ejpmr, 2018,5(12), 146-155

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

HEPATOTHERAPEUTIC POTENTIALS OF SIDA CORYMBOSA (WIRE WEED) ETHANOLIC LEAF EXTRACT ON CARBON TETRACHLORIDE (CCL4)-INDUCED ACUTE HEPATOTOXICITY ON MALE ALBINO WISTAR RATS

Charles Chijioke Dike[1,2]*, Friday Chuwuemeka Ezeonu[2], Hugh Clifford Chima Maduka[1], Ezeokafor Emmanuel Nonso[3] and Oguazu Chinenye Enoch[4]

[1]Department of Human Biochemistry, Faculty of Basic Medical Sciences, College of Health Sciences, Nnamdi Azikiwe University, PMB 5001, Nnewi, Anambra State, Nigeria.

[2]Department of Applied Biochemistry, Faculty of Biological Sciences, Nnamdi Azikiwe University, PMB 5025, Awka, Anambra State, Nigeria.

[3]Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Nnamdi Azikiwe University, PMB, 5001, Anambra State, Nigeria.

[4]Department of Biochemistry, College of Natural and Applied Sciences, Grepory University-Uturu, Abia State, Nigeria.

***Corresponding Author: Dr. Charles Chijioke Dike**
Department of Human Biochemistry, Faculty of Basic Medical Sciences, College of Health Sciences, Nnamdi Azikiwe University, PMB 5001, Nnewi, Anambra State, Nigeria.

Article Received on 14/10/2018 **Article Revised on 04/11/2018** **Article Accepted on 25/11/2018**

ABSTRACT

Aim: This work aimed at evaluating the hepatotherapeutic potentials of *Sida corymbosa* ethanolic leaf extract against carbon tetrachloride (CCL4)-induced hepatotoxicity on male Albino Wistar rats. Serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphate (ALP) were determined spectrophotometrically. Body and liver weights were measured using electronic weighing balance, while water consumption was measured using calibrated water bottle. Histopathological examination was carried out using hematoxyline and eosine (H and E) staining technique. Results were analyzed using ANOVA, using SPSS statistical software (version 21). The liver function (Serum AST, ALT, and ALP) assays carried out revealed significant decrease ($P<0.05$) in the levels of serum AST, ALT and ALP in groups of rats administered 5000, 3000 and 1000 mg/kgbw of the extract after inducing hepatotoxicity using CCL4 against groups induced hepatotoxicity without given any treatment from seven days to twenty eight days which had. These are suggesting that the treated rats with the extract may be recovering from the hepatic injury. The above changes were greatest in those administered the extract at 5000 mg/kgbw for 28 days. This suggests dose and time dependent effect. The treatment also showed positive effects on body weights and water consumption of the treated rats. The above findings were confirmed by the histological examination carried out. *Sida corymbosa* ethanolic leaf extract may therefore has some therapeutic effects on the livers of male Albino Wistar rats damaged by CCL4 toxicity.

KEYWORDS: Hepatic injury, Liver functions, sida extract.

INTRODUCTION

One of the major organs of the body is the liver. The liver is the main site for metabolism and excretion of unwanted materials. The Liver has mostly been destroyed by being exposed to xenobiotics and infections.[1,2] Whenever liver is affected by diseases, the synthesis of biomolecules such as protein, lipids, carbohydrates and minerals is altered. This is because they are metabolized in the liver. The rate at which liver diseases occur globally is alarming due to increase in industries.[3,4] Many researchers have used carbon tetrachloride (CCl4) as model for inducing toxicity in liver.[5,6] Research work has revealed that liver and kidney are susceptible to CCL4 damages.[7,8,9]

It had been the culture of Africans in using plants to treat diseases before the inception of orthodox medicine.[10] Traditional medicine has been considered a complementary and an alternative to orthodox medical system in many parts of civilized countries.[11] Sida plants belong to the family called Malvaceae. The plants are well known for their many medicinal values. There have been may reported cases of using *Sida corymbosa* extracts in treating diseases such as ulcer, gonorrhoea, bleeding, prolonged labour and wound but information are still scanty on the hepatotherapeutic activities of the plant. This research work, therefore seeks to close this gap by investigating if the plant's ethanolic leaf extract have some therapeutic potentials against CCl4-induced hepatic damage.

Fig. 1: Photograph of *Sida corymbosa*.

MATERIALS AND METHODS

Chemical and reagents

All chemicals used were of analytical grade and were gotten from British Drug House Ltd., England via their sales representative in Lagos State, Nigeria. These include diethyl ether, formalin (10%), sodium hydroxide (0.4M) and sodium chloride (0.9%). All the reagent kits used were gotten from Randox laboratory Ltd, United Kingdom via their sales representatives in Ikeja, lagos State, Nigeria. These include; AST, ALT, and ALP reagent kits. Distilled water used was obtained from the Human Biochemistry Laboratory, Nnamdi Azikiwe University, Nnewi Campus.

Collection of plant samples

Sida corymbosa plants were obtained from Nnewi, in Anambra State of Nigeria. It was authenticated by Prof. Okafor J.C of Department of Botany, Enugu State University of Science and Technology, Nigeria. The plant was reauthenticated by Dr. Ogbuozobe Okwudili Gabriel of Botany Department, Nnamdi Azikiwe University, Awka, Anambra State of Nigeria and Issued with voucher specimen number-NAU Herbarium N0 75G.

Preparation of plant samples

This was done according to the method of.[12] The Plant's leaves were washed with distilled water, dried under the air at room temperature and ground using blending machine (Model: HR2001, Philips, China). The ethanolic extracts were obtained by soaking 20 g of leaf samples in round bottom flasks containing 100 ml of absolute ethanol (98%) for 48 h with shaking using orbital shaker. The extract was filtered through muslin cloth and then 40mm Whatman filter paper. The crude extract was concentrated using a rotary evaporator (Model: TT22, USA) at 65^0C. It was then dried at 45^0C using oven.

Animal Studies

Ethical approval

Ethical approval was granted by the ethical committee of Faculty of Basic Medical Sciences, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus in line with the Principle of Laboratory Animal Care. The copy is attached to this work.

Acute toxicity studies (LD50)

Acute toxicity studies were done as described by the method of.[13]

Procedure

The procedure was carried out in stages. The outcome from each stage determined whether to proceed to the next stage or terminate the stage. Stage one involves four rats, which were grouped into four groups with each group containing one rat. Rats in groups one to four were administered 10, 100, 300 and 600 mg/kgbw of the extract orally. Since no mortality and signs of toxicity were observed, another three groups of rats containing one rat each were administered 1000, 1500 and 2000 mg/kgbw (Stage 2). Another three groups of rats with one rat each were administered 3000, 4000 and 5000mg/kgbw. A confirmatory LD50 test was carried out by administration comprising one rat each. The rats were observed for 1h after administration and 10min for every 2h interval for 24h.

LD50= (M0+M1) /2

Where M0= Highest dose of the test that gave no mortality

M1= Lowest dose of the test substance that gave mortality.

Mortality ratio= No of dead rats/n

Where n= number of rats used.

Experimental design

A total of hundred male Albino Wistar was used for this study. The rats were grouped into twenty, groups comprising five rats each. Sixteen groups of rats were induced hepatotoxicity by injecting 0.4 ml/kgbw of CCl4 intraperitoneally using olive oil as a vehicle in the ratio of 50:50. Four groups were not induced hepatotoxicity, but giving water and feed only (Normal rats or positive control groups).The rats were left seven days. After seven days, twelve groups were given a *Sida corymbosa* extract at 5000, 3000 and 1000mg/kgbw from seven to twenty eight days. Four groups that were induced hepatotoxicity were again left to stay throughout the period without administering any extract.

Animal handling

The rats were fed on a pellet feed obtained from Gland Cereals Ltd, a division of UAC Nigeria PLC, Zewana, Jos, Plateau State, Nigeria via her sales representative at

Nnewi, Anambra State, Nigeria. Care of and handling of the rats were done according to guidelines given by,[13,14] in line with the laid down rules and regulations given by the Ethical Committee of Faculty of Basic Medical Sciences, Nnamdi Azikiwe University, Nnewi, Anambra State, Nigeria. The rats were kept in cages, given feed and water ad libitum. The body weights of the rats were taken every seven days using electronic weighing balance (Camry J1106337616, China) while the water consumption was measured every day using calibrated water feeding bottles.

Volume of water consumed by each rat per day = V1-V2
Where V1= Initial volume of water in the water bottle,

V2= Final volume of water.

Blood samples were collected through ocular puncture using, heparin specimen bottles after anesthetizing the rats and serum separated by centrifugation at 3000 rpm for 15 min at 25^{o}C. The rats were sacrificed using liver tissues, weighed and stored in ten percent formalin at room temperature for histopathological examination.

Hepatotoxicity studies
Assessment of hepatotoxicity was conducted by using routine diagnostic indicators for liver function test (LFT). These include; AST, ALT and ALP. Liver function test was carried out using the method as described by.[14]

Determination of serum spartate aminotransferase (AST) activities
Principle
Aspartate aminotransferase catalyzes the transfer of amino group between L-aspartate and oxoglutarate forming oxoloacetate. The oxoloacentate formed reacts with NADH to form NAD+. The activities of this enzymes is determined by measuring the rate of oxidation of NADH.

Procedure
Hundred microliters of each sample was added into the respective test tubes for tests. This was followed by the addition of 0.5ml of AST reagent 1 to all the test tubes for test and that of blank. This was followed by the addition of hundred microliters of distilled water to blank. These were incubated for 30 min at 37^{o}C using incubator (DNP-9052A, China). After this, 0.5 ml of AST reagent 2 was added into all the test tubes. These were mixed and incubated at 25^{o}C for 20 min. This was followed by the addition of 5ml of sodium hydroxide into all the test tubes to stop the reaction and the absorbance taken at 544nm against the blank after allowing them to stay for five minutes using UV-VIS spectrophotometer (Model 752G, China). The activity levels of AST in the serum were then obtained from the AST chart by checking for the values that correspond with the absorbance readings.

Determination of serum Aalanine aminotranferase (ALT) Activities
Principle
The amino groups are transferred from alanine to oxoglutarate to form L-glutamate and pyruvate in the presence of alanine aminotransferate. The activity levels are determined by measuring the rate of oxidation of NADH.

Procedure
Hundred microliters of various serum samples were added into each test tube for tests. After this, 0.5ml of ALT reagent I was added into all the test tubes including that of blank. Hundred microliters of distilled water was added into the test tube for blank. These were incubated at 37^{0}C for thirty minutes using incubator (Model: DNP-9052A, China). These were followed by the addition of 0.5ml of ALT reagent 2 to all the test tubes. These were incubated at 25^{o}C for 20 min. These were followed by the addition of 5ml of sodium hydroxide (NaOH) into all the test tubes to stop the reaction and the absorbance read at 546nm against the reagent blank after five minutes using UV-VIS spectrophotometer (Model, 752G, China). The activity levels in the serum were obtained from the ALT chart by checking for the values that corresponds with the absorbance readings.

Determination of serum alkaline phosphatase (ALP) activities
Principle
Alkaline phosphate acts on p-nitrophenyl phosphate, thereby converting it to phosphate and p-nitrophenol. The absorbance of the colour developed is measured spectrophotometrically which is equivalent to the activities of the enzyme.

Procedure
Alkaline enzyme phosphate reagent (reagent enzyme) was constituted with ten mills of distilled water. 20 µl of various samples were added to the respective test tubes. This was followed by the addition of 0.5ml of ALP reagent. The absorbance was read three times at intervals of 1,2, and 3 min and average absorbance found for each sample using UV-VIS spectrophotometer (Model 752G, China).

The activities of the enzyme were calculated using the formular
ALP activity= 2760xA (U/L)
Where $\bar{\Delta}$average absorbance
2760 = correction factor.

Histopathological examination
This was done according to.[15] Ten percent formalin-fixed paraffin-embedded sections of liver tissues of various groups of rats were cut into 4mm thick and were mounted into slide with cover slips. Sections for histological studies were stained with hematoxylin and eosin and Malloy trichrome stain. The slides were

viewed using a microscope and photomicrographs of the liver sections taken.

Statistical Analysis

Results were expressed as mean ± standard deviation of triplicate determination. Results were analyzed using ANOVA, using SPSS statistical software (version21).

RESULTS

The results of serum enzyme assay (AST, ALT, and ALP) of Albino Wistar rats induced hepatotoxicity with CCL4 and treated with *Sida corymbosa* ethanolic leaf extract from seven to twenty eight days are hereby presented in figures 2 to 4. In all cases of significant differences, serum AST, ALT and ALP activity levels were higher ($P<0.05$) in rats induced hepatotoxicity without administering any treatment (untreated liver damage or negative control) than groups induced and administered the extract in 5000, 3000 and 1000mg/kgbw and the normal rats (groups with no CCL4 induction and extract administration). Those administered the extract at 5000 mg/.kgbw had lower levels of serum AST and ALT than those administered the extract at 3000 and 1000mg/kgbw at 28days of treatment.

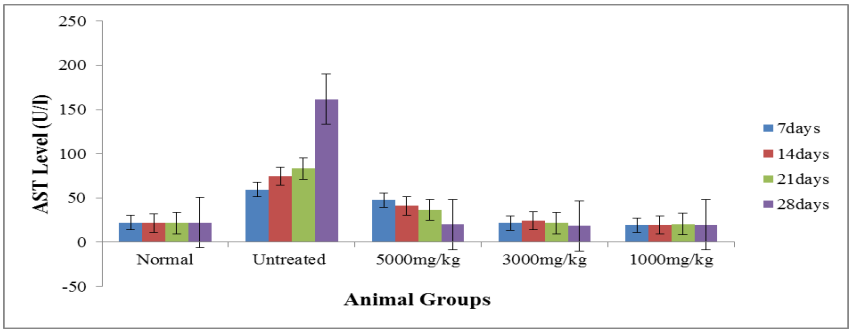


Fig. 2: Graph of mean serum AST levels of rats given *Sida corymbosa* ethanolic leaf extract before injecting CCL4 vs extract dosage. Ms Excel version 2007 was used to plot the graph.

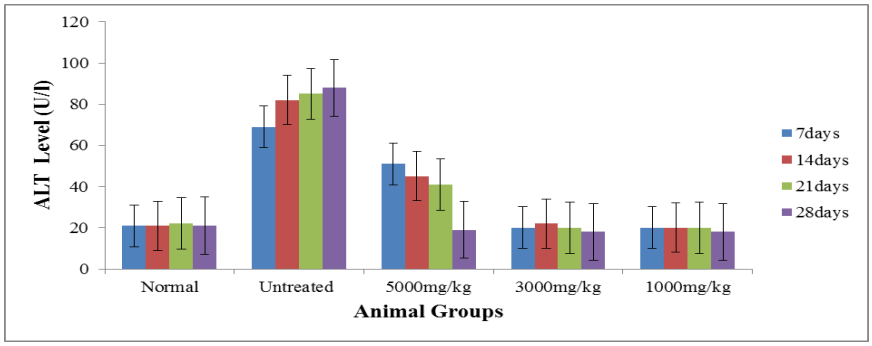


Fig. 3: Graph of mean serum ALT levels of rats given *Sida corymbosa* ethanolic leaf extract before injecting CCL4 vs extract dosage. The graph was plotted using Ms Excel version 2007.

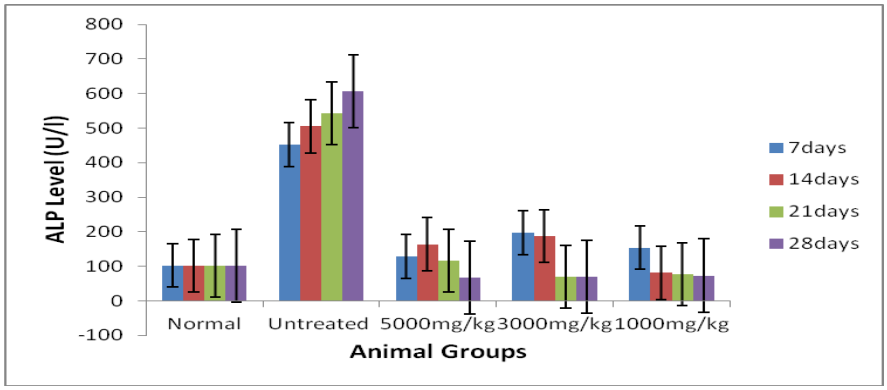


Fig. 4: Graph of mean serum ALP activity levels of rats given *Sida corymbosa* ethanolic leaf extract after inducing hepatotoxicity using CCL4 vs extract dosage. The graph was plotted using Ms excel version 2007.

The results of body and liver weights of Albino Wistar rats induced hepatotoxicity using CCl4 and administered *Sida corymbosa* ethanolic leaf extract orally are hereby presented in figures five to six. In all instances of significant differences ($P<0.05$), the body weights of rats induced hepatotoxicity without treatment

decreased throughout the period (7 to 28 days), while that of the normal rats increased progressively from seven to twenty eight days. That of other groups administered the extract in 5000, 3000 and 1000 mg/kgbw decreased after seven days and increased again from 14 to 28days. The liver weights of the treatment groups decreased from seven to twenty days of extract administration against the untreated liver damage groups which increased from seven to twenty days after the induction.

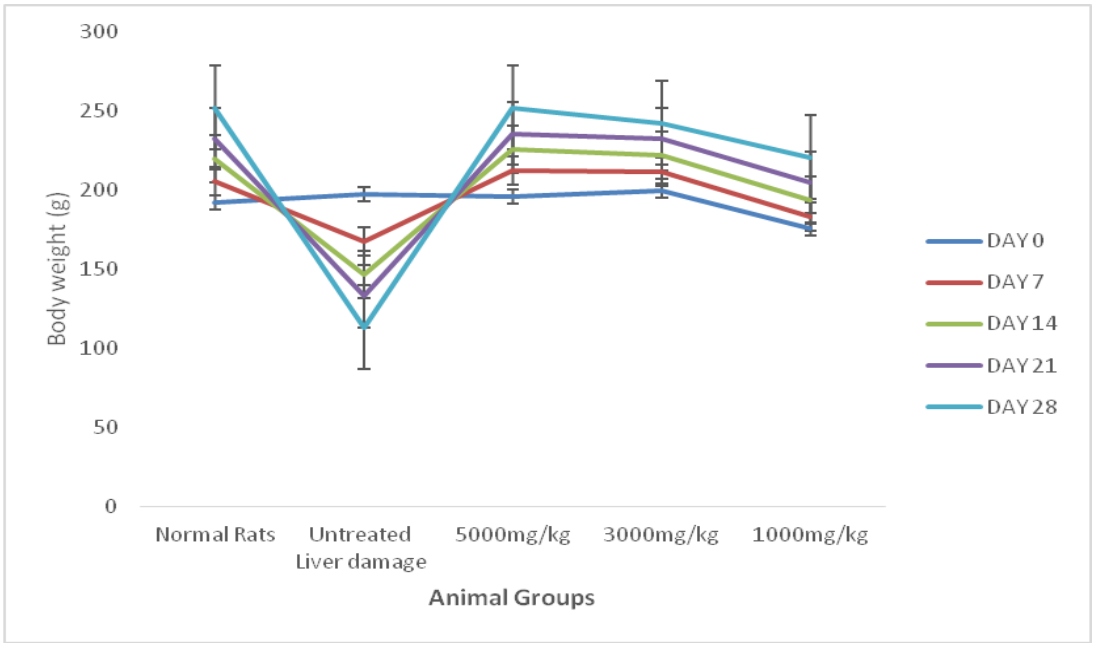


Fig. 5: Graph of mean body weights of rats given *Sida corymbosa* ethanolic leaf extract before injecting CCL4. The graph was plotted using Ms Excel version 2007.

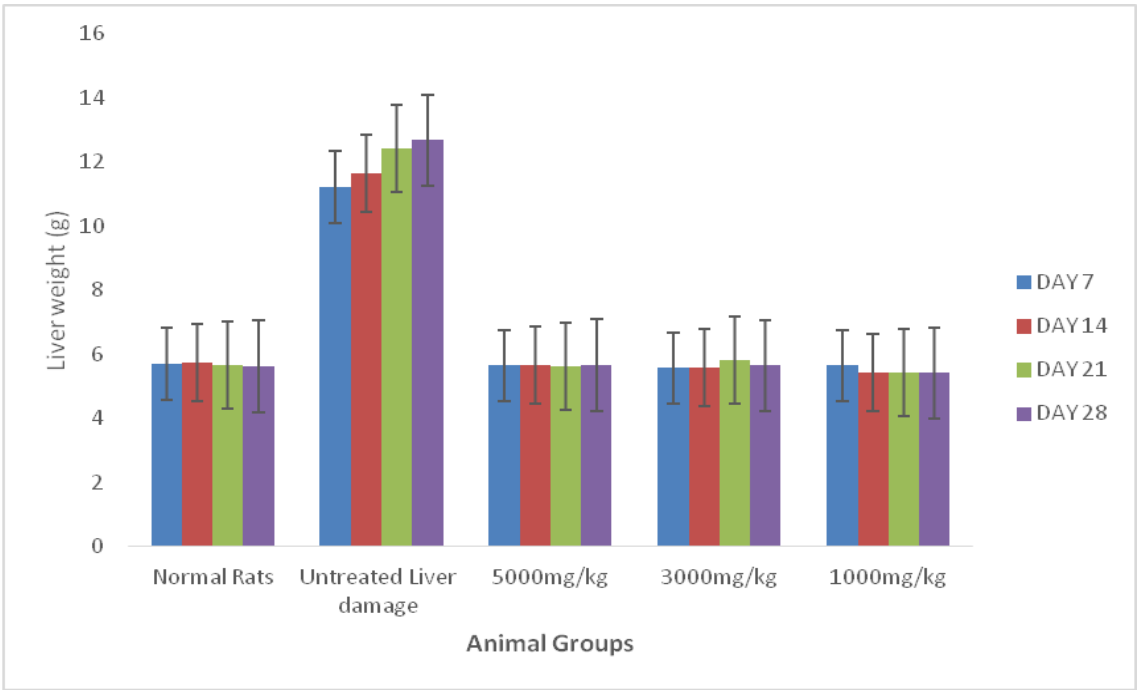


Fig. 6: Graph of mean liver weights of rats given *Sida corymbosa* ethanolic leaf extract before injecting CCL4. The graph was plotted using Ms Excel version 2007.

Figure 7 shows the results of mean water consumption of Albino Wistar rats induced hepatotoxicity with CCL4 and administered *Sida corymbosa* ethanolic leaf extract. In all instances of significant differences($P<0.05$) he water consumption of rats induced hepatotoxicity decreased, that of the treatment groups decreased at 7days and increased again at 21days and 28days of treatment. While that of normal rats increased progressively from seven to twenty eight days.

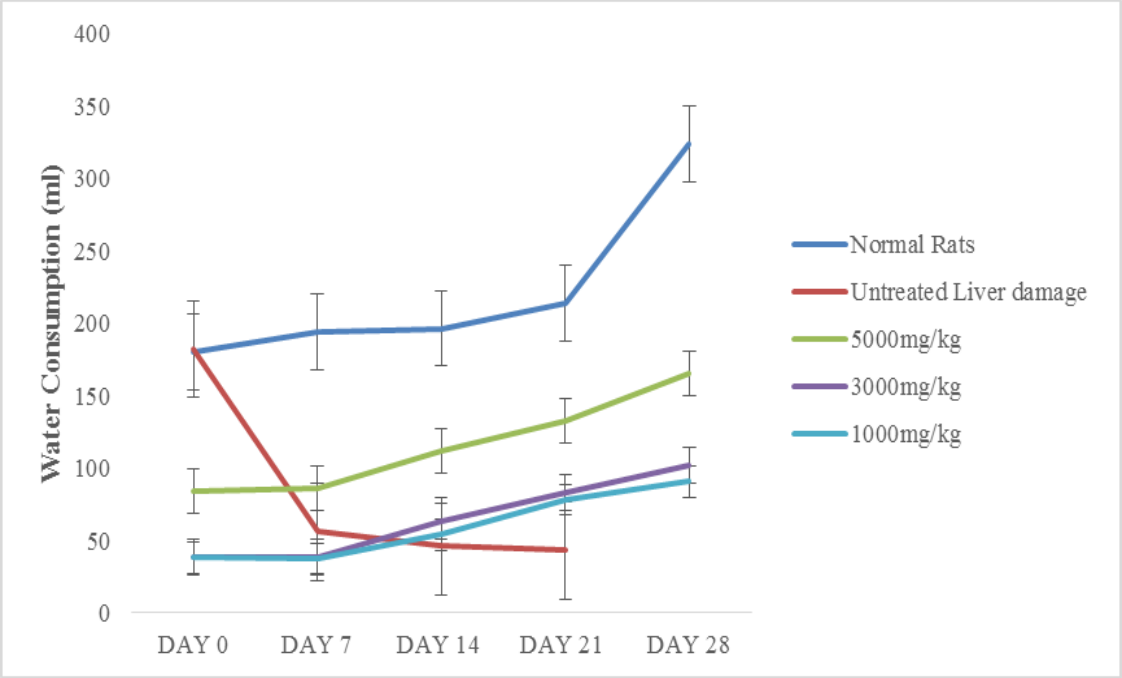


Fig. 15: Graph of mean water consumption of rats given *Sida corymbosa* ethanolic leaf extract before injecting CCL4. The graph was plotted using Ms Excel version 2007.

Plates 1-20 represent the photomicograms of liver sections of normal Albino Wistar rats, rats induced hepatotoxicity with Cl4 without any extract and those given *Sida corymbosa* ethanolic extract after inducing hepatotoxicy with CCl4. The physical examination carried out on liver tissues of rats showed all the liver tissues from the normal rats and that of the treatment groups from seven to twenty-eight had reddish brown colours with smooth surfaces. There were no morphological changes observed(Plates 1-4 and 9-20). While that of rats induced hepatotoxicity using CCl4 without any treatment had light brown colour with white spots all over the liver surfaces. The liver surfaces were rough (Plates 5-8).

Plate 1-20: Microscopy of liver tissues of rats

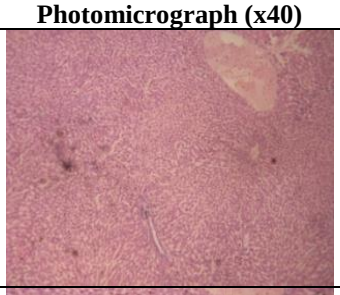
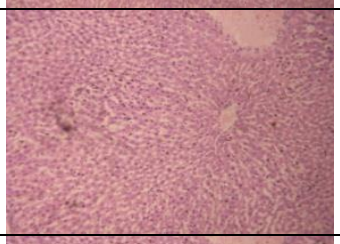
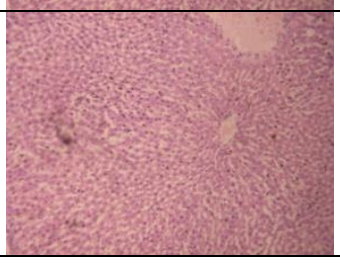
Description	Photomicrograph (x40)	Histological Observations
Plate 1: Normal rat liver for 7 days		well preserved liver architecture
Plate 2: Normal rat liver for 14days		well preserved liver architecture
Plate 3: Normal rat liver of for 21days		well preserved liver architecture

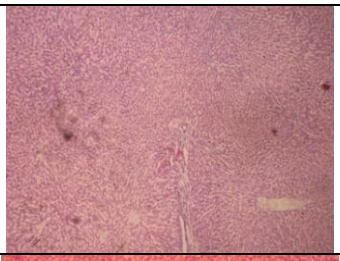
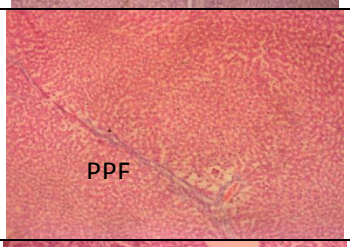
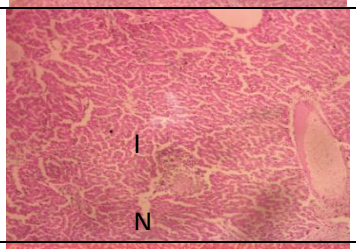
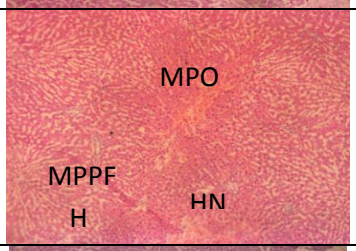
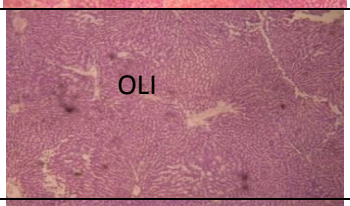
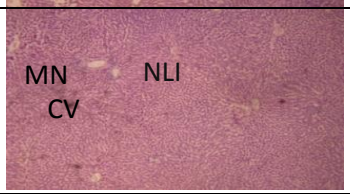
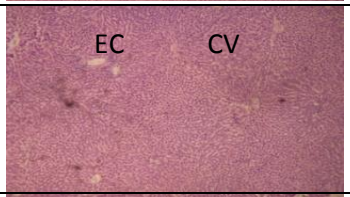
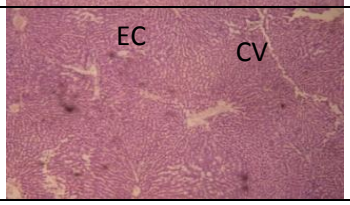
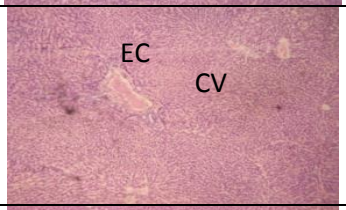
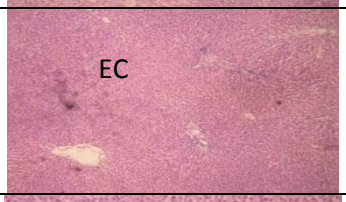
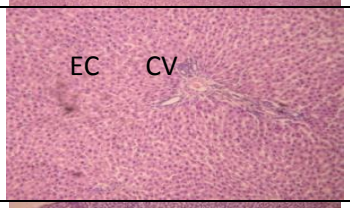
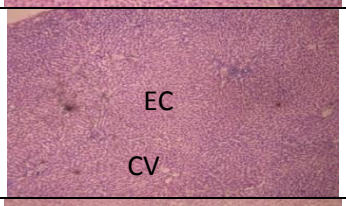
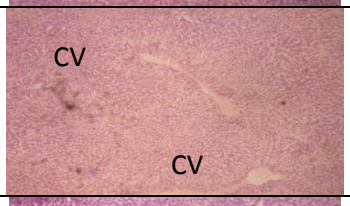
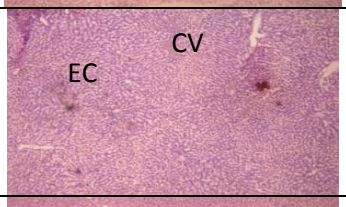
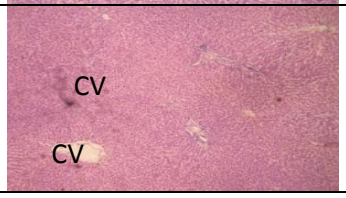
Plate 4: Normal rat liver for 28days		Well preserved liver architecture
Plate 5: Untreated liver damage for 7days		Classic micrograph of Liver damage showing portal to portal fibrosis(PPF)
Plate 6: Untreated liver damage for 14days		Classic micrograph of liver damage showing necrosis(N) and inflammation(I)
Plate 7: Untreated liver damage for 21 days		Classic micrograph of liver damage showing: 1.Mild parenchymal oedema(MPO) 2.Mild portal to portal fibrosis(MPPF) 3.Haemorrhage (H) and cells with hyperchromatic nuclei(HN)
Plate 9: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 5000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 7 days		There was well preserved architecture. The central vein(CV) showing mild congested blood vessels marked by black arrows and occasional lobular inflammation(OLI) without confluent necrosis. The erythrocyte cells were intact.
Plate 10: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 5000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 14 days		The liver architecture was intact The central vein(CV) with portal triads evenly spaced with mild peri-portal inflammation, mild necrosis (MN), no lobular inflammation (NLI). The erythrocyte cells were intact.
Plate 11: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 5000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 21 days		Normal liver tissue. The liver architecture was intact. The erythrocyte cells (EC) were intact. The central vein (CV) not clear. No necrosis nor lobular inflammation.
Plate 12: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 5000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 28 days		Normal liver tissue. The liver architecture was intact. The erythrocyte cells (EC) were intact. The central vein (CV) is clear. No necrosis nor lobular inflammation found.

Plate 13: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 3000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 7 days		Normal liver tissue. The liver architecture was well preserved. There is congested hepatic vessels(CHV)
Plate 14: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 3000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 14 days		Normal liver tissue. The liver architecture was well preserved. The central vein was not clear. The erythrocyte cells(EC) were intact
Plate 15: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 3000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 21 days		Normal liver tissue. The liver architecture was well preserved. The central vein was clear. The erythrocyte cells(EC) were intact.
Plate 16: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 3000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 28 days		Normal liver tissue. The liver architecture was well preserved. The central vein was not clear. The erythrocyte cells(EC) were intact.
Plate 17: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 1000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 7 days		Normal liver tissue. The liver architecture was well preserved. The central vein was clear. The erythrocyte cells(EC) were intact. There were no inflammation and necrosis
Plate 18: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 1000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 14 days		Normal liver tissue. The liver architecture was well preserved. The central vein(CV) was clear. The erythrocyte cells (EC) were intact. There was no inflammation and necrosis
Plate 19: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 1000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 21 days		Normal liver tissue. The liver architecture was well preserved. The central vein (CV) was clear. The erythrocyte cells (EC) were intact. There were no inflammation and necrosis
Plate 20: A photomicrograph of liver section of rat induced hepatotoxocity with CCl4 and treated with 1000 mg/kgbw of *Sida corymbosa* ethanolic leaf for 28 days		Normal liver tissue. The liver architecture was well preserved. The central vein (CV) was clear. The erythrocyte cells (EC) were intact. There were no inflammation and necrosis.

DISCUSSION

This research work investigated the therapeutic potentials of *Sida corymbosa* ethanolic leaf extract on Albino Wistar rats induced hepatotoxicity with carbon tetrachloride (CCL4) at 5000, 3000 and 1000mg/kgbw from seven days to twenty eight days. The oral acute toxicity (LD50) of the extract was found to be higher than 5000mg/kgbw. This suggests that the plant's extract may not be toxic when administered via oral route up to 5000 mg/kgbw. This implies that the extract may have a low toxic profile. This agrees with the earlier findings of.[16,17]

The results of the findings on hepatotherapeutic potentials of *Sida corymbosa* ethanolic leaf extract against CCL4-induced hepatotoxicty revealed that the levels of serum AST, ALT and ALP of all the groups of rats were significantly lower ($P<0.05$) than those of rats

induced hepatotoxicity using CCL4 without administering any treatment (Figures 2 to 4). The groups administered 5000, 3000 and 1000 mg/kgbw of the extract showed no significant difference in the values of AST and ALT when compared with those of the normal rats from seven days to twenty eight days of treatment. These are suggesting that liver injuries may have been induced in the rats injected CCL4 which might have been reversed as a result of the administration of the extract. This agrees with the similar findings of.[18,19,20]

The elevations of the hepatic enzymes (AST, ALP and ALP) in group of rats induced hepatotoxicity without treatment may be because the enzymes might have licked from the liver into the serum thereby elevating the serum levels of the enzymes. This assertion agrees with the similar report of[21] on evaluation of hepatoprotective activities of *Lamanea fluviatilis* on CCL4 -induced hepatotoxicity in rats. Hepatic enzymes such AST, ALT and ALP which are found in large amount in the liver are elevated in plasma or serum when there is severe hepatic cellular damage due to hepatitis, cirrohosis and hepatotoxicity drugs.[20]

It was observed that the levels of serum AST, ALT and ALP were significantly ($P<0.05$) lower in those rats administered 5000 mg/kgbw of the extract than those administered 3000 and 1000 mg/kgbw at 28days of treatment. This is suggesting dosage and time dependent effect. This is in line with the report of.[21]

The histopathological findings done so far supported the biochemical findings. Microscopic examination revealed that the liver architecture and the erythrocyte cells of both normal and treated groups were intact (plates 1-4 and 9-20), severe liver damages were noticed in the liver sections of the groups induced hepatotoxicity without treatment with any extract which progressed to fibrosis and necrosis (plates 5-8). This is collaborated by the findings reported by.[22]

The body weights of all the treatment groups (those given 5000, 3000 and 1000 mg/kgbw and the normal rats) were observed to have increased significantly ($P<0.05$) from seven days to twenty eight days. This is again suggesting weight loss might have been reversed in the treated groups as a result of treatment with the extract. This might have been as a result of increase in protein synthesis in treated rats.

However, it was observed that the water consumption of the treatment groups and the normal rats increased significantly ($P<0.05$) up to 28days of treatment while that of the groups induced hepatotoxicity without treatment decreased progressively up to 28days. The highest increase in water consumption for the treated groups was witnessed at 28days. This also suggests that a water imbalance caused as a result of CCL4 toxicity on the liver may have been reversed which is dependent on time. This agrees with the similar reports.[5,8]

CONCLUSION

Results analyzed so far showed that *Sida corymbosa* ethanolic leaf extract has reversed the elevated serum levels of hepatic biomarkers, (AST, ALT, ALP), decreased in body weights, water consumption and increase in liver weights of rats induced hepatotoxicity. The extract may therefore have hepatotherapeutic potentials against CCL4-induced hepatotoxicity, which is dependent on dosage and duration of the treatment. The best dose of the treatment may be 5000 mg/kgbw at longer duration. The extract may equally have a positive effect on body weight and water balance of the rats. These findings may not be extrapolated to human until epidemiological studies are carried out on the same issue.

Further studies

Research should be directed towards finding out the particular phytochemical compound responsible for hepatotherapeutic potentials in *Sida corymbosa* ethanolic leaf extract as witnessed in this work. The hypoglycemic, hematological and cardiological effects of the extracts on Albino Wistar rats should be investigated. The reproductive and antimalaria effects of the extract should equally be looked into. A comparative studies should be carried out on the hepatotherapeutic potentials of various parts of *Sida corymbosa* plant using various extracting solvent.

CONFLICT OF INTERESTS

No conflict of interest.

CONSENT TO PARTICIPATE

Not applicable.

REFERENCES

1. Hai ZB, Bing-Young YB, Yan GU. Hepatoprotective and antioxidant effects of Licorice extract against CCL4-induced oxidative damage in rats. Int J Mol Sci, 2011; 12: 6529-6543.
2. Adewale A, Abiodun O. Hepatoprotective and antioxidant effect of Hibiscus Polyphenol extract against carbon tetrachloride (CCL4) -induced damage in rats. British J Med Medi Res, 2013; 3(4): 1514-1586.
3. Dahiru D, Umaru H A, Vasira B, Agama AM. Antioxidant and antiperoxidative activities of aqueous extract of *Hibiscus gabdariffa L*. calyx on alcoholic-induced-hepatic lipid peroxidation in rats. Am J Biochem, 2013; 3(2): 62-65.
4. Al-Dosari A, Al-Sharif L, Khalil D, Shinwari J, Almuslamani A, Tassan N. Mapping of Loci for autistic spectrum disorder on chromosomes. Neurology, 2012; 74 (9):274.
5. Jamila MH. *Hibiscus sabdarriffa* calyx extract alleviates hepatotoxicity induced by carbon tetrachloride in male Albino rats. Nature Science, 2014; 12(6): 111-120.
6. Neetu D, Ajay KS, Piush S. Review on hepatoprotective plants. Int J Pharm Sci, 2011; 7(1): 15-25.

7. Nwokocha R, Owu D U, Ufearo CS, Iwuala MO. Comparative study and efficacy of *Garcinia kola* in reducing some heavy metal accumulation in the liver of Wistar rats. J Ethnopharmacol, 2011; 135: 438-491.
8. Nasir A, Abubakar MG, Shehu RA, Aliyu U, Toge BK. Hepatoprotective effect of aqueous leaf extract of *Andrographics paniculate* against carbon tetrachloride-induced hepatotoxicity in rats. Nigerian J Basic Appl Sci, 2013; 21(1): 45-54.
9. Mahmud Z, Bachar SC, Qais N. Antioxidant and hepatoprotective activities of ethanolic extracts of leaves of *Premina esculenta* Roxb against carbon tetrachloride-induced liver damage in rats. Journal of Young Pharmacists, 2013; 4(4): 228-234.
10. Marinmay D, Ashok KD. Pharmacological review of Althernanthera sessilis Linn. Int J Res Pharm Biol Sci, 2014; 1(1): 9-15.
11. Goutam G, Debajyoti D. An overview on therapeutic potentials and phytochemistry of *Sida rhombifolia*. Int J Pharm Sci Rev Res, 2015; 32(1): 209-216.
12. Enegide C, David A, Fidelis SA. A new methods for determining acute toxicity in animal models. Toxicol Int, 2013; 20(3): 224-226.
13. WHO. Recommendation for the preparation, characterization and establishment of international and other biological references standards. WHO Experimental Committee on Biological Standardization. Fifty-fifth report. WHO Technical Report Series NO 932. http://www.whoint/ bloodproducts/norms/en/.
14. Nubile T, Ukaejiofor EO, Nubila NI, Okwuosa N, Chijioke CP, Shu EN, Iyare EE. Sub-acute effects of crude methnolic leaf extract of *Mucuna filagellipes* (Vogel ex Hook) on haematological profile and hematinic activities in Albino Wistar rats. Int J Med Arom Plants, 2013; 3(4): 452-458.
15. Paola V, Filomena M, Giovanna M, Daniela CA, Maria T R, Antonietta R, Vinvenzo F, Nicola C, Giuseppe D. Coffee reduces liver damage in a rat model of steatohepatitis. The underlying mechanism and role of polyphenols and melanodins. Hepatology, 2012; 52(5): 1652-1661.
16. Lucy B J, Mercy A. Evaluation of the haemostatic activities of *Sida corymbosa* in rats. British J Pharm Res, 2015; 5(6): 431-436.
17. Lucy BJ, Tijani AY, Christianah YI. Antiulcer and wound healing activities of *Sida corymbosa* in rats. Afr J Tradit Compl Altern Med, 2014; 11(1): 87-92.
18. Geum-Hwa L, Hwa-Young L, Min-Kyung C, Han-Wool C, Seung-Wook K, Han-Jung C. Protective effect of *Curcuma Longa* L. extract on CCL4-induced acute hepatic stress. BioMed Central, 2017; 10: 77.
19. Maher AA, Mohamed AE, Aya A. The role of *Ficus carica* leaf extract in modulation of the experimentally- induced hepatotoxicity damage in male rats. Int J Advanced Res, 2015; 3(12): 572-588.
20. Alagammal M, Packia L, Mohan VR. Hepatoprotective and antioxidant effect of *Polygala rosmarinifolia* Wight and Ann against CCL4-induced hepatotoxicity in rats. J Pharmacogn, 2013; 2(1): 118-124.
21. Ejezie FE, Ikepeazu JE. Fundamentals of metabolism of lipids. 1st ed. Ezu books Ltd, 2010; 165-220.
22. Okafor IA, Ejimofor OC, Ezejindu DN, Chukwujekwu IE, Dike CC. The renoprotective effects of methonolic extract of *Portulacea oleracea* on cisplatin-induced nephrotoxicity in Wistar Rats. Adv Life Sci Technol, 2014; 19: 52-60.