

## Comparative Study of The Hepatoprotective Effect of Ethanolic Extract of *Telfairia occidentalis* (Ugu) Leaves And Silymarin on Paracetamol Induced Liver Damage in Wistar Rats

<sup>1</sup>Jibrin Danladi, <sup>1</sup>Kafeelat Bolajoko Abayomi, <sup>2</sup>Mairiga. A.A. and <sup>1</sup>Ahmadu Usman Dahiru

<sup>1</sup>Department of Human Anatomy, Faculty of Medicine Ahmadu Bello University Zaria, Nigeria

<sup>2</sup>Pathology Department, Faculty of Medicine Ahmadu Bello University Zaria, Nigeria

**Abstract:** *Telfairia occidentalis* is use as vegetable in number of countries. Extract of *Telfairia occidentalis* leaves have been reported to have medicinal use in traditional medicine system, in most often an hepatoprotectant agent. In this study, the effect of *Telfairia occidentalis* leaves and Silymarin on paracetamol induced liver damage was investigated in rats. A total number of 20 young adult wistar rats consisting of both sex and weighing between 150-350 g were use for the study. The animals were grouped in to (5) groups of four rats in each. Group 1, served as normal control and receive distilled water orally for 7 days. Group 2 receive 2000 mg/kg body weight of paracetamol orally for 3 days while Group 3 animals were administered 500 mg/kg body weight of plant extract orally for 7 days. Group 4 animals received 2000 mg/kg body weight of paracetamol orally for 3 days and 500 mg/kg body weight of the extract orally for 7 days while Group 5 received 2000 mg/kg body weight of paracetamol orally for 3 days and Silymarin orally for 7 days respectively. At the end of the experiment the animals showed increased in body weight which is highly significant in group 3 and showed significant decreased in organ weight (liver) of group 2 animals. Biochemical parameter shows that, there is significant decrease in the level of liver enzymes (ALT) in group 2 when compared to other groups, the level of AST showed significant decreased in group 5, 4 and 2 when compared to group 1 and 3 and the level of ALP showed a significant increased in group 2 when compared to other groups and significant decreased in group 4. The histological features of the liver showed central vein congestion with eroded endothelium and haemolised blood vessels, pkynotic nucleic, sinusoidal dilatation and fatty infiltration in group 2, normal liver appeared in group 3, 4 and 5. This study showed that, ethanolic extract of *Telfairia occidentalis* leave possess hepatoprotective property at a dose (500 mg/kg).

**Keywords:** ALP, AST, liver enzymes ALT, paracetamol, silymarin, *Telfairia occidentalis*, wistar rat,

### INTRODUCTION

Since early times, plants have provided medical remedies for the human race. The whole structure of medical pharmacopoeia is based on man's medical historical knowledge of flowers, herbs, plants and tree (Ernest and Johanna, 1973). It is apparent that many effective drugs could be produced from plants used in traditional medicine. These could be a source of raw material for local pharmaceutical industries to enhance self-reliance and reduce drug import bills as encouraged by WHO (1977). Since developing local medicines may be of greater value than importing the more expensive synthetic drugs, research on the efficacy and toxicity of plant product is particularly vital (Ethkin and Rose, 1983). Today science has isolated the medicinal properties of a large number of botanicals and their healing component has been extracted and analyzed. Many plant components are now synthesized artificially (Foster and Dunn, 1973). Fluted pumpkin

(*Telfairia occidentalis*) belongs to the family Cucurbitaceae and it is crop of commercial importance grown across the low land humid tropics of West Africa (Nigeria, Ghana and Sierra Leone). However, there is no identifiable information on the crop in terms of Sex and varieties (Schippers, 2000). It is a tropical vine grown mainly for the leaves which constitute an important component of the diet of many people in West African countries (Gill, 1992; Kayode *et al.*, 2009) and for its edible seed. The young shoots and leaves of the plant are the main parts used in soup. The plant also contain considerable amount of anti-nutrients such as phytic acid, tannin and saponin which could also have some health benefits to its consumers (Ladeji *et al.*, 1995; Ajibade *et al.*, 2006). Due to the richness of the leaves in iron it is used to cure aneamia (Ajibade *et al.*, 2006). The seeds are also rich in oil storage reserves however at present it has very low commercial value as an oilseed, but it is potentially valuable as a high protein oilseed for human and animal food (Okoli and Mgbeogu, 1983).

Table 1: Effects of ethanolic extract of the *Telfairia occidentalis* on organ (liver) and means body weight

Group	Dose (mg/kg bwt) oral	Liver weight	Initial body weight	Final body weight
Control	-	6.39±0.83	287.50±17.67	312.5±17.67*
Paracetamol	2000 mg/kg bwt	4.92±0.38*	190.00±17.79	225.0±35.35**
Extract	500 mg/kg bwt	6.15±0.69	175.00±35.35	309.0±35.35*
Paracetamol + extract	2000 mg/kg + 500 mg/kg bwt	5.75±0.98	156.25±31.45	231.3±31.45**
Paracetamol + silymarin	2000 mg/kg + silymarin/kg bwt	7.22±1.82	203.33±5.77	233.3±14.43**

Each value is expressed as mean±SD and are compared with control; Statistical significance: \*p<0.05; Statistical highly significance: \*\*p<0.5

## MATERIALS AND METHODS

**Collection of plant material:** The plant was obtained at samara market in August, 2011. The plant was identified and authenticated by Mallam Musa of the herbarium section in the Department of Biological Science, Ahmadu Bello University, Zaria and then processed and extracted at pharmaceutical science, Ahmadu Bello University, Zaria.

**Preparation of extract (ugu leaf):** Water extraction of Bitter melon seed was prepared according to the procedure of Saad *et al.* (2011). Fresh leaves Fluted pumpkin were collected, air dried at room temperature and pulverized with pestle and mortar. About 100 g of air dried powder was mixed with water/ethanol at different contact time from 1 to 72 h the temperature was maintained within the range of 30 to 80°C, respectively. The mixture was filtered and the filtrate was concentrated under a reduced pressure (bath temperature of 50°C and finally dried in a vacuum desiccator. The extract was suspended in normal saline to obtain a final concentration of 5000 mg/mL and used for the experiment. A total of 2 g of extracts was accurately weighed and emptied into a container containing 10 mL of distilled water.

**Preparation of paracetamol:** Paracetamol (2000 mg) was weighed using sensitive weighing balance and dissolved in 5 mL of water and stirred thoroughly.

**Preparation of silymarin:** Silymarin (300 mg) was weighed also using sensitive weighing balance and dissolved in 5 mL of water and stirred thoroughly.

**Animal and husbandry:** A total of 20 adult Wistar rats of either sex were purchased from the department of pharmacology, Ahmadu Bello University Zaria. The animals were housed in plastic cages in the animal house of the Department of Human Anatomy, Ahmadu Bello University Zaria. The plastic cages with stainless steel, mesh floor and top, for facilitating cross-ventilation and measuring 50×30×18 cm was used to house five rats of the same experimental group. Plastic

water bottle with stainless steel nozzles were used to provide water which was allowed *Ad libitum*. The animals were kept and maintained on standard

laboratory condition of room temperature, humidity and under 12 h dark-light cycle. The animals were fed with standard pellet diet and water. The animals were allowed to acclimatize to their new condition for 2 weeks before the commencement of the experiment. The cages were cleaned daily and washed weekly.

**Experimental protocol:** The rats were randomly divided into five groups. Each of the group comprises of four (4):

**Group 1:** Rats were administered normal Saline (Volume per body weight) for 7 days.

**Group 2:** Rats were administered 2000 mg/kg body weight orally of paracetamol for 3 days.

**Group 3:** (Plant control) rats were administered with ethanolic extract of ugu leaf at a dose of 500 mg/kg orally for 7 days.

**Group 4:** Rats were administered paracetamol at a dose of 2000 mg/kg body weight orally for 3 days and ethanolic extract of ugu leaf at a dose of 500 mg/kg body weight orally for 7 days.

**Group 5:** Rats were administered with paracetamol at a dose of 2000 mg/kg body weight orally for 3 days and silymarin at a dose of 300 mg/kg body weight orally for 7 days.

At the end of the experiment, the body weight of all rats were taken and recorded. The rats were then sacrificed and the blood obtained was subjected to biochemical investigation through the jugular vein of the animals under deep anesthesia with chloroform. The liver obtained was trimmed of any adherent tissue and the tissue was preserved in 10% formalin for subsequent histopathological examination.

**Statistical analysis:** Data are presented as mean±standard deviation. For establishing significant differences between groups data were analyzed by the One-way ANOVA of variance followed by the Tukey post hoc test. Values were considered statistically significant if p<0.05.

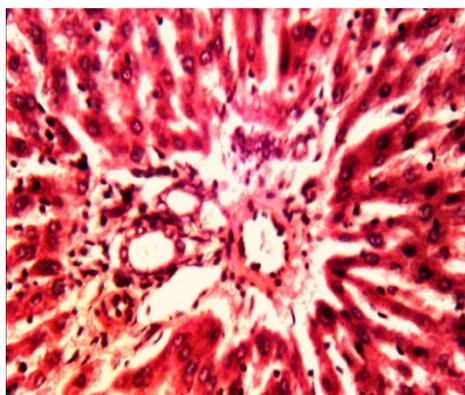


Fig. 1: Micrograph of the liver of a control rat showing normal arrangement of the central vein, sinusoid, portal triad and hepatocytes. H and E stain. Mag. x 400

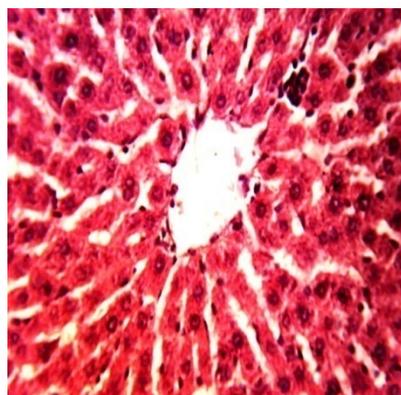


Fig. 4: Micrograph of rat administered with 500 mg/kg of plant extract and 200 mg/kg of paracetamol showing Central vein (Cv), Altration around the central vein (Av), Sinusiod (S) and Hepatocyte (H). H and E Stain. Mag X 400

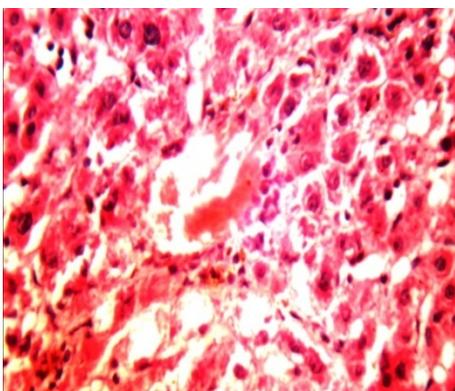


Fig. 2: Micrograph of liver from group administered 2000 mg/kg body weight of paracetamol, showing disruption around the central vein, mononuclear cells infiltration and pyknotic nuclei H and E stain. Mag x 400

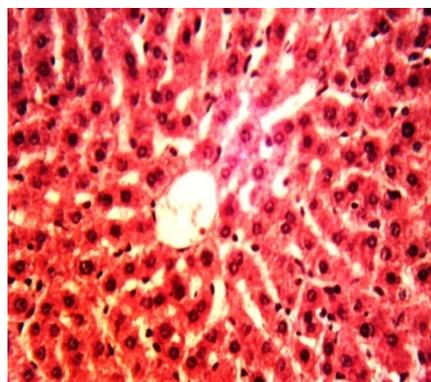


Fig. 5: Micrograph of rat administered with 300 mg/kg of Silymarin and 2000 mg/kg of paracetamol showing normal arrangement of the liver architecture with central vein Hepatocytes and Sinusiod. H and E Stain.

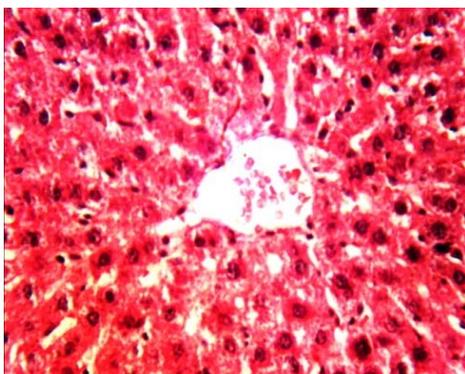


Fig. 3: Micrograph of the liver of a rat administered 500 mg/kg of the plant the Central vein (Cv), Sinusoid (S) and Hepatocytes (H). H and E Mag. x 400

## RESULTS

**Effects of ethanolic extract of the *Telfairai occidentalis* on organ (liver) and means body weight:** From the result of this study (Table 1), the animals showed increased in body weight which is highly significant in group 3 and showed significant decreased in organ weight (liver) of group 2 animals. Biochemical parameter shows that, there is significant decrease in the level of liver enzymes (ALT) in group 2 when compared to other groups, the level of AST showed significant decreased in group 5, 4 and 2 when compared to group 1 and 3 and the level of ALP showed a significant increased in group 2 when compared to other groups and significant decreased in group 4.

Table 2: Effect of ethanolic extract of *Telfairia occidentalis* on biochemical parameters

Group	Dose (mg/kg body wt.)	ALT	AST	ALP
Control	-	46.00±8.48	45.50±20.50	139.5±16.26
Paracetamol	2000 mg/kg	44.75±4.92	36.25±6.07*	156.5±36.81**
Extract	500 mg/kg	62.00±12.60**	42.50±3.69	137.8±25.51
Paracetamol + extract	2000 mg/kg + 500 mg/kg	58.00±12.3*	33.00±13.73*	106.5±20.04**
Paracetamol + silymarin	2000 mg/kg + 300 mg/kg	54.66±4.61*	18.00±4.35**	143.0±49.50

Each value is expressed as mean±SD and are compared with control; Statistical significance: \*p≤0.05; statistical highly significance: \*\*p≤0.5

**Histological finding:** The liver section from group 1 (control) showed normal architecture of the liver (Fig. 1). The liver section from group 2 (paracetamol 2000 mg/kg body weight orally) showed central vein congestion with eroded endothelium and haemolised blood vessels, pyknotic nucleic and fats infiltration (Fig. 2). The plant extract

(500 mg/kg body weight orally) showed no liver architectural changes (Fig. 3). But the liver section from group 4 and 5 (paracetamol 2000 mg/kg body weight plus 500 mg/kg body weight orally and paracetamol 2000 mg/kg body weight orally plus silymarin 300 mg/kg body weight orally) shows normal arrangement of the liver parenchyma cells (hepatocytes), central vein and sinusoid, Signifying protective property of the plant and silymarin (Fig. 4 and 5).

## DISCUSSION

Paracetamol (acetaminophen) is mostly converted in to inactive compound via phase ii metabolism by conjugation with sulphate and glucuronide, with small portion being oxidized via cytochrome P450 enzymes system. Cytochrome P450 2E1 (CYP2E1) and (CYP3A4) convert paracetamol to a highly reactive intermediary metabolite, N-Acetyl-P-benzo-Quinone Imine (NAPQI). Under normal condition, NAPQI is detoxified by conjugation with glutathione. In case of paracetamol toxicity, the sulphate and glucuronide pathways become saturated and more paracetamol is shunted to the cytochrome P450 system to produce NAPQI. As a result, hepatocellular supplies of glutathione become exhausted and NAPQI is free to react with cellular membrane molecules, resulting in widespread hepatocyte damage and death, leading to acute hepatic necrosis. However, when large quantities of paracetamol are taken, there is an increase in the production of NAPQI that may cause severe liver and kidney damage (Delvin, 2002).

Kapur *et al.* (1994) reported that paracetamol administered at high doses cause liver damage characterized by nuclear pyrosis, leucocytic infiltration and disarrangement of portal vessels. In the pilot study carried out in this study, paracetamol administered at a dose of 2000 mg/kg body weight orally, showed liver damage characterized by leucocytic infiltration, eroded endothelia of blood vessel containing haemolized

blood, disarranged portal vessels and appearance of pyknotic nuclei.

The present study, treatment of rats with 500 mg/kg of aqueous extract of *Telfairia occidentalis* alone did not alter the enzymes activities of thliver. But there is increase in body weight in the treated groups administered ethanolic extract of *Telfairia occidentalis* (500 mg/kg) in addition to 2000 mg/kg of paracetamol due to loss of appetite observed during the course of administration which lead to the decrease in food intake. While in paracetamol intoxication group trasaminase (AST, ALT and ALP) activities significantly increased Table 2. However, the rats pre-treated with ethanolic extract of *Telfairia occidentalis* has protective function against paracetamol toxicity in rats liver enzymes by increasing the level of the liver enzymes toward normal when administered orally at a dose of 500 mg/kg body weight prior to paracetamol intoxication.

The histopathological findings show normal liver architecture in the group 1 animals. The liver section from group 2 shows central vein congestion with eroded endothelium and haemolised blood vessels, pyknotic nucleic, sinusoidal dilatation and fatty infiltration. But the liver section from group 3, 4 and 5 shows normal arrangement of the liver parenchyma cells (hepatocytes), central vein and sinusoid, Signifying protective property of the ethanolic extract of *Telfairia occidentalis* and silymarin.

## CONCLUSION

In summary, it could be deduced that high doses or prolonged administration of paracetamol (acetaminophen) causes liver damage which could be remedied by continual administration of ethanolic extract of *Telfairia occidentalis* at appropriate doses (500 mg/kg/day orally) and duration in place of silymarin.

## ACKNOWLEDGMENT

I wish to acknowledge the technical assistance of the laboratory staff of the Department of Human Anatomy, Faculty of Medicine Ahmadu Bello University, Zaria, Nigeria.

#### REFERENCES

- Ajibade, S.R., M.O. Balogun, O.O. Afolabi and M.D. Kupolati, 2006. Sex differences in the biochemical contents of *Telfairia occidentalis* Hook f. *J. Food Agric. Environ.*, 4: 155-156.
- Delvin, T., 2002. *Test Book of Biochemistry*. 5th Edn., John Wiley and Sons Inc., New York, pp: 478-479.
- Ethkin, N.L. and P.J. Rose, 1983. Malaria-medicine and meal was among the Huasa and impact on diseases. *Anthro. Med. Culture Method*, pp: 231-259.
- Ernest, M. and L. Johanna, 1973. *Forklore and Odysseys of Food and Medicinal Plants*. Harrap, London, pp: 97-101.
- Foster, J.B. and R.T. Dunn, 1973. Stable reagents for determination of serum triglyceride by colorimetric condensation method. *Clin. Chem.*, 19: 338-340.
- Gill, L.S., 1992. *Ethromedical Uses of Plants in Nigeria*. Uniben Press, University of Benin, Benin City, Edo State, Nigeria, pp: 228-229.
- Kapur, J., V. Pillai, B. Hussaini and U.K. Balami, 1994. Hepatoprotective activity of Jingrine on liver Damage caused by Alcohol and paracetamol in rats. *Indian J. Phamarcol.*, 26: 35-40.
- Kayode, O.T., A.A. Kayode and A.A. Odetola, 2009. Therapeutic effect of *Telfairia occidentalis* on protein energy malnutrition-induced liver damage. *Res. J. Med. Plant*, 3: 80-92.
- Ladeji, O., Z.S.C. Okoye and T. Ojobe, 1995. Chemical evaluation of the nutritive value of leave of fluted pumpkin (*Telfairia occidentalis*). *Food Chem.*, 53: 353-355.
- Okoli, B.E. and C.M. Mgbeogu, 1983. Fluted Pumpkin, *Telfairia occidentalis*: West African vegetable crop. *Econ. Bot.*, 37: 145-149.
- Saad, M., A. Al-Said and S. Al-Barak, 2011. Extraction of insulin like compound from bitter melon plants. *Am. J. Drugs Disc. Dev.*, 1(1): 1-7.
- Schippers, R.R., 2000. *African Indigenous Vegetable: An Overview of the Cultivated Species*. Chatham, NRI/CTA, UK, pp: 66-75.