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Studies on some biochemical effects of aqueous leaf Extract of *landolphia owerrience* on albino rats

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ABSTRACT:

The effects of aqueous leaf extract (crude) of *Landolphia owerrience* on some biochemical parameters in adult male and female Albino rats were investigated. Administration of the plant leaf extract was by gavage at a dose level of 20 mg/kg, 30 mg/kg and 40 mg/kg body weight in 0.5 ml saline respectively, daily for 21 days. The concentration of ALT and AST were non-significantly increased as the dose increased. Alkaline phosphatase (ALP) level also increased non-significantly, but not dose dependent. Protein level also significantly increased in a dose dependent fashion. Hemoglobin concentration increased significantly, while lipid peroxidation level decreased non-significantly as the dose increased. The non-significant increase in liver enzyme concentrations in this study showed that the *Landolphia owerrience* leaf extract may not be toxic to the rat liver, while the low lipid peroxidation levels showed that it may have antioxidant activity.

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INTRODUCTION

Landolphia owerrience is a wild plant usually found growing wild in Africa and Madagascar. The plant belongs to the family Apocynaceae and it is distinguished by a corolla tube which is usually thickened above the anthers. It produces glabrous fruits, which is characterized by dense inflorescence (Person, 1962; Burkill, 1994). Other species of the genus include *Landolphia hirsute* and *Landolphia kirki*. The wild plant is rich in nutritional content as its composition parades rare food nutrients especially the vitamins, carotene and minerals (Ebi and Ofoefule, 1997).

In South East of Nigeria, the extract from *Landolphia owerrience* is used in the folklore treatment of venereal disease, colic diseases, teeth cleaning, curing and control of diabetes. The latex is drunk or used as an enema for intestinal worms, and in treatment of arrow poison. Preliminary photochemical tests on *Landolphia owerrience* have shown that it contains active cardio glycosides, saponins, tannins, flavonoids and steroids and also shows antimicrobial activities (Iwu 1993). The antimicrobial screening of *Landolphia owerrience* among other plants has shown that the extract inhibits *Escherichia coli, Bacillus subtilis, Candida albicans* and *Aspergillus niger* and the activities were linked to the presence of steroids, tannins and glycosides in the plants (Ebi and Ofoefule, 1997; Okeke *et al.,* 2001)

The liver is the central organ that co-ordinate and modulates most biochemical activities in the body. The metabolic activities of the liver are essential for providing fuel to the brain, muscle and other peripheral organs (Chang *et al*., 2004). Most compounds absorbed by the intestine go through the liver, which enables it to regulate the level of metabolites in the blood (Lehninger, 2005). The liver plays a central role in the regulation of lipid metabolism, detoxification and biotransformation of foreign compounds to more soluble forms for further breakdown and excretion (Hwang *et al*., 2002).

Alanine aminotransferase [ALT] activity rises in viral and toxic hepatitis and the degree and time course of its elevation parallel to those of Aspartate aminotransferase [AST] activity. An elevated ALT and alkaline phosphatase [ALP] activity also occurs in cirrhosis, extra hepatic biliary obstruction and hepatic metastasis, while inconsistent elevations occur in acute myocardial infarction and skeletal muscle disease (Jensen and Freese, 2009).

Diseases like severe burns, severe renal disease and chronic hepatitis and sarcoidosis cause rapid loss of plasma protein and hemoglobin. Lipid peroxidation plays a role in carcinogenesis and arteriosclerosis and by extension prevents damage to cells that result into disease condition (Hsieh *et al*., 2009).

Since the crude plant leaf extract of *Landolphia owerrience* is used for folklore treatment and management of various ailments: venereal disease, colic, diabetes, worm expulsion and teeth cleaning. This present study was conducted to investigate the effect of the plant leaf extract on the stability of the liver, vis-à-vis its effect on liver enzymes [ALT, AST and ALP], serum protein levels, hemoglobin and lipid peroxidation.

MATERIALS AND METHODS

Plant Material

The leaves of *Landolphia owerrience* were collected from the University campus where it is grown as ornamental plant; in January 2012. The plant was authenticated and taxonomically identified at the Department of Plant Science and Biotechnology, Abia State University, Uturu, Nigeria. Voucher specimen of the plant was deposited at the Departmental herbarium. The plant leaves were washed with distilled water to remove dirt and contaminants, and then sun dried.

Plant Extract

The dry leaf samples were milled into a fine powder using Arthur milling machine. 20g of the milled

leaf sample was soaked in 200ml of distilled water, and the mixture was left to stand for 48hrs with occasional stirring. Filtration was done with a muslin bag. The concentration of the extract was determined to be 27.2mg/ml.

Animals

Sexually matured adult albino rats (32 males and 32 females) of 6 weeks old and weighing between 185 to 200g were used for the investigation. The animals were kept in the laboratory under constant temperature (24±4°C) for at least one week before and throughout the experimental work. The animals were randomly divided into four groups of eight males and eight females each and housed in standard cages. The animals were allowed for food and water *ad libitum*. Approval for animal studies was obtained from the Animal Ethics Committee of College of Health Sciences, Abia State University, Uturu.

Group one animals served as control, and received (0.5ml) of normal saline which is the vehicle for the extract, while groups two, three and four received 20 mg/kg, 30 mg/kg and 40 mg/kg body weight of the plant extract respectively in 0.5ml sterile saline. The extract was administered once daily for 21 days.

Collection of Blood Sample

The animals were sacrificed under light chloroform anesthesia, and blood collected from the liver. The blood sample was centrifuged for 10min at 3000rev. to obtain a clear supernatant (serum) which was stored at -20°C until assayed for biochemical parameters.

Biochemical effects

ALT and AST

Assay of ALT and AST was done using Randox diagnostic kits. Determination was based on the principle described by Reitman and Frankel, (1957). The method is based on the determination of pyruvic acid as a product of the reaction catalyzed by alanine aminotransferase or as a product of decarboxylation of the oxaloacetate produced by aspartate aminotransferase catalyzed reaction. The assay procedure for ALT and AST are the same, except that for ALT, alanine citrate is added. The coloration produced with 2, 4 dinitrophenyl-hydrazine is read at 540nm on a spectrophotometer.

ALP

Alkaline phosphatase was determined using Randox diagnostic kits following the principle described by Neuman and Van Vreedenal, (1967). The assay is based on the action of alkaline phosphatase (ALP) on phenyl phosphate to liberate phenol and phosphate. The phenol released forms a chromogen with 4-aminoantipyrene in the presence of potassium ferrocyanide that absorbs at 540nm.

Total Protein

Total serum protein was determined by the Lowry method (1951). 1ml of each unknown protein solution (serum) was taken into 3ml of Biuret reagent. The mixture was warmed for 15min at 37^{o}C and allowed to cool. The absorbance of each test tube was read at 540nm.

Hemoglobin

Hemoglobin was determined according to the method described by Dacie and Lewis, 1990.

Lipid peroxidation

Lipid peroxidation was determined by the method of Wallin *et.al.,* (1993). Blood samples (0.5ml) were transferred to a test tube and 0.1ml of Triton X-100 was added and mixed properly. Next, 3ml of 30% TCA and 1ml of 0.6% TBA were added. The contents were shaken properly and the suspension was filtered. The clear filtrate (3ml) was mixed with 2ml of 0.6% TBA and heated for 15min in a boiling water bath. The mixture was allowed to cool and 2ml of chloroform was added. The mixture was centrifuged at 10,000g for 15min and the absorbance was read at 535nm. Lipid peroxidation products were extrapolated by a standard curve.

Statistical Analysis

Data obtained were subjected to two-way analysis of Variance (ANOVA) followed by Dennett's test to determine the statistical significance of the various changes in the parameters measured. SPSS software was used to analyze data. Values were considered significant when $p \leq 0.01$

RESULTS AND DISCUSSION

ALT concentration significantly increased ($p \leq 0.01$) in the test animals compared to control. (Table 1). There is also a non significant increase ($p \leq 0.01$) in ALT concentration for the male animals compared to the female animals as the dose of administered extract increased. The effect of the plant extract seems to be dose dependent as the enzyme concentration increased with increase in dose of plant extract administered.

Table 1 above also shows the variation in AST concentration in the test animals compared to the control. A significant increase ($p \leq 0.01$) is observed in the elevation of AST in test animals as the dose increased. The effect of the plant extract seem to be dose dependent as there was significant difference in enzyme concentration as the dose increased. There were no significant ($p \leq 0.01$) differences in enzyme concentration observed for the male and female test animals. The alkaline phosphatase activity in the test animals increased ($p \leq 0.01$) non-significantly with increase in dose of the extract compared with the control (Table 1). The males had non-significantly ($p \leq 0.01$) higher alkaline phosphatase activity compared to the females.

Table 2 shows the variations in total protein level in the test animals compared to control. Protein concentration increased significantly ($p \leq 0.05$) compared to control. There is no significant difference ($p \leq 0.05$) for the variation in protein concentration for the male and female albino rats. The effect of the plant extract seems to be dose dependent as increase in protein concentration is observed with increase in dose of extract administered. Hemoglobin concentration increased ($p \leq 0.01$) significantly in the test animals compared to the control (table 3). The increase is dose dependent. There was no significant ($p \leq 0.01$) difference in hemoglobin concentration between the male and female test animals. Lipid peroxidation levels decreased ($p \leq 0.01$) significantly in the test animals compared to the control. (Table 4). There are no significant ($p \leq 0.01$) difference in values for the male and the female rats. As the dose of administered extract increased there were significant ($p \leq 0.01$) reductions in lipid peroxidation values.

It is well known that the liver is the first target organ in toxicological prospects regarding its role in detoxification, biotransformation and excretion of xenobiotic. After enteric uptake of injurious materials, it is the first organ to be exposed to such hazards via the portal circulation (Ross and Kasum, 2002). The marker enzymes assayed are specifically located in some cell;

Table 1: Liver enzymes conc. (U/L)

Animal (n=5)	Group 1		Group 2		Group 3		Group 4	
Conc. of extract	Control		20mg/kg		30mg/kg		40mg/kg	
Sex	M	F	M	F	M	F	M	F
ALT	19.2±0.26	16.2±0.44	19.5±0.35	16.4±0.11	19.6±0.01	16.5±0.04	19.6±0.52	16.5±0.32
AST	16.3±0.05	13.3±0.21	16.4±0.25	13.5±0.13	16.5±0.06	13.5±0.71	16.5±0.04	13.6±0.46
ALP	23.4±0.06	20.5±0.29	23.6±0.02	20.6±0.16	23.6±0.24	20.6±0.93	23.5±0.16	20.7±0.46

***Values are mean ± SD of triplicate determinations M =Male, F=Female**

Table 2: Total Protein conc. (mg/dl)

Animal (n=5)	Group 1		Group 2		Group 3		Group 4	
Conc. of extract	Control		20mg/kg		30mg/kg		40mg/kg	
Sex	M	F	M	F	M	F	M	F
Σ	10.25±0.2	9.6±0.7	14.5±0.4	13.5±0.1	15.0±0.05	14.7±0.5	16.4±0.3	15.7±0.6

***Values are mean ± SD of triplicate determinations M =Male, F=Female**

however, they can leak into the serum or other parts as a result of injury to the cell where they are located (Adesokan and Akanji, 2003). The measurement of the various enzyme activities in the tissues and body fluids play a significant role in disease investigation, diagnosis and detection of tissue cellular damage (Malomo, 2000). The ALT concentration was elevated in all the test animals (Table 1). The increase in ALT concentration were non-significant ($p \leq 0.05$) compared to the control. The effect of the plant extract also seems to be dose dependent, as the increase in plant extract concentration resulted in slight increase in enzyme concentration. There were significant ($p \leq 0.05$) differences in ALT variation for the male and female animals, as dose of the plant extract increased. An elevated ALT level occurs in cirrhosis, extra hepatic biliary obstruction and hepatic metases (Effraim *et al.,* 2003). Inconsistent elevations also occur in acute myocardial infarctions and skeletal muscule disease. Normal activity of ALT is 1-20u/l, but in this study values ranged from 19.5±0.35u/l to 19.6±0.52 for males and 16.4±0.11u/l to 16.5±0.03u/l for females

AST concentration was also non-significantly ($p \leq 0.05$) elevated from 16.3±0.05u/l and 13.3±0.01u/l for the male and female control animals respectively, between 16.4±0.25u/l and 16.5±0.04u/l for the males and between 13.5±0.13 and 13.6±0.4 for females (Table 1). The slight increase in AST concentrations seems to be dose dependent, as elevations occurred as the plant extract dose increased. Normal activity of AST is 1-15u/l, but in this study AST elevation was observed to be from 16.3±0.05u/l and 13.3±0.01u/l for male and female animals respectively between 16.4.0±0.25 and 16.5±0.04 for males and between 13.5±0.13 and 13.6±0.04 for females administered the various concentration of the plant extract. ALP showed non-significant ($p \leq 0.05$) increase compared to control. Elevation of ALP is found in large number of disorders such as biliary cirrhosis. Although it is found both in the liver and the bile, it leaks into the blood stream in a manner similar to that of ALT and AST. ALP is found in other organs such as bone, placenta and intestine (Ranjna, 1996).

The plant leaf extract did not change significantly any of the liver enzymes including ALT, AST and ALP. This result showed that the leaf extract of *L .owerrience* does not have any apparent toxicity on the liver of rats. Green leafy plants are usually associated with hepatoprotective properties (Weber *et al*., 2003; Oboh, 2005; Roy *et al*., 2006, Iweala and Obidoa, 2010).

Table 3: Hemoglobin concentration (g/dl)

Animal (n=5)	Group 1		Group 2		Group 3		Group 4	
Conc. of extract	Control		20mg/kg		30mg/kg		40mg/kg	
Sex	M	F	M	F	M	F	M	F
Σ	9.8±0.50	9.5±0.41	11.7±0.54	11.0±0.31	12.1±1.05	12.4±1.12	12.8±0.73	12.5±0.65

***Values are mean ± SD of triplicate determinations M =Male, F=Female**

Table 4: Lipid peroxidation level [TBARS] (mg/ml)

Animal (n=5)	Group 1		Group 2		Group 3		Group 4	
Conc. of extract	Control		20mg/kg		30mg/kg		40mg/kg	
Sex	M	F	M	F	M	F	M	F
Σ	5.02±0.25	4.50±0.21	4.52±1.01	4.17±0.14	3.83±0.21	3.62±0.15	3.38±0.35	3.24±0.02

***Values are mean ± SD of triplicate determinations M =Male, F=Female**

Total protein levels were also significantly elevated ($p \leq 0.05$) (Table 2) from 10.25±0.2mg/l and 9.6±0.7mg/l for the male and female animals respectively between 14.5±0.4mg/l and 16.4±0.3mg/l for the males and between 13.5±0.1mg/l and 16.7±0.6mg/l for the females. The effect of the plant extract is also dose dependent, and the increase in protein concentration with increase in dose is significant ($p \leq 0.05$). Essentially, all the albumin and fibrinogen of the plasma protein and about 50 to 80% of the globulins are formed in the liver. The leaves of *L. owerrience* plant are rich in protein, essential amino acids and mineral elements (Ebi and Ofoefule, 1997). The serum protein of the experimental rats was significantly increased which is a reflection of the digestibility and hence availability of protein constituents of leaves of *L. owerrience* (Ross and Kasum, 2002).The elevation of serum protein could enhance the overall physiological function of the animals (Iweala and Obidoa, 2010).

Hemoglobin concentration significantly increased ($p \leq 0.05$) in the animals (Table 3). The plant extract most probably had no adverse effect on the red blood cells. The phytochemical constituents of *L. owerrience* which include flavonoids and phytosterol (Iwu, 1993) are possible candidates that increase white blood cells. The mineral and vitamin contents of *L. owerrience* (Ebi and Ofoefule, 1997) include haematinic factors such as iron which play a major role in the synthesis of haemoglobin (Alada, 2000; Tindal, 1965). This could explain the increase in haemoglobin seen in the experimental rats.

Lipid peroxidation levels significantly decreased ($p \leq 0.01$) in the test animals compared to control. (Table 4). The biological consequences of lipid peroxidation include structural damage to membranes and essential biomolecules. It is an underlying cause of degenerative diseases (Koba *et al*., 2002). In this study the plant extract had significant effect on lipid peroxidation and may not alter essential functions of cells that may lead to death (Hsieh *et al.,* 2009). The reduction in lipid peroxidation could be attributed to the presence of antioxidant phytochemicals including flavonoids and anthocyanidins in the *L. owerrience* whose phenolic structure favour their reaction with free radicals and reactive oxygen species (ROS) (Miller and Ruiz-Larrea, 2002). This reaction with ROS protects lipids from peroxidation and by extension prevents damage to cells. The reduction of lipid peroxidation by flavonoid prevents DNA damage, a critical event in most disease. (Cai *et al.,* 1997; Subashree *et al*., 2009; Mohd-Esa *et al*., 2010; MohanaSundaram *et al*., 2011).

Ethno-medicine practitioners'claims that it is effective to use the plant extracts either crude aqueous extract or the alcoholic extract for the treatment and management of various diseases. They claim it as effective in treating and managing venereal disease, colic disease, and control of diabetes and as enema for intestinal worms. The strong activity of the ethanolic extracts against known etiologic agents of diseases traditionally treated with *L. owerrience* root of similar preparations provides scientific justification for the use of the herb in ethnomedical practice in Nigeria.

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REFERENCES

Adesokan AA and Akanji MA. 2003. Effect of administration of aqueous extract of *Enantia chlorantha* on the activities of some enzymes in the small intestine of rats. Nigeria J. Biochem. Molec. Biol., 18(2):103-105.

Alada ARA. 2000. The haematological effect of *Telfairia occidentalis* diet preparation. Afr. J.Biomed. Res: 185-186.

Burkill HM. 1994. The useful plants of tropical West Africa. (2nd edition). Royal Botanic Gardens, Kew, ISBN: 0947643567

Cai Q, Rahan RO and Zang R. 1997. Dietary flavonoids, quercetin, luteolin and genistein, reduce DNA damage and lipid peroxidation and quench free radicals. *Cancer Lett.* 119:99-108

Chang JS, Chiang LC, Hsu FF and Lin CC. 2004. Chemoprevention against hepatocellular Carcinoma of *Comus officinalis* - invitro. *Am. J. Chin. Med*., 32(5):717-725

Dacie JV and Lewis SM. 1990. Practical Hematology. Churchill Livingstone New York 34.

Ebi GC and Ofoefule SI. 1997. Investigation into the folkloric antimicrobial activities of *Landolphia owerrience. Phyt. Res*., 11:149-151.

Effraim KD, Jacks TW and Sodipo OA. 2003. Histopathological studies on the toxicity of *Ocimum gratissimum* on some organs of Rabbits: *African J. Biomed., Res*. 6:21-25.

Hsieh YS, Kuo WH, Lin TW, Chang HR, Lin TH, Chen PN and Chu SC. 2009. Protective effects of Berberine against Low-Density Lipoprotein (LDL) oxidation and oxidized LDL- Induced cytotoxicity on endothelial cells. *J Agric Food Chem.*, 55:10437-1044

Hwang JM, Wang CJ, Chou FP, Tseng TH, Hsieh YS, Lin WL and Chu CY. 2002. Inhibitory effect of berberine on tert-butyl hydroperoxide-induced oxidative damage in rat liver. *Arch Toxicol.,* 76:664-670.

Iweala EEJ and Obidoa O. 2010. Studies on Some Biochemical and Histological Changes Associated with Long Term Consumption of Leaves of *Ocimum gratissimum L.* in Male Rats. *Am. J. Food Technol*., 5:376-384

Iwu MM. 1993. Handbook of African Medicinal Plants. CRC Press, Boca Raton, Ann. Arbor and London, Tokyo.

Jensen JE and Freese D. 2009. Liver Function Tests. Colorado Center for Digestive disorders 205s.Suite A Longmont Co. 80501. 151-163.

Koba K, Akahoshi A, Yamasaki M, Tanaka K, Yamada K, Iwata T, Kamegai T, Tsutsumi K and Sugano M. 2002. Dietary conjugated linolenic acid in relation to CLA differently modifies body fat mass and serum and liver lipid levels in rats. *Lipids*, 37:343-350.

Lehninger AL, Nelson OL and Cox MM. 2005. Text Book of Biochemistry. (6th edition) Worth Publishers. NY USA 450.

Lowry OH, Rosebrough NJ, Farr AL and Randall RJ. 1951. Protein measurement with the folin phenol reagent. *J. Biol. Chem*., 193:265-275

Malomo SO. 2000. Toxicological implication of Ceftriaxome administration in rats. *Nig. J. Biochem. Mol. Biol*., 15(1):33-35

Miller NJ and Ruiz-Larrea MB. 2002. Flavonoid and other plant phenols in diet: Their significance as antioxidants. *J. Nutr. Environ. Med*., 12:39-51.

Mohana Sundaram, Sivakumar Karthikeyan, Magesh Gopinath, Sheeladevi Thirumalai, and Pennarasi Prasanna. 2011. Studies on phytochemicals, antibacterial and Antioxidant effects of leaf extracts of lamprachaenium microcephalum.. Journal of Research in Biology 4: 279-284.

Mohd-Esa N, Hern FS, Ismail A and Yee CL. 2010. Antioxidant activity in different parts of roselle (*Hibiscus sabdariffa*) extracts and potential exploitation of their seeds. *Food Chem.,* 122:1055-1060.

Neuman HV and Vreedenal M. 1967. An improved alkaline phosphatase determination with p-nitrophenol phosphate. *Clinica Chimica Acta*.17(2):183-187.

Oboh G. 2005. Hepatoprotective property of ethanolic and aqueous extracts of *Telfairia occidentalis* (Fluted pumpkin) leaves against garlic-induced oxidative stress. *J. Med. Food* 8:560-563

Okeke MI, Iroegbu CU, Eze EN, Okoli AS and Esimone CO. 2001. Evaluation of extracts of the root of *Landolphia owerrience* for antibacterial activity. *J. Ethnopharmacol*., 78(2-3):119-27

Person JGM, Dilst FJH, Kuijpers RP, Leenwerberg AJM, Vonk GJA and Van-Dilst FJH. 1962. The African species of *Landolphia*. P.Beaux Series of Revisions of Apocynaceae. Xxxiv Wageningen Agricultural University Paper No.92. 323.

Ranjna O. 1996. Practical Clinical Biochemistry, Methods and Interpretations (2nd edition) Jaypee Brothers Medical Publishers. India 100-109

Reitman S and Frankel SL. 1957. Determination of ALT and AST concentrations in serum. *Am. J. Chem Path*., 28:56

Ross JA and Kasum CM. 2002. Dietary flavonoids: Bioavailability, metabolic effects and safety. *Ann. Rev. Nutr*., 22:19-34

Roy CK, Kamath JV and Asad M. 2006. Hepatoprotective activity of Psidium guajava Linn leaf extract. *Ind. J. Exp. Biol*., 44:305-311

Subashree B, Baskar R, Laxmi KR, Lijina SR and Rajasekaran P. 2009. Evaluation of antioxidant potential in selected green leafy vegetables. *Food Chem*., 115:1213-1220.

Tindal HD. 1965. Fruits and vegetables of West Africa. (1st Edition). Food and Agriculture Organization, USA

Wallin B, Rosengren B, Shertzer HG and Camejo G. 1993. Lipoprotein oxidation and measurement of thiobarbituric acid reacting substances formation in a single microtiter plate: its use for evaluation of antioxidants *Anal. Biochem.,* 208:10-15.

Weber LW, Boll M and Stampfl A. 2003. Hepatotoxicity and mechanism of action of haloalkanes: carbon tetrachloride as a toxicological model. *Crit. Rev. Toxicol*., 23:105-136.

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