ACTA SCIENTIARUM POLONORUM
Acta Sci. Pol. Technol. Aliment. 17(4) 2018, 387–397
www.food.actapol.net pISSN 1644-0730 eISSN 1898-9594 http://dx.doi.org/10.17306/J.AFS.2018.0601

ORIGINAL PAPER

Received: 13.08.2018
Accepted: 20.09.2018

EVALUATION OF THE SAFETY OF ORAL INTAKE OF AQUEOUS EXTRACT OF *STIGMA MAYDIS* (CORN SILK) IN RATS

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ABSTRACT

Background. Corn silk (*Stigma madyis*) is used in ethnomedicine for the management of diabetes, kidney stones, depression, fatigue, urinary infections and as a slimming tea. However, there is limited literature on its effect on body weight, lipid, hematological, hepatocellular, nephrological and histopathological indices which the present study evaluated.

Materials and methods. In the acute toxicity test, aqueous extract of *Stigma madyis* was orally administered to rats using a gavage, in doses of up to 5 g/kg body weight. The rats were observed for any behavioral changes, signs of toxicity or mortality. In the sub-acute toxicity, rats were orally administered 500, 1000 and 2000 mg/kg *Stigma madyis* extract for 28 days. On the 29th day, the rats were euthanized and the following parameters measured; lipid profile, hematology, serum chemistry and histopathology of the liver and kidney.

Results. In the acute toxicity test, *Stigma madyis* did not cause any mortality and was non-toxic at the dose of up to 5 g/kg body weight. In the sub-acute study, the extract caused an observable significant increase ($p < 0.05$) in triglycerides (TAG), low density lipoprotein (LDL) and very low density lipoprotein (VLDL), while the concentration of high density lipoprotein (HDL) decreased significantly ($p < 0.05$) when compared to the control group. AST and ALT increased significantly ($p < 0.05$) in rats treated with 1000 and 2000 mg/kg of *Stigma maydis* compared to their control. The histopathological results revealed degenerative changes in the liver at 2000 mg/kg body weight extract.

Conclusion. In long term treatment, toxic effects were observed in liver at the doses of 1000 and 2000 mg/kg. This study suggests that prolonged use of higher doses of aqueous extract of *Stigma maydis* ≥ 1000 mg/kg could be hepatotoxic. Therefore, only lower doses should be encouraged for therapeutic use.

Keywords: *Stigma maydis*, acute, sub-acute, hepatotoxic, histopathology

INTRODUCTION

Worldwide, medicinal plants and its pharmacological evaluations have gained significant attention among researchers. Today, there are many documented scientific studies on the potential uses of medicinal plants in the treatment of various diseases (Wachtel-Galor and Benzie, 2011). However, most of these scientific reports focused mainly on verifying the acclaimed traditional uses and efficacy of various parts of plants in the treatment of diseases, and few medicinal plants have been properly evaluated for possible detrimental toxic

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effects (Bello et al., 2016; Ekor, 2014). Therefore, there is need to investigate the short- and long-term toxic effects of medicinal plants before using them for therapeutic purposes.

The clinical significance of medicinal plants in the management of diseases is mainly due to their active ingredients, efficacy, availability and affordability (Ezekwesili et al., 2014). In recent times, developing countries have seen plants as a reliable method for the production of synthetic drugs (Kong et al., 2003). These groups of plants, which confer good health to humans when, used are generally referred to as medicinal plants. These plants have been utilized since time immemorial for shelter, food and treatments for different ailments and wounds (Jaleel et al., 2006; Ugbogu et al., 2016). The therapeutic elements of these plants can be found in various parts, such as the leaves, stems, barks and roots (Jaleel et al., 2006; Petrovska, 2012). Humans, in the search for a better source of healing, have gradually returned to plant sources as scientific evaluation further reveals the pharmacological properties of these plants in the treatment of disease. Medicinal plants have often been sought in preference to more expensive conventional medicine. One of such plants is *Stigma maydis* (corn silk).

Stigma maydis is an elongated stigma usually found in female growing maize flowers which resembles a cluster of threads, grass or hairs. It is a by-product from the planting of corn, and is generally discarded as waste due to the lack of utilization (Aukkanit et al., 2015). It is important in attracting pollens, which are further transferred from the anther to the stigma during pollination. Corn silk has been found to be rich in biomolecules such as proteins, volatile oils, vitamins and carbohydrates (Hasanudin et al., 2012). Also, the presence of calcium, potassium and magnesium ions, sodium salts, steroids, phenol and flavonoids are also believed to have contributed to their pharmacological potential (Ebrahimzadeh et al., 2008). Rahman and Rosli (2014) evaluated the proximate composition of corn silk and reported that corn silk consists of ash (5.51%), carbohydrate (29.74%), dietary fiber (51.24%), lipid (0.66%), moisture (3.90%) and protein (8.95%). The potential health benefits of corn silk include its anti-fatigue, anti-depressant, anti-diabetic, and hypoglycemic properties, as demonstrated in several reports (Guo et al., 2009; Wang et al., 2011; Zhao et al., 2012). The role of corn silk in the treatment of cystitis, edema, kidney stones, prostate disorder, urinary infections, bedwetting, obesity, and as a diuretic have also been reported (Grases et al., 1993). Corn silk has also been reported to be therapeutic in the management of pleurisy, and oxidative stress-induced inflammatory diseases (Wang et al., 2012). Rahman and Rosli (2014) reported that ethanol extract of corn silk has strong free radical scavenging capacity. Corn silk extracts could also help to improve kidney functions that have previously been inhibited by the use of nephritis causative agents (Sepehri et al., 2011). Urinary tract infections and kidney stones can be improved with the aid of corn silk tea. The diuretic properties of corn silk, which, when used as tea, soothes irritation in the urinary tract system, has increased its ethnomedicinal importance (Guo et al., 2009).

To the best of our knowledge, there is paucity of information on the toxicological evaluation of *Stigma maydis* at moderately high concentrations in the pharmacopeia. This present study therefore evaluates the oral toxicity effect of boiled aqueous extract of *Stigma maydis* in rats.

MATERIAL AND METHODS

Collection and identification of plant

Freshly white corn species (*Zea mays*) with intact corn silk were purchased at Eke Okigwe market in Okigwe Local Government of Imo state, Nigeria, in June 2017. After collection, the corn was carefully peeled to collect the intact corn silk. The corn silk was authenticated and deposited at the Department of Botany University of Nigeria Nsukka (Herbarium number UNN: 406).

Extraction of the plant material

The plant extract was prepared according to the method used by Saheed et al. (2015) with little modification. Exactly 100 g of corn silk was extracted by maceration in 1000 mL of distilled water. These heterogeneous mixtures were boiled with the aid of a heater for 4 hours at 100°C. After boiling the sample, the filtrate was separated from the corn silk residue with the aid of Whatman no. 1 filter paper and a funnel was placed into a beaker for separation. The resulting

filtrate was concentrated to dryness. The concentrated corn silk extract was reconstituted with distilled H_2O at the doses of 500, 1000, 2000 and 5000 mg/kg used in this study.

Experimental animals

Eighty-four Wistar rats, weighing 150–170 g, were used in this study. The rats were obtained from the Animal House of the University of Nigeria Nsukka and transported to the Animal House of the Department of Biochemistry, Abia State University Uturu. The experimental animals were allowed to acclimatize to their new environment for two (2) weeks prior to the commencement of the study. These animals were fed on growers' mash. All the animals were allowed to drink water *ad libitum*. The animal house was properly aerated and kept at an ambient room temperature. The entire assay employed in this study conformed to rules and tenets of United States National Institutes of Health for Care and Use (NIH, 1985) and in accordance to the principles of good laboratory procedure (WHO, 1998). This study was approved by the Abia State University Research Ethical Clearance Committee (ABSU/REC/BMR/020).

Oral acute toxicity test

The acute toxicity of the *Stigma maydis* was carried out using OECD (2001) guideline 423, with small modifications. The rats were randomly divided into five groups of 12 rats (6 males and 6 females) per group. Prior to this study, the animals were fasted overnight. Single doses of *Stigma maydis* extract (500, 1000, 2000 and 5000 mg/kg) were administered via oral gavage to the rats in each group, and the control group received 0.5 ml distilled water. The rats were monitored individually for any behavioral changes and signs of toxicity for a duration of 24 h and thereafter for 14 days.

Sub-chronic toxicity study

Post-acclimatization, the animals were divided into four groups of six (6) male rats per group. The groups were: I, 0.25 mL distilled water (control group); II, 500; III, 1000; and IV, 2000 mg/kg body weight. The required doses were administered once daily for 28 consecutive days (OECD, 1995) guideline 407 and the volume of aqueous boiled extract was administered to each animal according to their body weight for each concentration of the extract.

Hematology and serum clinical chemistry assay

Under light anesthesia with diethyl ether, the rats were euthanized and their blood was individually collected through cardiac puncture. One portion was transferred immediately into EDTA (ethylenediaminetetracetic acid) containing tubes for the measurement of hematological parameters such as hemoglobin level (Hb), packed cell volume (PCV), white blood cell count (WBC) and white blood cell differentials (Granulocytes and Agranulocytes), platelets and red blood cells (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), neutrophils, lymphocytes, basophils, monocytes and eosinophils. The hematological studies were performed as described by Dacie and Lewis (2001). Another portion of the blood was added to plain tubes for serum clinical chemistry assay. The blood was spun using a centrifuge at a fixed speed and time. The serum from the clotted blood was carefully collected from the packed red cells and used to determine lipid profiles and kidney and liver biomarkers. All the biochemical assays were determined using ready-to-use kits from Randox Laboratory Ltd, Co. Antrim, United Kingdom.

Histopathology

The toxicological organs, namely the liver and kidney, were subsequently fixed in 10% formalin saline solution and the samples were properly labeled. Exactly 5 μm of the excised tissue was embedded in paraffin wax and stained with hematoxylin and a basic dye eosin. The tissues were then mounted on the mechanical stage of light microscope and were examined by a skilled histopathologist as described by Fisher et al. (2002).

Statistical analysis

Means of the values and standard deviations were calculated (mean ±SD) using Microsoft (MS) Excel. The data was then subjected to one-way analysis of variance (ANOVA) and the difference between means was tested by Tukey *post-hoc* test using R-statistics software version 3.03. $p \leq 0.05$ was considered statistically significant.

RESULTS

Acute toxicity effects of *Stigma maydis* (corn silk)

Table 1 demonstrates results from rats that received boiled aqueous extract of *Stigma maydis*. There were no animal deaths recorded after oral administration of 5 g/kg of *Stigma maydis* extract. No toxicity signs were observed within 24 h and thereafter for 14 days. The LD_{50} of *Stigma maydis* in male and female rats is greater than 5 g/kg.

Table 1. Acute toxicity investigation (LD_{50}) of Wistar rats that received different doses of boiled aqueous extract of *Stigma maydis*

Group	Dose	D/T	Signs of toxicity
A	0.5 ml (H_2O)	0/12	no toxic effects
B	500 mg/kg	0/12	no toxic effects
C	1000 mg/kg	0/12	no toxic effects
D	2000 mg/kg	0/12	no toxic effects
E	5000 mg/kg	0/12	no toxic effects

D/T – number of albino rat deaths/total number of albino rats used.

Effect of oral administration of boiled aqueous solution of *Stigma maydis* on body weight and organ weights

The results of the effects of boiled aqueous extract of *Stigma maydis* on body weight of rats post-28 days of administration is presented in Figure 1. The result showed a manifold increase in the body weights of the extract-treated animals when compared to the control. When evaluated prior to the intake of the corn silk extract, the percentage weight change for the control and the 500 mg/kg, 1000 mg/kg and 2000 mg/kg groups increased as the extract administration increased.

Effect of aqueous *Stigma maydis* extract on relative organ weights of rats

There was no observed statistical difference ($p < 0.05$) in the results obtained from the relative organ weights of the liver, kidney, heart, lungs, intestines and testis of the groups that received the extracts when compared to the group that were not fed with the extract as shown in Table 2.

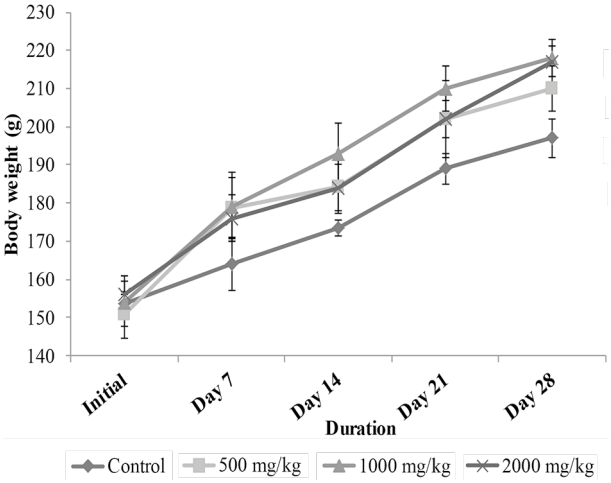

Fig. 1. Initial and 7, 14, 21 and 28 day body weight measurements of male rats in the sub-acute toxicity study of aqueous extract of *Stigma maydis*

Effect of oral administration of boiled aqueous extract of *Stigma maydis* on the lipid profile indices of rats

The effect of a 28-day regular intake of boiled aqueous extract of *Stigma maydis* at different concentrations (500 mg/kg, 1000 mg/kg and 2000 mg/kg) on the lipid profile parameters of rats are presented in Table 3. The extract caused observable significant increases ($p < 0.05$) in triglycerides (TAG), low density lipoprotein (LDL) and very low density lipoprotein (VLDL) while the concentration of high density lipoprotein (HDL) decreased significantly ($p < 0.05$) when compared to the control groups.

Effect of oral administration of boiled aqueous extract of *Stigma maydis* on hematological parameters

The effect of 28 days of administration of aqueous extract of *Stigma maydis* on the hematological indices of rats are presented in Table 4. There were no significant difference ($p > 0.05$) observed in red blood cell count (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), white blood cell count (WBC), total white blood cell differential, hemoglobin, mean corpuscular hemoglobin concentration, basophils and monocytes when compared to the control groups.

Table 2. Effect of aqueous *Stigma maydis* extract on relative organ weights of rats

Organ weight, g	Control	Corn silk extract dose, mg/kg		
		500	1000	2000
Liver	7.80 ±0.26	6.93 ±1.58	7.14 ±0.55	6.70 ±1.58
Kidneys	1.56 ±0.13	1.24 ±0.19	1.37 ±0.02	1.51 ±0.22
Heart	0.63 ±0.09	0.65 ±0.08	0.62 ±0.04	0.68 ±0.11
Lungs	1.73 ±0.30	1.25 ±0.06	1.54 ±0.09	1.33 ±0.12
Spleen	1.68 ±0.32	1.12 ±0.12*	0.98 ±0.21**	0.91 ±0.18**
Intestines	11.49 ±1.09	9.22 ±0.25	8.31 ±1.10	9.54 ±2.63
Testis	4.15 ±0.06	4.09 ±0.08	3.38 ±0.24	4.11 ±0.24

Data is expressed as the mean ±SD of 6 rats. Asterisk (*) shows significant difference from the control, $p < 0.05$.

Table 3. The influence of boiled aqueous extract of *Stigma maydis* on lipid profile indices of rats after 28 days of oral administration

Parameter mg/dl	Control	Corn silk extract dose, mg/kg		
		500	1000	2000
TC	78.42 ±3.83	82.65 ±1.83	82.91 ±2.00	85.52 ±1.30
TAG	126.83 ±5.78	153.10 ±1.89*	168.16 ±9.04*	176.87 ±2.48*
HDL	52.11 ±1.82*	47.26 ±2.37*	40.62 ±1.55	36.30 ±3.12
LDL	25.37 ±0.44	30.62 ±0.21*	33.63 ±1.13**	35.37 ±1.51**
VLDL	0.94 ±0.01	4.77 ±0.38*	8.66 ±0.81**	13.85 ±0.50**

Values are expressed as the mean ±SD of 6 rats. Asterisk (*) shows significant difference from the control, $p < 0.05$. TC – total cholesterol, TAG – triacylglycerol, HDL – high density lipoprotein, LDL – low density lipoprotein, VLDL – very low density lipoprotein.

Effect of oral administration of boiled aqueous extract of *Stigma maydis* on hepato-renal biomarkers

The influence of boiled aqueous extract of *Stigma maydis* on some liver and renal function indices of rats are presented in Table 5. Dose-dependent increase was observed in AST and ALT. AST and ALT significantly increased ($p < 0.05$) in rats treated with 1000 and 2000 mg/kg of *Stigma maydis* when compared to their respective controls. There was no significant difference ($p > 0.05$) observed in ALP, bilirubin, creatinine, K^+, HCO_3, total protein, urea, Na^+ and Cl^- between the treated groups and control groups.

Effect of oral administration of aqueous extract of *Stigma maydis* on the histology of the liver and kidney of rats

Microscopic examination of the liver revealed slight abnormalities in the examined hepatocellular structures of the rats that received 2000 mg/kg dose of the boiled aqueous *S. maydis*, with observable cellular injuries such as A – ballooning degenerative changes and several cystic spaces within the stroma; B – hepatocytes exhibiting pleomorphism, and C – the central vein appearing enlarged as shown in Figure 2. The histopathological study of the kidney showed no sign of abnormality in the renal architecture (Fig. 3).

Table 4. Influence of boiled aqueous extract of *Stigma maydis* on hematological parameters of rats after 28 days of oral administration

Parameter	Control	Corn silk extract dose, mg/kg		
		500	1000	2000
PCV, %	57.33 ±5.02	60.80 ±1.77	60.51 ±0.70	59.33 ±0.85
Hb, g/dL	15.27 ±0.70	14.20 ±0.30	14.23 ±0.40	14.03 ±0.50
RBC, $\times 10^{12}$/L	8.34 ±0.12	8.84 ±0.12	8.96 ±0.05	9.06 ±0.21
MCV, fl	70.73 ±1.10	68.77 ±1.91	67.57 ±0.40	65.50 ±2.26
MCH, pg	18.17 ±0.51	16.07 ±0.21	15.90 ±0.79	15.50 ±0.82
MCHC, g/L	257.30 ±4.58	233.50 ±9.64	236.20 ±14.18	236.33 ±5.13
WBC, $\times 10^{9}$/L	16.63 ±3.20	24.03 ±0.68	23.30 ±1.41	22.63 ±1.92
Neutrophil, %	51.67 ±1.53	42.33 ±3.51	42.33 ±2.08	37.33 ±5.69
Eosinophils, %	2.33 ±0.58	1.67 ±0.58	3.67 ±0.58	3.33 ±0.58
Basophils, %	0.67 ±0.58	0.67 ±0.58	0.33 ±0.58	0.33 ±0.58
Lymphocytes, %	41.67 ±1.53	52.67 ±3.06	50.67 ±1.53	54.00 ±5.29
Monocytes, %	3.67 ±1.53	2.67 ±1.53	3.00 ±1.73	5.00 ±1.00
Platelet, $\times 10^{9}$/L	781 ±12.01	875.10 ±15.24	895.33 ±9.64	820.68 ±8.16

Values are expressed as the mean ±SD of 6 rats. PCV – packed cell volume, Hb – hemoglobin, RBC – red blood cell, MCV – mean corpuscular volume, MCH – mean corpuscular hemoglobin, MCHC – mean corpuscular hemoglobin concentration, WBC – white blood cell.

Table 5. Influence of boiled aqueous extract of *Stigma maydis* on hepato-renal biomarkers of rats after 28 days of oral administration

Parameter	Control	Corn silk extract dose, mg/kg		
		500	1000	2000
AST, U/L	19.33 ±3.06	25.67 ±2.08	41.67 ±3.51*	48.00 ±4.00*
ALT, U/L	15.00 ±1.00	20.67 ±2.31	31.00 ±5.57*	42.67 ±3.06*
ALP, U/L	70.31 ±1.22	73.18 ±2.80	72.94 ±3.38	72.24 ±6.66
Total protein, mg/dL	6.67 ±0.45	5.64 ±0.23	5.53 ±0.33	5.35 ±0.11
Bilirubin, mg/dL	0.69 ±0.03	0.77 ±0.07	0.87 ±0.08	0.74 ±0.06
Creatinine, mg/dL	0.94 ±0.08	1.20 ±0.20	1.19 ±0.12	1.26 ±0.17
Urea, mg/dL	16.17 ±0.70	17.24 ±0.86	20.71 ±3.49	23.32 ±1.30
Na^{+}, mEq/L	137.76 ±0.96	133.98 ±2.17	126.04 ±1.47	133.32 ±5.16
K^{+}, mEq/L	5.18 ±0.13	5.37 ±0.39	5.43 ±0.17	5.58 ±0.35
Cl^{-}, mEq/L	100.88 ±1.59	101.24 ±0.92	92.30 ±0.79	90.92 ±1.37
HCO_3^{-}, mMol/L	25.89 ±1.00	26.38 ±1.13	24.71 ±0.87	25.05 ±2.03

Values are expressed as the mean ±SD of 6 rats. *Shows significant different from the control, $p < 0.05$. ALT – alanine amino transferase, AST – aspartate amino transferase, ALP – alkaline phosphatase, Na^{+} – sodium ion, K^{+} – potassium ion, Cl^{-} – chloride ions, HCO_3^{-} – bicarbonate ion.

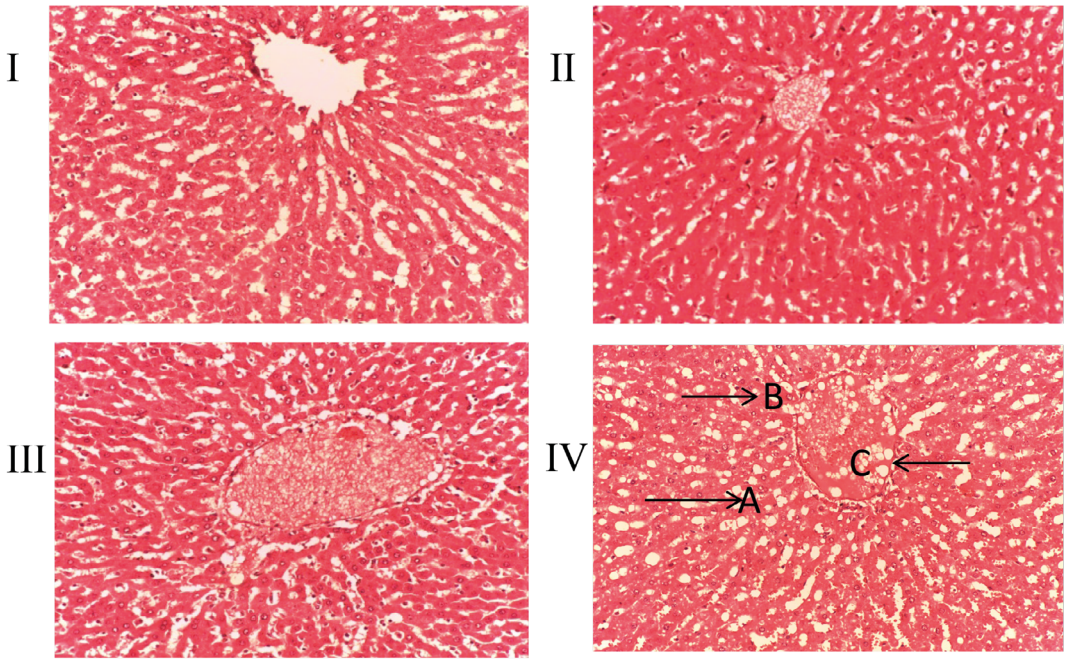

Fig. 2. Histology of liver sections showing the effect of aqueous extract of *Stigma maydis* after a 28-day sub-acute toxicity study in rats: I – control group, II – 500 mg/kg, III – 1000 mg/kg, IV – 2000 mg/kg; A – balloon degenerative changes and several cystic spaces within the stroma, B – hepatocytes exhibits pleomorphism, C – central vein appears enlarged

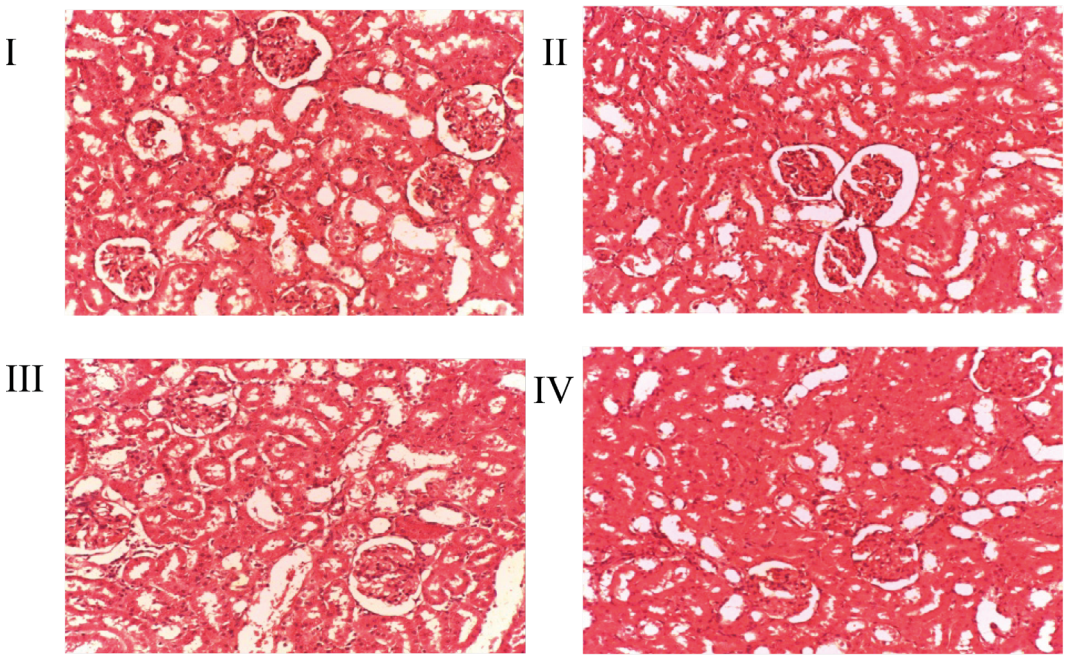

Fig. 3. Histology of kidney sections showing the effect of aqueous extract of *Stigma maydis* after a 28-day sub-acute toxicity study in rats: I – control group, II – 500 mg/kg, III – 1000 mg/kg, IV – 2000 mg/kg

DISCUSSION

Considering the wide-ranging phytotherapeutic potential of *Stigma maydis* in folk medicine, as reported by many researchers (Hasanudin et al., 2012; Maksimovic and Kovacevic, 2003; Velazquez et al., 2005), there is need to evaluate and establish the safety profile of *Stigma maydis*, as this may serve as a guide for its application in the treatment of diseases without any detrimental toxicity-related health risk to humans from the use of the extract.

Toxicological evaluation in animals gives a clearer view of the health risk and potential of pharmacological agents or plant extracts on humans due to their morphological similarities (Ajani et al., 2014). They may also assess and determine the benefits or potential hazards of administrating the extract at certain doses (Schulz et al., 2011).

In this study, single-dose oral administration of up to 5 g/kg body weight of *Stigma maydis* in male and female rats had no effect on behavioral changes. No death or sign of toxicity was observed. Therefore, the LD_{50} of *Stigma maydis* is greater than 5 g/kg. However, this safety assertion may be immaterial to medicinal plants consumed for a long period of time. Nevertheless, our acute toxicity study gave us the suggestions as to how to select appropriate doses or concentrations of *Stigma maydis* for the sub-acute study as presented below for more clinical relevance. Therefore, doses of 500, 1000, and 2000 mg/kg body weight were selected and administered to the rats for a period of 28 days so as to establish, with optimal precision, the doses of the extract that would be toxic or non-toxic when consumed for a longer period.

In animal experiments, monitoring body weight can serve as a good and sensitive indicator to assess their overall health (Borzelleca, 1996), as a decrease in body weight may be a sign of adverse effects (Tahraoui et al., 2010). There was no significant decrease ($p > 0.05$) in the body weight of the examined rats when compared to the untreated rats. This observation may be due to the fact that the extract did not disrupt the hormonal-metabolic processes of the tested animals for weight gain and loss regulations (Cajuday and Poscidio, 2010). This result is in agreement with the findings of Wang et al. (2011) who reported that up to 8% corn silk incorporated into the rats' feed has no effect on body weight after 90 days of consumption. Similar findings were reported by Guo et al. (2009), that daily administration of aqueous extract of corn silk over 20 days did not affect the body weight of alloxan-induced hyperglycemic mice. However, this result was at odds with the findings of Lee et al. (2016) who used C57BL/6J mice fed with high-fat diets and found that an increase in *maysin* corn silk competes with product formation of adipocyte activity, biosynthesis and accumulation of fats, as it inhibits the segment of DNA that codes for closely related proteins responsible for fat oxidation and lipolysis. These biochemical processes bring about body fat accumulation, which may result in abnormal body weight in experimental animals. This discordance in results may be attributed to the nutritional composition of the high fat diet fed to the mice during the administration of the corn silk.

Lipid profile is a panel of clinical chemical assays that serve as an initial preliminary broad medical screening for abnormalities associated with lipid metabolism. Imbalances in the concentration of key lipids in the system such as total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), and triglycerides (TAG) are held as major culprits to lipid-related metabolic diseases and the risk of cardiac diseases such as atherosclerosis, which can lead to coronary heart disease, hypoxia, infarction and necrosis (Oyedemi et al., 2010). Based on our findings, high density lipoprotein significantly decreased, while low density lipoprotein, significantly increased, indicating that this extract cannot serve as a hypolipidemic agent at the tested concentrations (Table 3). The result of our findings is in contrast with the findings of Saheed et al. (2015) who reported that the aqueous extract of *Stigma maydis* at concentrations less than or equal to 400 mg/kg is a good candidate in the management of coronary heart disease. However, the disparity between our results may be attributed to the higher doses which we have evaluated in the present study.

The evaluation of hematological indices could serve as health condition index on experimental animals that have been exposed to, ingested and metabolized xeno-compounds such as plant extracts (Ashafa and Kazeem, 2015). There was no statistical difference ($p < 0.05$) in all the hematological parameters

(Table 4). It has been noted that the measurement of MCV, MCH and MCHC relating to the status of RBC is essential in the diagnosis of red blood cell-associated diseases e.g. anemia (Saheed et al., 2015). From these results, it can be stated that there was a non-significant slight increase in red blood cell count and packed cell volume among the tested animals when compared to the untreated control groups. Based on these results, *Stigma maydis* extract did not interfere with the normal production of hemoglobin and RBC, and therefore has no potential to induce anemia. The slight increases observed in WBC, eosinophil, lymphocyte, monocyte and platelet counts suggest that *Stigma maydis* extract has no negative effects on the immune system of the rats. These results suggest that *Stigma maydis* extract at the tested doses is non-hematotoxic in rats. The liver and kidneys are key metabolic organs for central biochemical homeostasis that play crucial roles in xenobiotic metabolism, detoxification and biotransformation (Fouche et al., 2015). The analysis of liver and kidney function parameters may provide useful information on the safety or toxicity effects of therapeutic agents. The liver enzymes alkaline phosphatase (ALP), alanine transaminase (ALT) and aspartate transaminase (AST) are closely associated with hepatic injury when significantly increased in serum, as well as in total proteins and albumin (Saheed et al., 2015). The non-significant decrease in the serum concentration of total protein further confirms that the extract at the highest doses of 1000 and 2000 mg/kg body weight is likely to be hepatotoxic. The alterations in the hepatic biomarkers (AST and ALT) were dose-dependent, and as such could be considered treatment related. The loss of functionality and integrity of the renal system may be evaluated by the change in serum concentration of urea, creatinine, and electrolytes (Oloyede and Sunmonu, 2009). In the evaluated results, there were non-significant increases or decreases in the kidney biomarkers in all the tested doses. Sepehri et al. (2011) reported that aqueous extract of corn silk is nephroprotective against gentamicin-induced nephrotoxicity at moderate doses between 200 and 300 mg/kg. The results of this study imply that aqueous extract of *Stigma maydis* did not negatively affect the normal function of the kidney.

In the toxicological assessment, acute toxicity and biochemical parameters are not informative enough to ascertain the interaction of extracts with the physiological and biochemical processes taking place in the body of animals. Histological investigation of homeostatic and xenobiotic organs consequent upon exposure to pharmacological agents is inevitably beneficial in assessing the safety of such agents on organ injury (Saheed et al., 2015). In this study, the architectural features of the kidney were preserved in all the extract-treated animals, as demonstrated by microscopic examination, while that of the liver revealed slight abnormalities in the form of ballooning degeneration, hepatic pleomorphism and the enlargement of central veins at 2000 mg/kg dose, indicating injury (French et al., 1984; Schuppan and Afdhal, 2008). This observation, obtained from the histological examination of the liver, corroborates with the result of the liver function parameters in this study.

CONCLUSIONS

This study has provided clear evidence that boiled aqueous extract of *Stigma maydis* could be toxic at high concentrations greater than or equal to 1000 mg/kg when used for a long period. The present study also established that there was no significant decrease ($p < 0.05$) in the body weight of the tested rats when compared to the untreated rats (control groups). Again, the result of the lipid profile indicates that high density lipoprotein were significantly reduced. The observable non-significant decrease in the body weight and the reduction in high density lipoproteins may be strong evidence that the extract may not be used as slimming tea for weight control. Based on our findings, low density lipoprotein (LDL) significantly increased, indicating that the boiled aqueous extract of *Stigma maydis* cannot serve as a hypolipidemic agent at the tested doses.

ACKNOWLEDGMENTS

The authors wish to thank the dynamic and research-loving Vice Chancellor of Abia State University, Professor E.U. Ikonne, and his management team for providing a conducive environment to carry out this study.

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