BIOLOGY, MEDICINE, & NATURAL PRODUCT CHEMISTRY ISSN 2089-6514 (paper)
Volume 14, Number 2, October 2025 | Pages: 1529-1536 | DOI: 10.14421/biomedich.2025.142.1529-1536 ISSN 2540-9328 (online)

Hepatoprotective Activities of Seed Extract and Fractions of *Telfairia occidentalis* on Doxorubicin-Induced Hepatotoxicity in Rats

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Manuscript received: 02 October, 2025. Revision accepted: 29 November, 2025. Published: 12 January, 2026.

Abstract

Telfairia occidentalis Hook (cucurbitaceae) seeds, which is used in the preparation of soups and as medicine traditionally to treat various diseases by the Ibibios was investigated for effect against doxorubicin-induced hepatotoxicity. The seed extract (138 -553 mg/kg) and fractions; dichloromethane (DCM) and aqueous, 276 mg/kg) were evaluated for hepatoprotective activity against doxorubicin-induced liver injury in rats. Liver function parameters, liver oxidative stress markers and liver histology were used to assess the liver protective potential of the extract and fractions. The seed extract and fractions significantly ($p<0.05$-0.01) reduced the serum levels of AST, ALT, ALP, total and direct bilirubin that were elevated by doxorubincin. Also, the reduced levels of total protein and albumin by doxorubicin were increased by the extract coadministration. The levels of GSH, GST, SOD, GPx, and CAT that were decreased by doxorubicin were significantly ($p<0.01$) elevated and raised MDA level was reduced by the seed extract and fractions. Histology of the liver sections of extract -treated animals showed reductions in the pathological features compared to the organotoxic-treated animals. The chemical pathological changes were consistent with histopathological observations suggesting marked hepatoprotective potential. The anti-toxic effect of this plant may in part be mediated through the chemical constituents of the plant. The seeds of *Telfairia occidentalis* possess anti-toxicant properties which can be exploited in the treatment of doxorubicin related toxicities.

Keywords: *Telfairia occidentalis*; anti-toxicant; oxidative hepatoprotective; antioxidant.

INTRODUCTION

Telfairia occidentalis Hook is a fluted pumpkin of the *Cucurbitaceae* family widely consumed as food in Nigeria (Okokon *et al*., 2009). It is a popular vegetable all over Nigeria, especially in the Niger-Delta region and the Eastern part of the country; varieties of meals are prepared from the leaves, stem and seeds of the plant (Usunomena and Okpiabhele, 2023). The seeds are very nutritious and are eaten roasted or boiled. The seed has history of being effective in the treatment and prevention of prostrate disorders. The seed extract has been reported to exert antidiabetic (Eseyin *et al.*, 2007), cellular antioxidant, immunodulatory, anticancer, antiinflammatory (Okokon *et al.,* 2012a), antiplasmodial (Okokon *et al.,* 2009), antioxidant (Osukoya *et al,* 2016) and analgesic (Okokon *et al.*, 2012b; Osukoya *et al,* 2016), genotoxic and cytotoxic (Magnus *et al.*, 2024) and in vivo inhibitory effect alpha amylase and alpha glucosidase (Enin *et al.,* 2023). while the leaf extract possesses antioxidant, antibacterial (Oboh *et al.,* 2010), hepatoprotective (Nwanna *et al*., 2007) antidiabetic (Nwozo *et al*., 2004), antiplasmodial (Okokon *et al.,* 2009) genotoxic and cytotoxic (Magnus *et al*., 2024) and antiprostatic (Fabian *et al.*, 2025) activities. Phytochemical studies of the extract have shown the presence of alkaloid, flavonoid, tannins, terpenes, saponin, and cardiac glycosides (Ebong *et al.,* 2020). Okokon *et al*. (2012) reported the presence of compounds such as pentadecanoic acid, hexadecanoic acid; 16-octadecenoic acid methyl ester; 9, 12-octadecadienoyl chloride (Z,Z); 9- octadecadienoic acid (Z)-, 2, 3-dihydroxypropyl ester; octadecanoic acid; hexadecanoic acid,2,3-is[(trimethylsilyl) oxy] propyl ester, 2,4-heptadien-6-ynal,(E,E); benzoic acid; dodecanoic acid; linoleic acid ethyl ester; hexadecanoic acid, methyl ester; α-phellandrene; α-campholene aldehyde; terpinen-4-ol; trans-β-ocimene; borneol and stigmastan-3- ol, in the seed extract.

The present study was designed to evaluate the activities of seed extract and fractions of *T.occidentalis* against doxorubicin-induced liver injury in rats.

MATERIALS AND METHODS

Plant collection

Fresh seeds of *Telfairia occidentalis* were purchased from Itam market in Itu L. G. A, Akwa Ibom State, Nigeria, in June, 2023. The seeds were previously identified and authenticated by a taxonomist in the Department of Botany, University of Uyo, Uyo, Nigeria. Herbarium specimens (UUPH 1(b)) were deposited at Department of Pharmacognosy and Natural Medicine Herbarium, University of Uyo.

The fresh seeds of the plant were dried on laboratory table for 2 weeks and reduced to powder. The seeds powder (1 kg) was separately macerated in 50% ethanol (5000 mL) for 72 hours. The liquid filtrate obtained were concentrated at 40˚C and all the ethanol was completely removed. The crude extract (20 g) was dissolved in 500 mL of distilled water and partitioned with equal volume of dichloromethane (DCM, 5 x 500 mL) till no colour change was observed, to obtain DCM and aqueous fractions. The extract and fractions were stored at 4˚C in a refrigerator until used for the experiment.

Animals

In this study, male albino Wistar rats (150-200 g) were used. The animals were sourced from University of Uyo Animal house and sheltered in plastic cages. The rats were fed with pelleted standard Feed (Guinea feed) and given unlimited access to water. The study was approved by College of Health Sciences Animal Ethics Committee, University of Uyo.

Experimental design

In this study, repeated dose model earlier described by Raskovi *et al.* (2011) and Olorundare et al., (2020), which lasted for 14 days was used. Groups I rats which served as the untreated control were orally pretreated with 10 mL/kg/day of distilled water. Group 2 rats were given normal saline (10 mL/kg/day) but equally treated on alternate days with 1.66 mg/kg of doxorubicin hydrochloride dissolved in 0.9% normal saline administered on alternate days for 14 days. Groups 3-5 rats were orally pretreated with 138 mg/kg/day, 276 mg/kg/day, and 553 mg/kg/day of *Telfairia occidentalis* dissolved in 10% Tween 80, 2 hours before treatment with 1.66 mg/kg of doxorubicin in 0.9% normal saline administered intraperitoneally on alternate days for 14 days, respectively. Groups 6 and 7 were pretreated with 276 mg/kg of DCM and aqueous fractions respectively. Group 8 rats which served as the positive control group were equally pretreated with 100 mg/kg/day of silymarin two hours before treatment with 1.66 mg/kg of doxorubicin in 0.9% normal saline administered intraperitoneally on alternate days for 14 days.

Collection of blood samples and organs

After 14 days of treatment (24 hours after the last administration) the rats were weighed again and sacrificed under light diethyl ether vapour. Blood samples were collected by cardiac puncture and used immediately. Blood samples were collected into plain centrifuge tubes. The blood samples were centrifuged at 2500 rpm for 15 mins to separate the serum at room temperature and stored at -20^{o}C until used for biochemical determinations. The livers of the rats were surgically removed, weighed. Each liver was gently and carefully divided into two parts; a part was fixed in 10 % formaldehyde for histological processes, while the other part of the liver was briskly rinsed in ice cold 1.15% KCl solution and put in a clean sample bottle. These were stored in ice cold 0.9% NaCl.

Assessment of the effect of extract on liver function parameters of rats

The collected serum was used for the estimation of biochemical parameters such as total protein, albumin, total and direct bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphotase (ALP), total cholesterol. All biochemical parameters estimations were done using automated analysers and Fortress Diagnostic Kits® (Fortress Diagnostic Limited, UK) according to standard procedures of manufacturer's protocols at University of Uyo Teaching Hospital.

Oxidative Stress Markers

The antioxidant enzymes assays were performed on liver homogenates of rats that were used in this study. These oxidative stress markers were used to assess antioxidative stress potentials of the extract and fractions.

Preparation of liver Homogenate

After the rats were sacrificed humanely under inhaled diethyl ether, the livers of the rats were surgically removed and weighed. They were briskly rinsed in ice cold 1.15% KCl solution and put in a clean sample bottle. These were stored in ice cold 0.9% NaCl. Homogenates were made in a ratio of 1 g of wet tissue to 9 ml of 1.25% KCl by using motor driven Teflon-pestle. The homogenates were centrifuged at 7000 rpm for 10 min at 4˚C and the supernatants were used for the assays of superoxide dismutase (SOD) (Marklund and Marklund, 1974), catalase (CAT) (Sinha,1972), glutathione peroxidase (GPx) (Lawrence and Burk,1976), reduced gluthathione (GSH) (Ellman,1959) and malondialdehyde (MDA) content (Esterbauer and Cheeseman, 1990). The assays were performed on liver homogenates of rats that were used in this study.

Histopathological studies

The excised livers fixed in 10 % buffered formalin were used for histological processes. They were processed and stained with haematotoxylin and eosin (H&E) (Drury and Wallington, 1980), according to standard procedures at

Department of Chemical Pathology, University of Uyo Teaching Hospital, Uyo. Morphological changes observed and recorded in the excised organs of the sacrificed animals. Histologic pictures were taken as micrographs.

Statistical analysis

Data collected were analyzed using one way analysis of variance (ANOVA) followed by Tukey's multiple comparison post-test (Graph pad prism software Inc. La Jolla, CA, USA). Values were expressed as mean ± SEM and significance relative to control were considered at $p<0.001$ and $p<0.05$.

RESULTS

Effect of seed extract and fractions of *Telfairia occidentalis* on body and liver weights of rats with doxorubicin-induced toxicity

Administration of *T.occidentalis* seed extract and fractions to rats with doxorubicin-induced organs toxicities caused considerable improvement of the body weights compared to the organotoxic group. The crude extract (276 mg/kg) and dichloromethane fraction treated groups recorded the highest body weight gains compared to the organotoxic group. The liver weights of the group treated with doxorubicin only were found to be increased when compared to those of the normal control group though not statistically significant ($p>0.05$). However, concommitant treatment of rats with doxorubicin and seed extract and fractions of *T. occidentalis* improved the liver weights though insignificantly ($p>0.05$) relative to the group treated with doxorubicin only (Table 1)

Effect of *T. occidentalis* seed extract and fraction on liver function parameters of rats with doxorubicin-induced hepatotoxicity: Administration of doxorubicin (1.66 mg/kg, i.p) on alternate days for 14 days to rats caused a significant ($p<0.05$-0.001) elevation in the level of AST, ALT, ALP, total and combined bilirubin and decreases in total protein and albumin levels when compared to control. Concomitant administration of seed extract and fractions of *T.occidentalis* (138 -553 mg/kg) with doxorubicin (1.66 mg/kg,i.p) for 14 days caused significant ($p<0.05$-0.001) and dose-dependent reductions in the levels of the liver enzymes (AST, ALT, ALP), total and combined bilirubin in the extract/fractions-treated groups when compared with the organotoxic group with the aqueous fraction exerting the highest reduction. However, the decreases were non dose-dependent. Similar significant ($p<0.05$) reductions were observed in the group treated with silymarin. Total protein and albumin levels were significantly ($p<0.05$-0.001) elevated dose-dependently in the extract/fractions -treated groups when compared to the doxorubicin group with aqueous fraction exerting the most effect (Table 2).

Effect of *T. occidentalis* seed extract and fraction on liver oxidative stress markers of doxorubicin-induced liver toxicity: Table 3 shows the effect of *T. occidentalis* seed extract/fractions on liver oxidative stress markers of the rats. Administration of doxorubicin (1.66 mg/kg i.p) on alternate days for 14 days caused significant ($p<0.01$-0.001) decreases of liver antioxidant enzymes activities (SOD, GPx, CAT) and GSH levels when compared to control. The MDA level was also elevated by doxorubicin treatment significantly ($p<0.01$) when compared to control. However, concomitant administration of seed extract/fractions of *T.occidentalis* (138 - 553 mg/kg) with doxorubicin for 14 days caused significant ($p<0.05$-0.001) and non dose-dependent elevations of the enzymatic and non enzymatic endogenous antioxidants in the treated rats groups when compared to the organotoxic groups. DCM fraction exerted the most significant ($p<0.001$) effect on SOD level, while aqueous fraction and silymarin had the highest effect on CAT level. Similarly, GPx activity and GSH levels were non dose-dependently and significantly ($p<0.05$) elevated when compared to control with the highest dose (553 mg/kg) followed DCM fraction producing higher increases (Table 3).

Effect of seed extract and fractions of *T. occidentalis* on histology of rat liver in doxorubicin-induced hepatotoxicity: Histologic sections of livers of rats receiving various treatments at magnification (x400) stained with H&E method revealed that normal control (Group 1, CONT) treated distilled water (10 mL/kg) had normal hepatic architecture with well protected portal vein, hepatic artery and Bile duct, within the portal area, well-protected hepatocytes, presence of kupffer cells, and radiating sinusoids within the hepatic lobules. No pathological changes was seen. The organotoxic group (Group 2, T+CONT) treated with doxorubicin (1.66 mg/kg) only showed moderately affected livers with atrophying hepato-architectures with areas of degenerated hepatic and ductal cells, degenerating and vacoulated hepatocytes, and wide spread micro-vesicular steatosis. Group 3 (T+STD), which was treated with silymarin (100 mg/kg) and doxorubicin (1.66 mg/kg) showed a mildly altered hepato-architecture with spreading micro-vesicular steatosis, and increase proliferation of kupffer cell within the hepatic lobules. Group 4 (T+LDE) treated with 138 mg/kg of *T. occidentalis* seed extract and doxorubicin (1.66mg/kg) showed a mildly altered hepato-architecture with proliferating fibrocytes within the interstitial connective tissue, and increasing proliferation of kupffer cell within the hepatic lobules.lobular architecture of the liver with normal hepatocytes and averaged sized central vein and sinusoid. Group 5 (T+MDE), treated with 276 mg/kg of *T.occidentalis* seed extract and doxorubicin (1.66 mg/kg) showed a mildly altered hepato-architecture with spreading micro-vesicular steatosis, proliferating fibrocytes within the interstitial connective tissue and

increase proliferation of kupffer cell within the hepatic lobules. Group6 (T+HDE), treated with 553 mg/kg of *T. occidentalis* seed extract and doxorubicin (1.66 mg/kg) showed a moderately altered tissues demonstrating an atrophying hepato-architecture with areas of degenerated hepatic cells, degenerating and vacoulated hepatocytes, and wide spread micro-vesicular steatosis within the hepatic lobules. Rats treated with aqueous fraction (276 mg/kg) of *T. occidentalis* seed and doxorubicin (1.66 mg/kg) in group 7 (T+AQE), had liver section that revealed an atrophying hepato-architecture with areas of degenerated hepatic cells within the hepatic lobules lobular architecture of the liver demonstrating a moderate effect. Liver section of group 8 (T+DCME) rats treated with dichloromethane fraction (276 mg/kg) of *T. occidentalis* seed and doxorubicin (1.66 mg/kg showed an atrophying hepato-architecture with areas of degenerated hepatic cells revealing a moderate effect (Figure 1).

Table 1. Effect of *T.occidentalis* seed extract on body and liver weights of rats with doxorubicin-induced toxicity.

Parameters/ Treatment	Dose mg/kg	Liver	Body weight		
			Before	After	% increase in body weight
Normal control	-	5.30±0.51	176.28±17.97	198.25± 6.61	12.46
Doxorubicin	1.66	6.34±0.24	169.66 ± 6.80	181.66±13.24	5.72
Silymarin+DOX	100	5.62±0.60	180.33± 10.86	190.66± 13.24	5.72
Extract+DOX	138	6.10±0.92	176.0± 11.13	191.0± 6.08	8.52
	276	5.63±0.28	167.0± 7.57	185.0 ± 8.73	10.77
	553	5.65±0.15	177.66± 7.42	193.33 ± 5.48	8.82
Aqueous fraction	276	6.60±0.77	187.66± 17.89	195.33± 17.70	4.08
DCM fraction	276	5.07±0.38	162.66± 12.66	180.33± 9.56	10.86

Data are expressed as mean ±SEM. significant at dp<0.001 when compared to normal control; ap< 0.05, bp< 0.01, cp< 0.001 when compared to organotoxic control. n = 5.

Table 2. Effect of *T. occidentalis* seed extract and fractions on liver oxidative stress markers of rats with doxorubicin-induced toxicity.

Treatment	Dose mg/kg	SOD (U/mL)	CAT (U/g of protein)	GPx (µg/mL)	GSH (µg/mL)	MDA (µMol/mL)
Control	10	0.41±0.01	6.34±0.72	0.038±0.005	1.69±0.01	0.38±0.02
Doxorubicin	1.66	0.20±0.001^{b}	4.11± 0.90^{b}	0.030±0.001^{b}	1.31±0.01^{b}	0.52±0.02^{c}
Crude extract	138	0.26±0.01^{b}	6.07±0.32	0.041±0.001^{f}	1.84± 0.04^{e}	0.42±0.08^{d}
	276	0.31±0.02^{d}	7.87± 0.25^{f}	0.034±0.002	1.54± 0.11	0.22±0.01^{c,f}
	553	0.35±0.02^{e}	6.94±0.42^{d}	0.044±0.002^{f}	2.00± 0.10^{f}	0.43±0.07^{d}
Aqueous Fraction	276	0.22±0.01^{b}	8.20±0.06^{f}	0.041±0.002^{f}	1.89± 0.12^{f}	0.42± 0.08^{d}
DCM fraction	276	0.36±0.01^{d}	5.33±0.67	0.039±0.005^{f}	1.79± 0.02^{f}	0.31± 0.02^{f}
Silymarin	100	0.33±0.05^{d}	9.28±0.34^{f}	0.039±0.003^{f}	1.78±0.03^{f}	0.48±0.03^{a}

Data are expressed as MEAN ± SEM, Significant at ^{a}p<0.05, ^{b}p<0.01, ^{c}p<0.001, when compared to control;Significant at ^{d}p<0.05, ^{e}p<0.01, ^{f}p<0.001 compared to organotoxic group. (n=5).

Table 3. Effect of *T. occidentalis* seed extract and fractions on liver oxidative stress markers of rats with doxorubicin-induced toxicity.

Treatment	Dose mg/kg	SOD (U/mL)	CAT (U/g of protein)	GPx (µg/mL)	GSH (µg/mL)	MDA (µMol/mL)
Control	10	0.41±0.01	6.34±0.72	0.038±0.005	1.69±0.01	0.38±0.02
Doxorubicin	1.66	0.20±0.001^{b}	4.11± 0.90^{b}	0.030±0.001^{b}	1.31±0.01^{b}	0.52±0.02^{c}
Crude extract	138	0.26±0.01^{b}	6.07±0.32	0.041±0.001^{f}	1.84± 0.04^{e}	0.42±0.08^{d}
	276	0.31±0.02^{d}	7.87± 0.25^{f}	0.034±0.002	1.54± 0.11	0.22±0.01^{c,f}
	553	0.35±0.02^{e}	6.94±0.42^{d}	0.044±0.002^{f}	2.00± 0.10^{f}	0.43±0.07^{d}
Aqueous Fraction	276	0.22±0.01^{b}	8.20±0.06^{f}	0.041±0.002^{f}	1.89± 0.12^{f}	0.42± 0.08^{d}
DCM fraction	276	0.36±0.01^{d}	5.33±0.67	0.039±0.005^{f}	1.79± 0.02^{f}	0.31± 0.02^{f}
Silymarin	100	0.33±0.05^{d}	9.28±0.34^{f}	0.039±0.003^{f}	1.78±0.03^{f}	0.48±0.03^{a}

Data are expressed as MEAN ± SEM, Significant at ^{a}p<0.05, ^{b}p<0.01, ^{c}p<0.001, when compared to control;Significant at ^{d}p<0.05, ^{e}p<0.01, ^{f}p<0.001 compared to organotoxic group. (n=5).

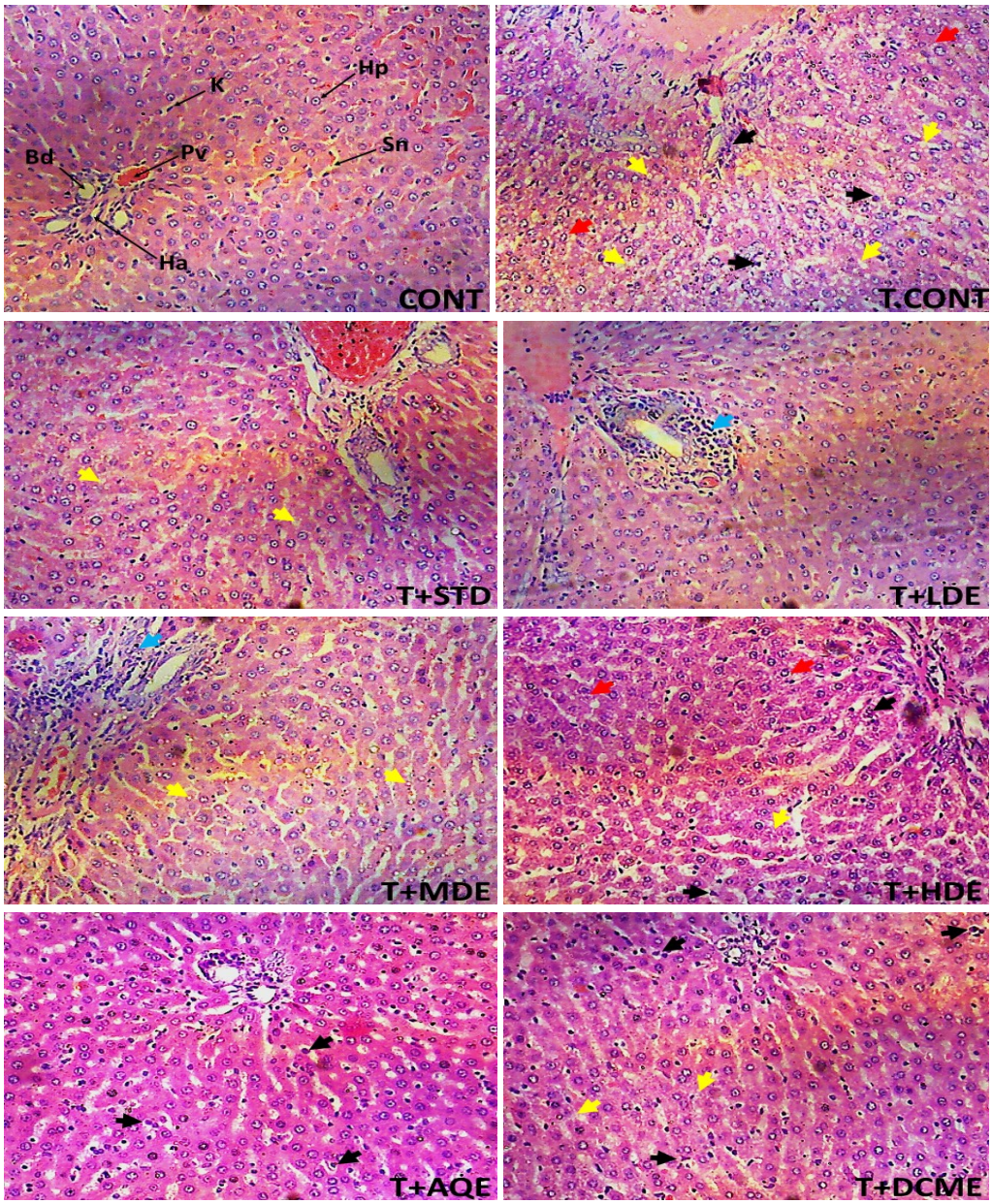

Figure 1. Photomicrographs of sections of livers of rats treated with distilled water (**CONT**), doxorubicin only,1.66 mg/kg (**T.CONT**), Sylimarin,100 mg/kg and DOX(**T+STD**), *T occidentalis*, 138 mg/kg and DOX (**T+LDE**), *T.occidentalis*, 276 mg/kg and DOX (**T+MDE**), *T.occidentalis,* 553 mg/kg and DOX (**T+HDE**), Aqueous fraction, 276 mg/kg and DOX (**T+AQE**) and DCM fraction, 276 mg/kg and DOX (**T+DCME**) showing well protected portal vein (Pv), hepatic artery (Ha) and Bile duct (Bd), within the portal area, well-protected hepatocytes (Hp), presence of kupffer cells (K), and radiating sinusoids (Sn),areas of degenerated hepatic and ductal cells (black arrow), degenerating and vacoulated hepatocytes (red arrow), and wide spread micro-vesicular steatosis (yellow arrow) within the hepatic lobules (H&E x100).

DISCUSSION

This work was designed to evaluate the effect of seed extract and fractions of *Telfairia occidentalis* on doxorubicin-induced liver toxicity in rats. Doxorubicin is an anthracycline glycoside antibiotic that possesses a potent and broad spectrum antitumour activity against a variety of human solid tumours and haematological malignancies (Calabresi and Chamber, 1990). However its use in chemotherapy has been limited largely due to its diverse toxicities, including cardiac, hepatic, hematological and testicular toxicity (Yilmaz *et al.,* 2006). The semiquinone form of doxorubicin is a toxic short-lived metabolite which interacts with molecular oxygen and initiates a cascade of reactions, producing reactive oxygen species (ROS). ROS generation, inflammatory processes and lipid peroxidation have been suggested to be responsible for doxorubicin-induced cardio and hepatotoxicity (Injac *et al.,* 2009; Kalender *et al.,* 2005).

It has been proposed that DOX-semiquinone, an unstable metabolite of DOX, reacts with O_2, producing H_2O_2 and O_2^- (superoxide). In addition, DOX enhances the activity of extramitochondrial oxidative enzymes such as xanthine oxidase and NADPH oxidase and also

interferes with mitochondrial iron export, resulting in formation of ROS (reactive oxygen species) (Bachur *et al.,* 1979).

Doxorubicin administration was found in this study to have increased the liver weights insignificantly, while co-administration of the seed extract and fractions was observed to cause insignificant decrease in weight of liver. Generally, internal organs weights are considered as important indicator to injury and toxicities (Farah *et al.,* 2013). Hypertrophy of organs often indicates toxicity and damaged to organ (Ping *et al*., 2013). This often results from oedema due to inflammation of the organs. Free radicals generated during doxorubicin metabolism cause destruction of hepatic, cardiac and kidney cells and tissues. The decrease in weights of liver by the extract and fractions maybe as a result of protective effect of the extract against the effect of free radicals generated by doxorubicin. The antioxidative burst and antioxidant activities of the seed extract and fractions of *T.occidentalis* had previously been reported (Oboh *et al.,* 2010; Okokon *et al.*, 2012a; Osukoya *et al.,* 2016). Moreso, the antioxidative stress activities of the seed extract and fractions observed in this study further support the antioxidant potentials of the plant. These activities may have contributed to the observed protective effects in this study.

In this study, administration of doxorubicin (1.66 mg/kg, i.p) on alternate days for 14 days to rats was found to caused a significant ($p<0.001$) elevation in the level of AST, ALT, ALP, total and combined bilirubin and decreases in total protein and albumin levels when compared to control, as manifestations of serious damage to the liver. Concomitant administration of seed extract and fractions of *T. occidentalis* (138 - 553 mg/kg) with doxorubicin (1.66 mg/kg, i.p) for 14 days caused observable significant ($p<0.001$) decreases of these enzymes levels and that of total and combined bilirubin in the extract-treated groups when compared with the organotoxic group. Assessment of liver function can be made by estimating the activities of serum ALT, AST, ALP, bilirubin (total and direct), total cholesterol, total protein and albumin which are originally present in the cytoplasm (Manokaran *et al.,* 2008). When there is liver damage, these enzymes and molecules leak into the blood stream, which serves as an indicator for the liver damage (Nkosi *et al.,* 2005). The reduction of the levels of these enzymes and molecules by the seed extract and fractions in this study is as a result of their free radical scavenging potentials, thereby protecting the liver against oxidative stress by free radicals generated by doxorubicin. The effect may have resulted from the antioxidant activities of its phytoconstituents. This result agrees with earlier studies by Nwanna *et al.* (2007) and Fabian *et al*. (2025) in which significant protection of the liver against paracetamol and testosterone-induced liver injuries by the seed extract of this plant were reported.

The findings of this study show that administration of doxorubicin (1.66 mg/kg, i.p) on alternate days for 14 days to rats caused significant decreases ($p<0.05$) in levels of liver enzymatic and non enzymatic endogenous antioxidants (SOD, CAT, GPx and GSH) when compared to control. Elevated level of MDA was also observed. Lipid peroxidation is a marker of oxidative stress and elevations in the amount of malondialdehyde (MDA), a lipid peroxidation product, have been reported following Dox treatment (Rashid *et al.,* 2013, Rehman *et al.,* 2014, Khames *et al.,* 2019). This trend was observed in this study. Concomitant administration of seed extract and fractions *T.occidentalis* (138 - 553 mg/kg) with doxorubicin caused significant ($p<0.05$-0.001) non dose-dependent elevation in the levels of the liver antioxidant enzymes (SOD, CAT, GPx) when compared to control. Similarly, GSH level was significantly ($p<0.001$) elevated following treatment with the extract/fractions when compared to control. Also, there were significant ($p<0.05$-0.01) reductions in the level of MDA of the extract/fractions-treated rats. It has been documented that DOX inhibits the activities of endogenous enzymatic and nonenzymatic antioxidants as was the case in this study. So, an imbalance between ROS generation and neutralization leads to oxidative stress and injury to the liver (Abushouk *et al.,* 2017; Abdel-Daim *et al.,* 2017; Aboushouk *et al.,* 2019). The reduction of MDA level by the extract and fractions demonstrates a reduction in lipid peroxidation and free radicals generation which might have been scavenged by the phytoconstituents present in this extract and fractions, hence the protective effect on the liver.

Doxorubicin was found in this study to cause necrosis of liver cells leading to damages and obstruction of liver functions. This effect was however counteracted by the seed extract/fractionst. DOX mediated hepatotoxicity are seen as focal damage in hepatocytes, vascular damage and steatosis (Pedrycz *et al.,* 2004). DOX in the form of DOX semiquinone, which generates free radicals, has been suggested to play a major role in its hepatotoxic action (Bachur *et al.,* 1979). The antioxidant potentials of the phytoconstituents in the seed extract/fractions may have been responsible for the hepatoprotective effect observed in this study.

CONCLUSION

The findings of this study show that the seed extract and fractions of *Telfairia occidentalis* has the potentials to counteract the injurious effect of doxorubicin on the liver. This activity can be attributed to the antioxidant and antioxidative stress activities of it's phytochemical constituents. Thus, the seed can be used to alleviate and/or prevent doxorubicin-induced hepatotoxicity.

Acknowledgements: The authors are grateful to staff of Animal house, Pharmacology and Toxicology Department of University of Uyo for providing technical assistance.

Conflicts of Interest: There is no conflict of interest

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