, Delta State University, Abraka. The fruit was peeled and the seeds were collected. The seeds were air dried and later grounded. The grounded *C. papaya* seed was weighed, 170 g of the grounded seed was soaked with 2000 ml of distill water for 72 hours and the residue was separated from the solvent. The solvent was concentrated to a paste like solid with a heating mantle yielding 36 g. The extract was kept in a clean container and refrigerated until use.

Animal Handling

Thirty two (16 male and 16 female) wistar albino rats (205 – 280g) obtained from the

animal house of the Faculty of Basic Medical Sciences, University of Benin, Benin City, were used for the study. They were kept in rat cages in a well ventilated house, at the Animal House of the Faculty of Basic Medical Sciences, Delta State University and were exposed to 12 hours light and 12 hours darkness and they were fed with clean tap water and rat chow once daily (8.00am - 9.00am). They were allowed to acclimatize for fourteen (14) days prior to the experiment.

Experimental Design

A total of thirty two (32) wistar albino rats were randomly divided into four groups of eight rats each.

Group A: (Male Control): Male rat fed with rat chow and water daily.

Group B: Male rat fed with rat chow and water daily, and then received a dose of 100mg/kg of aqueous extract of C. *papaya* seed.

Group C: Male rat fed with rat chow and water daily, and then received a dose of 200mg/kg of aqueous extract of C. *papaya* seed.

Group D: Male rat fed with rat chow and water daily, and then received a dose of 300mg/kg of aqueous extract of C. *papaya* seed.

Collection of Samples

The rats were weighed weekly for five (5) weeks and mean weight was obtained and recorded after which they were sacrificed by decapitation after an overnight fast. Blood samples were collected from the heart by cardiac puncture in heparinzed tubes and the plasma was immediately separated and stored until used for analysis of liver enzymes. This was done twenty four (24) hours after the last treatment.

Serum Biochemical Assay

The activities of alanine aminotransferase (ALT), aspartate amino transferase (AST) and alkaline phosphatase (ALP) were determined according to according to the method of **[21, 22]**.

Statistical Analysis

Results were expressed as mean ± SD. The evaluation of data for statistical significance between control and experimental groups was done using Students t-test. Statistical software, SPSS 17, was used to analyze the data. A $P<0.05$ was accepted as statistically significant.

RESULTS

In this experiment, changes in the level liver enzymes of the *Carica papaya* treated rats were compared to those of the control rats over a period of four weeks this was to ascertain the effect. The treated rats were administered with separate dose of the drug **(Table1)**.

Effect on Aspartate Aminotransferase (AST) in male wistar rats

There was an initial increase in the level of the enzyme but there was no significant difference ($P > 0.05$). As the dose is further increased, there is a reduction in the mean level of the aspartate aminotransferase (AST) and subsequent increase of the dose in Groups C and D further reduced the liver enzymes level. The decrease in the liver enzyme showed significant difference ($P < 0.05$) **(Figure 1)**.

Effect on Alanine Aminotransferase (ALT) in Male Wistar Rats

A dose dependent decrease in the level of ALT was observed with Group B and C having no significant difference while the Group D has a statistical significant difference ($P < 0.05$). Results can be better understood from the **Figure 2** below.

Effect on Alkaline Phosphatase (ALP) in Male Wistar Rats

Carica papaya extract caused an initial significant ($p<0.05$) increase in the level of the ALP enzyme at a dose of 100mg/kg, but with subsequent increase in the doses, the level of the enzyme significantly reduced. The results can be seen below in **Figure 3**.

Effect on Total Bilirubin in Male Wistar Rats

The effect of *Carica papaya* caused an increase in the level of the Total Bilirubin, with Group B having an initial significant ($p<0.05$) increase and the Groups C and D recording significant ($p< 0.05$) reduction in the liver enzyme level. Results have been represented in **Table 4** below.

Table 1: Effect of *Carica papaya* on the Liver Enzymes of Male Wistar Rats

Enzymes	Group A (Control)	Group B (100mg/kg)	Group C (200mg/kg)	Group D (300mg/kg)
AST (U/L)	12.50±1.73	13.00±4.62	9.50±0.58*	8.00±0.82*
ALT (U/L)	12.00±0.82	10.00±3.46	9.50±2.89	5.50±1.73*
ALP (U/L)	79.00±9.24	120.00±23.0*	48.50±5.26*	40.00±2.31*
Total Bilirubin (mg/dl)	3.90±0.35	10.60±0.69*	4.90±0.35*	3.65±0.17*

Values are presented as means ± SD; *P < 0.05 compared with control group. (n=8)

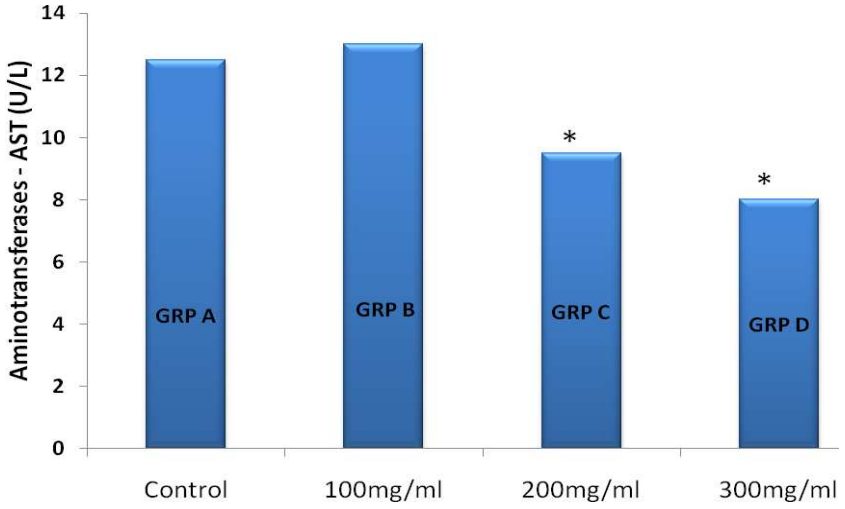

Figure 1: Effect of *Carica papaya* on Aspartate Aminotransferase (AST) in Male Wistar Rats [(n=8); *P < 0.05 compared with control group]

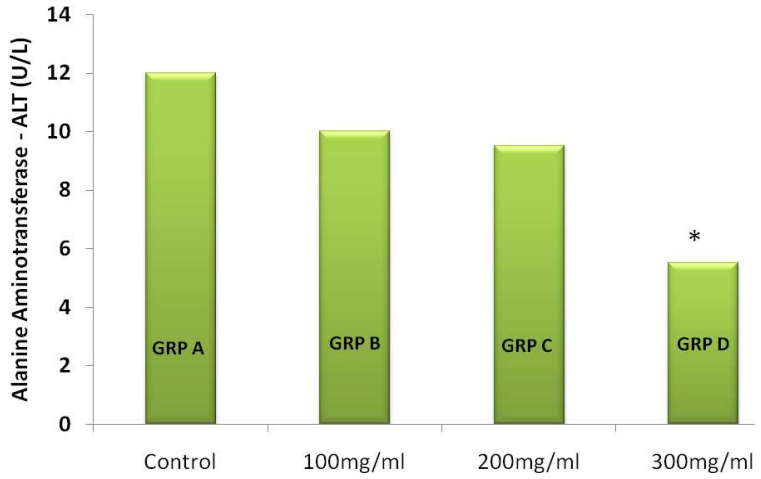

Fig 2: Effect of *Carica papaya* on Alanine Aminotransferase (ALT) in Male Wistar Rats [(n=8); *P < 0.05 compared with control group]

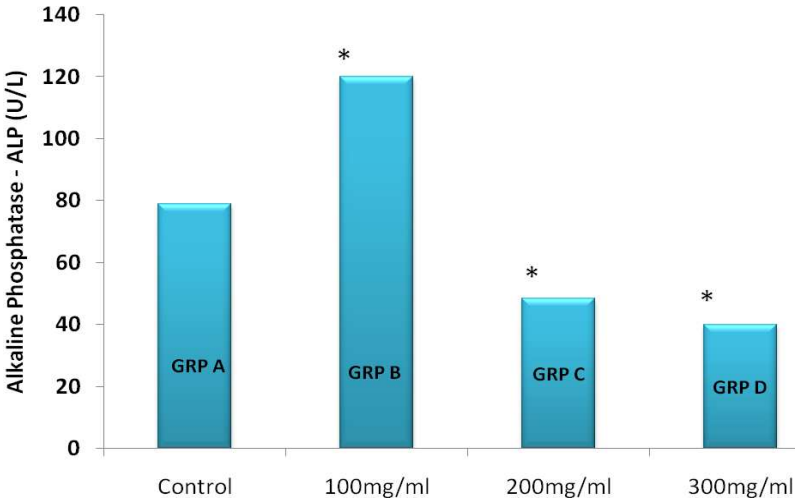

Fig 3: Effect of *Carica papaya* on Alkaline Phosphatase (ALP) in Male Wistar Rats [(n=8); *P < 0.05 compared with control group]

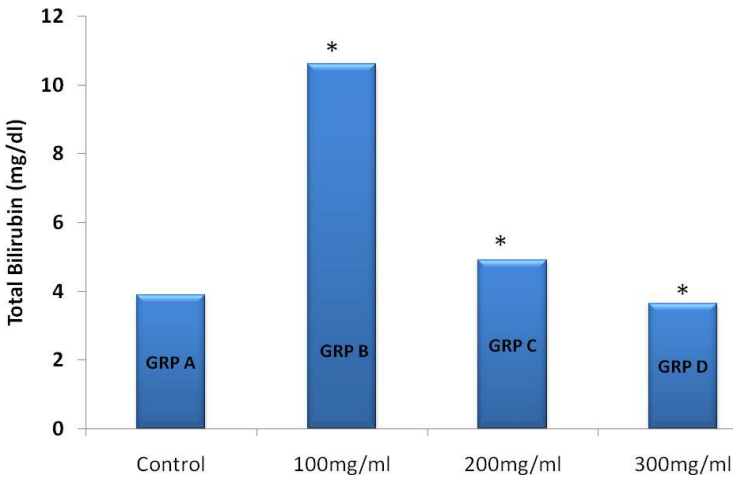

Fig 4: Effect of *Carica papaya* on Total Bilirubin in Male Wistar Rats [(n=8); *P < 0.05 compared with control group]

DISCUSSION

According to World Health Organization, medicinal plants would be the best source to obtain a variety of drugs. Therefore, such plants should be investigated to understand their properties, safety and efficacy.

Studies have revealed that change in liver enzymes like alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and bilirubin are the tests employed in the assessment of hepatic integrity or diseases **[23, 24]**.

In the present study, it was found that there is a dose-dependent and significant ($p<0.05$) decrease in the liver enzyme parameters (ALT, AST, ALP and Bilirubin) which may be an indication of the hepato-protective effects of the extract of *Carica papaya*. However, it was observed that at a lower dose of the extract (100mg/kg) there was an initial significant ($P<0.05$) increase in the level of ALP and Bilirubin only, which could be the initial hepatic response to the administration of the extract.

In an earlier study, the presence of alkaloids, flavonoids, saponin, tannin, anthraquinones, and anthacyanosides in *C. papaya* extract was reported **[25]**. Also, previous independent studies have reported that the hepatoprotective actions of medicinal plants are mediated by their flavonoids or alkaloids components or by their combination via antioxidant and free radicals scavenging activities **[26, 27]**. This phytochemical components may therefore be responsible for the results obtained in the present study.

CONCLUSION

From the findings in this present study, C. *papaya* seed extract is found to have a hepatoprotective effect which could be employed in management of acute liver injury.

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