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Original Research Article

Evaluation of sub-acute toxicity profile of methanol extract of *Adansonia digitata* leaves in Wistar rats

[1*]Chima M.U., [2]Ozioko C. A., [1]Onoja S. O., [3]Odo R. I., [4]Udeh N. E., [5]Igwe A. O., [6]Ezeh G. C., [7]Ezeh C., [7]Ogemdi M. & [7]Omeh Y. N.

[1]Department of Veterinary Physiology and Pharmacology, Michael Okpara University of Agriculture, Umudike, Abia State, [2]Department of Veterinary Microbiology, Michael Okpara University of Agriculture, Umudike, Abia State, [3]Department of Veterinary Physiology and Pharmacology, University of Nigeria Nsukka, Enugu State, [4]Department of Veterinary Biochemistry and Animal Health in Production, Michael Okpara University of Agriculture, Umudike, Abia State, [5]Department of Veterinary Pathology, Michael Okpara University of Agriculture, Umudike, Abia State, [6]Department of Agriculture, Alex Ekwueme Federal University Ndufu Alike Ikwo, Ebonyi State, [7]Department of Veterinary Biochemistry, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria

*Corresponding author: chima.macnissi@mouau.edu.ng, +234803600090

ABSTRACT

This study evaluated the sub-acute toxicity profile of methanol extracts of *Adansonia digitata* leaves on Wistar rats. Cold maceration method was used to prepare the methanol extract of *Adansonia digitata* leaves (MEADL). Twenty-four (24) adult male Wistar rats were randomly divided into 4 groups of 6 rats each. Group A (control) received 5% dimethylsufoxide (DMSO) at 5 ml/kg, while groups B -D received MEADL at 100, 200 and 400 mg/kg, respectively. All treatments were administered orally and once daily for 28 consecutive days. The weight, haematological and lipid profile, antioxidant status as well as liver and kidney function tests were evaluated. The extract (200 and 400 mg/kg) caused a significant ($p<0.05$) reduction in the triacylglycerol and very low density lipoprotein cholesterol levels of the treated groups when compared with the control group. The platelet count of the MEADL treated groups were significantly ($p < 0.05$) elevated when compared with the control group. The extract did not cause significant ($p > 0.05$) change in the serum markers of liver and kidney function test, but produced histopathological changes in the kidney and liver section of the treated rats in a dose-dependent manner. These findings justify its use in folkloric medicine for treatment of several diseases, but caution should be exercised as it is associated with histopathological changes in the liver and kidney at high doses.

.**Keywords:** *Adansonia digitata*, haematology, sub-acute toxicity, Wistar rats

INTRODUCTION

Adansonia digitata Linn also called the Baobab tree, is a deciduous tree commonly found in the hot, dry savannah of sub-saharan Africa. It is also referred to as the "tree of life" due to its longevity (it can live for hundreds of years) as a result of its water-holding capacity and its several ethnomedicinal and nutritional uses (Wickens & Lowe, 2008). It is a massive tree that belongs to the family Malvaceae, sub family Bombacaeae. It has a large trunk, with diameter of over 10 m and can grow to a height of 25 m (Kabore *et al.*, 2011). Every part of the tree has been reported to be very useful (Igboeli *et al.*, 1997). The leaves, bark and fruits are used in several African cultures as food condiments and for fibre. They are also used as medicinal herbs which is the reason the tree is sometimes referred to as the *small pharmacy* (Vertuani *et al*, 2002). The powdered leaves serve as a tonic and possess antihistamine and anti-tension properties (Irondi *et al.*, 2016). The leaves also possess antioxidant (Vertuani *et al.*, 2002), anti-inflammatory and anti-viral properties (Vimalathan and Hudson, 2009). The fruit pulp is used as an antipyretic, anti-dysenteric, diaphorectic, immune-stimulant, anti-inflammatory, analgesic and probiotic agent (De Caluwe *et al.*, 2010; Kabore *et al.*, 2011). The stem bark is used to clean wounds, promote weight gain and growth in infants (De Caluwe *et al.*, 2010). These numerous medicinal uses have triggered huge research and pharmaceutical interests on

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the plant in recent times. There is paucity of information concerning the sub-acute and acute toxicity of *Adansonia digitata* leaf extracts in biological systems. This study evaluated the sub-acute toxicity profile of methanol extracts of *Adansonia digitata* leaves in Wistar rats.

MATERIALS AND METHODS

PLANT COLLECTION AND IDENTIFICATION

The plant material was collected from the Michael Okpara University of Agriculture, Umudike environment. Prof. M. C. Dike of College of Natural Resources and Environmental Management, Michael Okpara University of Agriculture, Umudike, Nigeria, identified the leaves sample. A voucher sample (MOUAU/VPP/2017/04) was kept at the Department of Veterinary Physiology and Pharmacology herbarium.

Plant preparation and extract

The leaves were air dried and extracted according to the method described by Nwafor *et al*., (1996) with slight modification. The dried leaves were pulverized with a grinding machine to obtain a coarse powder. 342.41 g of the powder was soaked in a mixture (4:1) of methanol and distilled water for 72 h and stirred intermittently. The extract was filtered using Whatman No 1 filter paper and concentrated in a hot air oven at 40°C. The methanol extract of *Adansonia digitata* leaves (MEADL) was then stored in a refrigerator at 4 °C throughout the duration of the experiment.

HANDLING OF EXPERIMENTAL ANIMALS

Male Wistar rats weighing between 103-171 g were obtained from University of Nigeria, Nsukka. The rats were housed at the animal house, Department of Veterinary Physiology and Pharmacology, Michael Okpara University of Agriculture, Umudike, Nigeria. The animals were kept in aluminium cages at room temperature of 24± 3°C under a 12 h dark/light cycle. They were fed with standard rat pellets and allowed access to water *ad libitum*. The study was performed in accordance with the ethical guidelines stipulated by the ethical committee of Michael Okpara University of Agriculture, Umudike, Nigeria and was assigned the following ethical approval number; MOUAU/CVM/REC/202209. These guidelines were in accordance with the international accepted guidelines for laboratory animal use and care.

EXPERIMENTAL DESIGN

Twenty-four (24) adult male Wistar rats were randomly divided into 4 groups of 6 rats each. Group A (control) received 5% dimethyl sufoxide (DMSO) at 5 ml/kg, while groups B-D received MEADL 100, 200 and 400 mg/kg, respectively. All treatments were administered orally and once daily for 28 consecutive days. Their weights were recorded weekly and after the last treatment, the animals were fasted for 16 hours and the blood sample was collected through ocular puncture into a plain and EDTA containing containers. The blood in EDTA container was used for hematology analysis, while the blood in the plain container was allowed to clot and the serum harvested was used for antioxidant and biochemical analyses.

DETERMINATION OF THE LIPID PEROXIDATION (LPO) IN SERUM

The level of the thiobarbituric acid reactive substance (TBARS) and malondialdehyde (MDA) production was measured by the modified method described by Draper & Hadley (1990). The serum (50 µl) was deproteinized by adding 1ml of 14% trichloroacetic acid (TCA) and 1 ml of 0.6% thiobarbituric acid. The mixture was heated in a water bath for 30 minutes. After centrifugation at 2000 rpm for 10 minutes, the absorbance of the coloured product (TBARS) was measured at 535 nm with ultraviolet spectrophotometer. The concentration of TBARS was calculated using the molar extinction coefficient of malondialdehyde ($1.56 \times 10^5\ M^{-1}cm^{-1}$) using the formula below:

$A = \sum CL$

Where A = Absorbance, $\sum$ = Molar coefficient, C = Concentration and L= path length.

The result was expressed in nmol/mg of protein.

ESTIMATION OF SUPEROXIDE DISMUTASE (SOD) ACTIVITY

Superoxide dismutase activity was assayed as described by Onoja *et al.*, (2014). In this method, xanthine oxidase system was used to generate a peroxide flux and nitrobluetetrazolium (NBT) was used as an indicator of superoxide production. SOD activity was then measured by the degree of inhibition of the reaction unit enzyme providing 50 % inhibition of NBT reduction. Results were expressed per g protein.

ESTIMATION OF CATALASE ACTIVITY

The catalase activity in serum was determined using the modified method (Atawodi, 2011). The method is briefly described as follows: serum (10 µl) was added to a test tube containing 2.80 ml of 50 mg potassium phosphate buffer (pH 7.10). The reaction was initiated by adding 0.1ml of fresh 30 mm hydrogen peroxide and was measured at 240 nm for 5 minutes on a spectrophotometer. A molar extinction coefficient of $0.04/M^{-1}cm^{-1}$ was used to calculate catalase activity.

DETERMINATION OF BIOCHEMICAL PARAMETERS

A commercially available reagent kit (Randox Diagnostic Laboratories, United Kingdom) was used to evaluate the serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP)

activities as well as serum total bilirubin, total protein, albumin, urea creatinine, total cholesterol, triacylglycerol and high-density lipoprotein cholesterol (HDL-C) concentration. The assay was carried out as instructed by the manufacturer. Serum low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein-cholesterol (VLDL-C) were calculated using Friedewald's equation as follows:

LDL-C = TC–HDL-C+ TG/5; VLDL-C = (TG/5) (Onoja *et al*., 2018).

DETERMINATION OF HEMATOLOGICAL INDICES

Hematological analysis including total white blood cell count (TWBC), red blood cell count (RBC), hemoglobin count (Hb) and packed cell volume (PCV) were carried out on the blood collected in the EDTA bottles using improved Neubauer hemocytometer and Wintrobe's hematocrit as described by Dacie and Lewis (1991). The mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were determined according to the method decribed by Jain (1986).

DATA ANALYSIS

Data were expressed as mean ± standard error of the mean (mean ± SEM). Statistical analysis was performed by one way-analysis of variance (one way ANOVA) at 95 % confidence level using SPSS statistical software. Mean differences were separated using Least Significant Different (LSD).

RESULTS

EFFECTS OF MEADL ON LIPID PROFILE

The effect of MEADL on lipid profile is presented in Table i. The extract did not produce any significant ($p>00.5$) difference in the serum cholesterol and LDL-C level in the treated groups when compared with the control group. The extract (200 and 400 mg/kg) caused a significant ($p<0.05$) reduction in the triacylglycerol and VLDL-C levels of the treated groups when compared with the control group. The extract (100, 200 and 400 mg/kg) treatment produced a significant ($p<0.05$) increase in the serum level of HDL-C of treated rats when compared with the control.

EFFECTS OF MEADL ON ANTIOXIDANT PARAMETERS

The effect of MEADL on *in vivo* antioxidant activity is represented in Table ii. The extract (200 and 400 mg/kg) caused a significant ($p<0.05$) dose-dependent decrease in the activities of SOD of the treated groups when compared with the control group. However, at 100 mg/kg the extract did not cause a significant ($p>0.05$) decrease in the SOD of the treated group when compared with the control group. The extract (100, 200 and 400 mg/kg) produced a significant ($p<0.05$) dose-dependent reduction in catalase activities in the treated groups when compared with the control group. The extract (200 mg/kg) treatment produced a significant ($p<0.05$) decrease in the MDA level of the treated groups when compared with the control group.

EFFECTS OF MEADL ON LIVER FUNCTION MARKERS

The effects of MEADL treatment on serum enzyme markers of liver function in the rats is represented in Table iii. The extract (100 mg/kg) caused a significant ($p<0.05$) increase in the serum AST activity of the treated group when compared with the control group. The extract treatment did not produce any significant ($p>0.05$) difference in the serum ALT and ALP activities as well as the serum levels of total protein, albumin, and globulin of the treated groups when group compared with the control group.

EFFECTS OF MEADL ON KIDNEY FUNCTION MARKERS

The effect of MEADL treatment on serum levels of creatinine and urea is presented in Table iv. The extract did not produce any significant ($p>0.05$) change in the serum creatinine level in the treated groups when compared with the control group. The extract (400 mg/kg) caused a significant ($p<0.05$) increase in the serum Urea level of the treated groups when compared with the control group.

EFFECTS OF MEADL ON HEMATOLOGICAL PROFILE

The effects of MEADL treatment on the hematological profile is presented in Table v. The extract did not produce a significant ($p > 0.05$) change in the TWBC, RBC, HB, PCV, MCV, MCH and MCHC levels of the treated groups when compared with the control group. The platelet count of the MEADL treated groups were significantly ($p < 0.05$) elevated when compared with the

Table I: Effects of MEADL on lipid profile

MEADL = methanol extract of *Adansonia digitata* leaves, CHOL = total cholesterol, TAG = triacylglycerol, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, VLDL-C = very low-density lipoprotein cholesterol

Treatment	CHOL (mg/dL)	TAG (mg/dL)	HDL-C (mg/dL)	VLD-C (mg/dL)	LDL-C (mg/dL)
5%DMSO, mg/kg	58.60 ± 5.91	48.18± 1.41	3.59 ± 0.33	9.64 ± 3.07	45.38 ± 6.12
ADE 100, mg/kg	63.38 ± 2.46	50.00± 0.42	11.09 ± 3.78*	10.00 ± 2.61	42.29 ± 6.92
ADE 200, mg/kg	50.00 ± 1.41	19.09 ± 8.05*	7.50 ± 1.72*	3.82 ± 1.61*	38.68 ± 3.97
ADE 400, mg/kg	62.74 ± 7.02	16.36 ± 1.08*	17.28 ± 6.95*	3.27 ± 1.30*	42.18 ± 7.44

*p<0.05 when compared with the control group,

control group.

Table II: Effects of MEADL on antioxidant parameters

MEADL = methanol extract of *Adansonia digitata* leaves, SOD = superoxide dismutase, CAT = catalase, MDA = malondialdehyde

Treatment	SOD (U/g protein)	CAT (µmol/g protein)	MDA (µmol/g protein)
5% DMSO, 5ml/kg	14.32 ± 1.01	14.13 ± 1.07	1.15 ± 0.27
ADE 100, mg/kg	11.37 ± 1.84	6.31 ± 1.48*	0.77 ± 0.07
ADE 200, mg/kg	5.91± 1.81*	6.10 ± 2.23*	0.42 ± 0.21*
ADE 400, mg/kg	5.61 ± 1.64*	5.78 ± 1.86*	0.62 ± 0.19

*p<0.05 when compared with the control group

Table III: Effects of MEADL on Liver function markers

MEADL = methanol extract of *Adansonia digitata* leaves, ALT = alanine aminotransferase, AST = aspartate aminotransferase, ALP = alkaline phosphatase, TP = total protein, ALB = albumin, GLB = globulin

Parameters	**5% DMSO, 5 mg/kg**	**ADE, 100 mg/kg**	**ADE, 200 mg/kg**	**ADE, 400 mg/kg**
TP (g/dl)	5.00 ± 0.19	5.29 ± 0.23	5.50 ± 0.40	5.30 ± 0.34
ALB (g/dl)	2.76 ± 0.05	2.76 ± 0.11	2.82 ± 0.04	2.80 ± 0.13
GLB (g/dl)	2.24 ± 0.23	2.53 ± 0.12	2.68 ± 0.38	2.51 ± 0.31
AST (U/L)	18.08 ± 3.12	31.03 ± 4.47*	15.03 ± 2.55	16.70 ± 1.60
ALT (U/L)	14.20 ± 0.69	11.60 ± 1.54	17.00 ± 3.29	15.58 ± 1.31
ALP (U/L)	15.60 ± 3.03	17.44 ± 1.67	19.65 ± 1.67	20.63 ± 1.97

*P < 0.05 when compared with the control

Table IV: Effects of MEADL on kidney function markers

MEADL = methanol extract of *Adansonia digitata* leaves

Treatment	**Creatinine (mg/dL)**	**Urea (mg/dL)**
5% DMSO, 5 ml/kg	0.71 ± 0.01	31.16 ± 4.33
ADE, 100 mg/kg	0.81 ± 0.04	24.11 ± 2.69
ADE, 200 mg/kg	0.76 ± 0.03	22.63 ± 2.81
ADE, 400 mg/kg	0.77 ± 0.07	41.99 ± 3.01*

*p < 0.05 when compared with the control group

HISTOPATHOLOGY

The photomicrograph section of the liver is shown in Figure 1. The liver section of MEADL 100 mg/kg treated group showed area of mild inflammatory cells infiltration in the hepatic parenchyma and mild bile duct proliferation. The liver section of MEADL 200 mg/kg treated group showed area of severe proliferation and hyperplasia of the bile duct and fibrosis of the portal canal. The liver section of MEADL 400 mg/kg treated group showed area of severe proliferation and hyperplasia of the bile duct and multifocal extensive necrosis of the hepatocytes.

The photomicrograph section of the kidney is shown in Figure 2. The kidney section of MEADL 100 mg/kg treated group showed moderate congestion of the peritubular capillaries and detachment of the epithelial lining of the tubules from the basement membrane. The kidney section of MEADL 200 mg/kg treated group showed multifocal extensive coagulative necrosis of the renal tubule and the glomerulus (glomerulopathy). The kidney section of MEADL 400 mg/kg treated group showed severe coagulative necrosis of the glomerulus (glomerulopathy) and renal tubules as well as venous congestion, arteritis, and fibrosis.

DISCUSSION

The sub-acute profile of methanol extract of *Adansonia digitata* leaves was evaluated in Wistar rats. MEADL treatment led to a significant decrease in triacyglycerol and VLDL-C, and elicited an increase in HDL-C. These effects can be attributed to the presence of bioactive phytochemicals such as flavonoids in the extract. These finding agree with the findings of Ngatchic *et al.* (2020) who reported that in rats treated with different fractions of *Adansonia digitata*

Table V: Effects of MEADL on haematological profile

MEAD; methanol extract of Adansonia digitata leave, TWBC; total white blood cell, HB; haemoglo
RBC; red blood cell, PCV; packed cell volume, MCV; mean corpuscular volume, MCH; mean corpuscular volume, MCH = mean corpuscular haemoglobin, MCHC = mean corpuscular hemoglobin concentration

Parameter	**5% DMSO, 5 ml/kg**	**ADE, 100 mg/kg**	**ADE, 200 mg/kg**	**ADE, 400 mg/kg**
TWBC ($x10^3$/µL)	15.47 ± 1.20	14.77 ± 2.41	16.43 ± 3.66	17.53 ± 3.23
HB (g/dL)	13.30 ± 0.75	12.60 ± 0.26	13.33 ± 0.07	13.70 ± 0.62
RBC ($x10^6$/µL)	7.40 ± 0.35	6.94 ± 0.03	7.75 ± 0.22	8.00 ± 0.20
PCV (%)	43.70 ± 3.11	41.57 ± 1.20	44.77 ± 0.98	45.30 ± 1.39
MCV (fL)	58.97 ± 1.77	59.93 ± 1.52	57.90 ± 1.40	56.57 ± 0.38
MCH (pg)	17.90 ± 0.21	18.10 ± 0.32	17.17 ± 0.55	17.43 ± 0.71
MCHC (g/dL)	304.33 ± 6.33	302.67 ± 2.33	297.67 ± 7.84	306.67 ± 9.13
Platelets ($x10^3$/µL)	377 ± 45.21	541.33 ± 34.79*	619.00 ± 27.43*	553.00 ± 11.36*

*p < 0.05 when compared with the control group

pulp powder particles, there was a significant decrease in total cholesterol, LDL-cholesterol and an increase in HDL-cholesterol compared tocontrol. Abdelgadir *et al.* (2019) also reported a significant decrease in triglyceride level, LDL-C and cholesterol level in ethanol extracts of *Adansonia digitata* pulp. Flavonoids have been reported to have antihyperlipidemic activity (Ngatchic et al., 2020). The mechanology of the antihyperlipidemic activity include increasing fecal evacuation of cholesterol, triglycerides and complex bile salts, blocking the synthesis of cholesterol by inhibiting 3-hydroxy-3-methylglutaryl coenzyme A (HMG-COA) reductase and suppressing the transcription gene responsible for fatty acid synthesis.

Superoxide dismutase (SOD) and catalase (CAT) constitute the first line of antioxidant defense system in the body (Ighodaro and Akinloye, 2017). SOD catalyzes the breakdown of two molecules of superoxide anion to hydrogen peroxide (H_2O_2) and molecular oxygen (O_2), thereby rendering the potentially hazardous superoxide anion less harmful. Catalase catalyzes the breakdown of two molecules of hydrogen peroxide (H_2O_2) to water (H_2O) and molecular oxygen thereby completing the detoxification process initiated by SOD. In the present study, it was observed that the extract treatment (200 and 400 mg/kg) caused a significant increase in SOD and CAT activities when compared with the control. This is in accordance with the report of Ngatchic *et al.*(2020) who reported an increase in enzymatic activities of SOD and CAT in rats treated with <50 µm particle size of *Adansonia digitata* pulp powder and Ebaid *et al.* (2019) who reported an increase in CAT and SOD levels in *Adansonia digitata* leaf extract treated diabetic rats. Phenolic compounds contained in MEADL have been reported to play a role in improving the synthesis of antioxidant enzymes which in turn protect cells against reactive oxygen species (Althwab *et al*., 2019).

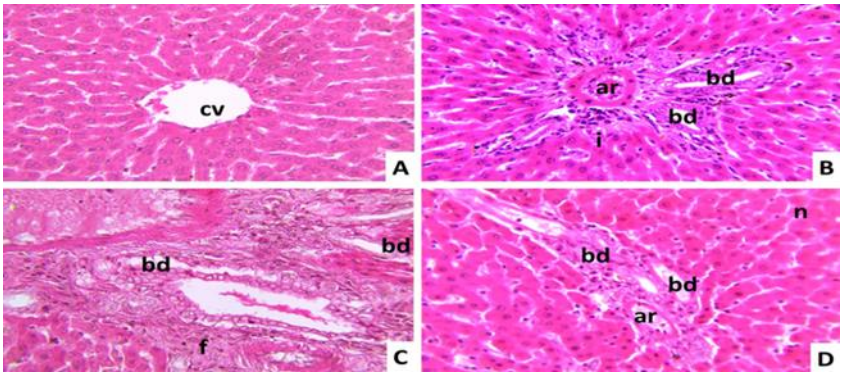

Figure I: Photomicrograph of sections of the liver of rats treated with MEADL (H&E, × 400).

A = 5% dimethylsufoxide (DMSO), 5 ml/kg treated group, B = MEADL 100 mg/kg treated group, C = MEADL 200 mg/kg treated group, D = MEADL 400 mg/kg treated group, "ar" shows the artery, "f" shows areas of fibrosis, "bd" shows bile ducts, "cv" shows the central vein, and "n" shows area of necrosis, "i" shows area of inflammatory cell infiltration

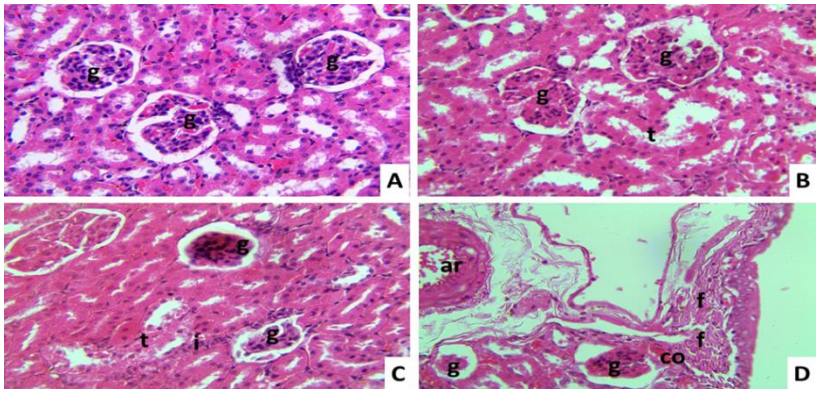

Figure II: Photomicrograph of sections of the liver of rats treated with MEADL (H&E, x400).

A = 5% dimethylsufoxide (DMSO), 5 ml/kg treated group, B = MEADL 100 mg/kg treated group, C = MEADL 200 mg/kg treated group, D = MEADL 400 mg/kg treated group, "ar " shows the artery, "f" shows area of fibrosis, "g" shows the glomerulus, "t" shows the tubules, "co" shows area of venous congestion, "i" shows area of inflammatory cell infiltration

Free radicals are responsible for the lipid peroxidation that occur in the cells of an organism. Malondialdehyde (MDA) is one of the final products of lipid peroxidation in cells. Therefore, excessive production of MDA is caused by an increase in free radicals. In the present study, MEADL(200 mg/kg) treatment caused a significant ($p<0.05$) decrease in MDA production. This concurs with the findings of Ebaid *et al.* (2019) who reported a significant decrease in MDA level of diabetic rats treated with MEADL compared with control and Ngatchic *et al.* (2020) who reported a decrease in MDA level in rats treated with <50 µm granules of *Adansonia digitata* pulp powder when compared with rats treated with the unsieved powder. These reduction in MDA levels by MEADL could be due to its rich flavonoids content (Yakubu *et al*., 2019; Ebaid *et al*., 2019). Studies have shown that flavonoids have the capacity to trap free radicals, which gives them an inhibitory effect on the peroxidation of membrane lipids. They also prevent the production of free radicals via their ability to chelate pro-oxidants metals through a process known as Fenton reaction (Ngatchic *et al.*, 2020).

Changes in serum protein levels and elevated activities of AST, ALT and ALP can be indicative of liver damage and loss of functional cellular integrity. In the present study

MEADL treatment did not cause any significant change in the biochemical markers of liver function (Table III), but there were histopathological lesions in the liver (Figure 1). This is in contrast with the findings of Sa'id *et al.* (2020) who reported that aqueous fruit pulp extract of *Adansonia digitata* exhibited hepatoprotective effects by reducing significantly ($p<0.05$) the elevated levels of serum proteins and liver enzyme markers due to CCl_4 induced toxicity. This could be linked to the possible difference in the phytoconstituents of the extracts used in both studies. Though, both extracts were products of polar solvents, different vegetative parts of the plant were used and they were harvested from different geographical locations. The phytoconstituents of plant extracts varies with the vegetative part used, stage of growth and geographical conditions of where the plant was grown (Farhadi *et al*., 2020; Semerdjieva & Zheljazkov, 2019).

The MEADL treatment also caused no significant ($p > 0.05$) difference inthe biochemical indicators (urea and creatinine) of renal function when compared to the control, but produced histopathological changes in the kidney. The presence of histopathological lesion in the liver and kidney with the absence of biochemical lesion could be attributed to reserve functional capacity and compensatory increase in function (Sharma *et al.*, 2014). Hyperfiltration often occur in residual nephrons when kidney damage has occurred and renal mass is decreased. In case of kidney damage with upto 50% of functioning tissue, hyperfiltration in the remnant nephrons is the compensatory mechanism that ensures that glomerular filtration rate remains within the normal range (Sharma *et al.*, 2014).

The extract (200 mg/kg) produced a marginal increase in the TWBC, HB, PCV, and RBCwhich was not significant ($p >0.05$) when compared with the control. This suggest that it can be used to ameliorate anaemia and provide evidence supporting its use in the ethnomedical management of anaemia (Abubakar *et al.*, 2019; Kamatou *et al.*, 2011). The extract produced a significant ($p < 0.05$) increase in the platelet count of the treated groups when compared with the control group. This suggests that it can be used to control blood clotting dysfunction. Platelet play a crucial role in the blood clotting cascade and low platelet count is an indicator of poor clotting mechanism, while elevated platelet count suggests enhanced clotting mechanism (Hartmann *et al*., 2016; Thachil & Warkentin, 2017).

CONCLUSION

The present study assayed the sub-acute effects of methanol extract of *Adansonia digitata* in Wistar rats. The extract showed good antioxidant and antihyperlipidemic effects as well as proved to be partially toxic to the liver and kidneys. These findings justify its use in folkloric medicine for treatment of several diseases, but caution should be exercised as it is associated with histopathological changes in the liver and kidney at high doses.

CONFLICT OF INTEREST

The authors declare no conflict of interest

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