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Original Research Article

Antioxidant and Hepatoprotective Potentials of Methanol Extract of *Ficus platyphylla* Stem Bark (Moraceae) in Wistar Rats

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ABSTRACT

Ficus platyphylla Delile has been used in Nigerian traditional medicine for the management of pain, epilepsy and inflammation. The aim of this study is to evaluate the antioxidant and hepatoprotective potentials of methanol extract of *F. platyphylla* stem bark in Wistar rats. The hepatoprotective properties of methanol extract of *F. platyphylla* stem bark was tested both *in vitro* and *in vivo* by evaluating oxidative stress markers, liver function parameters and changes in the morphology of liver in carbon tetrachloride (CCl_4) induced hepatotoxicity in Wistar rats. *In vitro* antioxidant studies of methanol extract of *F. platyphylla* stem bark was evaluated using 2, 2-diphenyl-2-picryhydrazyl (DPPH) model. Treatment of Wistar rats-induced hepatotoxicity with CCl_4 with methanol extract of *F. platyphylla* stem bark at 100, 200 and 400 mg/kg revealed significant decrease in *in vivo* stress markers levels ($p < 0.05$, $p < 0.001$). Methanol extract of *F. platyphylla* stems bark at doses of 100 mg/kg and 400 mg/kg significantly reversed the increasing transaminases activities induced by the CCl_4 toxicity ($p < 0.05$) in the Wistar rats. Histologically, there were differences in the liver morphology as compared to the control and silymarin group. These results provide scientific evidence that the liver pathology in CCl_4 induced hepatotoxicity is improved by methanol extract of *F. platyphylla* stem bark.

Keywords: Antioxidant, Hepatoprotective, *Ficus Platyphylla*, CCl_4.

Introduction

Liver serves as an important organ in the detoxification of various drugs and xenobiotics in the body and drug-induced liver diseases is said to accounts for about 50% of all hospital admissions and 50% of all acute liver failure resulting in the withdrawal of some approved drugs from the market. [1,2] The withdrawal of these drugs appears to be as a result of enormous toxicities arising from the liver such as unique vascular, secretory, synthetic and metabolic effects.[3] Excessive production of pro-oxidants and ROS in the liver can result in the damage of both structural and functional integrity of the liver cells amounting to widespread liver toxicities.[4]

Antioxidants protect the human body against the damage caused by reactive oxygen species (ROS).[5] These ROS are produced *in vivo* through various biochemical reactions and respiratory chain coming from occasional leakage.[6] The leakages are the main agents in lipid peroxidation and several anti-inflammatory, digestive, anti-neurotic, neuroprotective, and hepatoprotective drugs have recently been shown to have antioxidant and/or radical scavenging activities.[7]

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These antioxidant activities seen in the agents are due to the presence of flavones, isoflavones, flavonoids, anthocyanins, coumarinlignans, catechins and isocatechins.[8] Disturbances in the normal redox state of cells can cause toxic effects through the production of peroxides and free radicals that damage all components of the cell, including proteins, lipids and DNA. Several biochemical and physiological processes in human body are said to probably produce oxygen centered free radicals and other reactive oxygen species as by-products and over production of this free radical can cause chronic diseases in human.[9]

In other words abnormal antioxidant production with dysfunctional detoxification defense system is also said to play an important role in the pathophysiology of liver disorders.[10] In view of the above, the development of hepatoprotective agents to reduce or eliminate ROS production and to strengthen the functional antioxidant disposition will be an effective plan for Figurehting oxidative stress that causes liver toxicities and diseases.

ROS and oxidative stress abundance can be introduced by many factors, including exposure to xenobiotics such as acetaminophen, lead poisoning and carbon tetrachloride (CCl_4).[11] CCl_4 model is a reductive halogenations by cytochrome P450 2EI to the highly reactive trichloromethyl radical (CCl_3), which is subsequently converted into a trichloromethylperoxyl radical ($^{\cdot}OOCCl_3$) in the presence of oxygen.[12] In liver injury trichloromethyl free radicals ($^{\cdot}OOCCl_3$) served as the hepatotoxic metabolites of CCl_4 which are mainly associated with CCl_4-induced hepatic damage.[13] Removal of hydrogen atoms from the unsaturated fatty acids by the radicals tends to generate carbon-centered lipid radicals. The lipid radicals quickly add molecular oxygen to form lipid peroxyl radicals, thereby initiating the process of lipid peroxidation (LPO). Unless neutralized by radical scavengers,

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these peroxyl radicals in turn attract hydrogen atoms from other lipid molecules, thereby propagating the process of lipid peroxidation.[14] Despite the enormous benefit for hepatoprotective agents to offer protection against liver injuries, only few numbers of efficacious and reliable drugs were used successfully and some of them have increased number of adverse effects.[15]

In the modern medicine of today, numerous drugs are directly or indirectly derived from higher plants as dietary supplements and therapeutic intervention strategies for health benefits with less harmful effects than that of synthetic agents.[16] The traditional system of medicine has incorporated several hepatoprotective plants like *Silybum marianum, Picrorrhizakurroa, Tephrosiapurpurea, Phyllantusamarus,* and *Asparagus racemosus* to treat hepatic body ailments.[17] Plants and plant substances have been the original medicines for humanity for most of human history and medicinal plants have played a vital role in world health.[18] Most cultures on earth have evolved rich systems of medicine focused on using plants to alleviate medical conditions from time immemorial. Modern science has recently focused on studying medical uses for plants and many plants have now been studied to justify scientifically their use in traditional medicine.

Ficus platyphylla Delile (Family: Moraceae) is a deciduous plant mainly found in the savannah regions of the Western African coast. Preparations of this plant have been used in Nigeria's folk medicine to manage epilepsy, depression, psychosis, pain and inflammation for many years, and their efficacies are widely acclaimed among the rural communities of Northern Nigeria.[19] Several studies of this plant have been demonstrated which revealed that the methanol extract of its stem bark is said to be safe in rodents[20] with potential central nervous system activity, analgesic and anti-inflammatory properties.[21,22] A report of the psychopharmacological and anticonvulsant effects of the saponins rich fraction of this medicinal plant has also been revealed.[23] The present study is stem up from the previous studies showing this plant to have an anti-inflammatory which by extension could have antioxidant activities that may probably assist to protect the liver from pain and excessive damages.

Materials and Methods

Plant materials and extraction

The plant was collected in September, 2014 in Zaria, Kaduna state, Nigeria and was identified and authenticated by Mallam I. Muazzam of the Department of Medicinal Plant Research and Traditional Medicine, National Institute of Pharmaceutical Research and Development (NIPRD), Abuja. A voucher specimen (No. 4035) was deposited at NIPRD Herbarium for future reference.

Preparation of the extract

The stem bark of *F. platyphylla* was freed from sand particles by carefully scrapping with a spatula. It was chopped to pieces, air dried and milled into coarse powder using pestle and mortar. Extraction was carried out by cold maceration of 500 g of the coarse powder with 2.5 L of 70% aqueous methanol for 72 hrs, with constant shaking using the Gesellschaft für Labortechnik (GFL shaker No. 3017 mbH, Germany). The resultant mixture was filtered using Whatmann filter paper (No.1) and the filtrate was evaporated to dryness *in vacuo* at 40^{o}C using rotary evaporator to give a yield of 25% of the methanol extract of *F. platyphylla* stem bark (MEFpSB). Aliquots of the extract were weighed and dissolved in distilled water for use in the study.

Phytochemical screening

The preliminary phytochemical screening of MEFpSB was carried out using standard method for presence of phyto-constituents. The MEFpSB was tested for carbohydrates, cardiac glycosides, anthraquinones derivatives, saponins, flavonoids, tannins and alkaloids.[24]

Acute toxicity studies

Median lethal dose (LD_{50}) determination was conducted using Lorke's method[25] for both intra-peritoneal and oral routes in rats selected for the work. This method was carried out in two phases. In the first (initial) phase, 3 rats per group of different weights were treated with MEFpSB at a dose of 10 mg/kg, 100 mg/kg and 1000 mg/kg body weight orally and were observed for signs of toxicity and death for 24 hours. In the second phase, 4 rats of different weights were administered with four more specific doses of the extract at 1000 mg/kg, 1600 mg/kg, 2900 mg/kg, and 5000 mg/kg body weight respectively based on the result of phase 1. The procedure was also repeated for intra-peritoneal route (i.p). The LD_{50} value was determined by calculating the geometric mean of the highest non-lethal dose (0/1) and lowest lethal dose (1/1) as shown in the formula below:

$$LD_{50} = \sqrt{}\text{ (Highest non-lethal dose) x (lowest lethal dose)}$$

In vitro antioxidant activity

The scavenging activity of MEFpSB for the radical 2, 2- diphenyl-2-picrylhydrazyl (DPPH) was determined using the method described by Goyal *et al.*[26] The DPPH solution (50 mg/mL) was prepared in 95% methanol. Also using 0.1 mg/ml, 7.5 µg of the MEFpSB was dissolved in 75 ml of 95 % methanol and an additional of 225 mls of 95 % methanol was added to prepare the stock solution of 300 µg/ml in a baker and this was later divided into concentrations of 10 µg – 280 µg/ml using five test tubes. Finally 0.45 µg of ascorbic acid was dissolved in 15 ml of distilled water for the first dissolution which was later added up to prepare a stock solution of 30 µg/ml and were then divided into five test tubes in a concentration of 1 µg – 28 µg/ml. Freshly prepared DPPH solution was added to the test tubes and MEFpSB were added followed by serial dilutions (10 µg-280 µg/ml) to every test tube such that the final volume was 2.5 ml and absorbance was measured at 517 nm wavelength after incubation for 15 min in the dark using Jen-way 6405 UV/VIS spectrophotometer. Measurements were performed in triplicate. Ascorbic acid was used as a reference standard and dissolved in 95 % methanol to make a stock solution with the same concentration (0.1 mg/ml). The control sample was prepared, which contained the same volume without any extract and 95 % methanol was used as the blank. All values were converted to percentage anti-oxidant activity using the formula below:

$$\text{Antioxidant activity \% (AA \%)} = 100 - \left[\frac{\text{A Sample} - \text{A Blank}}{\text{A Control}} \times 100\right]$$

A sample = Extract + DPPH, A blank = Extract + Methanol, A control = Methanol + DPPH.

The actual decrease in absorbance induced by the test extract (F. platyphylla) was compared with the positive controls (Ascorbic acid). The EC_{50} value was calculated after plotting the graph of % inhibition against sample concentration using Microsoft excel software.

In vivo antioxidant and hepatoprotective activities

Selection of animals, caring and handling

The albino rats (Wistar strain 140-250 g) of either sex were used. Randomized into various groups, animals were acclimatized for period of 14 days under standard husbandry condition. All the animals were kept in plastic cages and fed on Vital Grower feeds (Vital feeds, Jos Plateau State, Nigeria) and water was allowed ad libitum under strict hygienic condition. All the experimental procedures followed the ethical guidelines for the care and use of laboratory animals as provided and approved by Ahmadu Bello University Research Policy (Revised, 2010) and accepted internationally (NIH 1985, Revised 1996). Animals were divided into six groups with each group having six animals.

Study design and experimental protocol

Albino rats of Wistar strain weighing 140-250 g were selected and divided into 6 groups of each containing 6 animals. Group I served as control and received normal saline 0.9 % solution for 14 days. Group II to VI were injected daily with carbon tetrachloride, CCl_4 at dose of 0.1 ml/kg/day i.p for 14 days. Group III served as the standard group and administered Silymarin (100 mg/kg/day p.o.). Group IV, V and VI were treated with MEFpSB in the doses of 100 mg, 200 mg and 400 mg/kg/day p.o. for 14 days respectively. All the animals that survived

after 14 days post-treatment were sacrificed under light anesthesia. The blood samples were collected separately into 40 sterilized dry centrifuge tubes and were allowed to coagulate for 30 min at room temperature. The clear serum was then separated at 2500 rpm for 10 min using a centrifuge and biochemical investigations were carried out to assess liver function parameters such as serum glutamic pyruvic transaminases (SGPT), serum glutamic-oxaloacetic transaminase (SGOT), alanine phosphatase (ALP) and antioxidant parameters namely malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx).

Histological examination

The liver was removed from the group representative rats, weighed, examined and stored in 10 % buffered formalin for 48 hrs for histopathological studies. The harvested organs fixed in 10 % buffered formalin were grossed and placed in tissue cassettes. They were loaded into tissue processor machine where they underwent further fixation in formalin, dehydration in gradient alcohol from 70 % to absolute. The tissue were later impregnated with paraffin and later made into tissue blocks. The paraffin-embedded tissues were sectioned with microtome and placed on labeled frosted slides. After removing the paraffin with xylene, reverse dehydration took place in absolute to 70% alcohol and stained with haematoxylin and eosin. The slides were examined under the microscope and photomicrographs of the section were taken (magnification x 10).

Statistical analysis

Data were expressed as mean ± SEM, with number of animals per group (n) = 6 for a given experimental procedure. Data were analysed by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparisons test. Results were considered significant at $p< 0.05$.

Results and Discussion

The demand for natural herbal medicine for therapeutic purpose and health supplement is increasing because of their ability to prevent and reduce the risk of oxidative damage with minimal toxic effects.[27, 28] The present study was designed to establish a scientific justification for the use of *F. platyphylla* stem bark as an antioxidant and treatment of liver diseases. The results of preliminary phytochemical screening of *F. platyphylla* revealed the presence of carbohydrate, cardiac glycoside, saponins, flavonoids, triterpenes, tannins, alkaloids but anthraquinones was absent (Table 1). Some of these constituents present are said to be an active secondary metabolites responsible for the important pharmacological activities of medicinal plants.[28] The phytochemical constituents present may also be responsible for the observed antioxidant and hepatoprotective potential of *F. platyphylla* stem bark extract in this study as earlier demonstrated. [28,13].

The antioxidant and hepatoprotective potentials were studied using oxidative stress markers and CCl_4 induced liver injury respectively. Oxidative stresses as well as hepatic injury induced by CCL_4 were assessed by some oxidative stress markers like superoxide dismutase (SOD), malondialdehyde (MDA), catalase (CAT) and gluthatione peroxidase (GPx) and liver function parameters such as serum glutamic pyruvic transaminases (SGPT), serum glutamic-oxaloacetic transaminase (SGOT) and alanine phosphatase (ALP).

The acute toxicity study showed that the MEFpSB is relatively safe both orally and intra-peritoneally at a dose above 5000 mg/kg with no visible signs of toxicity nor mortality in the Wistar rats supporting the earlier research conducted using the same plant.[20]

In the *in vitro* DPPH scavenging activities of MEFpSB, the result revealed that there was absorption band at 517 nm in visible region and DPPH solution decolourized as the colour changes from deep violet to light yellow. From the regression coefficient (R^2) of the resulting models, it was observed that the MEFpSB had strong positive effects on scavenging 2, 2-DPPH with an EC_{50} of 36.40 µg/mL calculated from $y = 0.8009x – 3.6563$ (as showed in Table 2 and Figure 1a, where $x = 50$) and R^2 of 0.9847 as compared with ascorbic acid of EC_{50} of 75.78 µg/mL also calculated from $y = 1.6204x – 5.2403$ (as shown in Table 3 and Figure 1b, where $x = 50$) with R^2 of 0.8764. The results revealed that both MEFpSB and ascorbic acid promoted an inhibition of DPPH radical with increasing concentration (Table 2, Figure 1 and Table 3, Figure 2, respectively). However, the percentage inhibition of the DPPH radical by the extract was higher than that of ascorbic acid proven the extract to be a strong in vitro antioxidant agent. The strong DPPH activities exhibited by our plant as comparable to that of ascorbic acid being a known standard antioxidant agent can also be postulated of the enriched flavonoids and saponins found in the MEFpSB. [8, 20]

In CCl_4 induced liver injury model, oxidative stress can exaggerate and promote lipid peroxidation resulting into the damage of hepatocellular membrane and this can be followed by the release of pro-inflammatory chemokines and cytokine.[29, 30] Several studies had showed that overdose of CCl_4 can produce centrizonal hepatic necrosis in both human and experimental animals.[31] CCl_4 hepatic injury model is commonly used as an experimental method for the study of hepatoprotective effects of medicinal plants extracts and the extent of hepatic damage is assessed by in vitro and in vivo antioxidant, liver biochemical parameters and histological evolution. CCl_4 model is a reductive halogenations by cytochrome P450 2EI to the highly reactive trichloromethyl radical (CCl_3), which is subsequently converted into a trichloromethylperoxyl radical ($^{\cdot}OOCCl_3$) in the presence of oxygen.[12] It produces hepatotoxicity by altering liver microsomal membranes in experimental animals. Removal of hydrogen atoms from the unsaturated fatty acids by the radicals tends to generates carbon-centered lipid radicals. The lipid radicals quickly add molecular oxygen to form lipid peroxyl radicals, thereby initiating the process of lipid peroxidation (LPO). Unless neutralized by radical scavengers, these peroxyl radicals in turn attract hydrogen atoms from other lipid molecules, thereby propagating the process of lipid peroxidation.[14]

In the CCl_4-induced hepatotoxicity studies, administration of CCl_4 (0.1 ml/kg) caused significant ($p< 0.05$) increase of the oxidative parameters when compared to control rats treated with normal saline. Post-treatment of the rats with sylimarin (100 mg/kg) after CCl_4 administration (0.1 mL/kg) caused significant ($p > 0.05$) decrease levels in SOD, CAT and GPx (1.48 ± 0.01, 43.40 ± 1.17 and 39.80 ± 1.28 respectively) as compared with CCl_4 toxic group only (1.58 ± 0.10, 44.40 ± 1.03 and 39.60 ± 0.51 respectively) (Figures 2 and 3). Similarly, post-treatment of rats with 100, 200 and 400 mg/kg of MEFpSB after CCl_4 induced hepatotoxicity also caused significant ($p > 0.05$) decrease in oxidative stress parameters of SOD (1.60±0.07-100 mg/kg, 1.46 ± 0.10-200 mg/kg and 1.30 ± 0.07-400 mg/kg), CAT (42.80 ± 1.07-100 mg/kg, 41.40 ± 1.08-200 mg/kg and 40.0 ± 0.71-400 mg/kg) and GPx (33.6 ± 1.03-100 mg/kg, 35.6 ± 0.71-200 mg/kg and 37.00 ± 0.71-400 mg/kg) respectively when compared with CCl_4 toxic group only (Figures 3a and b). However, post-treatment with MEFpSB (100, 200 and 400 mg/kg) after CCl_4 administration (0.1 mL/kg) did not cause significant ($p > 0.05$) decrease in oxidative stress marker of MDA levels when compared to only CCl_4 toxic group (Figure 2). In this present study, we have shown that there is decrease in hepatic levels of SOD, CAT and GPx (Figures 3a and b) which are often regarded as indicators of oxidative stress response as reported by Ding *et al*, 2006 and Swem *et al*., 2020.[32, 33] We can evidently present that the oxidative scavenging properties of our plant can be linked to the previous work conducted using the same plant which demonstrated its anti-inflammatory and anti-nociceptive activities of the plant.[21] Our plant exerted a strong antioxidant property in DPPH scavenging activity hence with significant decreased noted in the in vivo oxidative markers implies the potential of MEFpSB in the prevention or attenuation of oxidative stress-mediated liver injury which conformed with the work of Swem *et al*.[33] and Yusuf *et al*.[34]

This hypothesis was further studied by measuring the liver function parameters (SGPT, SGOT and ALP) in the Wistar rats induced with CCl_4 liver injury model by treating them with our MEFpSB and then comparing with standard drug, silymarin and control groups, normal saline (Figure 4). These parameters are considered as the major sensitive liver tissue damage indicators.[34,35] However, it can be said

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Table 1: Phytochemical constituents of methanol extract of *F. platyphylla* stem bark.

Constituents	Remark
Carbohydrate	Present
Saponins	Present
Tannins	Present
Flavanoids	Present
Triterpenes	Present
Alkaloids	Present
Anthraquionones	Absent

Table 2: Effect of ME*Fp*SB on DPPH *in vitro* inhibition

Treatments ME*Fp*SB (µg/mL)	Mean AA (%)
280	75.01 ± 1.45
125	97.20 ± 0.30
50	36.80 ± 3.80
25	09.50 ± 4.80
10	09.97 ± 2.70

Where ME*Fp*SB= methanol extract of *F. platyphylla* stem bark, AA = Antioxidant activities. Wavelength is 517 nm

Table 3: Effect of Ascorbic acid on 2, 2- DPPH *In vitro* Inhibition

Treatment Ascorbic Acid (µg/mL)	Mean (AA %)
28	44.0 ± 3.50
12.5	4.6 ± 0.30
5	4.8 ± 0.70
2.5	3.0 ± 0.60
1	5.2 ± 0.70

AA = Antioxidant activities. Wavelength is 517 nm

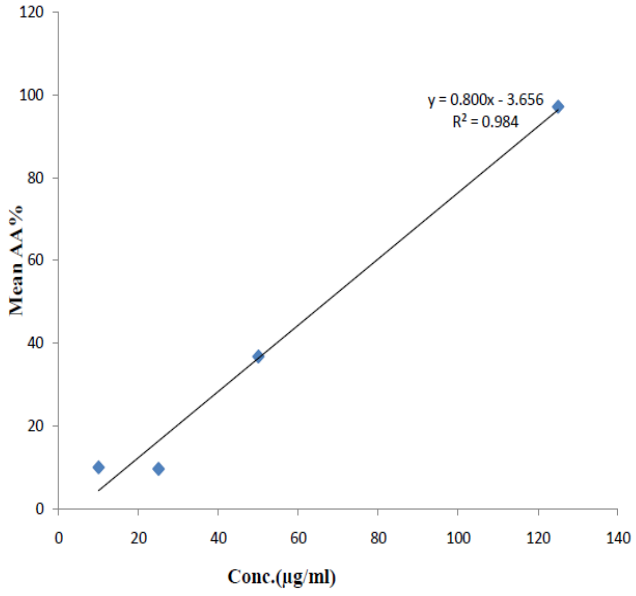

Figure 1: Regression coefficient graph of methanol stem bark extract of *F. platyphylla* on DPPH inhibition.

that our plant extract prevent elevation of liver function parameters in CCl_4 induced hepatic injury, suggesting that the structural and functional integrity of hepatic cellular membrane is preserved with protection of the liver tissues against toxic effects of CCl_4. From the results, the administration of the extract 400 mg/kg gives more protection against the CCl_4 (0.1 mL/kg) concurrent administration for 14 days with a significant ($p > 0.05$) decrease in SGPT, SGOT and ALP (42.8 ± 1.28, 36.4 ± 1.21 and 64.0 ± 1.51, respectively) as compared with silymarin (100 mg/kg) {43.2 ± 1.36, 38.6 ± 2.10 and 68.6 ± 1.50 respectively} and CCl_4 (0.1 mL/kg) group {42.80 ± 1.28, 36.40 ± 1.21 and 64.00 ± 1.51 respectively} (Figure 4).

The histological examination of the liver sections revealed that the normal liver architecture was disturbed by the hepatotoxin intoxication using CCl_4 (0.1 mL/kg) but this was retained in those experimental rats treated with the MEFpSB as compared to silymarin and control groups which further support our hepatoprotective hypothesis. There were differences in the histopathology of the liver in the different groups where 100 mg/kg, 200 mg/kg and 400 mg/kg of the methanol extract of *F. platyphylla* stem bark were administered per kg body weight of the animals for 14 days with concurrent administration of the CCl_4 (0.1 mL/kg) as showed in the photomicrograph when compared with the group treated with standard drug, silymarin and normal saline (Plate I - VI). In plate I where only normal saline was administered to the rats for the 14 days, it showed that normal hepatocyte with central vein are intact. Also in plate II, where CCl_4 was only administered to the rats, there was hepatitis with apoptosis bodies and necrosis of the hepatocytes with massive destruction of the liver cell. In plate III with administration of CCl_4 (0.1 mL/kg) and concurrent administration of silymarin, there was bridging necrosis of the hepatocytes with mild protection of the liver cells from the silymarin. In plate IV with CCl_4 (0.1 mL/kg) and 100 mg/kg of the extract, peri-portal hepatitis with inflammation within the portal tract and bridging necrosis was noticed showing mild protection when compared with plate II & III. For 200 and 400 mg/kg of the extract, the liver cell was noticed to have diffused mild hepatitis with inflammatory cell within the hepatocytes and mild inflammation of hepatocytes with preserved cyto-architectures of the cells respectively.

This results clearly showed that MEFpSB have protective ability against the CCl_4 induced hepatotoxicity especially in their increase doses which agreed with the previous works.[7, 28 and 16] The likely possible mechanism eliciting this action of MEFpSB may be associated with the scavenging activities of the free radicals that are responsible for CCl_4 toxicity. Antioxidants serve as a protective mechanism in oxidative stress-related diseases thereby reducing the mortality rate.[34,36]

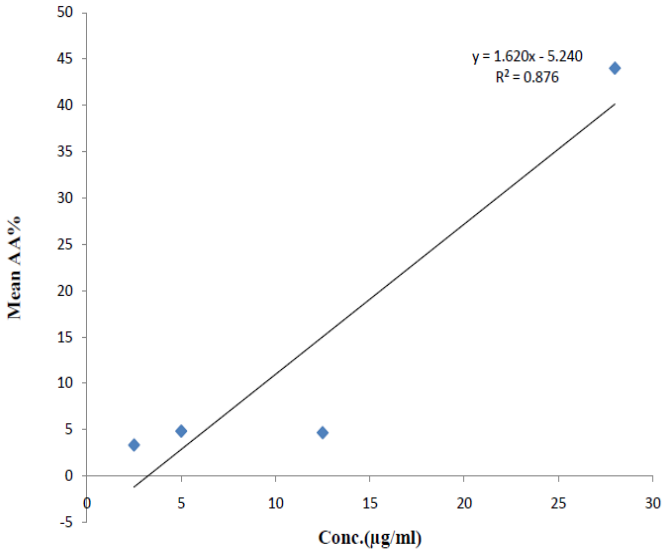

Figure 2: Regression coefficient graph of Ascorbic acid on DPPH inhibition.

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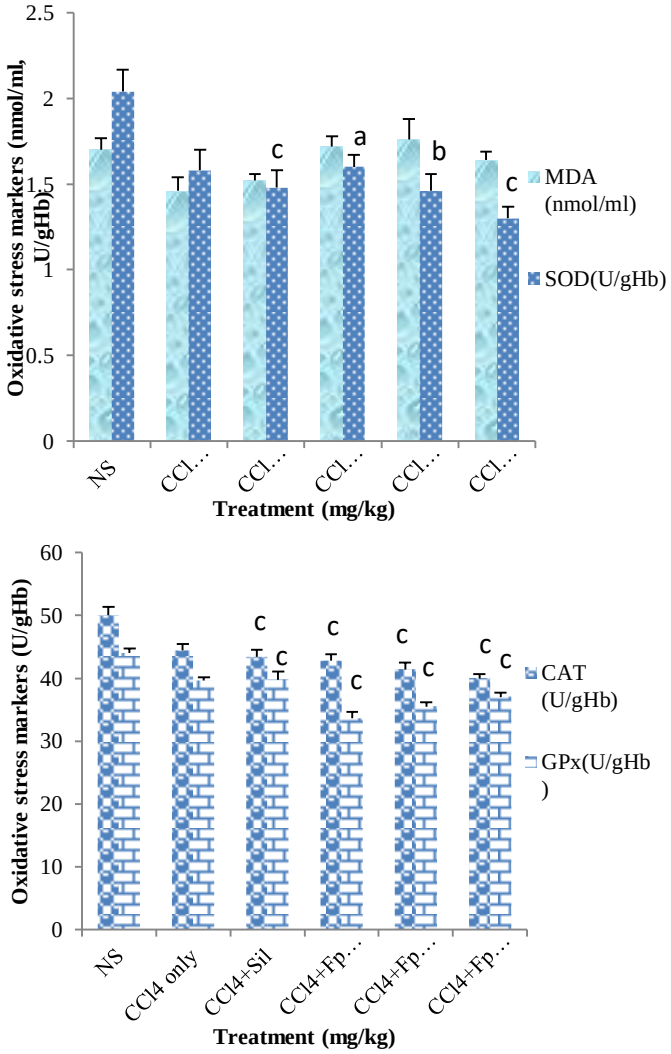

Figure 3: Effect of ME*Fp*SB on MDA, SOD, CAT and GPx oxidative stress markers.

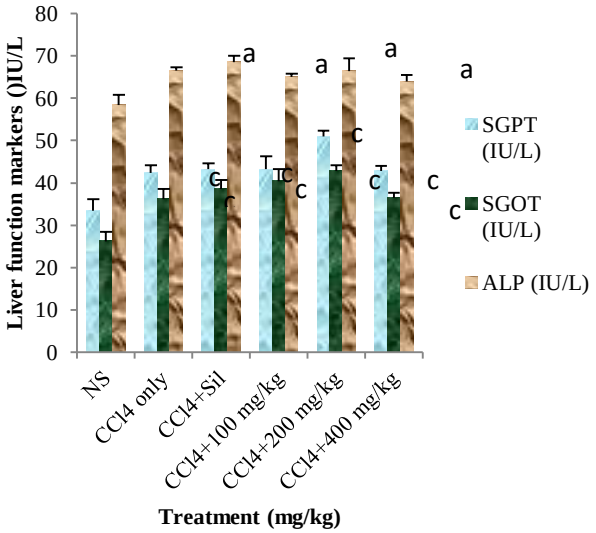

Figure 4: Effects of MSBE*Fp* on liver function test parameter.

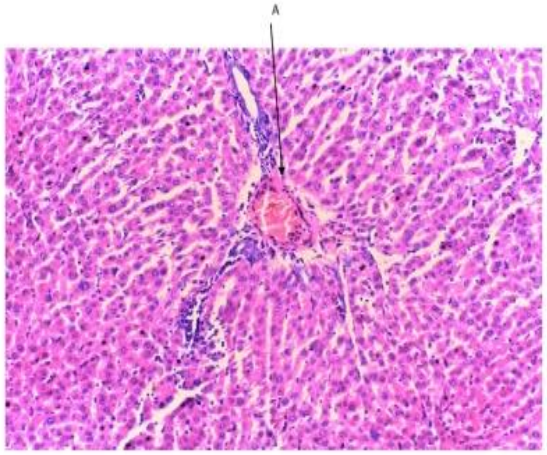

Plate I: Rat liver administered normal saline showing normal hepatocyte with central vein (A)

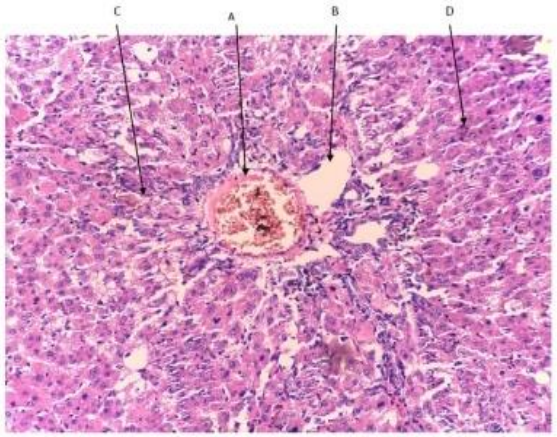

Plate II: Rat liver administered only CCl_4 showing necrosis of the liver (B), apoptosis (C) and severe hepatitis (D)

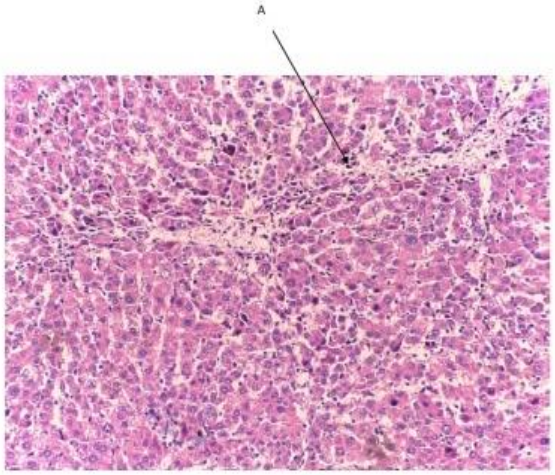

Plate III: Rat liver administered CCl_4+slymarin showing bridging necrosis with mild protection from CCl_4 (A)

Phenolic acid and flavonoids are implicated in the antioxidant effect of natural products like food.[37,38] Flavonoids are usually seen in the epidermal cells of plant organs such as flowers, leaves, stems, roots, seeds and fruits.[16,39] The observed free radical scavenging activity of our extract as shown in the DPPH study as compared to that of the standard, ascorbic acid can be deduced to the presence of flavonoids as shown in other work.[2,40,41]

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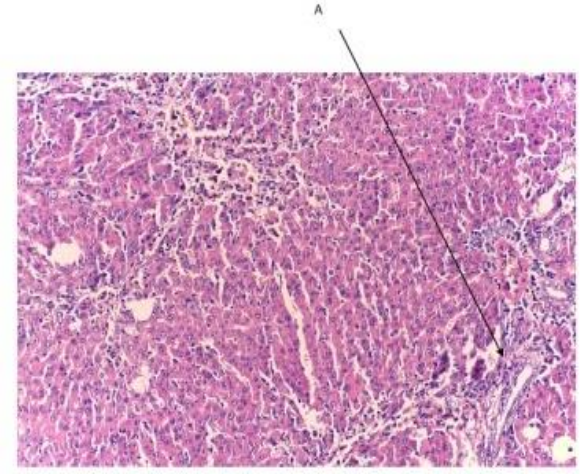

Plate IV: Rat liver administered with CCl4+MEFpSB 100 mg/kg showing bridging necrosis and peri-portal hepatitis (A)

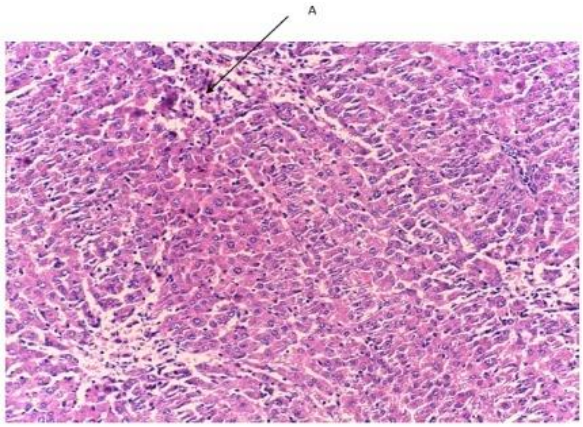

Plate V: Rat liver administered CCl4+MEFpSB 200 mg/kg showing diffused mild hepatitis with inflammatory cell within the hepatocytes (A)

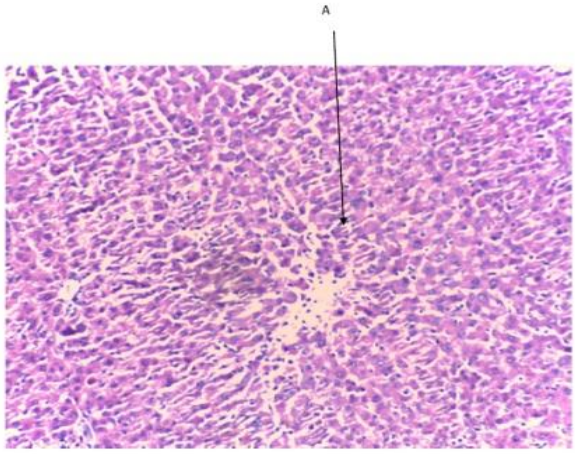

Plate VI: Rat liver administered CCl4+MEFpSB 400 mg/kg showing mild inflammation of hepatocytes with preserved cyto-architectures (A)

Conclusion

The results from this study clearly demonstrated that MEFpSB has a protective effect against CCl_4-induced acute hepatotoxicity in Wistar rats, as evidenced by dose-dependent lowering of oxidative stress markers, liver function parameters and significant changes in the morphology of the liver after treatment justifying its use for management of liver disease in traditional medicine. These findings suggest that MEFpSB can be utilized as a natural source to protect the liver from oxidative damage serving as an important source of antioxidant and hepatoprotective compounds in hepatotoxin liver injury.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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