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Original Article

Toxic effect of *carica papaya* bark on body weight, haematology, and some biochemical parameters

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ABSTRACT: **Toxic effect of *Carica papaya* bark on body weight, haematology and some biochemical parameters was investigated. Two-five out of thirty-five male albino rats allocated to five groups were sacrificed for the analysis. One group served as the control and the rest were test groups. The control group was placed on pelletized rat feed while that of the test groups were compounded feed of pelletized rat feed and ground sample of *C. papaya* bark. The rats were placed on tap water while the feed administration lasted. Results obtained showed that % average weight change, haematological and some biochemical parameters were significantly ($p<0.05$) affected in test rats against those of the control. This study has shown the toxic effect of *C. papaya* bark on body weight, haematology and some biochemical parameters**

KEYWORDS: Key words here

INTRODUCTION

Sequel to the renewed interest on traditional medicine brought by WHO (1978) declaration at Alma Ata, the importance of phytomedicine in healthcare delivery especially in developing countries of the world, cannot be overstated. In Africa and Asia, it will not be a gainsaying to state that some appreciable level of efficiency has been actualized in healthcare delivery in these continents by complementing orthodox medicine with traditional medicine. For instance in Africa, about 80% of the populace depend on plant medicine for healthcare (Okwu and Uchegbu, 2009; Ajose, 2007; Okigbo and Mmeka, 2006; Calixto, 2000; Neuwinger, 2000). The high dependency rate could be as a result of its efficacy, low cost, relative affordability and acceptability (Wurochekke *et al*., 2008; Sofowora, 1993). Phytomedicine makes use of medicinal plants as raw materials. Sofowora (1993) noted that a medicinal plant is any plant used for the extraction of pure substances either for direct medicinal compounds which can be used for the synthesis of useful drugs. Edeoga *et al*., (2005), Okwu (2005); and Okwu and Ekeke (2003) reported that the therapeutic value of medicinal plants lie in some chemical substances that produce definite physiological actions on the human body, against bacteria and other microbes. Okwu (2005) noted that extracts from the roots, seeds, fruits, and barks of medicinal plants are used in the preparation of concoctions, infusions, or syrups, against cough, cirrhosis, hepatitis, etc.

Carica papaya, a *Caricaceae* commonly known as pawpaw is among such medicinal plants used to prepare concoctions, infusions, or syrup which are effective against diseases in phytomedicine. For instance, sap from unripe fruit of *C. papaya* or trunk is used to treat eczema, razor bumps, and nematode infestation (Okigbo and Mmeka, 2006). A decoction made from unripe *C. papaya* fruit is effective against malaria while the seeds are anthelmintic in nature (Mantok, 2005). Iweala *et al.* (2012) noted the *in vitro* antisickling property of crude juice extract of *C. papaya*; Asaolu *et al.* (2010) reported the antihypertensive property of *C. papaya*; Ayoola and Adeyeye (2010) reported the phytochemicals and nutrient evaluation of *C. papaya* leaves; Bennet *et al*., (1997) noted the production of compounds such as benzylglucosinolate, cyanogenic glucosides and phenylpropanoids in *C. papaya*; Flath and Forrey (1997) reported on the volatile components of solo variety of *C. papaya*; Franco *et al*., (1993) gave appraisal on possible volatile components and flavour of pawpaw (Waugh *et al*., 1993) related age of fruit of *C. papaya* to yield and quality of crude of papain produced; and Brochlehurst and Salih (1985) isolated the enzyme forms found in fresh non-latex fruit of *C. papaya.* The above mentioned literature on *C. papaya* addressed bioactive constituents or pharmacology hence little seems to have been done to address and document toxicological studies on the plant. Just like most synthesised drugs, it has also been noted that there is inherent toxicity in the use of medicinal plants (Wurochekke *et al*., 2008). It

is therefore important to extend the study on *Carica papaya* to its toxicology. The present study investigated the potential toxic effects of *Carica papaya* bark on body weight, haematology and some biochemical parameters using Wister albino rats.

MATERIALS AND METHODS

Sample collection

Carica papaya plants used were collected from Imo State University school farm and got identified in the Department of Plant Science and Biotechnology, of the same school by Dr. F. N. Mbagwu. The barks were carefully separated from the entire plants and dried for Seven days. The dried barks got milled into powder with the aid of an electric blender. The ground sample was stored in air tight container till needed for analysis.

Experiment animals

Thirty-five male Wister albino rats weighing between 80g-100g obtained from the animal colony of Department of Biochemistry, Abia State University, Uturu, Abia State Nigeria were used in this study. The animals were housed in clean and dry plastic cages with good ventilation, and were given pelletized commercial rat feed (Pfizer Livestock Co., Ltd, Aba, Nigeria) and tap water *ad libitum*. The rats were given the same feed before acclimatization. The acclimatization period lasted for 5 days. After acclimatization period, the animals were allocated to five groups of seven rats each. Their weights were equalised as nearly as possible. Aside the control group, the remaining groups were given compounded rat feed for twenty-eight days. Treatments for the rats were as follows.

Control group (Normal feed + tap water); Group I_5 (5% of ground bark+ Normal feed + Tap water); Group I_{10} (10% of ground bark + Normal feed + Tap water); Group I_{15} (15% of ground bark + Normal feed + Tap water); Group I_{20} (20% of ground bark+ Normal feed + Tap water). The treatment of experimental animals was in accordance to the National Institute of Health (NIH) guidelines for the care and use of laboratory animals (NIH, 1985). After the treatment period, a total of two-five rats; five from each group were sacrificed for analysis.

Blood sample collection

At the end of twenty-eight days treatment period, the rats were reweighed, and sacrificed by making incisions at their cervical regions with sterile blade after being to sleep using ether in a closed container. Their organs were excised and their weights were taken. Blood was collected by cardiac puncture into anticoagulant free tubes with corks for biochemical parameters test while that of haematology was collected in anticoagulant tubes. The tubes were used for analysis.

Serum assay

The levels of alkaline phosphatase (ALP) were determined by Wriht *et al.*, (1972). Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were determined as described by Reitman and Frankel (1957). The assay of bilirubin both conjugated and total was carried out using the Jendrasik and Groff (1938). Creatinine was determined as described by Heinegard and Triderstorm (1973) while urea was done using Urease-Berthlot method.

Haematological analysis

Blood percentage (Hb) and red blood cell (RBC) levels were determined using Sahli`s and Alexander and Griffith (1993a) methods respectively. Westergreen`s method was used for erythrocyte sedimentation rate (ESR), Counting chamber and slide methods were used for white blood cell total count (WBC) and differential counts respectively. Haematocrit method (Jones, 1961) was used for packed cell volume (PCV) whereas, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC), were determined as described by Alexander and Griffith (1993b).

Statistical analysis

The statistical analysis was conducted using the student t-test as described by Steel and Torris (1960) .Each test group was compared to control group at 5% significant level.

RESULTS

A total of five deaths occurred during treatment period of the rats, one from group $I_{10,}$ and two each from groups I_{15} and I_{20} (Table 1). There was a significant ($p<0.05$) loss in body weight of test rats when compared to those of the control (Table 2). There was observed changes especially in the movement of the test rats against those of the control. The observed loss in body weight of the test rats could be as a result of the androgenic activity of *Carica papaya* bark in the body of these rats.

TABLE 1 **Rat status before and after commencement of treatment**

Parameter	Control	I_5	I_{10}	I_{15}	I_{20}
Total no. of rats before the commencement of treatment	7.00	7.00	7.00	7.00	7.00
Total no. of rats after treatment	7.00	7.00	6.00	5.00	5.00
Total no. of dead rats during treatment period	0.00	0.00	1.00	2.00	2.00
No. of rats used for the experiment	5.00	5.00	5.00	5.00	5.00

The haematological parameters could be used to explain blood relating functions of a plant extract and its products (Yakubu *et al.*, 2007; Yakubu *et al.*, 2008; Adebayo *et al.*, 2010b). Okeke *et al.*, (2006) noted that haematological parameters have been associated with health indices and are of diagnostic importance in the routine chemical evaluation of state of health. Hb, RBC and PCV of rats in test groups I_{10}, I_{15}, and I_{20} reduced significantly ($p<0.05$) against those of the control group. The observed decrease in PCV in the

TABLE 2 Body weight changes of rats given *Carica papaya* bark for 28 days

Parameter	Control	I_5	I_{10}	I_{15}	I_{20}
Average weight of rats before administration of water and feed (g)	100.12±0.17	100.51±0.00	100.63±0.32	100.74±0.01	100.86±1.34
Average weight of rats after administration of water and feed (g)	187.01±1.40	181.32±0.11	174.30±0.14	167.11±0.10	148.94±2.63
Average weight change of rats after administration of water and feed (g)	86.89±0.74*	80.81±1.31*	73.67±1.92*	66.37±0.03*	48.08±0.57*
% average weight change of rats after administration of water and feed	24.42±0.13*	22.71±1.74*	20.70±0.49*	18.55±1.06*	13.51±1.50*

Values are expressed as mean of five determinations ± standard deviations. Values asterisked (*) are statistically significant from control group at 5% significant level.

TABLE 3 Haematology results of rats given *Carica papaya* bark for 28 days

Groups / Parameters	Control	I_5	I_{10}	I_{15}	I_{20}
Hb (g/dl)	17.12±0.41	17.01±1.13	13.76±1.05*	12.50±1.24*	12.09±1.13*
PCV (%)	38.75± 0.12	45.42± 0.15*	45.93± 0.33*	45.13±1.61*	45.84±2.34*
RBC (10^{12}/L)	6.80±0.10	6.51±0.91	4.16±0.30*	4.04±0.53*	3.86±0.60*
WBC (10^9/L)	7.09±0.74	7.81±0.12	10.11±0.96*	10.30±1.02*	10.75±2.22*
Neutrophil (%)	24.04.±2.12	25.31±1.31	29.41±1.10*	29.94±2.17*	31.54±1.07*
Lymphocyte (%)	65.10±1.10*	79.00±2.10*	83.34±1.18*	83.96±1.04*	85.21±2.01*
Eosinophil (%)	0.33±0.10	0.35±0.07	0.37±0.12	0.39±0.02	0.40±0.11
Monocyte (%)	1.40±0.31	1.43±0.18	1.49±0.60	1.49±0.16	1.51±0.91
Basophil (%)	0.62±0.08	0.83±0.01	0.84±0.12	0.87± 0.14	0.90±0.26
MCH (pg)	33.11±0.84	32.36±0.13	32.27±0.29	32.37±0.64	32.26±0.14
MCHC (%)	6.98±0.12*	3.01±0.21*	3.20±0.94*	3.09±0.17*	3.12±0.59*
ESR (mm/hr)	8.15±0.23*	4.12±0.66*	4.73±1.01*	4.33±0.60*	4.08±1.09*

Values are expressed as mean of five determinations ± standard deviations. Values asterisked (*) are statistically significant from control group at 5% significant level.

TABLE 4 Haematology results of rats given *Carica papaya* bark for 28 days

Group / Parameters	Control	I_5	I_{10}	I_{15}	I_{20}
AST (U/L)	91.64±1.06*	94.00±0.56*	109.01±0.17*	113.02±1.85*	117.56±0.63*
ALT (U/L)	65.61±1.23*	67.12±2.10*	83.01±1.04*	87.40±1.01*	89.05±0.17*
ALP (IU/L)	96.80±2.11*	94.15±1.64*	102.10±1.33*	119.03±0.62*	118.35±2.15*
Urea (mg/dl)	46.31±1.13*	51.05±0.93*	53.98±1.07*	61.04±1.19*	67.17±2.01*
Creatinine (mg/dl)	0.54±0.07	0.61±0.09	0.83±0.01	0.97±0.04	1.01±0.07
Total bilirubin(mg/dl)	0.21±0.06	0.27±0.02	0.56±0.09	0.93±0.07	1.08±0.05
Direct bilirubin(mg/dl)	0.10±0.01	0.18±0.04	0.17±0.00	0.39±0.01	0.48±0.10

Values are expressed as mean of five determinations ± standard deviations. Values asterisked (*) are statistically significant from control group at 5% significant level

test rats in the present study is normal in a system with decreased Hb level (Krishan and Venna, 1980). The combined effects of physiological and chemical factors in the metabolic system of animals could lead to increase in WBC (Okeke *et al*., 2006). This could be the case with test rats in the present study. WBC of test rats in groups I_{10}, I_{15}, and I_{20} were significantly ($p<0.05$) increased against those of the control. The mechanism of WBC and its components are defensive against foreign substances. Lymphocytes are associated to immunoglobulin while neutrophils aid in the protective work. Neutrophil levels of the present study increased significantly ($p<0.05$) in test groups I_{10}, I_{15}, and I_{20} against those the control rats whereas lymphocyte levels increased significantly ($p<0.05$) in test rats when compared to the control. The observed increase in both lymphocyte and neutrophil levels could be an indication of presence of toxic substances in the system of test rats. Eosinophil, monocyte and basophil levels were insignificantly ($p>0.05$) affected in the test rats against those of the control in this study. The implication may be that *C. papaya* bark could not trigger their production. The increased blood parameters observed in test rats in this study may have significantly ($p<0.05$) reduced the erythrocyte sedimentation rate (ESR) in test rats against those of the control rats. Adebayo *et al*., (2005); Abiodun *et al*., (2010) noted that MCV, MCH and MCHC are related to individual red blood cells. MCH levels in the present study were insignificantly affected ($p>0.05$) in test rats against those of the control. MCHC reduced significantly ($p<0.05$) in test rats when compared to those of the control rats. Low MCHC could be indication that *C. papaya* bark can be linked with hypochromic condition in the system. Low MCHC can occur in iron deficiency anaemia where red cells are produced as a result of the lack of iron to support haemoglobin synthesis. The reduced Hb, PCV, RBC, and MCHC could mean that incorporation of haemoglobin into red blood cells, the morphology and osmotic fragility of the red blood cells were altered (Adebayo *et al*., 2005; Abiodun *et al*.,2010).

Toxic materials cause peroxidative degradation in the adipose tissue resulting in infiltration of the hepatocytes (Mankani *et al*., 2005). Hepatocytes perform the functions of detoxification, production of urea, break down excess ammonia by deamination, and storage of iron and some vitamins (Haper, 1975; Chris, 1998; Robert *et al*., 2003). Primary and secondary hepatic disease can cause an elevation of both AST and ALT (Enemor *et al*., 2005; Almer, and Olosson, 2006; Wuruchekke *et al*., 2008). ALP leaks in a manner similar to AST and ALT (Wright *et al*., 1972; Nsirim, 1999,). Serum AST, ALT and ALP increased significantly ($p<0.05$) in test rats against those of the control. The increases could be an indication of cellular leakage and loss of functional integrity of the cell membrane of the hepatocytes. Levels of bilirubin indicate the depth of jaundice induced by toxic substances (Mathew, 2000; Mathew, 2001). The direct and total bilirubin of the present study increased insignificantly ($p>0.05$) in test rats when compared to those of the control rats. Although the observed bilirubin increase was insignificant, the increase was dose dependent on the test rats. This could be an indication that *C. papaya* bark could induce jaundice with time. The kidneys perform the haemostasis function in the body. Urea and creatinine are indices of kidney function. Urea is the main end product of protein catabolism. Decrease in urea is seen in severe liver disease. Urea increased significantly ($p<0.05$) in test rats against those of the control. The retention of creatinine in the blood is evidence of kidney impairment. Creatinine was insignificantly ($p>0.05$) affected in test rats when compared to those of the control rats.

CONCLUSION

Although the efficacy of herbs against diseases has been confirmed in phytomedicine but in recent times there are quite a number of accumulating reports about organ injuries and other effects after intake of some herbs. This could be the case of *C. papaya* bark. The present study has revealed the toxic effect of *C. papaya* bark on body weight, hematology and some biochemical parameters

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