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Tetrapleura Tetraptera Fruit Protects Against Cyanide Induced Toxicity in Rats

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Abstract

At present there is no approved food antidote for cyanide poisoning. Therefore, plants are being tested as possible antidotes for cyanide (CN) toxicity. This study aimed to evaluate the possible protective role of the ethanolic extract of *Tetrapleura tetraptera* (*T. tetraptera)* against cyanide nephrotoxicity and hepatotoxicity in male rats. Forty five male albino rats divided into nine groups were used for the experiment: Group 1 received water only, Group 2 received CN only, Group 3 received CN + thiosulphate, Groups 4, 5 and 6 received 100, 250 and 500 mg/kg *T tetraptera* extract, respectively. Groups 7, 8 and 9 received CN in addition to 100, 250 and 500 mg/kg *T tetraptera*, respectively. The results showed elevated levels of lipid peroxidation, aminoaspartate transferase, alanine amino transferase, alkaline phosphatase, creatinine, and urea in the serum and tissues of cyanide treated rats. Significant decreases in superoxide dismutase and catalase activities were also observed in the liver and kidney of cyanide treated rats. Histological analysis showed CN- induced structural distortions of the liver and kidney tissues. However treatment with *T. tetraptera* fruit extract was able to mitigate these damages. This study indicates that *T. tetraptera* fruit extract possesses hepato-and-nephro-protective properties and can be used as an antidote for cyanide poisoning.

Keywords: Cyanide, *Tetrapleura tetraptera*, antidote, renal toxicity, hepatotoxicity

Introduction

Cyanide is a component of many industrial products such as insecticides, rodenticides, metal polishes and fumigant.[1] Certain bacteria and fungi also synthesize cyanide naturally as a component of cyanogenic glycosides to provide a source of nitrogen and for self-defence making this poisonous substance ubiquitous.[2] Cyanide is also as a common environmental pollutant associated with several adverse health consequences such as carcinogenesis, hepatotoxicity, renal impairment as well as disruption of normal endocrine and reproductive functions [2]

Most importantly, cyanide occurs naturally as glycosides in over 2000 plants [2, 3, 4] and ingestion of such plants has been reported to cause acute cyanide toxicity and mortality of live stocks as well as humans [2]. Also, as a result of the increasing use of cassava in particular, in the compounding of animal feeds as a carbohydrate substitute, there is a greater exposure to dietary toxins from cyanogenic glycosides [2, 3]. Toxic effect of cyanide is attributed mainly to the production of anoxia following inhibition of cytochrome oxidase, a terminal mitochondrial respiratory chain enzyme [4]. This is predicated on the affinity of cyanide for the heme iron and the reaction of cyanide with the multimeric iron enzyme complex facilitated by first penetration of cyanide to protein crannies, with initial binding of cyanide to the protein followed by binding of cyanide to heme iron. Thereby, cyanide-heme cytochrome oxidase complex is formed which renders the enzyme incapable of utilizing oxygen.[4] In fact, cyanide is dangerous to all forms of aerobic life and has been demonstrated to induce oxidative stress and cause damage to several biological systems [5].

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Earlier studies on several antidotes for cyanide poisoning such as dicobalt edetate, sodium thiosulphate and sodium nitrite has demonstrated that they are associated with several limitations [1, 6]. This stimulated the search for more efficient antidotes, by testing plants-based materials with antioxidant potentials, for cyanides toxicity in animals. Medicinal plants continue to attract global attention for effective ways of using plant parts (such as seeds, leaves, stems, roots, etc.) to treat many diseases affecting humans [7] .

Tetrapleura tetraptera (*T. tetraptera)* is a plant commonly grown in the tropical regions of the world with nutritional and health promising benefits [8]. It is a deciduous tree belonging to the family "Minosaceae" [9] and is commonly called Aidan tree in English Language. In Nigeria, it is called Aridan or Aidan by the Yoruba tribe, Edeminang by the Efiks, Uyayak by the Ibibios, Oshosho by the Igbos, Dawo by the Hausas, and Oraora, Ighimiakia, Ihokiriho and Imiminje by the people of Awka, Bini, Ngwa and Etsako respectively[10]. Phytochemical screening of ethanolic extract of *T. tetraptera* fruit revealed the presence of polyphenols, flavonoids, tannins alkaloids, sugar, saponins, cardiac glycosides, magnesium, phosphorus, potassium, calcium, sodium, zinc and vitamins A, C and E [11]. The medicinal effect of *T. tetraptera* is well known and widely documented and this includes anti diabetic, anticonvulsant anti-inflammatory properties [10].There is little or no information on its antidote effect for cyanide poisoning. Again there is a scarcity of information on the nephro- and-hepatic protective abilities of *T. tetraptera* and hence the need for this study.

Materials and Methods

Plant Material

Dry fruit of *T. tetraptera* was bought from Abraka big market in Abraka, Ethiope East local government area of Delta state Nigeria. It was identified by a taxonomist from the University of Benin and given voucher number UBH-T4T2. The plant was air dried for two weeks at an open space within the laboratory confinement of the Department of Biochemistry, Delta State University, Abraka, Nigeria, at room temperature. After air drying the pods were cut into small sized pieces and ground into a powder with an electric blender (Binatone, BLG 500, and Japan).

Preparation of plant extract:

Three hundred gram of the powdered plant (*T.tetraptera)* was first soaked for 30 min in 300 ml of hexane to de-fat. The extract was collected and filtered and the residue soaked in 900 ml of 70% ethanol for 5 days. The extract was filtered again and concentrated at 78^{o}C using rotary evaporator and further concentrated by using a water bath at 48^{o}C.

Experimental Animal

Forty five male white albino rats with average weight of between 110-150g were used for the research. They were obtained from the Department of Basic Medical Science, Delta state University, Delta State, Nigeria. The rats were housed in plastic cages and left to acclimatize for one week during which they were fed with grower's mash throughout the acclimatization period. All animals used were maintained in accordance with the guidelines for laboratory animal care (as stipulated by NIH publication no 85-93, revised [12]).

Study design

Rats were divided in to nine groups each with five rats. The plant extract was given by gavage at an oral dose of 100,250and 500mg/kg/day.

- Group 1 (Control) received distilled water for 21 days,
- Group 2 (Negative Control) received cyanide in form of KCN by gavage.
- Group 3 (Positive Control) received cyanide in form of KCN and was treated with 500mg/kg/day sodium thiosulphate (synthethic cyanide antidote)
- Group 4 received 100mg/kg/day of *T. tetraptera* extract
- Group 5 received 250mg/kg/day of *T. tetraptera* extract
- Group 6 received 500mg/kg/day of *T. tetraptera* extract
- Group 7 received cyanide in form of KCN and was treated with 100mg/kg/day of *T .tetraptera* extract
- Group 8 received cyanide in form of KCN and was treated with 250mg/kg/day of *T .tetraptera* extract
- Group 9 received cyanide in form of KCN and was treated with 500mg/kg/day of *T. tetraptera* extract

All groups given cyanide received it in form of potassium cyanide at a concentration of 4 mg/kg body weight a sub lethal dose [6]. All treatments were given orally by gavage and according to body weights. The experiment lasted for 21 days. The dose of the plant extract used was in the range of the safe dose reported by Ojewole and Adewunmi, [13]

Collection of experimental samples

After 21 days of treatment, the rats were sacrificed chloroform euthanization. Prior to the day of sacrificing, the rats were subjected to an overnight fast. Sterile test tubes were labelled accordingly and blood samples were collected by cardiac puncture. The blood samples collected were spurn in a table top centrifuge at 3200*g* for 15 min to obtained blood serum which was further used for biochemical analysis. Kidneys and livers of each rat were harvested and weighed. 0.5g was cut out from the tissue of each rat into labelled containers under cold conditions (-4^{o}C). The kidney and liver wet tissues were homogenized in 9.0 mL of normal saline using mortar and pestle and the resulting supernatant was stored in the refrigerator and used for biochemical analysis following standard procedures within 48 h.

Biochemical analysis

Alanine aminotransferases (ALT) and Aspartate aminotransferase (AST) activities in serum and liver were determined by the method of Reitman and Frankel [14]. Alkaline phosphatase activity in the serum and liver was determined by the method of Deutsche Gesellschaft fur klinischeChemie DGKC ([15]. Total Protein concentration in the serum and liver was determined by the method of Tietz [16]. Albumin concentration in the liver and serum was determined by the method of Doumas et al., [17] (1971).Liver and kidney catalase activity was determined by the method of Aebi [18]. Superoxide dismutase activity in the liver and kidney was measured according to the method of Sangeetha [19]. Lipid peroxidation level (LPO) in the liver and kidney was determined according to the method of Buege and Aust [20], Thiobarbituric acid (TBARS) values are estimated with a molar extinction coefficient of 1.56 x 10^5 M/cm and expressed as nm malondialdehyde per gram protein (MDA/g protein). The method of Lowry et al., [21] was used to estimate the protein content

Histopathology of the Liver and kidneys from treated rats

A portion of the pairs of livers and kidneys harvested were rinsed in 0.9% normal saline and fixed in 10% formo-saline. The liver and kidney histology was analyzed according to the methods given by [22] Avwioro (2015)

Statistical analysis

The data from all the analyses were collected and statistically analysed and expressed as the mean ± SD (n=5) for each group of rats using one-way analysis of variance (ANOVA). Results were considered statistically significant at $P < 0.05$.

Results

Effect of ethanolic extract of *T. tetraptera* on some liver function markers in the serum of rats intoxication with cyanide

The effect of *T. tetraptera* on AST, ALT, ALP, TP and Albumin level in the serum of cyanide induced rats is indicated in Table- 1. A significant ($P<0.05$) increase in the activities of AST, ALT, ALP was observed in the serum of negative control rats when compared with the normal control. However no significant difference was observed in Groups 4, 5 and 6 given an increasing dose of the extract without cyanide poisoning. Treatment of cyanide intoxicated rats with 100,250 and 500 mg/kg body weight of the ethanolic extract of *T. tetraptera* (Groups 7, 8 and 9) significantly reduced ($P>0.05$) AST, ALT and ALP activities in the serum in a dose dependent manner when compared with the untreated Group 2. Conversely significant decrease ($P>0.05$) in total protein and albumin levels was indicated when negative control rats were compared with the normal control. Again, treatment of cyanide intoxicated rats with different doses of the plant extract significantly increased ($P<0.05$) the level of total protein and albumin when compared with the untreated Group. In addition there was no significant difference($P>0.05$) in the serum activities of AST, ALT, ALP, TP and albumin in Groups 7,8 and 9 rats treated with the different doses of the plant extract when compared with the positive control (treated with sodium thiosulphate). Thus the study indicates that *T. tetraptera* ameliorated the effect of cyanide on level of serum AST, ALT, ALP, TP and Albumin comparable to a known synthetic antidote (sodium thiosulphate) and the effect of the extract was dose dependent.

Table 1-Effects of ethanolic extract of *T. tetraptera* fruit on some liver function enzymes in the serum of cyanide intoxicated rats

Groups	AST	ALT	ALP	Albumin	Total Protein
1	50.0 ± 5.83^{a}	16.0 ± 354^{a}	420.30 ± 27.4^{a}	19.19 ± 0.74^{a}	36.27 ± 6.92^{a}
2	89.25 ± 7.96^{b}	29.13 ± 7.75^{c}	610.35 ± 48.62^{b}	15.62 ± 2.38^{b}	27.61 ± 4.01^{b}
3	60 ± 7.90^{b}	22.63 ± 4.41^{b}	480.61 ± 41.62^{c}	16.23 ± 5.22^{a}	36.50 ± 4.39^{b}
4	48.13 ± 7.64^{a}	14.0 ± 4.0^{c}	408.42 ± 16.71^{a}	16.0 ± 7.34^{a}	37.42 ± 5.26^{a}
5	40 ± 4.24^{a}	12.13 ± 2.66^{c}	380.46 ± 11.85^{a}	20.48 ± 3.23^{a}	38.27 ± 7.05^{a}
6	42 ± 5.83^{a}	13.0 ± 3.0^{c}	392.31 ± 20.79^{a}	18.23 ± 2.27^{a}	36.53 ± 5.99^{a}
4	67.0 ± 7.07^{c}	22.13 ± 3.65^{b}	490.55 ± 18.56^{c}	17.42 ± 3.15^{a}	35.41 ± 4.36^{a}
5	60.13 ± 7.65^{c}	21.25 ± 3.13^{b}	470.25 ± 11.9^{c}	18.78 ± 2.82^{a}	35.67 ± 5.19^{a}
6	54.13 ± 5.87^{a}	17.13 ± 3.82^{a}	438.51 ± 14.99^{c}	19.55 ± 2.18^{a}	35.70 ± 5.74^{a}

Values are presented as mean ± standard deviation. (n=5). Values with different superscript letter in the same column differ significantly at $p < 0.05$

Effect of ethanolic extract of *T. tetraptera* fruit on some kidney function markers in rats exposed to cyanide intoxication

The effect of *T. tetraptera* on the urea and creatinine concentrations in the serum and kidney of rats induced with cyanide toxicity is indicated in Table- 2. The result shows that urea and creatinine concentrations were significantly increased in the serum and kidney of negative control rats when compared with the normal control. However no significant difference was observed in Groups 4, 5 and 6 given an increasing dose of the extract without cyanide poisoning. Again, treatment of cyanide intoxicated rats with 100,250 and 500 mg/kg body weight of the ethanolic extract of *T. tetraptera* (Groups 7, 8 and 9) significantly reduced the level of creatinine and urea in the serum of the treated rats when compared with the negative control not treated.

Table 2-Effects of ethanolic extract of *Tetrapleura tetraptera* fruit on renal function enzymes of cyanide intoxicated rats

GROUPS	Serum Urea	Serum creatinine	Kidney Urea	Kidney Creainine
1	16.69 ± 2.23^{a}	2.12 ± 0.81^{a}	24.38 ± 3.66^{a}	9.37 ± 1.75^{a}
2	32.54 ± 3.66^{b}	4.30 ± 0.98^{b}	39.62 ± 4.06^{b}	16.56 ± 4.74^{b}
3	20.54 ± 3.48^{c}	2.72 ± 0.17^{c}	30.81 ± 3.38^{c}	10.62 ± 1.99^{a}
4	15.43 ± 2.21^{a}	1.64 ± 0.43^{a}	22.12 ± 3.26^{a}	8.22 ± 2.37^{a}
5	13.64 ± 3.19^{a}	1.86 ± 0.08^{a}	27.46 ± 2.41^{a}	7.56 ± 1.49^{a}
6	19.51 ± 2.17^{c}	1.31 ± 0.78^{a}	26.25 ± 5.05^{a}	10.68 ± 1.41^{a}
7	23.57 ± 4.47^{c}	2.80 ± 0.73^{ac}	31.62 ± 5.03^{c}	9.39 ± 1.67^{a}
8	21.53 ± 5.11^{c}	2.51 ± 0.19^{a}	30.41 ± 3.65^{c}	8.65 ± 0.92^{a}
9	19.57 ± 3.26^{c}	2.21 ± 0.38^{a}	27.28 ± 6.06^{a}	8.52 ± 0.79^{a}

Values are presented as mean ± standard deviation. (n=5). Values with different superscript letter in the same column differ significantly at $p < 0.05$.

Effect of ethanolic extract of *T. tetraptera* on fruit on lipid peroxidation level in the liver and kidney of rats intoxicated with cyanide.

The effect of *T. tetraptera* on the level of LPO, in the liver and kidney of rats induced with cyanide toxicity is indicated in Figure-1. Induction with cyanide significantly increased the LPO levels from 0.60± 0.22 in the kidney and 2.61±0.14 in the liver of the normal control to 6.38± 0.99 and 8.14± 1.15 respectively in the negative control induced with cyanide without treatment. However there was no significant increase (P>0.05) in LPO in Groups 4, 5 and 6 given an increasing dose of the extract without cyanide poisoning. Treatment with different doses of the plant extract was however able to significantly reduce LPO levels in a dose dependent manner in both the kidney and the liver of the rats.

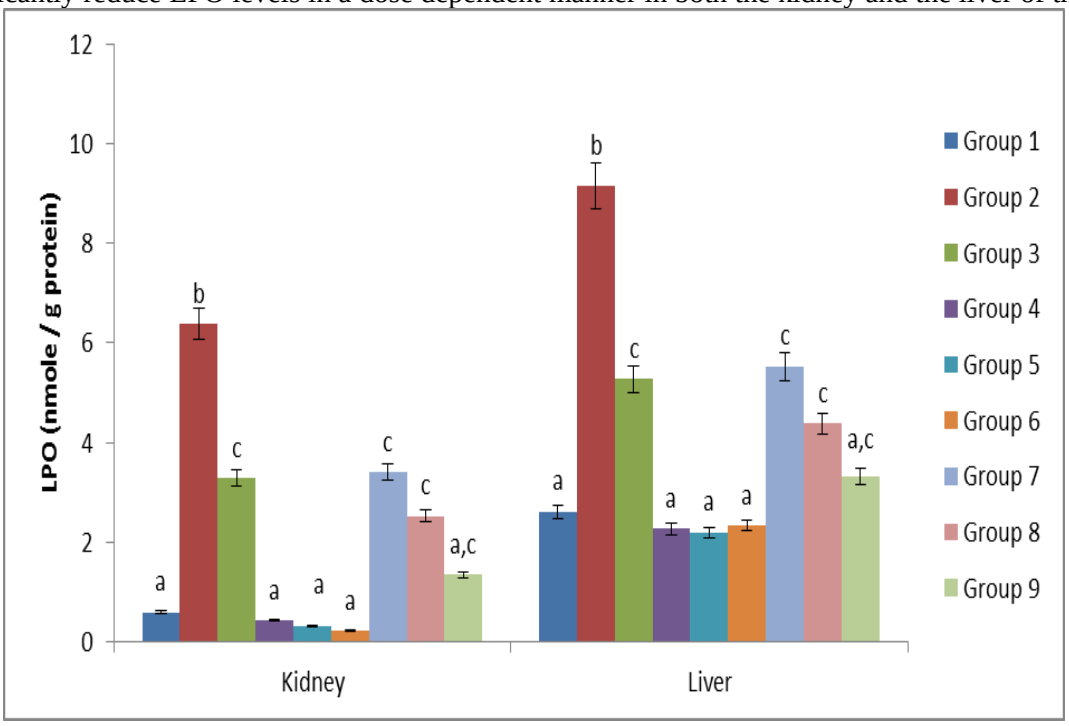

Figure 1-Effect of Ethanol extract of *T.te**traptera*** on lipid peroxide levels in the kidney and liver of rats intoxicated with cyanide.Values are presented as mean ± standard deviation. (n=5). Values with different superscript letter in the same column differ significantly at p< 0.05.

Effect of *T. tetraptera* on some antioxidant enzymes in the liver and kidney of rats induced with cyanide toxicity

The effect of *T. tetraptera* on the level of Superoxide dismutase (SOD) and catalase (CAT) activities in the liver and kidney of rats induced with cyanide toxicity is indicated in Figures-(2, 3) respectively. SOD and CAT activities were significantly reduced (P<0.05) in the kidney and liver homogenate of the untreated negative control rats when compared with the normal control. However no significant difference was observed in Groups 4, 5 and 6 given an increasing dose of the extract without cyanide poisoning. Treatment of cyanide intoxicated rats with 100,250 and 500 mg/kg body weight of the ethanolic extract of *T. tetraptera* (Groups 7, 8 and 9) significantly increased the activity of these two enzymes in the kidney and liver in a dose dependent manner when compared with the negative control. The study therefore indicates that *T. tetraptera* ameliorated the effect of cyanide on level LPO, SOD and CAT in the liver and kidney comparable to a known synthetic antidote and the effect of the extract was dose dependent.

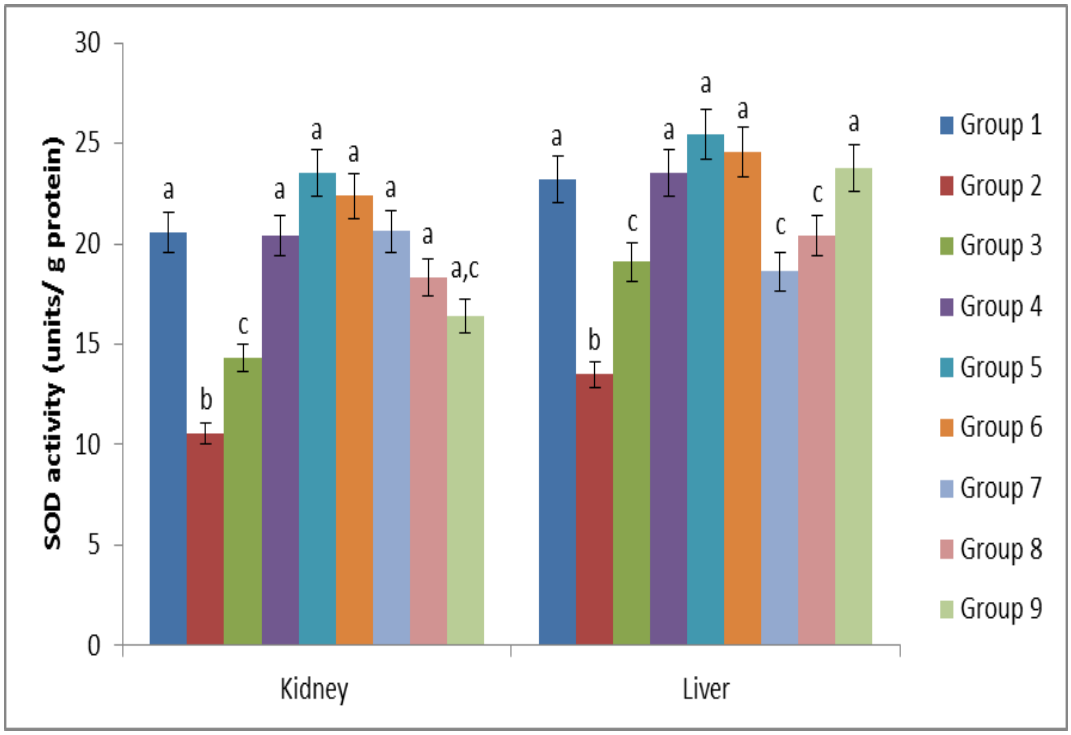

Figure 2-Effect of Ethanol extract of *T.traptera* on Super oxide dismutase activity in kidney and liver of rats intoxicated with cyanide.Values are presented as mean ± standard deviation. (n=5). Values with different superscript letter in the same column differ significantly at p< 0.05.

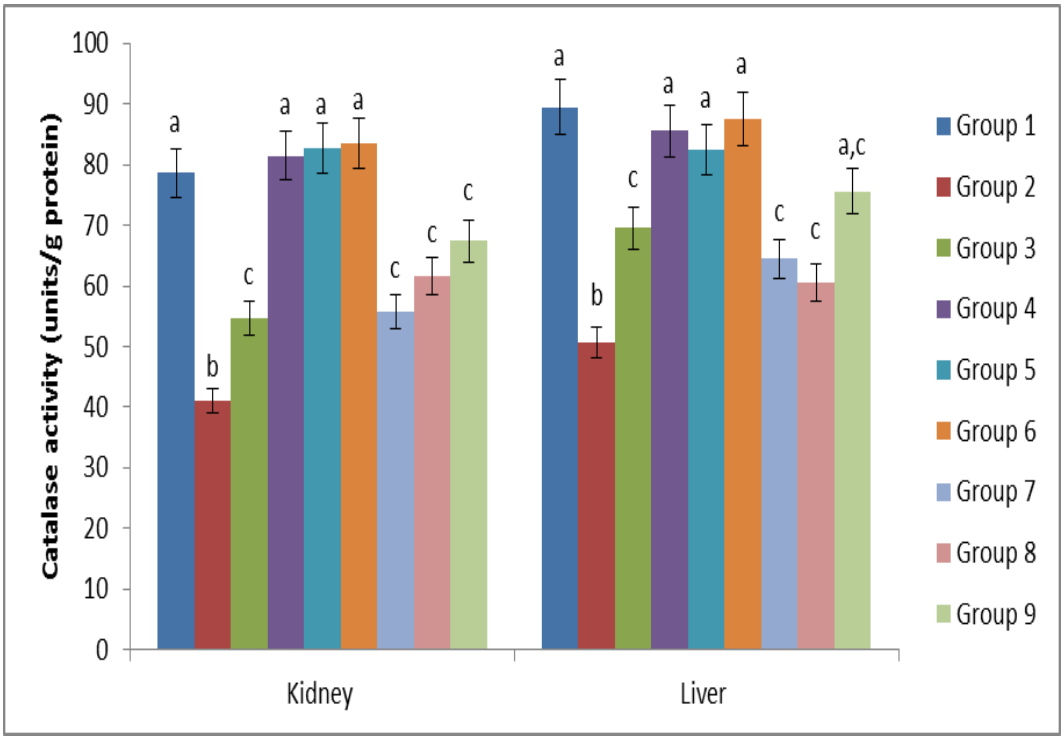

Figure 2-Effect of Ethanol extract of *T.treptera* on superoxide dismutase activity in kidney and liver of rats intoxicated with cyanide.Values are presented as mean ± standard deviation. (n=5). Values with different superscript letter in the same column differ significantly at p< 0.05.

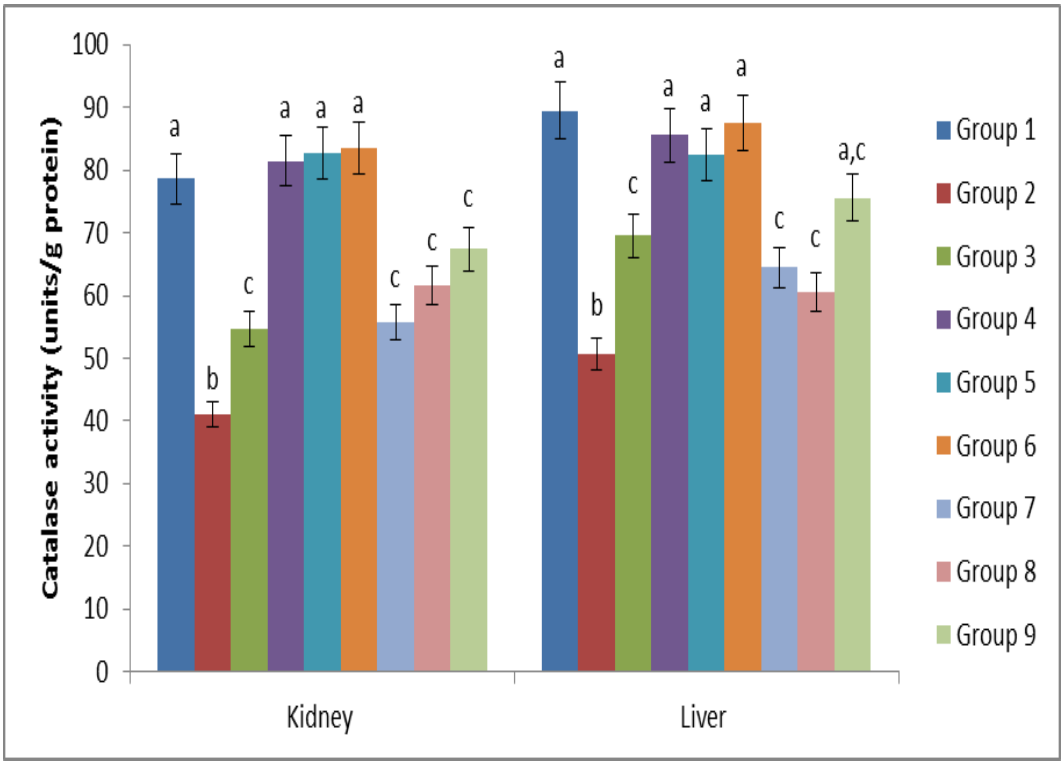

Figure 2-Effect of Ethanol extract of *T.treptera* on Super oxide dismutase activity in kidney and liver of rats intoxicated with cyanide.Values are presented as mean ± standard deviation. (n=5). Values with different superscript letter in the same column differ significantly at $p< 0.05$.

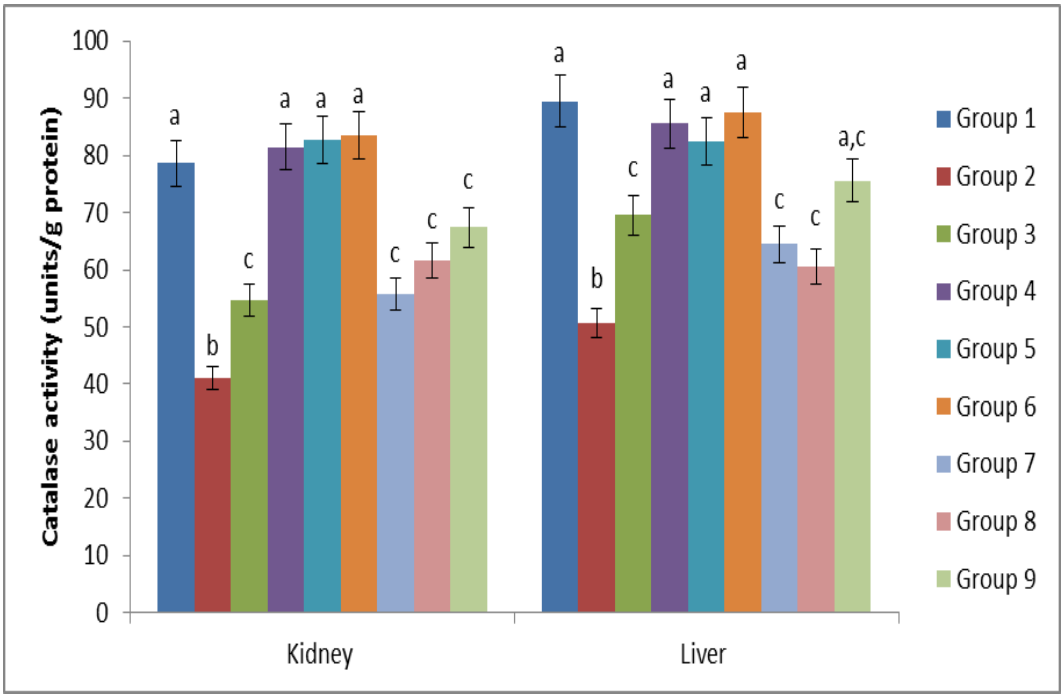

Figure 3-Effect of Ethanol extract of *T.treptera* on catalase activity in kidney and liver of rats intoxicated with cyanide. Values are presented as mean ± standard deviation. (n=5). Values with different superscript letter in the same column differ significantly at $p< 0.05$.

Liver and Kidney histopathology of rats intoxicated with cyanide and treated with ethanolic extract of *T. tetrapleura* fruit

Liver and kidney histopathology was indicated in Figure-4A-F and Figure-5G-L respectively. The result indicated that treatment with the three doses of the extract conferred protection to the liver and kidney in a dose dependent manner.

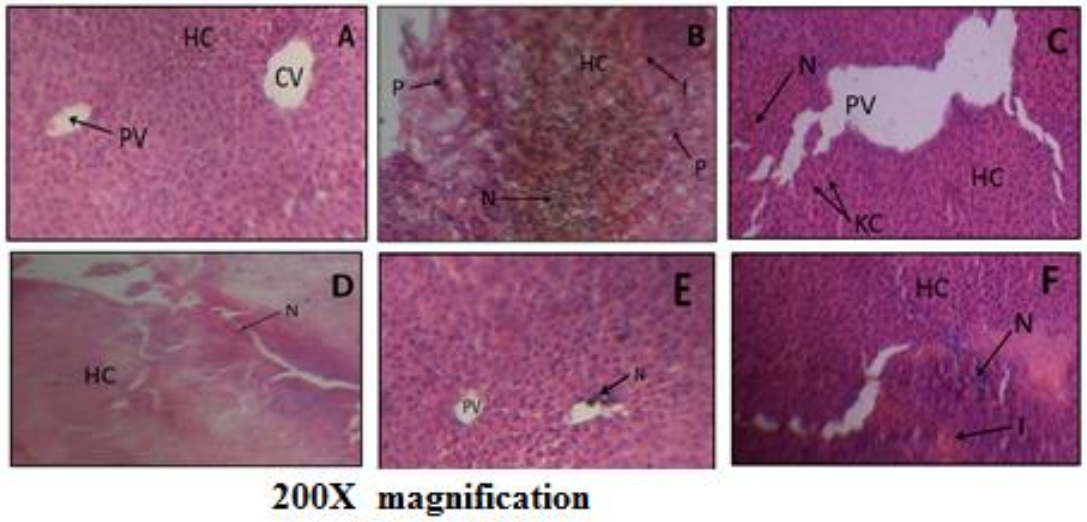

Figure 4A-F: Photomicrograph of the liver of rats intoxicated with cyanide and treated with ethanolic extract of *T. Tetrapleura* fruit A= Normal hepatic cell (HC),portal vein (PV)and central vein (CV). B= Severe degenerated hepatic cell (HC), necrosis (N) multi pyknotic nuclei (P). C = Regeneration of hepatic cell (HC) kupffer cells (KC), portal vein (PV) D = Moderate regeneration of hepatic cell (HC) and mild necrosis (N). E= Moderate improvement of portal vein (PV), kupffer cells (KC), and reduced necrosis (N). F = Normal hepatic cells with mild inflammation (I) and reduced hepatic necrosis (N).

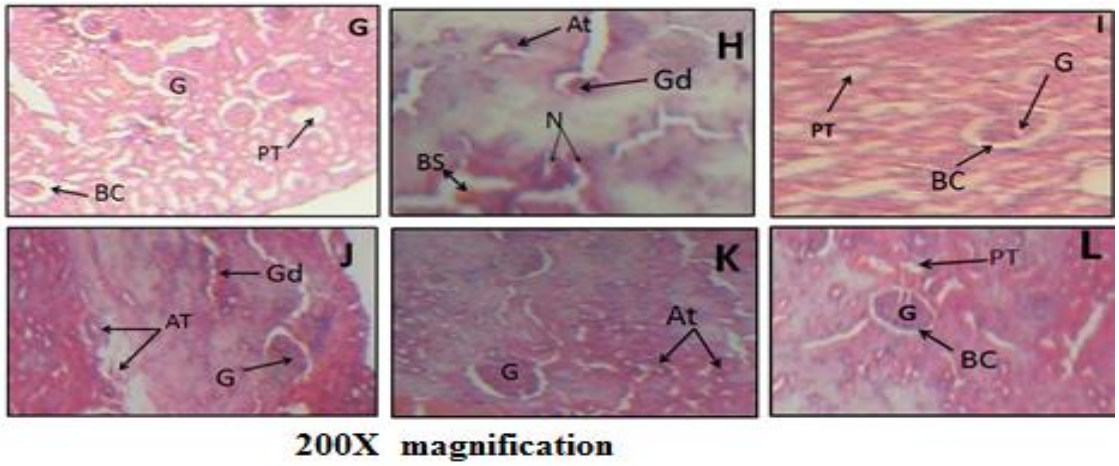

Figure 5G-L: Photomicrograph of the kidney of rats intoxicated with cyanide and treated with ethanolic extract of *T. Tetrapleura* fruit. G = Normal renal cells. H = Renal cells with severe damage of renal tubules, glomerular distortion (Gd), atrophy (At) of tubules with multi necrotic (N) tubular cells and increased bowman space (BS). I= Normal renal cells with regeneration of proximal tubules (PT). J= Renal cells with moderate improvement of renal tubules atrophy (At) and glomerular distortion (Gd). K = Renal cells showing a reduction of renal tubules atrophy (At). L= Normal renal cells with mild distortion of proximal tubules (PT).

Discussion

Cyanide is a very poisonous chemical and study indicates that sub lethal dose induces signs of toxicity [2]. Presently, there is no food and drug approved antidote that is specifically used for oral cyanide poisoning. Hence there is need for counter measure to oral cyanide exposure [23]. Previously, cyanide has been established to cause liver damage in different organisms [3, 4] and cyanide-induced

hepato-toxicity was confirmed in this study by the increase in the activities AST, ALT and ALP in the serum of rats and the decrease in the levels of TP and albumin in the cyanide treated rats. Activities of ALT, AST and ALP and the levels of total protein (TP) and albumin are routinely been measured clinically as diagnostic tools in assessing hepato-cellular injuries and health status of the liver [24, 25]. Moreover, the no significant difference in the activities of ALT, AST and ALP and the levels of total protein and albumin in the rats exposed to the extract in an increasing dose without cyanide intoxication is an indication that *T.tetraptera* fruit has no hepatotoxic effect. In addition, the reversal of the effect of cyanide by *T.tetraptera* on the activity and level of the hepatic enzymes in increasing dose is an indication of the hepato-protective potential of the extract probably due to its rich flavonoid content which has been indicated in earlier studies [8, 9, 26]. Also, increase in TP and albumin levels resulting from treatment by the plant extract maybe due to the ability of the plant to stabilize the endoplasmic reticulum and increase protein synthesis. This study is in agreement with the works of Saague et al. [27], where they demonstrated the hepato-protective ability of *T.tetraptera* on rats induced with liver injury using CCl_4.

Measurements of the levels of excretory metabolites such as urea, and creatinine are widely used methods in the assessment of renal function [28, 29]. Cyanide has been established to cause kidney damage in different organisms. [30,31].The result from this present study is in agreement with these findings as renal toxicity was indicated by the recorded increase in creatinine and urea concentrations in the serum and kidney. However co-treatment with *T. tetraptera* restored the concentration of creatinine to near normal level. The reduction in creatinine and urea concentrations is an indication that the *T. tetraptera* must have had a protective effect due to its antioxidant properties which has been investigated in earlier studies carried out on *T. tetraptera* [9]. The antioxidant properties of *T. tetraptera* can be ascribed to the presence of phytochemicals in the plants [9, 26].

The overall degenerative potency of cyanide on the liver and kidney tissues has been related to its ability to increase LPO and suppress the antioxidants enzymes, SOD and CAT [32]. The is consistent with this study which showed that cyanide intoxication resulted in increase in lipid peroxidation as evidenced in the increased MDA level and a reduction in catalase and SOD activities in the liver and kidney establishing hepatic and renal toxicity. However, administration of increasing dose of *T. tetrapleura* fruit extract alleviated the observed oxidative stress in the liver and kidney of cyanide treated rats by decreasing the level of lipid peroxidation and increasing the activities of antioxidant enzymes, CAT and SOD (Table- 3). Thus the reversal of oxidative stress by the extract is an indication that the extract has antioxidant properties and this is one of the mechanisms by which the extract alleviates the toxic effect of cyanide in the liver and kidney. The antioxidant effect of ethanolic extract of *T. tetrapleura* fruit is due to the presence of phytochemicals such as flavonoids, phenols, cardiac glycosides and terpenes [9, 10, 26] which are known for their chelating property and protection against free radical attacks [33]. Several studies have also shown that certain flavonoids can induce the activity and expression of enzymes by inducing the expression of antioxidant defense enzymes such as SOD and CAT. These flavonoids have the potential to produce long lasting effects on cellular function and this could be highly beneficial to cells exposed to chronic oxidative stress [34]

The structural distortions of liver and kidney by cyanide is in tandem with increase in lipid peroxidation and the corresponding decrease in the activities of SOD and catalase observed in this study. Study from Fulda et al., [35], shows that cells respond histopathologically to toxic insult by the following processes: degeneration, proliferation, inflammation, and repair. These pathological changes in the liver and kidney of cyanide intoxicated rats in this present study is also in agreement with previous studies by kadiri and Asagba [3]and Tulsawani [5] who reported that cyanide induces pathological aberrations in the liver and kidney of birds and in the liver and kidney of rats following exposure to sublethal concentrations of cyanide. In agreement with other biochemical parameters monitored, histological examination showed the protective ability of *T. tetrapleura* extract against cyanide insult.

On the whole, the findings of this study may be the reason for the extensive use of *T. tetraptera* to manage an array of human ailments such as hypertension, arthritis, diabetes mellitus, and epilepsy. However it's renal and hepato-protective potential against cyanide toxicity has not been exploited. This present study therefore established the potential renal and hepatic protective ability of *T. tetraptera* against cyanide toxicity.

Conclusion

In conclusion, this study has demonstrated that ethanolic extract of *T. tetraptera* fruit has potentials to serve as hepato-protective and renal protective agent as well as a good antidote to cyanide poisoning. Thus it can be considered as an oral source of antidote for cyanide poisoning as it compares favourably with the known synthetic cyanide antidote.

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