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Effects Of *Annona Muricata* On Total Protein, Albumin, Globulin And Body Weight In Paracetamol Overdose-Induced Liver Damage In Albino Rats

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Abstract: *Effects of ethanolic leave extract of Annona muricata on paracetamol-induced liver damage in albino rats were investigated. Liver damage was induced by oral administration of 800mg/kg of paracetamol for seven days. The induced liver damage was indicated by abnormal fall in serum levels of total protein, albumin, globulin and weight loss. Serum levels of total protein, globulin, albumin and weight changes were monitored for 14 days at 7 days intervals in all the groups. The results showed that the levels of total protein, albumin and globulin were significantly increased (P<0.05) in the treated groups (C-E) compared to the negative control (B, induced but not treated), while the levels were highest in the positive control (A) which neither received paracetamol nor leave extract. This indicated that the extract had curative effect on paracetamol induced liver damage. There was significant (P<0.05) loss in weight among the liver damaged rats than the control, but administration of Annona muricata for 7 days and 14 days caused significant (P<0.05) regain in weight. The study showed that ethanolic extract of Annona muricata can be used for treatment of liver damage.*

Key words: *Annona muricata, Rats, Paracetamol total protein, albumin, globulin and weight*

I. Introduction

Using plants for medicinal purposes is an important part of culture and tradition in Nigeria. Thus, up to 80% of the populations depend directly on the traditional medicine for primary health care (Keenwe and Bekalo, 1996). This traditional medicine uses numerous plants, one of which is *Annona muricata*. *Annona muricata* is commonly called sour sop in most part of Nigeria. The plant has a large and rich history of profits to human beings (Santos, 2001). The first people who knew about this plant species were undoubtedly, the several Amerindian ethnic groups who lived in central and South America (Santos, 2001) the first use attributed to it was probably as food, but as time passed and as a consequence of the extended act of living together of man and this species, a series of curative properties were gradually discovered and transmitted from generation to generation by the different native people of the several regions in America (schulte*et al.*, 1999).

In ethnomedicine,*Annona muricata* is employed in the treatments of variety of diseases ranging from arthritic pains, asthma, bronchitis, catarrh, colic cough, diabetes, dysentery, oedema, fever, gallbladder disorder, hypertension, liver disorders, malaria, nervousness, neuralgia, palpitation, parturition, rashes, rheumatism, ringworm, skin disorders, spasms, tumors and ulcers (Shahidi *et al*., 1999).

Considering the importance of this plant, which is commonly used in herbal medicine, it is necessary to evaluate its potentiality in the treatment of liver damage due to paracetamol overdose. Liver damage due to paracetamol overdose is very rampant world wide (Temple and Himmel, 2002). This may be due to easy accessibility and cheap cost of paracetamol in the market compared to other prescription drugs (Cripin, 1993). In a recommended dose of 500-1000mg in adults, paracetamol is safe in relieving fever, headaches and other minor aches and pains (Kostrubsky, *et al*., 1995).

Paracetamol toxicity can lead to liver failure and death within days (Blazka *et al*., 1995). According to the United States agency for food and drug administration, acute liver failure accounts for more than 50% of liver failure cases, 39% of which is caused by paracetamol overdose and 13% is due to idiosyncratic liver injury triggered by other drugs (Heathcost, 2003). In this study, the effects of *Annona muricat*a extract on paracetamol induced liver damage were investigated in albino rats. Liver damage was induced in the rats with 800mg/kg of paracetamol and the extract was administered at different concentrations for 14 days. The effect of the extract was monitored via determination of total protein, albumin, globulin and body weight changes. The results will help to suggest the potentiality of the extract in correcting paracetamol induced liver damage in albino rats.

II. Materials And Methods

Collection of Plant Materials

A fresh young leaf of *Annonamuricata* was obtained from Umuoghara in Ezza North Local Government Area of Ebonyi State, Nigeria, for preparation of the extract.

Experimental Animals

The animals used in the study were albino rats weighing between 75g and 180g of both sexes obtained from University of Nigeria Nsukka and were allowed to acclimatized for seven days at the Animal House of the Department of Biochemistry, Ebonyi State University, Abakaliki. They were kept in rat cages and fed with grower's mash and equally allowed free access to clean water throughout the duration of the study.

Experimental Design

A Total of 33 albino rats were divided into groups A, B, C, D and E. Groups A and B contained 3 rats each while groups C, D and E contained 9 rats each. These groups served the following purposes in the experiment.

Group A was the normal control. This group was fed with only water and grower's mash throughout the experiment.

Group B served as negative control. This group was given water, grower's mash and paracetamol over dose (800mg/kg) for seven days without treatment

GroupsC, D and E were thetest animals; they were given water, growers mash and paracetamol over dose (800g/kg) for seven days, and were also administered with 200, 500, and 700mg/kg of extract respectively at 7th and 14th days of the experiment.

At the end of the seven days, one rat from groups A and B were selected and killed. Blood were obtained for Biochemical analysis.Albumins, total protein, Globulin weremeasured. Rats remaining in-groups A and B were kept under normal fed (grower mash) and water alone. Three rats from each of groups C, D and E were selected and killed after 7 days of extract administration. Blood was also obtained for the analysis of the aforementioned clinical parameters. The remaining rats in the whole groups were killed after additional 7 days (14 days) of extract administration for another round of the same analysis.

Ethanolic Extraction of Plant Materials

Leaves of *Annona muricata* were plucked and dried in heated oven at a temperature of 80^{O}Cuntil constant weight was obtained. The dry leaves were pulverized using mortar and pestle. The resultant powdered material was used for the extraction process. The extraction was carried out by the method of Harbone (1972) using ethanol (99%) as solvent. In the extraction process, the powdered sample was soaked in 1000ml of ethanol in a beaker, stirred for about 6 minutes and allowed overnight in a shaker. The solution was filtered using whatman No 1 filter paper and the filtrate was evaporated in an oven at 90^{o}C for about 10 hours. The resultant solid extract weighing 158g was diluted with 450ml of water before administering it to the rats.

Measurement of Rat Weights

The weight of each rat was monitored daily throughout the 14 days of the experiment as an index of the physical status of the rat during the period of the study using compression spring balance.

Collection of Blood Samples from the Rats

Blood was drawn at three different intervals from all the groups on the 7^{th} day of paracetamol administration, 7^{th} day of extract administration and on the last 14th day of extract administrationusing ocular puncture.

CHEMICALS: All chemicals used for various assays were purchased from Aldrich Chemicals, Poole, UK

Biochemical Analysis

Determination of total protein, albumin and globulin in the serum were determined using standard methods by Tietz (1995**).**

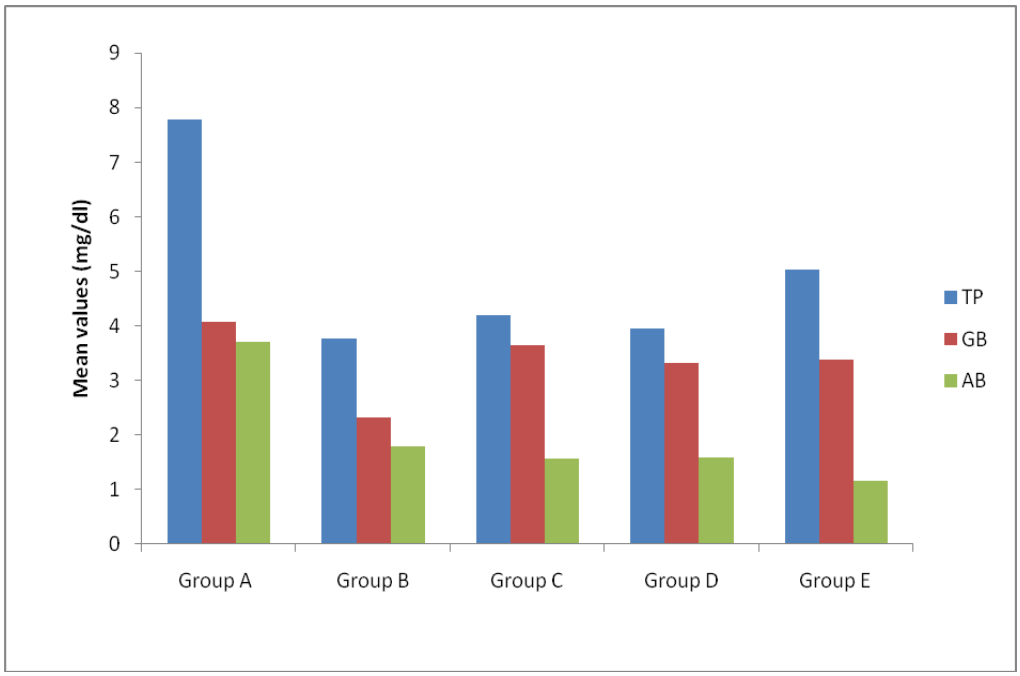

Figure1: Effect of 7 Days of *Annona Muricata* Treatment on Total Protein, Globulin and Albumin Levels in Liver Damaged Rats due to Paracetamol Overdose.

Values are means of 3 determinations, groups C, D and E =groups treated with 200, 500, and 700mg/kg of extract respectively, TB = total protein, GB = globulin and AB = albumin, Group B= negative control, Group A = positive control.

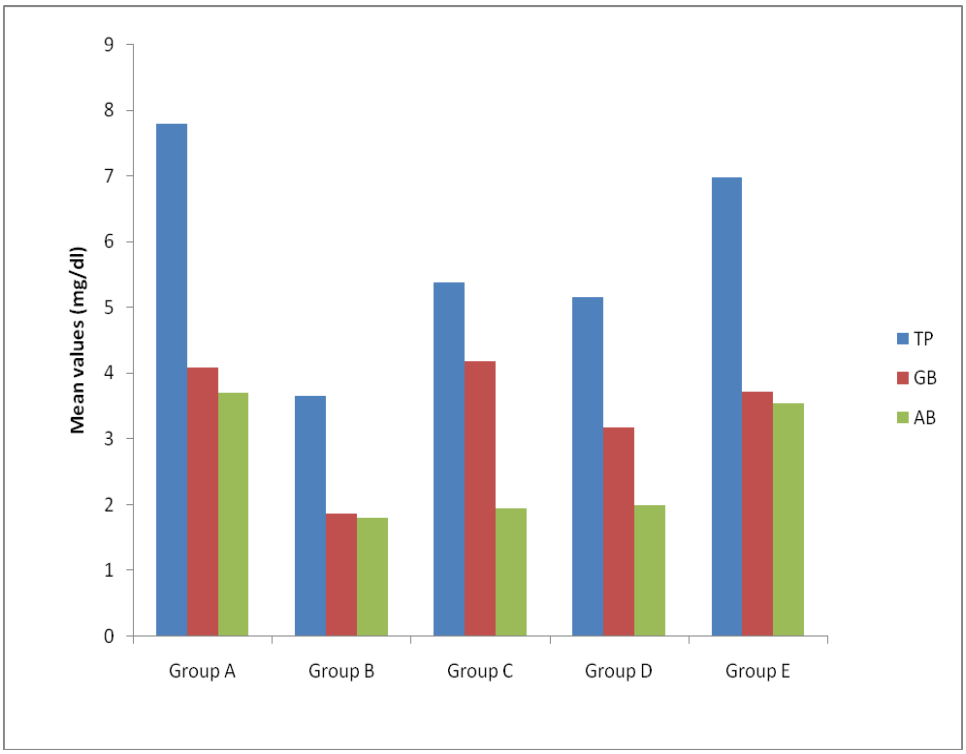

Figure2: Effect of 14 Days of *Annona Muricata* Treatment on Total Protein, Globulin and Albumin Levels in Liver Damaged Rats due to Paracetamol Overdose.

Values are means of 3 determinations, groups C, D and E =groups treated with 200, 500, and 700mg/kg of extract respectively, TB = total protein, GB = globulin and AB = albumin, Group B= negative control, Group A = positive control.

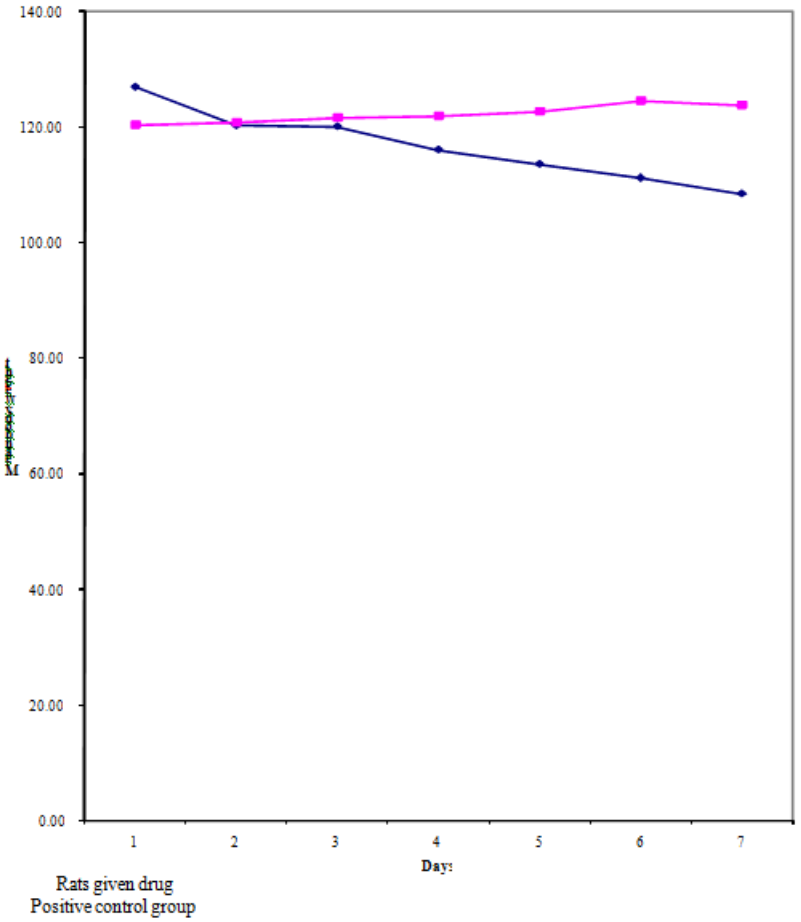

Figure 3: Mean body weight (g) given over dose of Paracetamol

This showed the effect of paracetamol overdose on mean body weight of Albino Rats after 7days of extract administration. It showed that paracetamol lowered the weights of the rats

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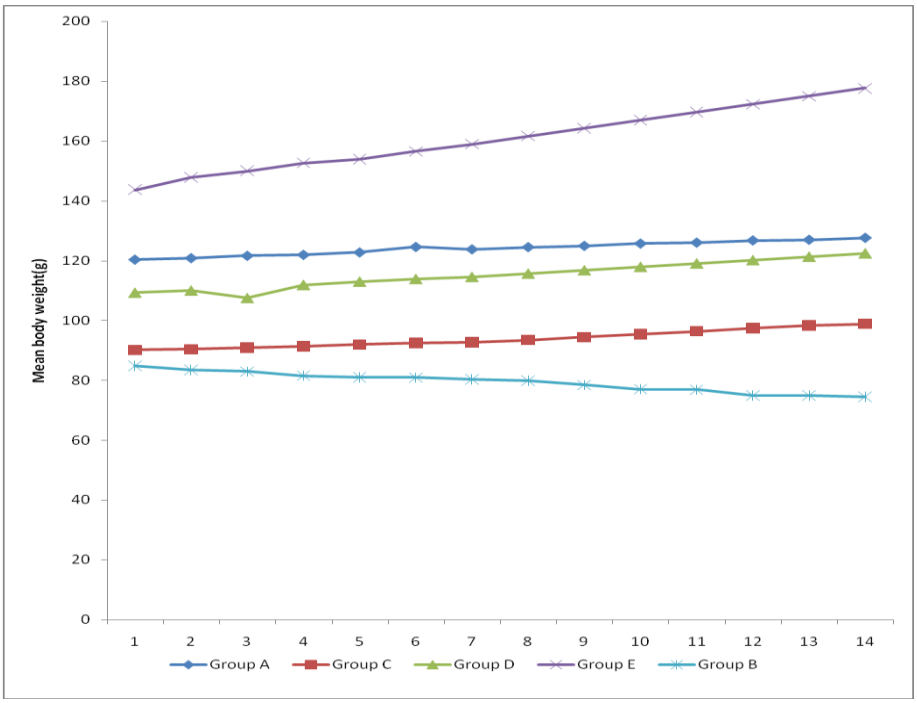

Figure 4: Effect of different doses of *Annona muricata* extract treatment on mean body weight of Rats given paracetamol overdose.

It showed that the rats gradually regained weights as a result of the extract treatment when compared to the negative control (group B)

III. Discussion:

Drug-induced liver injury is a health problem that challenges not only health care professionals but also the pharmaceutical industry and drug regulatory agencies (Buckely *etal*., 1999). Paracetamol, a common analgesic and antipyretic drug used in relieving fever, headache and other minor aches and pains is known to be deadly if taken overdose, causing different pathological changes ranging from liver inflammations, fibrosis, cirrhosis and liver failures (Sorensen *et al.*, 2003). Liver damage, which is a chronic disease of various disorders that damage the liver overtime, seems to have no specific treatment (Bourd *et al*., 2002).

In the present study, effects of *Annona muricata* extract treatment on paracetamol induced liver damage were investigated. Liver damage in albino rats was induced by oral administration of paracetamol overdoses at 800mg/kg per days for seven days. There were significant ($P<0.05$) increases in serum protein, albumin and globulin levels, which were significantly decreased by paracetamol overdose (fig 1 and 2). Administration of the extract also coursed the animals to regain their weights, which were lost due to paracetamol overdose (fig 4). Protein, albumin and globulin levels significantly ($P <0.05$) decreased as a result of paracetamol overdose (Fig 1). This may be indicating chronic hepatoctye damage or degeneration of the liver as a result of the toxin which may have damaged the liver beyond its ability to produce normal levels of total protein, albumin and globulin which are principally made by various liver cells (Hunter *et al*., 1999). Steady weight loss from the second day of paracetamol induction, clearly indicated the negative effects of the drug on the physiological status of the rats (fig 3).

After two weeks of *Annona muricata* extract administration at graded doses of 200, 500 and 700mg/kg),there were a significant ($p < 0.05$) increases in the levels of total protein, albumin and globulin (Fig 1 and 2)compared to the negative control (group B). This may also be due to the protective properties of the extract in hepatocyte regeneration, necrosis healing and anti-inflammatory actions, which may have enabled the liver to regain its functions (Bourd *et al*., 2002). The highest increase in the levels of total protein, globulin and albumin was observed in-group E (those treated withthe highest dose (700mg/kg) of the extract. This may be suggesting that the effect of the extract of *Annona muricata* is concentration dependent. Administration of the extract also resulted in steady weight regain across the groups (fig4). This study clearly demonstrated that *Annona muricata* extract has great promise for use in the treatment of liver damage.

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