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EFFECT OF METHANOL EXTRACT OF THE UNRIPE PEELS OF *MUSA PARADISIACA* ON SOME HAEMATOLOGICAL AND BIOCHEMICAL INDICES IN MALE ALBINO WISTAR RATS.

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ABSTRACT

Studies have demonstrated the potential of the fruit pulp of *Musa paradisiaca* in nutrition and in the treatment of various ailments. However, there is a dearth of information on the efficacy of the peels which are often discarded as waste. In the search for useful products from organic wastes, the present study evaluated the phytochemical composition of the unripe peels of *Musa paradisiaca* and investigated the effects of its methanol extract on some haematological/biochemical indices in male albino wistar rats. Phytochemical analysis of the unripe peels was carried out using standard methods. Twenty (20) male albino wistar rats were randomly assigned into 4 groups of 5 rats per group. Treatment involved the administration of 44.72 mg/kg, 89.44 mg/kg and 134.16 mg/kg body weight respectively of methanol extract of the unripe peels for 14 days. Blood samples were collected by cardiac puncture and used for hematological and biochemical studies. Phytochemical screening of the unripe peel extract indicated the presence of alkaloids, tannins and cardiac glycosides. Administration of the extract caused a dose dependent decrease in white blood count, hemoglobin concentration, mean cell volume and mean cell hemoglobin levels. Platelets were high compared to control. Total cholesterol, triglycerides, very low density lipoprotein and low density lipoprotein fractions were increased while the high density lipoprotein decreased. Aspartate aminotransferase, alanine

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aminotransferase and alkaline exhibited a dose dependent increase across the treatment groups. These findings suggest that the unripe peels of *M. paradisiaca* are toxic, with pro-inflammatory potentials and can induce anemia.

Keywords: Phytochemical screening, unripe peels, hematology, liver enzymes, anemia

INTRODUCTION

Musa paradisiaca Linn. (Plantain) is an evergreen plant with an aerial pseudostem, an underground rhizome and a height of 2 to 9 m (Ekunwe and Ajayi, 2010). The leaves are oblong, deep green and narrowed to the base (Iman and Akter, 2011). The fruits are edible, contain about 220 Calories and are traditionally used in the treatment of various ailments (Lakshmi et al., 2015). Plantain production in Africa is estimated at more than 50% of worldwide production (FAO, 1990). About 70 million people in West and Central Africa derive more than 25% of their carbohydrate from plantains, making them one of the most important sources of food energy throughout the African lowland humid forest zone (Swennen and Ortiz, 1990). During the processing the plantain fruits for human consumption, the epicarp (peels) are often discarded as waste. Ighodaro (2012) reported that the unripe plantain peels contain 48.18% carbohydrate, 6.87% protein, 16.20% fibre, 17.59% ash, 7.47% of moisture. Unripe plantain peels have also been reported to be rich in mineral elements (Ighodaro, 2012; Oduje et al., 2015; Okorie et al., 2015). The isolation and characterization of starch from the unripe plantain peels has been reported (Ogechukwu et al., 2017). Ogunsipe and Agbede (2010) provided data on the replacement value of unripe plantain peels on growth performance and carcass characteristics of rabbits.

In an effort to obtain useful products from agricultural wastes, the present study was undertaken to evaluate the phytochemical composition of the unripe peels of *Musa paradisiaca* and assess the effects of its methanol extract on some haematological/biochemical indices in male albino wistar rats. It is expected that the results will provide useful data on the toxicological profile of the unripe plantain peels.

MATERIALS AND METHODS

Mature unripe fruits of Musa paradisiaca were obtained from a local market in Itu, Akwa Ibom State, Nigeria. They were authenticated at the Herbarium of the Department of Pharmacognosy and Natural Medicine, University of Uyo, Nigeria. The fruits were washed and the peels were carefully separated from the pulps with a sharp stainless steel knife. The peels were sun dried and pulverised using a laboratory mortar and pestle. The crude extract was prepared as described by Kagbo and Nwafor (2012). Briefly, the pulverized plantain peels were macerated in methanol

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for 72 hours, the mixture was shaken at intervals of 24 hrs. At the end of 72 hrs, the mixture obtained was filtered using a Whatman No.1 filter paper and the filtrate was concentrated to dryness in a water bath at 45^oC. The resulting crude extract was preserved in a refrigerator at 4^oC until required for use.

Twenty male albino rats of the wistar strain weighing 100 – 120 g were used for this study. Animals were obtained from the animal house of Department of Pharmacology and Toxicology, University of Uyo, Nigeria, housed in wire-meshed cages; maintained under standard environmental conditions of temperature, 22±5^oC; relative humidity 50-60% and a 12 hour light/dark cycles. All animals were fed with grower's pellets and water *ad libitum* then allowed an acclimatization period of seven days before commencement of the experiment. The rats were randomly selected into four groups of five animals each; with group I as the control receiving distilled water. Groups II, III and IV were administered 44.72 mg/kg, 89.44 mg/kg and 134.16 mg/kg representing low, medium and high dosages respectively of the unripe plantain peel extract. Extract administration was carried out by oral gavage once daily between the hours of 8-10 am before administration of feed for a period of 14 days. Institutional approval was obtained from the Postgraduate School, University of Uyo, Nigeria. The animal studies were carried out in accordance with the "Guide for the Care and Use of Laboratory Animals" (National Research Council, 1999). At the end of the 14 days treatment, all experimental animals were anaesthetized using chloroform fumes 24 hrs after the last administration of the extract. Blood samples were collected via cardiac puncture using a 5 ml syringe attached to a needle (21 SWG) into sterile EDTA (anti-coagulant) bottles and used for whole blood analysis. Blood samples were also collected into sterile plain test tubes for sera preparation. Serum samples were obtained from the clotted blood into sterile plain test tubes after centrifugation at 3000 rpm for ten minutes using a bench- top centrifuge (MSE Minor, England). The sera were stored in the refrigerator for analysis of biochemical parameters.

The LD_{50} of the unripe peel extract was determined by the method of Lorke (1983) using twelve albino mice. In the first phase, nine albino mice were divided into three groups of nine animals per group and were respectively treated with doses of 100, 200 and 300 mg/kg of the extract. In the second phase, the animals were treated with 400, 500 and 600 mg/kg of extract. In the third and final phase the animals received 1000, 3000 and 5000 mg/kg of the extract. They were observed for mortality within a 24 hour period. The LD_{50} was calculated as geometrical mean of a and b, expressed mathematically as $LD_{50}=\sqrt{ab}$, where a is the maximum dose producing 0% mortality and b, the minimum dose producing 100% mortality.

Phytochemical screening was carried out using standard procedures as described (Trease and Evans, 1989; Sofowara, 1993).

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Haematological parameters were determined within two hours of sample collection using Mindray 5 differential Haematology Auto Analyzer, model BC 5300. The haematological indices estimated include Haemoglobin concentration [Hb], Packed cell volume (PCV)/ haematocrit, White blood cell count(WBC), Red blood cell count (RBC), Platelet count, Mean cell haemoglobin (MCH), Mean cell volume and Mean cell haemoglobin concentration (MCHC).

Estimation of serum enzymes; alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) were carried out using the Randox kit (Randox Laboratories, England), according to manufacturer's instructions. Serum total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) were estimated using the diagnostic reagent kit supplied by Randox Laboratories, England according to the manufacturer's instructions.

STATISTICAL ANALYSIS

Results were expressed as mean ± standard error of the mean. Data was analysed using the one-way analysis of variance (ANOVA). Difference between groups was compared using Least Significance Difference (LSD) and values of $p<0.05$ were considered significant (Yockey, 2011).

RESULTS AND DISCUSSION

The phytochemical analysis of the methanol extract of the unripe plantain peels revealed the presence of alkaloids, saponins, tannins and cardiac glycosides. (Table1). Other authors have reported similar findings (Ighodaro, 2012; Oduje et al., 2015). The biological and pharmacological properties of plants have been attributed to these bioactive components (Ighodaro, 2012; Larrauri, 1999).

Table 2 shows the result of acute toxicity test. All the test animals showed some physical signs of toxicity (such as writhing, gasping, palpitation, decreased respiratory rate, reduced mobility) but no mortality was recorded in the first stage of the test. In stage two, all animals from the groups treated with 500 and 600 mg/kg of the unripe extract died within 24 hours in addition to the physical signs of toxicity. In stage three, all the animals died within 24 hours. Thus the median lethal dose (LD_{50}) of the extract in mice was calculated as geometric mean of the two doses, that is, 400 and 500 mg/kg body weight:

$$LD_{50} = \sqrt{axb}$$

$$LD_{50} = \sqrt{400x500} = 447.21 \text{ mg/kg}$$

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Hence, the median lethal dose for the unripe peel extract was given as 447.21 mg/kg body weight. This value indicates that the sample could be harmful if ingested (Walum, 1998).

The determination of haematological indices could serve as a useful biomarker for evaluating the haematoxic potentials of a plant extract (Sunmonu and Oloyede, 2010). In this study (Table 3), administration of methanol extract of the unripe peels of Musa paradisiaca induced a significant decrease in total WBC count. This is an indication of the immunosuppressive potentials of this extract (Odesanmi, 2000). Haematological studies also showed dose dependent decreases in [Hb], PCV, RBC, MCV, MCH and MCHC across the extract treated groups, suggesting the possibility of developing anaemia as a consequence of administration of the extract (Selvi and Alagesan, 2017). Thrombocytosis was observed in the groups treated with low, medium as well as high doses of the unripe peel extract. This indicates that the extract might contain some compounds capable of inducing the release of thrombopoietin which is involved in the stimulation of platelet proliferation (Muriithi et al., 2015). Platelets play an important role in the maintenance of normal homeostasis (Sharp et al., 1995).

Lipid profile studies (Table 4), indicated that total cholesterol, LDL, VLDL and triglyceride levels increased significantly ($p<0.05$) in all test groups. The serum concentration of HDL cholesterol was significantly lower ($p<0.05$) in medium and high dose groups. Alterations in these lipid fractions provide useful information concerning the status of lipid metabolism as well as predisposition to atherosclerosis and its associated coronary disease (Singh et al., 2012). Increase in serum total cholesterol and LDL-cholesterol following the administration of the extract could be attributed to an enhanced β-oxidation resulting in increased levels of acetyl coenzyme A (CoA), a key substrate in the biosynthesis of the cholesterol (Naik, 2010). Elevated serum concentrations of triglycerides as observed in the present study could also be attributed to increased lipolysis which may ultimately deplete the body store of fatty acids. It has been reported that patients with cardiovascular disease exhibit high serum levels of triglycerides (Singh et al., 2012). HDL-cholesterol (the good cholesterol) mediates the reverse transport of cholesterol from extrahepatic tissues to the liver for degradation and excretion as bile acids and therefore has been reported to possess anti-atherogenic properties (Kwiterovich, 2000; Das, 2003). There is an inverse relationship between HDL-C and coronary heart disease (Yakubu and Afolayan, 2009). Administration of methanol extract of the unripe peels of *M. paradisiaca* was observed to significantly decrease serum concentrations of HDL-cholesterol indicating increased risk of cardiovascular disease detrimental to the health of the animal.

Measurement of the activities of aminotransferases (AST, ALT) and alkaline phosphatise (ALP) is of clinical and toxicological importance as changes in their activities are indicative of tissue damage by toxicants or disease conditions (Kuete et al., 2010). Alanine aminotransferase (ALT)

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and aspartate aminotransferase (AST) have been established as markers of hepatocellular injury while alkaline phosphatase is a marker of cholestasis. Persistent elevation of serum ALT, AST and ALP serve as reliable markers for hepatotoxicity (Eleazu et al., 2013). These enzymes are usually raised in acute hepatotoxicity or mild hepatocellular injury, but tend to decrease with prolonged intoxication, because of severe damage to the liver (Yang et al., 2014). An increase in the activity of serum ALT in methimazole-induced hepatotoxicity in mice has also been reported (Heidari et al., 2014) while Papackova et al., (2018) reported an elevation in ALT activity as a consequence of acetaminophen-induced hepatotoxicity in rats. In this study (Table 5), AST, ALT and ALP showed significant ($P<0.05$) increases in test groups III and IV compared with the control indicating the hepatotoxic potentials of this extract.

CONCLUSION

This study has shown that the unripe peels of *M. paradisiaca* contain bioactive compounds such as alkaloids, saponins, tannins and cardiac glycosides. The value obtained for LD_{50} indicates that the extract could be harmful if ingested. The extract has the potential to suppress the immune system by decreasing WBC count and could induce anemia based on its ability to reduce [Hb], PCV, RBC, MCV and MCH. However, the unripe peels of *Musa paradisiaca* could have positive pharmacological potentials due to the content of bioactive compounds.

Table 1: Phytochemical composition of the methanol extract of unripe peels of *Musa paradisiaca*

Constituent	Composition
Alkaloids	+ +
Saponin	+ +
Tannin	+
Flavonoids	-
Cardiac glycosides	+

Key: + present; ++ moderately present; - absent

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Table 2: Results of acute toxicity test (LD_{50}) on albino mice treated with methanol extract of unripe peels of *Musa paradisiaca*.

Stage	Dose (mg/kg body weight)	Fraction of death	%Mortality
1.	100	$^{0}/_{3}$	0
	200	$^{0}/_{3}$	0
	300	$^{0}/_{3}$	0
2.	400	$^{0}/_{3}$	0
	500	$^{3}/_{3}$	100
	600	$^{3}/_{3}$	100
3.	1000	$^{3}/_{3}$	100
	3000	$^{3}/_{3}$	100
	5000	$^{3}/_{3}$	100

Table 3: Effect of methanol extract of the unripe peels of *M. paradisiaca* on haematological indices of male albino wistar rats

Group	Hb (g/dl)	PCV (%)	WBC ($x10^{12}$/L)	RBC ($x10^{12}$/L)	PLT ($x10^{9}$/L)	MCV (fl)	MCH (pg)	MCHC (g/dl)
1(control)	14.5 ± 1.8	38 ± 0.0	15.6 ±1.2	7.14 ±0.2	749 ± 29.1	63 ± 3.2	19 ± 0.4	32 ± 1.1
2(44.72mg/kg) (Low dose)	12.3± 2.1*	39 ± 1.0	15.1 ± 2.3	6.48 ± 0.3	768 ± 29.3*	58± 0.2*	18 ± 0.2	31 ± 0.4
3(89.44mg/kg) (Middle dose)	10.6 ± 2.4^{*a}	35 ± 0.4^{*a}	13.0 ± 1.2*	5.77 ± 0.3*	789± 18.6*a	50 ± 3.3^{*a}	17.2 ± 0.7	30 ± 0.4
4(134.16mg/kg) (High dose)	9.9± 2.1^{*ab}	28 ± 0.1^{*ab}	10.6± 1.6^{*ab}	4.48 ± 0.4^{*ab}	868± 32.4^{*ab}	42± 0.8^{*ab}	15 ± 0.4	29.8± 0.5

Values are expressed in mean ± SEM,

** Statistically significant at $P<0.05$ compared to control group*

a = $P<0.05$ indicates a significant difference compared with low dose;

b = $p<0.05$ indicates a significant difference compared with medium dose;

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Table 4: Effect of methanol extract of the unripe peels of *M. paradisiaca* on lipid profile of male albino wistar rats

Groups	**TC** (mmol/L)	**TG** (mmol/L)	**VLDL** (mmol/L)	**HDL** (mmol/L)	**LDL** (mmol/L)
1(control	2.2 ± 0.1	0.76 ± 1.1	0.43 ± 0.2	4.4 ± 1.2	0.00± 0.1
2(44.72mg/kg) (Low dose)	2.3 ± 1.1	0.81± 0.4	0.41± 0.1	3.2 ± 1.1	0.0 ± 0.0
3(89.44mg/kg) (middle dose)	2.4 ± 0.0	0.90 ± 0.1[*a]	0.37± 1.3[*a]	2.1 ± 0.1*	0.04 ± 0.1
4(134.1g/kg) (high dose)	2.5 + 0.0	0.99 ± 0.1[*ab]	0.24± 1.3[*ab]	1.1 ± 0.6*[a]	0.73 ± 2.1[*ab]

Values are expressed in mean ± SEM,
** Statistically significant at $P<0.05$ compared to control group*
a = $P<0.05$ indicates a significant difference compared with low dose;
b = $p<0.05$ indicates a significant difference compared with medium dose;

Table 5: Effect of methanol extract of the unripe peels of *M. paradisiaca* on serum enzymes of the male albino wistar rats

Groups	**AST (U/L)**	**ALT (U/L)**	**ALP (U/L)**
1(control)	42 ± 1.0	19± 0.1	101 ± 0.1
2(44.72mg/kg) (Low dose)	48 ± 0.1	21 ± 0.5	102 ± 0.4
3(89.44mg/kg) (middle dose)	49 ± 0.3[*]	23 ± 0.0[*]	109 ± 0.5[*]
4(134.16mg/kg) (High dose)	69 ± 0.3[*ab]	24 ± 0.0[*ab]	111 ± 0.0[*ab]

Values are expressed in mean ± SEM,
** Statistically significant at $P<0.05$ compared to control group*
a = $P<0.05$ indicates a significant difference compared with low dose;
b = $p<0.05$ indicates a significant difference compared with medium dose;

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