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HEPATOPROTECTIVE ACTIVITY OF AFRICAN BREADFRUIT (*Treculia africana* DECNE) SEEDOIL AGAINST CHEMICAL- INDUCED LIVER DAMAGE

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ABSTRACT

Hepatoprotective activity of African Breadfruit (*Treculia africana* DECNE) seed oil was studied using carbon tetrachloride induced liver injuries in rats. The hepatotoxicity produced by chronic $CC1_4$ administration was found to be inhibited by *Treculia africana* seed oil with evidence of decreased levels of liver markerenzyme ALT, AST, ALP and TB. Histopathological findings also suggest that *Treculia africana* seed oil prevents development of chronic liver damage. The changes in body weights in the rats assigned to the study groups supported these biochemical and histopathological findings. The results of this study clearly indicate that *Treculia africana* DECNE seed oil has potent hepatoprotective action against carbon tetrachloride induced liver damage.

Keywords: African Breadfruit (ABF), *Treculia africana* DECNE, Hepatoprotective, Liver Damage

INTRODUCTION

African Breadfruit (*Treculia africana*) belong to the Moraceae Family of Trees grown along coastal forest zone of Southern part of Nigeria**[1],** Senegal, Sudan, Angola, **[2].**The tree grows up to 30m high with a girth of 4 – 6m, with a dense spreading crown and fluted trunk. The African breadfruit is a big round shaped, greenish yellow in colour with a spongy texture when ripe. It contains numerous brown seeds

embedded in the fleshy pulp **[3]** with a fibrous coating. The seeds are highly nutritious and provide a cheap source of protein, carbohydrate, fats, vitamins and minerals **[4]**. The seeds when processed (dehulled) are an important food source, very popular amongst the South-East and South-South people of Nigeria **[5]**. It is severally prepared into pottage, roasted and combined with garden egg as snacks. It is processed into flour for pastries **[6]** used as flavor in alcoholic drinks and prepared as a non-alcoholic bereverage **[7, 8]**. Irvine **[9]** reported obtaining edible oil from the processed seeds. The seed is named according to the tribes in Nigeria; "Ukwa" (Igbo), "Afon" (Yoruba), "Barafuta" (Hausa), "Onyan" (Ijaw) etc. **[9]**. Unconfirmed reports have it that water extracted from the boiled seeds help to cleanse the stomach when taken. Proximate analysis revealed that the seed contains 38.3% CHO, 17.7% Protein, 3.8% Moisture, 15.9% Fibre, 4.0%Ash and 15.9% Fat **[10]**.

The liver which is the largest organ of the body and play important role in metabolism, secretion and excretion, glycogen storage, decomposition of red blood cells, protein synthesis and detoxification, is continuously exposed to environmental pollutants, xenobiotics and chemotherapeutic agents **[11].** Based on the increase in liver diseases the use of conventional drugs seems inadequate and necessitates the use of alternative methods of treatment. In this study we highlighted the hepatoprotective effect of the African Breadfruit (*Treculia africana*) seed oil on carbon tetrachloride induced liver damage in rats.

MATERIALS AND METHODS

Plant Materials

Seed Preparation

About 10kg of African breadfruit (*T. africana*) seeds were purchased from Mbiama Main Market, Rivers State, Nigeria. They were cleansed by hand picking to remove extraneous matters, the seeds were then per-boiled at 100^{o}Cfor 15minutes. The per-boiled seeds were drained and threshed in a commercial mill, they were then de hulled manually to remove the husk.

The Kernels were sun dried for 24hrs and milled in a blender (Moulinex 276, France) to fine powder flour. 50g of the flour were weighed into a thimble in the Soxhlet extractor fitted with a conical flask using 250ml of ethanol as solvent. The ethanol solvent was boiled under reflux for about 5hrs. The seed oil was calculated by weight difference of the sample before and after extraction.

Proximate Composition of African Breadfruit (*Treculia africana)* Flour

Proximate analysis of dehulled African breadfruit seed was determined for moisture, crude protein using micro kjeldhal method, crude fat using soxhlet method,

crude fiber and ash according to methods described in AOAC **[12]**. The carbohydrate was determined by difference.

Physico-Chemical Properties of *Treculia africana* Seed Oil

The physico-chemical properties of the *Treculia africana* seed oil determined included yield, colour, specific gravity, melting and smoke points, pH, saponification value, iodine value, free fatty acid value, peroxide value as described by the standard methods **[12]**.

Specific gravity was determined by use of specific gravity bottle at 27^{o}C, the colour index was determined by method described by Pike **[13]**.

Animals Used

Wistar albino rats of either sex weighing 150 – 200g were maintained in the Animal House Unit, Department of Biochemistry, University of Port Harcourt. The animals were housed in cages under standard conditions and were fed with standard laboratory chow from Pfizer foods Plc, water ad libitum. The animals were adapted to laboratory conditions for 7days before the experiments.

Acute Toxicity Study

The acute toxicity tests were carried out in accordance to Organization for Economic Cooperation and Development (OECD) guideline 423 **[14]**. Five rats were used the control group received 2ml Olive Oil, the others received African breadfruit oil (ABFO) at different volumes 4, 6, 8 and 10ml/kg BW by oral gavage. The rats were kept overnight fasting prior to administration of ABFO and food was withheld for further 4hrs after administration of seed oil. The rats were observed individually once during the first 30 minutes after dosing, then periodically during the first 4hrs for the first day and daily thereafter for 7days for behavioral changes and mortality, if any. The LD_{50} was found to be 10ml/kg BW, One-tenth of the LD_{50} dose was selected as the therapeutic dose for the evaluation of hepatoprotective activity.

Hepatoprotective Acivity

All experimental animals weighing between 150 – 200g were randomly divided into six groups of six rats each (n=6).

- Group I (Control) received 0.9% Normal Saline (NS) 1ml/kg daily for 7days.
- Group II received 0.1ml/kg BW of $CC1_4$ in olive oil ($1:1^{v}/_{v}$) for 7days.
- Group III received 100mg/kg BW of standard drug Silymarin and 0.1ml/kg BW of $CC1_4$ orally for 7days, and serve as standard control.
- Group IV received 0.1ml/kg BW of $CC1_4$ (i.p) with 0.2ml/kg BW ABFO daily for 7days
- Group V received 0.1ml/kg BW $CC1_4$ (i.p) with 0.4ml/kg BW ABFO for 7days.

- Group VI received 0.1ml/kg BW $CC1_4$ (i.p) with 1.0ml/kg BW ABFO for 7days.

Animals of all the groups were sacrificed under light ether anesthesia on the 8th day. Blood samples of each animal was collected by cardiac puncture using sterile disposable syringe and kept in plain tubes. The blood samples were allowed to clot for 45mins at room temperature. The clear serum was separated by centrifrigation at 2500 rpm at 30°C for 15mins and utilized for the estimation of serum alanine animotransferase (ALT), serum aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin (TB) using a Hitachi – 902 – Roche Japan Auto Analyzer.

After collection of blood samples, the animals livers were exercised immediately, and the liver weight/100g body weight was measured and fixed in 10% buffered neutral formalin for histopathology examination.

Body weights of the rats were measured before and after treatment and changes in body weight were recorded as percentages; using the formula:

$$\text{Change in body weight (\%)} = 100 \times \left(\frac{Wn - Wo}{Wo}\right)$$

Histopathological Study

Pieces of liver tissues in each group were immersed in 10% formalin for proper fixation. The tissue were processed and dipped in paraffin wax. Sections of 5mm in thickness were cut and stained with Hematoxylin and Eosin **[15]**. These sections were examined under light microscope for histological changes.

Statistical Analysis

The results are expressed as mean ± standard error of mean (S.E.M). The values were analyzed statistical by one way Analysis of Variance (ANOVA) followed by Dunnet Multiple Comparison Test. Significance was accepted at levels of $P<.05$.

RESULTS AND DISCUSSION

The proximate composition of de hulled sun-dried breadfruit seed flour is shown in **Table 1**. The results showed moisture content of 9.6%, protein content was 17.75% which agrees with value reported by previous researcher **[6]**. The ash content was 2.30% indicating a good source of minerals **[16]**, the fat content of 9.00%, fiber 2.80% and carbohydrate content 58.45 suggest that the seed will be of high energy meal. The high carbohydrate content makes the African breadfruit seed flour a composite flour in bakeryand confectionary product **[6, 17]**.

African Breadfruit Seed Oil (ABFO) Yield and Physical Chemical Properties

The Oil Yield and Physico-Chemical Properties of African Breadfruit Seed Oil are as presented in **Table 2**. The oil yield obtained from the soxhlet extraction using ethanol solvent was 18.95%. The ABFO oil yield tallies with reports by previous

workers **[17, 18]** who obtained oil yield of 20.83% and 19.85% respectively from African breadfruit and a yield of 20% in maize **[19]**. The specific gravity of ABFO recorded was 0.87g/ml, it compares with that reported for palm oil 0.91 and groundnut oil 0.84 **[20]**.

The melting point of 33.7^{o}C and smoke point of 250.0^{o}C suggest that African breadfruit seed oil could be used for cooking and frying. The iodine value of African breadfruit in this study was 44.80g/100g, this value is low compared to values obtained for pumpkin (109g/100g), **[21]**. Iodine Value is a measure of oil or fat stability and resistance to oxidation **[22]**, this indicate that ABFO cannot be suitable as a drying oil.

Saponification value is a measure of the average molecular weight of the triglycerols in an oil sample. The smaller the saponification number i.e, less than 100 indicate large average molecular weight of the triglycerol and high saponification value of 200 and above indicate low molecular weight **[23**]. The value obtained for this study was 210meq/kg, it suggests that it will be very good for soap and shampoo production **[18]**. Peroxide value is an indicator of the rancidity of the oil caused by peroxide and hydro-peroxide oxidation. The peroxide value for this study was 4.20meq/kg which is low compared to values obtained for palm oil (12.8meq/kg) pumpkin seed (25meq/kg).

The free fatty acid value obtained in this study is 4.74% which is high, it will thus require some form of purification (refining) to enhance stability and storage.

Acute Toxicity Studies of ABFO

No changes were observed in behavioral and mortality with oral administration of the highest volume of 10ml/kg African breadfruit seed oil.

Effect of ABFO on Body Weight

The effect of African breadfruit seed oil (ABFO) on the body weight of Carbon tetrachloride treated rats is presented in **Table 3**. The $CC1_4$significantly ($P<0.05$) increased the rats body weight in group II when compared to group I pre-treated with Normal Saline (NS) alone. There was also an increase in body weight of rats in groups IV and V who received 0.2 and 0.4ml/kg ABFO and $CC1_4$ respectively, but there was a reverse to normal bodyweight in rats treated with Silymarin (group III) and 1.0ml/kg ABFO (group IV).

Effect of ABFO on Biochemical Parameters

The effect of African Breadfruit Oil (ABFO) on serum level of hepatic enzymes, viz; serum alanineaminotransferase (ALT), serum aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin (TB) are shown in **Table 4**. The hepatic enzyme ALT (18.50 ± 1.3), AST

(22.40± 3.5), ALP (310.10 ± 13.9) and TB, (1.50 ± 0.4) in serum was significantly ($p<0.05$) elevated in $CC1_4$ (group II) treated animals when compared to control (group I). Treatment with 10ml/kgBW Silymarin and 1.0ml/kgBW ABFO significantly ($P<0.05$) decreased the marker enzymes ALT (4.20± 09 and 8.20 ± 0.9 respectively), AST (3.75 ± 0.70 and 7.10 ± 0.2 respectively), ALP (170.50± 10.8 and 200.2 ± 12.6 respectively) and TB (0.7 ± 0.5 and 0.9 ± 0.5 respectively) when compared to rats treated with $CC1_4$. **Effect of ABFO on Liver Weight**

Table 5 shows result of the effect of ABFO on the liver weights of rats. Administration of $CC1_4$ significantly ($P<0.05$) increased the liver weight to 3.7g/100g BW for rats in group II when compared to the normal control rats of group I. Treatment with 10ml/kg BW of Silymarin reduced the liver weight to 2.4g/100g BW while only the 1.0ml/kg BW of ABFO (group VI) also significantly ($P<0.05$) reduced the liver weight close to normal, suggesting the hepatoprotective action of ABFO.

Histopathological Findings

Histology of liver section of normal control rats (group I) showed normal hepatic cells with preserved cytoplasm, prominent cytoplasm and nucleolus and well brought out central vein (**Figure 1a**). The rats in the $CC1_4$ treated group II showed a loss of hepatic architecture with hepatic necrosis, fatty changes, vacuolization and congested sinusoids, hyperplasia, crowding of central vein and apoptosis (**Figure1b**). Treatment with ABFO with different concentrations of 0.2, 0.4, ml/kg BW showed weak to moderate activity in protecting the liver cells from $CC1_4$ damage **(Figures 1c** and **d respectively)**. Treatment with 1.0ml/kg BW ABFO returned the injured liver close to normal (**Figure 1e**) suggesting that hepaprotective activity of ABFO was dose dependent.

Liver cells are involved in several enzymatic metabolic activities and injury to this vital organ will lead to obstruction of the body metabolism **[24]**. $CC1_4$ was specifically chosen for this study because it has a direct destructive effect on membranes of hepatocytes and consequent interface with cellular metabolism and transport **[25]**. The $CC1_4$ damages the liver cells causing leakages of the enzymes in the cells resulting to elevation of the levels of plasma transaminases **[26]**.

The metabolism of $CC1_4$ releases $CC1_3$ free radicals that cause the process of peroxidation by attacking the methylene bridge of unsaturated fatty acids side chain of microsomal lipids **[26]**. Within a few minutes of a single dose of $CC1_4$, it causes injury to the endoplasmic reticulum leading to dysfunction of the hepatocyte and multiple biochemical manifestation of liver injury. This study revealed a significant

increase in the activities of liver marker enzymes (ALT, AST, ALP) and bilirubin on exposure to $CC1_4$ indicating hepatocellular damage. Treatment with 1.0ml/kgBW ABFO ameliorated the damage by reducing the elevated level of enzymes caused by $CC1_4$ bringing about the normalization of the liver similar to the known hepatoprotectant Silymarin. The results of this study agree with values obtained fomwork with coconut oil **[27].** This finding is further substantiated with the histopatological examinations of the animals' liver which showed the hepatoprotective activity of ABFO in a dose dependent manner. The fact that at low concentration of ABFO (0.2 and 0.4ml/kg BW), there is little protection of the liver from $CC1_4$ damage. This can be attributed to the oil's fatty acid content where about 50% of the fatty acid consist of Medium Chain Fatty Acids (MCFA's) which include C_6 to C_{12} fatty acids **[28]**. These MCFA's are easily digested and absorbed in the intestines and passed to the liver without further metabolism.

Dayrit **[29]** in his work suggested that the other MCFA's and monoglyceride molecules that are not metabolized will enter the system and exert their protective action. It is thus suggestive that at higher concentration of 1.0ml/kg BW ABFO exhibited hepatoprotective activity.

Table 1: Proximate Composition of Dehulled African Breadfruit Seed Flour

Parameters	African Breadfruit Seed Flour
Moisture (%)	**9.6**
Protein (%)	**17.75**
Ash (%)	**2.30**
Fat (%)	**9.00**
Fibre (%)	**2.80**
Carbohydrate (%)	**58.45**

Mean ± SD of Triplicate Determination

Table 2: Physico-Chemical Properties of African Breadfruit Seed Oil

Physico-Chemical Parameters	African Breadfruit Seed Oil (ABFO)
Oil Yield (%)	**18.95**
Specific gravity (g/ml)	**0.87±0.001**
Melting Point (^oC)	**33.70±0.001**
Smoke Point (^oC)	**250.0±0.02**
Colour Index	**470.50±0.02**
pH	**5.8 ± 0.001**
Iodine Value (g/100g)	**44.80±0.01**
Saponification Value (meq/kg)	**210.50±0.01**
Peroxide Value (meq/kg)	**4.20±0.01**
Free Fatty Acid (%)	**4.74±0.001**

Mean ± SD of Triplicate Determination

Table 3: Effect of ABFO on the Percentage Change of Body Weight in $CC1_4$ Treated Rats

Groups	Change in Body Weight (%)
I NS	3.60± 0.95
II NS + $CC1_4$	11.50 ± 0.50
III Silymarin + $CC1_4$	3.90 ± 0.60
IV 0.2ml/kg ABFO + $CC1_4$	13.60± 1.80
V 0.4ml/kg ABFO + $CC1_4$	13.80 ± 2.00
VI 1.0ml/kg ABFO + $CC1_4$	6.50 ± 1.10

Table 4: Effect of ABFO on the Hepatic Enzymes Levels in Serum of $CC1_4$

Group/Treatment	ALT	AST	ALP	TB
I NS	2.00± 0.7	2.00±0.7	16.15±2.5	0.42±0.1
II NS+$CC1_4$	18.50 ± 1.3	22.40±3.5	310.10±13.14	1.50±0.9
III 10ml/kg Silymarin + $CC1_4$	4.20 ± 0.9	3.75±1.3	170.50±10.8	0.7±0.8
IV 0.2ml/kg ABFO+$CC1_4$	14.80± 2.8	17.5±0.35	296.5±15.0	1.2±0.7
V 0.4ml/kg ABFO + $CC1_4$	13.6 ± 1.9	16.8±0.20	290.1±16.4	1.2±0.7
VI 0.1ml/kg ABFO + $CC1_4$	8.2 ± 0.9	7.1±0.20	200.4±12.6	0.9±0.5

Values are Expressed as Mean ± SEM for (n=6); Significance Level at P<0.05

Table 5: Effect of ABFO on the Liver Weight of $CC1_4$ Treat Rats

Groups	Liver Weight (g/100g BW)
I NS	2.10± 0.1
II NS + $CC1_4$	3.70 ± 0.2
III Silymarin + $CC1_4$	2.40 ± 0.2
IV 0.2ml/kg BW ABFO + $CC1_4$	3.50± 0.1
V 0.4ml/kg BW ABFO + $CC1_4$	3.30 ± 0.1
VI 0.1ml/kg BW ABFO + $CC1_4$	2.70 ± 0. 2

Values are Mean ± SEM for n=6; Significance Level at P<0.05

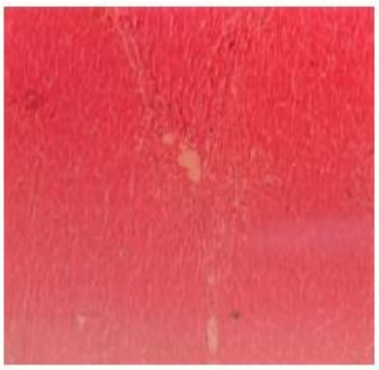

Figure 1a: Normal Saline (NS)

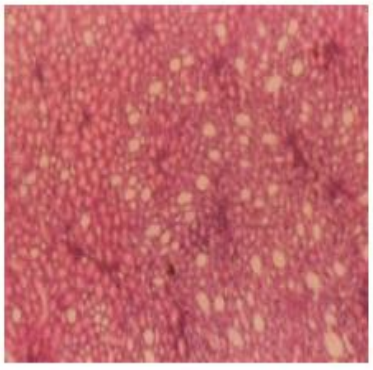

Figure 1b: NS + $CC1_4$

Figure 1c: 0.2ml/kg ABFO + $CC1_4$

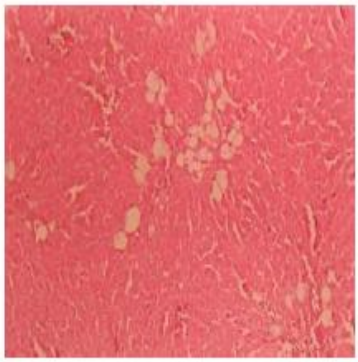

Figure 1d: 0.4ml/kg ABFO + $CC1_4$

Figure 1e: 0.1ml/kg ABFO + $CC1_4$

CONCLUSION

Based on the above observations of biochemical parameters, this study have been able to demonstrate that African Breadfruit (*Treculia africana*) Seed Oil at 1.0ml/kg has a reasonable potential in regenerating injured liver cells. Thehepatoprotective effect of ABFO may be ascribed partly to antioxidants activities present in the oil; but the active ingredients and the mechanism by which ABFO carry out its hepatoprotectivity is still obscure to the authors. We therefore recommend further investigation for the isolation of the pure components and its path of mechanism.

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