MERIT RESEARCH JOURNALS
www.meritresearchjournals.org
Merit Research Journal of Medicine and Medical Sciences (ISSN: 2354-323X) Vol. 7(3) pp. 100-105, March, 2019
Available online http://www.meritresearchjournals.org/mms/index.htm

Original Research Article

Hepatoprotective effect of the methanol leaf extract of *Lophira lanceolata teigh* (Ochnaceae): An experimental study

***Onyeto C. A., Ihim S. A. and Akah P. A.**

Department of Pharmacology andToxicology, Faculty of Pharmaceutical Sciences, Nsukka, 410001, Enugu State, Nigeria.

***Corresponding Author's E-mail: collins.onyeto@unn.edu.ng. Tel: +2348034004221**

Abstract

The hepatoprotective effect of methanol leaf extract (ME) of *Lophiralanceolata* Tiegh (Ochnaceae) was investigated against carbon tetrachloride (CCl_4) induced hepatotoxicity in rats. Rats were randomly divided into 7 groups(n=6) and ME were administered at 100, 200, and 400mg/kg/day p.o to groups III-V, while groups I, VI and VII received 1ml/kg tween 80, Vitamin C and Silymarin at 25 mg/kg/day p.o respectively while group II received only CCl_4.. CCl_4 was given every 72 hours to all the groups except group1.ThenSerum level of blood samples was assayed by alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), malondialdehyde (MDA), total protein, total bilirubin, albumin and globulin. ME significantly ($p < 0.05$) reduced in the serum levels of the liver enzymes when compared with the control group (CCl_4). The levels of ALT, AST and bilirubin at 100 and 400mg/kg were reduced significantly ($p< 0.05$).Also, ALP levels was lowered at 100 mg/kg but not significant difference ($p>0.05$). At 100mg/kg, MDA levels was lowered more significantly ($p<0.05$) than controls (Silymarin and vitamin C).Serum globulin level at 200mg/kg dose of extract was significantly increased when compared to CCl_4 control group.

In conclusion, ME can be protective against oxidative stress caused by liver toxicitylike CCl_4.

Keywords: Hepato-protective effect, *Lophiralanceolata,* methanol extract, rats, carbon tetrachloride

INTRODUCTION

The liver is the main body organ responsible for the metabolism of xenobiotics. It is an important modulator of lipid metabolism, and it has a critical role in the synthesis of lipoproteins, triglycerides, gluconeogenesis from fatty acids, and cholesterol metabolism (Sherwood, 1997). As the body has the most important metabolism and detoxification organ, the liver may be subject to potential damage from a wide range of pharmaceutical and environmental chemicals. These Injury results indirect toxicity, due to hepatic conversion of a xenobiotic to an active toxin (Farrel et al., 2002).

Hepatotoxicity is a growing concern for today's modern society. The increasing incidence of industrial pollutions, occupational hazards and unhealthy lifestyle options such as alcoholism, cigarette smoking, substance abuse and consumption of fatty foods is contributed to the morbidity and mortality due to liver disease (Scott, 1998). Many drugs, toxic substances and infectious organisms are associated with hepatotoxicity due to the ability to generate free radicals and to cause a disturbance in hepatocyte biochemistry (Fernandez-Checa and Kaplowitz, 2005). The free radical formation

leading to hepatic damage in the form of jaundice, cirrhosis and fatty liver, which remain one of the serious health problems can only be removed with natural defensive.

Carbon tetrachloride (CCl_4) is a toxic substance to the liver (Al-Shabanah et al., 2000). It causes to ROS. It is widely used to develop experimental animal models of liver failure (Yoshioka et al., 2016) Excessive production of the reactive species manifests in tissue thiol depletion, lipid peroxidation, plasma membrane damage etc., culminating into severe hepatic injury (Wargovich et al., 2001).

Lophiralanceolata among other folkloric medicinal uses has been used to treat diarrhoea, dysentery, menstrual pain, liver diseases etc. However, these claims are yet to be studied.

In this study aimed investigate hepato-protective activities of the methanol leaf extract of *Lophiralanceolata.* Interest in herbal medicines is increasing due to their effectiveness, minimal side effects in their clinical experience and relatively low cost. Herbal medicines have been used traditionally worldwide for the prevention and treatment of various diseases. According to the WHO, 80% of the world population use plant-based remedies for their primary form of healthcare (Evan et al., 1998). Herbal drugs play a role in the management of various liver disorders most of which speed up the natural healing processes of the liver (Subramoniam et al., 1998). Recent studies have reported that the hepatoprotective activity of plants of family Rutaceae like *Murrayakoenigii, Citrus limon, Citrus aurantium* and *Tephrosiapurpur* (Gupta, 2009). Several other medicinal plants have also shown potential hepatoprotective effects include the rhizomes of *Zingiberofficinale* (Saadet al., 2017), *Alchorneacordifolia* leaves (Kouakon et al., 2017), *Thymus vulgaris* (Nagwa and Manar 2017), *Tylophoraindica* and*Hoslundia opposite (*Rachna, 2018), *Viola canescens* (Abdullah et al., 2017)*, Stachyspilifera* (Esmaeel et al., 2017)*, Sphaeranthusamaranthiodes* (Somnath et al., 2017)*, Spondiasmombin* (Luky et al., 2017)*, Polygonumamplexicaule* (Faiza et al., 2017)*, Homaliumletestui* (Jude et al., 2017), *Garcinia Morella* (Nabajyoti et al., 2017), *Pseudocedralakotschyi* (Moise et al., 2017).

MATERIALS AND METHODS

Materials

Chemicals, reagents, solvents and Standard Drugs

Carbon tetrachloride (CCl_4) (JHD, China), liquid paraffin (Quilikems, India), , tween 80 ((JHD, China)), ethylene diamine tetra acetic acid (EDTA), ALT substrate solution, NaOH solution, AST substrate solution, trichloroacetic acid, ALP substrate solution, distilled water (Lion water, UNN), Silymarin, Vitamin C (Vinco Pharmaceutical, Nigeria) were used

Instruments

Electrical animal weighing balance (B. Bran Scientific and Instruments Co., England), analytical weighing balance, spatula, beakers, measuring cylinders, test tubes, centrifuging tubes, incubator, electrical centrifuges (B. Bran Scientific and Instruments Co., England), UV-Visible spectrophotometer (Easy-Way Medical England 752 W, England),a milling machine (Lab mill, serial No. 4745, Christy and Norris Ltd., England), Soxhlet apparatus, large extraction vessels and rotary evaporator (B. Bran Scientific and Instruments Co., England).

Plant collection and identification

The fresh leaves of *L. lanceolata* were collected from Nsukka, Enugu state, Nigeria in the month of May, in 2016, identified and authenticated by Mr Alfred Ozioko of the International Centre for Ethno medicine and Drug Development (Inter CED), Nsukka, Enugu state. A dried voucher specimen was preserved at the Pharmacognosy Herbarium, Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka (specimen number: PCG/UNN/0311) thereafter.

Preparation of plant extract and fraction

The leaves of *L. lanceolata* were air-dried at room temperature and ground into powder by a grinder (ADDIS, Nigeria). The powdered material (2370 g) was macerated with 4.5 L of 70% methanol for 72 h with constant shaking. The resultant mixture was filtered using Whatman (No. 1) filter paper and the filtrate was concentrated on dryness under vacuum at 40^{o}C using rotary evaporator.

Animals

Adult Swiss albino rats (150 - 200 g) were used for the study. Rats were obtained from the department of pharmacology and toxicology at the University of Nigeria was recorded from the laboratory animal facility. In Nigeria, Nsukka. The animals were maintained freely on standard pellets and water. The animal use ethical approval was obtained from the Institutional Ethics committee of the University of Nigeria, Nsukka and was in compliance with the National Institute of Health Guide for Care and Use of Laboratory Animals (Pub No. 85 – 23, revised 1985).

Methods

Pharmacological Tests

Carbon Tetrachloride Induced Toxicity

The carbon tetrachloride induced biologic oxidation model was used as described by previously methods (Suja et al., 2004). After seven days of acclimatization, the 35 rats of both sexes were divided into seven groups, each group containing five animals. Group I received tween 80 (Negative control), group II received CCl_4 (CCl_4: liquid paraffin (1:2); (1 ml/kg/day p.o), the animals in the test groups (III to V) received 100, 200 and 400 mg/kg of the methanol extract respectively. Group VI received vitamin C (25 mg/kg p.o), and group VII were given Silymarin (25 mg/kg.). The treatments were lasted for seven days and 1ml/kg of carbon tetrachloride (CCl_4) was given to groups II to VII once every 72 hours to induce the liver damage. On the 8^{th} day, blood sample was collected forthe assay of serum enzymes alanine aminotransferase (ALT) and serum aspartate aminotransferase (AST) activities (Reitman et al., 1957),serum alkaline phosphatase (ALP) activity (Klein et al., 1960; Babson et al., 1966), malondialdehyde (MDA) determination by Thiobarbituric acid method (Plaser et al., 1966), determination of Serum Total Proteins (Lubran, 1978), determination of serum albumins (Doumas et al., 1971; Doumas and Peters, 1997), calculation of serum globulin, determination of total bilirubin and clinical biochemistry using orbital technique (Stone, 1954).

Statistical analysis

Results obtained were expressed as mean ± SEM. The data were analyzed using one way ANOVA, followed by DUNNET post hoc using Graph pad Prism version 5.03 software. $p<0.05$ was considered statistically significant.

RESULTS

The percentage yield

The percentage yield of the ME was calculated to be 4.59 % w/w.

Phytochemical analysis

The ME of *Lophiralanceolata* gave positive test for flavonoid, alkaloid, glycoside, saponins, and terpenoids, reducing sugar, oils and carbohydrates as reported by Onyeto et al., (2014).

Pharmacological test

Acute toxicity test

There was no mortality recorded in the mice upon oral administration at 5000 mg/kg (Onyetoet al., 2014).

Effect of methanol extract of *Lophiralanceolata* on serum ALT activity induced carbon tetrachloride rats

The serum ALT activity of the group treated with 100 and 400 mg/kg was significantly ($p<0.05$) lower than that of the untreated (CCL_4) control. The effects of the 100 and 400mg/kg was comparable ($p>0.05$) to that of Silymarin (Table 1).

Effect of methanol extract of *Lophiralanceolata* on serum AST activity induced carbon tetrachloride rats

The serum AST activity of the group treated with 100 and 400 mg/kg was also significantly ($p<0.05$) lower than that of the untreated (CCL_4) control, and comparatively better than Silymarin (Table 1).

Effect of methanol extract of *Lophiralanceolata* on serum ALP activity induced carbon tetrachloride rats

Animal groups treated with various doses of methanol extract had lower serum ALP activity but the difference was not significant ($p>0.05$) when compared to the untreated CCL_4 control. Silymarin treatment had a significantly ($p<0.05$) better effect on serum ALP than the extracts (Table 1)

Effect of methanol extract of *Lophiralanceolata* on MDA activity induced carbon tetrachloride rats

Treatment with methanol extract of 100 mg/kg significantly lowered ($p<0.05$) the MDA levels (Products of Oxidative stress) far better than all other treatments including Silymarin (Table 1)

Effect of methanol extract of *Lophiralanceolata* on serum protein, globulin and albumin activity induced carbon tetrachloride rats

Liver damage using CCL_4 and treatment with methanol extract or vitamin C or Silymarin had no significant ($p>0.05$) effect on serum proteins and albumin levels. However, damage using CCL_4 led to higher albumin levels in animal groups given CCL_4 and treated with varied doses of methanol extracts. The effect on the

Table 1. The serum enzyme activity and malondialdehyde levels in rats given carbon tetra chloride (CCL_4) and treated with varied doses of methanol extract of *Lophiralanceolata*

Treatments	Means of serum enzyme activity and malondialdehyde levels, with standard error in bracket.							
	Alanine aminotransferase (IU/L)		Aspartate aminotransferase (IU/L)		Alkaline phosphatase (IU/L)		Malondialdehyde (µmol/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Tween 80 control	45.58 (2.08)	47.25 [a] (2.07)	72.08 (1.90)	74.34 [a] (2.77)	318.10 (17.96)	327.20 [a] (19.59)	1.43 (0.06)	1.42 [acd] (0.05)
CCL_4 only	45.90 (1.59)	88.71 [b] (0.56)	72.39 (2.22)	107.80 [b] (1.89)	313.7 (16.24)	504.80 [b] (9.87)	1.41 (0.05)	1.85 [b] (0.10)
CCL_4 + 100mg/kg b.w. extract	47.35 (2.13)	63.47 [c] (8.69)	71.54 (2.20)	94.11 [c] (6.99)	322.20 (16.77)	456.00 [b] (21.40)	1.40 (0.08)	1.27 [c] (0.05)
CCL_4 + 200mg/kg b.w. extract	45.03 (2.22)	83.43 [b] (1.20)	73.16 (2.25)	109.50 [b] (3.59)	319.30 (17.76)	478.00 [b] (14.56)	1.44 (0.08)	1.50 [d] (0.09)
CCL_4 + 400mg/kg b.w. extract	47.40 (2.49)	67.07 [c] (5.61)	72.31 (3.06)	95.21 [c] (5.01)	300.80 (18.02)	434.40 [b] (54.44)	1.42 (0.07)	1.51 [d] (0.11)
CCL_4 + Vitamin C	46.96 (1.53)	78.45 [b] (3.71)	72.85 (2.33)	102.80 [bc] (4.16)	320.30 (17.53)	462.40 [b] (23.04)	1.45 (0.06)	1.50 [d] (0.07)
CCL_4 + Silymarin	44.45 (1.95)	69.20 [c] (4.96)	75.51 (2.64)	97.53 [bc] (6.74)	336.20 (20.82)	317.90 [a] (2.07)	1.46 (0.05)	1.40 [acd] (0.05)

[a, b, c, d] Different alphabetical superscripts in a column indicate significant difference between the means, $p < 0.05$

Table 2. The serum protein and bilirubin levels of rats given carbon tetra chloride (CCL_4) and treated with varied doses of methanol extract of *Lophiralanceolata*

Treatments	Means of serum proteins and bilirubin, with standard error in bracket.							
	Total protein (g/dl)		Albumin (g/dl)		Globulin (g/dl)		Bilirubin (mg/dl)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Tween 80 control	6.43 (0.14)	6.67 (0.05)	3.38 (0.09)	3.75 (0.17)	3.05 (0.12)	2.92 [a] (0.17)	0.22 (0.03)	0.23 [a] (0.02)
CCL_4 only	6.56 (0.27)	6.93 (0.18)	3.47 (0.08)	3.60 (0.24)	3.09 (0.22)	3.33 [ab] (0.26)	0.25 (0.02)	0.51 [b] (0.05)
CCL_4 + 100mg/kgb.w. extract	6.31 (0.19)	6.95 (0.13)	3.41 (0.08)	3.82 (0.13)	2.91 (0.15)	3.13 [ab] (0.13)	0.26 (0.04)	0.28 [ac] (0.02)
CCL_4 + 200mg/kg b.w. extract	6.64 (0.11)	6.98 (0.23)	3.42 (0.09)	3.47 (0.23)	3.22 (0.12)	3.51 [b] (0.31)	0.27 (0.03)	0.31 [c] (0.02)
CCL_4 + 400mg/kg b.w. extract	6.69 (0.21)	6.90 (0.30)	3.76 (0.08)	3.82 (0.17)	3.22 (0.24)	3.36 [ab] (0.15)	0.25 (0.03)	0.30 [ac] (0.01)
CCL_4 + Vitamin C	6.42 (0.16)	6.77 (0.17)	3.50 (0.12)	3.77 (0.12)	2.91 (0.19)	3.00 [ab] (0.08)	0.27 (0.04)	0.28 [ac] (0.03)
CCL_4 + Silymarin	6.49 (0.19)	6.61 (0.18)	3.49 (0.15)	3.48 (0.16)	2.70 (0.14)	3.12 [ab] (0.16)	0.23 (0.03)	0.27 [ac] (0.02)

[a, b, c] Different alphabetical superscripts in a column indicate significant difference between the means, $p < 0.05$

globulin levels was most severe on the group treated with 200mg/kg extract (Table 2)

Effect of methanol extract of *Lophiralanceolata* on serum bilirubin activity induced carbon tetrachloride rats

The serum bilirubin levels of the animal groups treated with the extracts, vitamin C, and Silymarin were all significantly lower ($p<0.05$) than that of the CCL_4 untreated control. The serum bilirubin of animal groups treated with 100 and 400 mg/kg, vitamin C and Silymarin were comparable to that of the tween 80 control (Table 2).

DISCUSSION AND CONCLUSION

Discussion

The efficacy of any hepatoprotective drug is essentially dependent on its capacity of either reducing the harmful effects or maintaining the normal physiologic function which has been disturbed by hepatotoxic agents, (Tripathi et al., 1999). Mechanisms of drug induced hepatotoxicity includes: Interference with bilirubin transport and conjugation; cytotoxic injury; cholestasis; mixed cytotoxic/cholestatic injury; fatty liver (steatosis); chronic active hepatitis, cirrhosis and sub-acute necrosis; phospholipidosis; liver tumours; and non-specific changes, (Davis et al., 1977). Mechanisms of hepatoprotectective effect includes: Glycine-mediated cytoprotection which protects the liver, kidney and other cells against cell death in various models of hypoxia and ATP depletion, (Lemasterset al.,1981); estradiol and ethinylestradiol reduce the degree of liver injury caused by hepatotoxic as well as ischemia-reperfusion.

In liver damage, total protein, albumin and globulin synthesis are impaired leading to their decrease in serum concentrations (Grant, 1987).

Carbon tetrachloride was reported to produce free radicals, which affect the cellular permeability of hepatocytes leading to elevated levels of serum biochemical parameters like ALT, AST and ALP (Vinoth et al., 2009). The levels of serum aspartate amino transaminase (AST), Alanine amino transaminase (ALT), Alkaline Phosphate (ALP) and Malondialdehyde (MDA) were taken as an index for oxidative stress induced by CCl_4.

The results of this study shows that daily oral supplementation of the methanol extract of *Lophiralanceolata* significantly ($p<0.05$) reduced the escalation of mean serum concentration of AST and ALT induced by CCl_4in a dose dependent manner. The administration of 100 and 400 mg/kg of the ex-tract produced more reduction in serum AST and ALT as compared to the standard drug, Silymarin. This reduction suggest the protection of the structural integrity of hepatocyte cell membrane or regeneration of damaged liver cells caused by CCl_4. ALT is a better index of liver injury, as liver ALT activity represents 90% of total enzymes present in the body (Moss and Butterworth, 1974).

Serum levels of ALP were reduced by the methanol extracts of *Lophiralanceolata* though not significant. A more significant reduction was seen with the standard drug, Silymarin. Administration of vitamin C did not reduce the serum level of the enzyme ALP. Overall, the progressive decrease in the levels of serum liver enzymes implies that the free radicals, which were generated due to the CCl_4 induction, were being mopped up by the plant extract treated with ME of *Lophiralanceolata* after seven days post treatment and also indicates an early improvement in the cellular membrane integrity of the hepatic cell.

The reduction of the serum level of MDA by the ME (100 mg/kg) was very high. This confirms the antioxidant mediated mechanism incorporation.

In liver diseases, there is elevation of conjugated and unconjugated bilirubin concentrations (Hass, 1999). At dose levels of 100mg/kg, 200mg/kg and 400mg/kg, the extract reduced total bilirubin concentration relative to the control groups. However, these reductions were not significant when compared to any of the control groups. Suppression of increased activity of ALP correlating with a decrease in raised bilirubin level indicates the stability of the biliary dysfunction in the rat liver during hepatic injury with CCl_4 (Gole et al., 1997).

One of the major functions of the liver is the synthesis of serum protein and its metabolism. Hepatotoxicity can impair the protein synthesis function of the liver (David, 1999). The extract showed an increase in the serum total protein, albumin and globulin concentrations at dose levels of 100mg/kg, 200mg/kg and 400mg/kg, relative to the negative control and CCL_4 control group. The extract also showed sufficient increase in albumin and total protein concentrations at dose levels of 100mg/kg and 400mg/kg, relative to the positive control group. There is sufficient increase in globulin concentrations at dose levels of 200mg/kg, relative to the positive control group. This implies that the extract is effective in reversing liver damage caused by carbon tetrachloride at different dose levels.

CONCLUSION

Taken together, the results of the present study suggest that the ME of *Lophiralanceolata* Teigh, possesses potent hepatoprotective effects against carbon tetrachloride induced toxicity in rats. However, further work is required to elucidate the phytochemical constituents of *Lophiralanceolata* Teigh, in order to verify any other

advantages the extract may possess over other hepatoprotective agents.

REFERENCES

Abdullah M, Waqar A, Manzoor A, Mohammad N (2017). Hepatoprotective effect of the solvent extractsof *Viola canescens*wall. Ex Roxb. Against CCL4 induced toxicity through antioxidant and membrane stabilizing activity. BMC Compl Alter Med. 17(10): 1-11

Al-Shabanah OA, Alam KS, Nagi MN, Al-Rikabi AC, Al-Bekairi AM (2000). Protective effect of aminoguanidine, a nitric oxide synthetase inhibiter against CCl4 induced hepatotoxicity in mice. Life Sci. 66: 265-270.

Babson LA, Greeley SJ, Coleman CM, George EP (1966). Phenolphthalein monophosphate as a substrate for serum alkaline phosphatase.Clin. Chem. 12: 482.

David EJ (1999). Special consideration in interpreting liver function tests. American Family physician. V. 59 No. 8.

Davis M, Williams R. Hepatic Disorders. (1977). In: Davies DM, editor. Textbook of Adverse Drug Reactions, Oxford: Oxford University press. pp 146-172.

DoumasBT, Watson WA, Biggs HG (1971). Albumin standards and the measurement of serum albumin with bromocresol green. ClinChimActa. 31: 87 – 96.

DoumasBT, Peters TJr (1997). Serum and urine albumin: a progress report on their measurement and clinical significance. ClinChimActa. 258(1): 3 – 20.

Esmaeel PK, Kyomarth A, Heibatollah S, Hossein S, Fahemeh D, Nazanin D, Mahmoud RA (2017). Hepatoprotective effect of *Stachyspilifera*ethanol extract in carbon tetrachloride–induced hepatotoxicity in rats. Pharm Biol.55 (1): 1389 -1393

Evan WC: Trease and Evan's Pharmacognosy. 14th Edn. WB Saunders, London; 1998. ISBN: 0-7020-1899-6.

Faiza M, Tanvir I, Ammad AF, Muhammad SA (2017). *Polygonumamplexicaule*extract: An effective herbal cure to CCL4 induced liver damage *in vivo*. J rare DisordDiagnTher. 3(3):1 -8

Farrel GC, Liddle C (2002). Hepatotoxicity in the twenty-first century. Semin. Liver Disease. 22: 109-206.

Fernandez – Checa JC, Kaplowitz N (2005). Hepatic mitochondrial glutathione: Transport and role in disease and toxicity. ToxicolApplPharmacol.204: 263 – 273.

Gole MK, Dasgupta S, Ghosal RK (1997). Hepatoprotective effect of *Amoora Rohitu.* Int J Pharmacog.5: 138 – 322

Grant GH (1987). Amino acids and proteins: Fundamentals of clinical chemistry, Tietz, N.M. (ed), 3rd Edition, 328-329.

Gupta S. (2009). Antioxidant Activity of MurrayaKoenigii Linn Leaves" [Internet] Available from <http://www.pharmacologyonline.com> 1: 474-478 (Accessed June 19, 2009)

Hass PL. (1999). Differentiation and diagnosis of jaundice. AACN Clin. Issues10: 433-441.

Jude EO, Joseph OS, Emem EU (2017). Hepatoprotective activity of the extract of *Homaliumletestui*stem against PCM induced liver injury. J Phytomed. 7(1):27-36

Klein S. (1960). Protein-energy malnutrition. In: Goldman L, Schafer AI, eds. Cecil Medicine. 24th ed. Philadelphia, Pa: Saunders Elsevier; 2011: chap 222.

Kouakou EE, Sylvain LK, Genevieve IG, N'Doua GK (2017). Antioxidant activity and hepatoprotective effect of an aqueous extract of *Alchorneacordifolia*leaves. Pharmacol Pharm.8:369-380.

Lemasters JJ, Ji S, Thurman RG (1981). Centrilobular injury following hypoxia in isolated, perfused rat liver. Science 2131-3.

Lubran MM. (1978). The measurement of total serum proteins by the Biuret method.Annals of ClinicLab Sci.8 (2): 106 – 110.

Luky LN, Ekramy E, Oboma IY, Wayne GC (2017). Hepatoprotective and antioxidant effects of *Spondiasmombin*and stem extracts upon carbon tetrachloride induced hepatotoxicity and oxidative stress Basic Clin Pharm8:S11 –S19

Moise LN, Sylvie WN, Nobert K, Sylviane KP, Pepin AN, Albert K (2017). Hepatoprotective and antioxidant effect of stem bark extracts: Methanolic and aqueous of *Pseudocedrelakotschyi* (Meliaceae) on paracetamol induced hepatic damage in rats. Asian J biomed PharmSci7 (63):1-9

Moss DW, Butterworth PJ (1974). In: Enzymology and Medicine, Pitman Medical, London

Nabajyoti G, Ankur G, BijoyNeog, Dibyojyoti B, Khumanthem D (2017). Antioxidant and hepatoprotective activity of fruit and extract of *Garcinia Morella* (Gaertn.) Desr. Ind J Nat ProdtResr. 8(2): 132-139

Nagwa ME, Manar ER (2017). Hepatoprotective activity of *Thymus vulgaris* extract against *Toxoplasma gondii* infection. Asian Pac J Trop Med.7 (5): 280-285

Onyeto CA,Akah PA, Nworu CS, Okoye TC, Okorie N.A, Mbaoji FN, Nwabunike IA, Okumah N, Okpara O. (2014). Anti-plasmodial and antioxidant activities of methanol extract of the fresh leaf of *Lophira lanceolata* (Ochnaceae). *African J. Biotechnol.* 13(16) 1731-1738.

Plaser ZA, Crushman L, Johnson BC (1966). Estimation of product of lipid peroxidation (malondialdehyde) in biochemical systems. Anal Biochem.16:359–64

Rachna V (2018). A review on hepatoprotective activity of medicinal plants. J Med Plants Study.6 (1): 188 - 190

Reitman S, Frankel S (1957). A colorimetric method for determination of serum glutamic oxaloacetic and glutamic pyruvic transaminases. Amer J of ClinicPathol. 28:56 – 62.

Saad AG, Enayat MH, Dalia MK (2017). Hepatoprotective effect of aqueous extract of some medicinal plant mixtures on CCL4-induced liver toxicity. J Pharm BiolSci.12 (1): 43-52

Scott ND (1998). A review of plants used in the treatment of liver disease: Part-I. Alt med Rev. 3 (6):410

Sherwood L. (1997). Human physiology from cells to systems, *Belmont*: Wadsworth publishing company.

Somnath D, Ramalingam S, Akula M, Siddabathuni A (2017). *In vivo*hepatoprotective activity of methanolic extracts of Sphaeranthusamaranthoides and Oldenlandia umbellate. Pharmacogn. J 9(1): 98-101

Stone SH (1954): Method for obtaining venous blood from orbital sinus of rat or mouse. Science.119:100.

Subramoniam A, Evans DA, RajasakhranSP (1998).Hepatoprotective activity of *Trichopuszeylanicus* extracts against paracetamol induced damage in rats. Ind J ExptBiol. 36: 385-389.

Suja SR, Latha PG, Pushpangadan P, Rajasekharan S (2004). Evaluation of hepatoprotective effects of *Helminthostachyszeylanica* (L) Hook against carbon tetrachloride induced liver damage in Wistar rats. J Ethnopharmacol.92: 61. [doi:10.1016/j.jep.2004.01.019]

Tripathi SC, Patnaik GK, Dhawan BN (1999). Hepatoprotective activity of picroliv against alcohol-carbon tetrachloride induced damage in rats. Indian J. Pharmacol.23 (3):143-48.

Vinoth K, Sivaraj A, Elumalai EK, Senthil K (2009). Carbon Tetrachloride-induced Hepatotoxicity in Rats – Protective Role of Aqueous Leaf Extracts of *Cocciniagrandis*. Int. J. Pharm. Tech. Res.1 (4):1612-16m, 15.

Wargovich MJ, Woods C, Holli DM,Zander ME (2001).Herbals, Cancer Prevention and Health.J of Neutraceutical.131: 3034-3036.

Yoshioka H, Tanaka M, Fujii H, Nanogaki H. (2016).Sasa veitchii extract suppresses carbon tetrachloride-induced hepato- and nephrotoxicity in mice. Environ Health Prev Med.21 (6): 554–562.