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Toxicity Studies of the Extracts of *Parkia biglobosa* Stem Bark in Rats

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Research Article

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ABSTRACT

Extracts of *Parkia biglobosa* stem bark is used in Nigerian traditional medicine (NTM) to treat malaria, diarrhea and pains. To establish the toxicity profile of the medicine such parameters as the lethal dose (LD_{50}) as well as effects on body functions and organs were evaluated in albino Wistar rats. The bioactive constituents of the water and methanol extracts were also evaluated as a link to toxicity. The LD_{50} was greater than 5000mg/kg per oral (p.o) for both extracts. No significant ($P< 0.05$) changes in body weights and vital organs of treated animals. However, at 5000mg/kg of water extract, a significant increase in relative weight of the kidneys and hyper -cholesterolemic effects were observed. The extract also elicited significant increase in blood glucose level. The kidneys and livers of animals treated with *P. biglobosa* water extract for 14 days revealed histopathological evidence of pathological lesions. The methanol extract did not show any changes in the levels of hepatic and hematological parameters, histopathological evidence of pathological lesions, and serum level of urea, uric acid, bilirubin, creatinine and total protein concentrations. Treatment elicited hypo -cholesterolemic effects and significant reduction in blood glucose level occurred in all the groups. The phytochemical screening revealed the presence of tannins, flavonoids, saponins, terpenes, cardiac glycosides, phenols and reducing sugars in the methanol extract, the water extract showed the presence of similar constituents with the absence of flavonoids and cardiac glycosides. This study has shown the toxicity characteristics of the methanol and water extracts of the stem bark P*. biglobosa* in short time treatment with the extracts.

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Keywords: Acute; P. biglobosa; subacute; toxicity; wistar rats.

1. INTRODUCTION

Plants from different botanical sources have been used by many Traditional Medical Practitioner (TMPs) in Nigeria for the treatment and cure of numerous diseases that are locally endemic (Builders et al., 2007; Asase et al., 2005; Jullian et al., 2006). Numerous claims by the TMPs on the potency and use of many of these plants have been scientifically authenticated thus establishing there potency and efficacy especially in the management of certain diseases in rural communities. *Parkia biglobosa* represents one of such plants.

P. biglobosa (Jacq.) R.Br. ex G. Don belongs to the family Fabaceae formerly Leguminosae and the subfamily Mimosoideae. Some major synonyms for *P. biglobosa* are: *P. africana* R. Br., *P. intermedia* Oliver, *P. oliveri* J.F. Macbr., *P. clappertoniana* Keay and popularly known as the African locust bean tree, is a perennial deciduous tree with a height ranging from 7-20 m, bole stout, not buttressed, low-branching, bearing a large wide-spreading crown, flowering while leafless; flowers in pendulous capitula bearing also pendulous, large fruit-pods.

P. biglobosa have been used in the Nigeria and other West African rural communities to treat a variety of diseases (Abbiw, 1990; Shao, 2002). The efficacy of the various preparations of *P. biglobosa* is widely acclaimed by the Hausa communities of northern Nigeria for the treatment of such diseases as malaria, diabetes mellitus and pains. The stem barks is boiled in water and taken as a decoction for the treatment of malaria, inflammatory diseases, and infections to diarrhea (Asase et al., 2005; Shao, 2002; Gronhaug et al., 2008; Tijani et al ., 2009), the bark soaked in ethanol are also used in some communities for anti-diarrhoeal properties and as an effective anti- snake venoms that protects against neurotoxic, haemotoxic and cytotoxic effects of poisonous snakes (Agunu et al., 2005 ; Asuzu and Harvey, 2003) . Also, the leaves, fruits and seeds of *P. biglobosa* have also been used to manage various diseases (Builders et al., 2011; Asase et al., 2005; Abo and Fred-Jayesimi, 2008; Gronhaug et al., 2008), thus making *P. biglobosa* a plant of importance in the West African sub regional rural communities. Though most of the claims of efficacy of the extracts derived from *P. biglobosa* stem bark have been scientifically established little information on their toxicities are however, available.

The aim of the present study therefore was to determine the acute and sub acute toxicity profile of the water and alcohol extracts of the stem bark of *P. biglobosa*.

2. MATERIALS AND METHODS

2.1 Plant Materials

The stem barks of *P. biglobosa were* collected in the month of February, 2009 in Chaza village in Niger state of Nigeria. The identification and authentification were done by (Ethno botanist) Mallam Muazam Wudil of Department of Medicinal Plant Research and Traditional Medicine of National Institute for Pharmaceutical Research and Development, (NIPRD), Abuja, Nigeria where a voucher specimen (NIPRD /H/6225) was deposited at the herbarium for reference.

2.1.1 Extraction of plant materials

The plant material was cleaned, air dried under shade and pounded into fine powder using mortar and pestle. A 100 g quantity of the powder was boiled with 1 L of distilled water for 30 mins. The decoction was decanted, centrifuged at 4500 rpm (Erweka, Germany) for 30 min and freeze dried. The total yield of dark brown extract was 12.76% w/w of crude starting material. The freeze dried powder was stored in an airtight container and used for the study. The methanol extract was prepared by extracting coarse powdered stem barks (100g) with IL methanol for 48hrs using Soxhlet apparatus (Quicket UK). The extract was filtered through Whatmann No. 1 (Whatmann International Ltd, Maidstone, UK) paper and evaporated under reduced pressure using a rotary evaporator. The filtrates were freeze-dried using lyophilizer to yield dark brown extract of 20.17%w/w referred as crude extract. The dried extract was stored in an airtight container and used for the study.

2.1.1.1 Chemicals and Reagents

All chemicals were purchased from Sigma – Aldrich, USA.

2.1.2 Phytochemical tests

The phytochemical screening of *P. biglobosa* stem bark extracts were carried out to determine the presence of the following compounds; alkaloid, flavonoids, tannins, anthraquinones cardiac glycosides, saponins, glycosides, sterols, resins, volatile oil, terpenes and phenols using standard procedures described by (Builders *et al.,* 2011).

2.2 Animals

Adult Wistar rats (180 – 250 g) of either sex maintained at Animal Facility Centre (AFC) of the Department of Pharmacology and Toxicology, National Institute for Pharmaceutical Research and Development (NIPRD), Abuja, Nigeria were used for the study. The animals were fed *ad libitum* with standard feed (Ladokun feeds, Ibadan, Nigeria) and had free access to water. They were also maintained under standard conditions of humidity, temperature and 12 h light/ darkness cycle. The animals were acclimatized for two weeks before the commencement of the study. A standard protocol was drawn up in accordance with the Good Laboratory Practice (GLP) regulations of the ENV (1998). The principle of laboratory animal care (NIH publication, 1985) was also followed in this study.

2.3 Acute Toxicity Study

The LD_{50} of the extract was determined using Lorke's method (Lorke, 1983) with modifications. Briefly, the test was carried out in two phases. Phase 1: Nine rats were divided into three groups of three rats per group. The three groups were administered orally with graded doses (10, 100 and 1000 mg/kg respectively) of the extract. Phase 2: Another nine rats were divided into three groups of three rats per group, which received graded doses (1600, 2900 and 5000 mg /kg) of the extract respectively. The number of deaths in each group within 24 h was recorded and the final LD_{50} values were calculated as the geometric mean of the highest non-lethal dose (with no deaths) and the lowest lethal dose (where deaths occurred).

2.4 Sub Acute Toxicity Study

Twenty four (24) rats were selected by randomization and then divided into four groups of six each. The first group served as control while the remaining three groups were given 1000, 3000 and 5000 mg/kg of *P. biglobosa* single oral dose. The first day of dosing was taken as D0 whereas the day of sacrifice was designated as D14. This was carried out according to the method of Orisakwe *et al., (*2003*).*

2.4.1 Weekly body weight

The body weight of each rat was assessed using a sensitive balance during the acclimatization period, once before commencement of dosing, alternate day during the dosing period and once on the day of sacrifice (Aniagu et al., 2004).

2.4.2 Relative organ weight

On day 14 of the dosing period, all the animals were euthanized by exsanguinations under chloroform anesthesia. Different organs namely the heart, liver, lungs, spleen and kidneys were carefully dissected out and weighed in grams (absolute organ weight) as described by (Uma, 2010). The relative organ weight of each animal was then calculated using equation 1.

$$\text{Relative Organ Weight} = \frac{\text{Absolute organ weight (g)}}{\text{Body weight of rat on sacrifice day (g)}} \times 100 \quad \ldots . 1$$

2.4.3 Histopathological study

Histopathological investigation of the kidney, heart, liver, lung and spleen were done according to the method Pieme *et al.,* (2006) .The organ pieces (3-5 µm thick) were fixed in 10% formalin for 24 h and washed in running water for 24 h. Samples were dehydrated in an autotechnicon and then cleared in benzene to remove absolute alcohol. Embedding was done by passing the cleared samples through three cups containing molten paraffin at 50°C and then in a cubical block of paraffin made by the "L" moulds. It was followed by microtome and the slides were stained with Haematoxylin-eosin. Detailed microscopic examination was carried out in those organs of both control and treatment groups.

2.4.4 Hematological assay

Blood samples collected in the heparinized tubes were used to investigate White Blood Cells (WBC), Red Blood Cells (RBC), Packed Cell Volume (PCV), Haemoglobin, (Hb), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC) and platelets estimation. The microhaematocrit and cyanmethanemoglobin methods of ReyV ´ azquez and Guerrero (2007) were used for the assay. The method of Orisakwe *et al.,* (2003), was employed to determine the total leucocyte counts (TLC) whereas the longitudinal method of Uma (2010) provided a good assay for the differential leucocyte Count (DLC).

2.4.5 Biochemical analysis of serum

Blood collected into non heparinized tubes were then centrifuged at 3000 rpm for 10 min. The serum separated was analysed to evaluate the liver enzymes [Aspartate

aminotransferase (AST), alanine aminotransferase (ALT) and Alkaline phosphatase (ALP), using the method of Pieme et al., (2006). Glucose concentration was determined by the method of Dou et al., (1996). Serum urea, uric acid, creatinine, bilirubin and protein were evaluated by the method of Aniagu et al., (2006), and total serum cholesterol and triglyceride by the method of Taga et al., (1998). The serum was also analysed for electrolytes (sodium, potassium and chloride ions) levels using the method of Henry (2001).

The change in glucose /serum lipids was evaluated with equation 2.

$$\% \text{ Change in glucose/ serum lipid concentration} = \frac{\text{Final concentration}}{\text{Base line concentration}} \times 100 \quad \ldots . 2$$

2.5 Statistical Analysis

Results were expressed as the mean ± standard error of mean (SEM). Statistical analysis of data was carried out using one-way analysis of variance (ANOVA).

3. RESULTS

3.1 Phytochemical Tests

The result of the phytochemical screening of the extracts of *P. biglobosa* is presented in Table 1. The analysis revealed the presence of saponins, tannins, terpenes, and phenols, reducing sugars and sterols in the extracts. Flavonoids and cardiac glycosides were also found in the methanol extract. However resins, volatile oil and anthraquinones were absent.

3.2 Acute Toxicity Studies

There was no mortality in animals at all doses of the extracts up to 5000 mg /ml. The absence of death at doses up to 5000 mg extract /kg showed that LD_{50} of the extracts of *P. biglobosa* is greater than 5000mg/kg P.O. Rubbing of nose and mouth on the floor of the cage and restlessness were the only behavioral signs of toxicity shown by the animals, these disappeared within 24 hrs of extracts administration.

3.3 Weekly Body Weight

During the 14 days of observation, there were no significant changes in the bodyweights of the treated rats compared to the control rats.

3.3.1 Relative organ weights

There were no significant changes in the relative weight of the heart, kidneys, liver, lung and spleen of the rats treated with methanol extract in relation to the control groups. A significant increase in relative weight of the kidneys was observed with the group administered 5000mg/kg of water extract (Table 2).

Table 1. Phytochemical screening of the extracts of stem bark of *P. biglobosa*

Chemical compounds	Test methods	Water extract	Methanol extract
Alkaloids	Dragendorff's test	_	_
	Wagner's test	_	_
	Mayer's test	_	_
Flavonoids	Sodium hydroxide test	_	+
	Ferric chloride test	_	+
	Lead acetate test	_	+
Tannins	Lead acetate test	++	+
	Ferric chloride test	++	+
Anthraquinones	Borntrager's test	_	_
Saponins	Foam test	+	+
	Liebermann's test	+	+
Cardiac glycosides	Keller Killiani's test	_	+
Terpenes	Salkowski's test	_	+
Sterols	Liebermann's test	+	+
Phenols	Ferric chloride test	+	+
Reducing sugars	Fehling's test	+	+
Volatile oil	Boiling test	_	_
Resins	Boiling test	_	_

+ represents Compound present; ++ represents appreciable amount; - represents Compound absent.

Table 2. Effects of the extracts of *P. biglobosa* on relative organ weights of rats

Treatment (mg/kg/day)	Hearts	Lungs	Livers	Spleens	Kidneys
Control	0.34 ± 0.05	0.73 ± 0.06	3.90 ± 0.13	0.38 ± 0.10	0.79 ± 0.05
W1000	0.35 ± 0.07	0.72 ± 0.07	3.86 ± 0.16	0.35 ± 0.10	0.75 ± 0.11
W3000	0.34 ± 0.03	0.75 ± 0.02	3.92 ± 0.12	0.37 ± 0.07	0.79 ± 0.09
W5000	0.35 ± 0.06	0.75 ± 0.09	3.94 ± 0.03	0.37 ± 0.14	0.87 ± 0.02^{x}
M1000	0.32 ± 0.10	0.70 ± 0.13	3.86 ± 0.10	0.34 ± 0.08	0.77± 0.09
M3000	0.35 ± 0.08	0.74 ± 0.03	3.91 ± 0.06	0.36 ± 0.12	0.80±0.03
M5000	0.34 ± 0.04	0.72 ± 0.10	3.93 ± 0.02	0.38 ± 0.16	0.76±0.15

W= Water extract, M= Methanol extract.
Note: values represent the mean ± SEM (n=6); ^{x} $p<0.05$. Significantly different from controls.

3.4 Gross and Histological Pathology

In control group no structural changes were identified by histopathology in the heart, liver, lung, spleen and kidneys suggesting that these animals were healthy and the conditions under which the experiment was conducted were proper.

Infiltration, necrosis and fatty degeneration were noted with 5000mg/kg of water extract of *P.biglobosa* treated rats. No adverse effects were observed with methanol extract treated rats in our study (Fig.1-5).

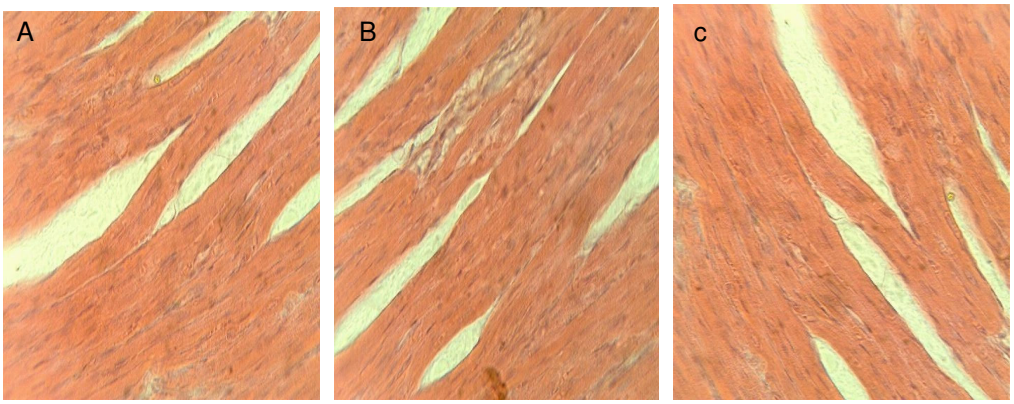


Figure 1. Photomicrographs of heart tissue of rat.
All sections were stained with hematoxylin and eosin.
A: Section of control rat showing normal histological appearance of heart.
B: Section of rat treated with 5000mg/kg of water extract of P. biglobosa showing normal architecture.
C: Section of rat treated with 5000mg/kg of methanol extract of P. biglobosa showing normal architecture. (X 40 magnifications).

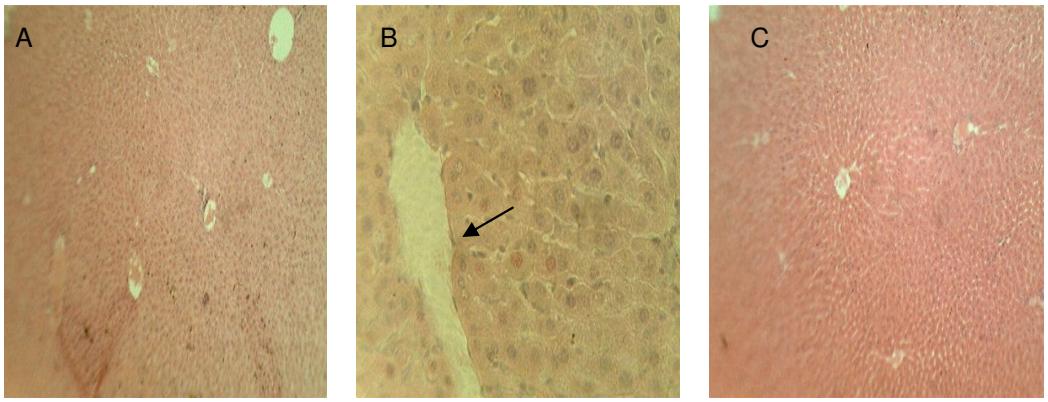


Figure 2. Photomicrographs of liver tissue of rat.
All sections were stained with hematoxylin and eosin.
A: Section of control rat showing normal histological appearance of liver.
B: Section of rat treated with 5000mg/kg of water extract of P. biglobosa showing fatty degeneration (black arrow).
C: Section of rat treated with 5000mg/kg of methanol extract of P. biglobosa showing normal architecture. (X40 magnifications).

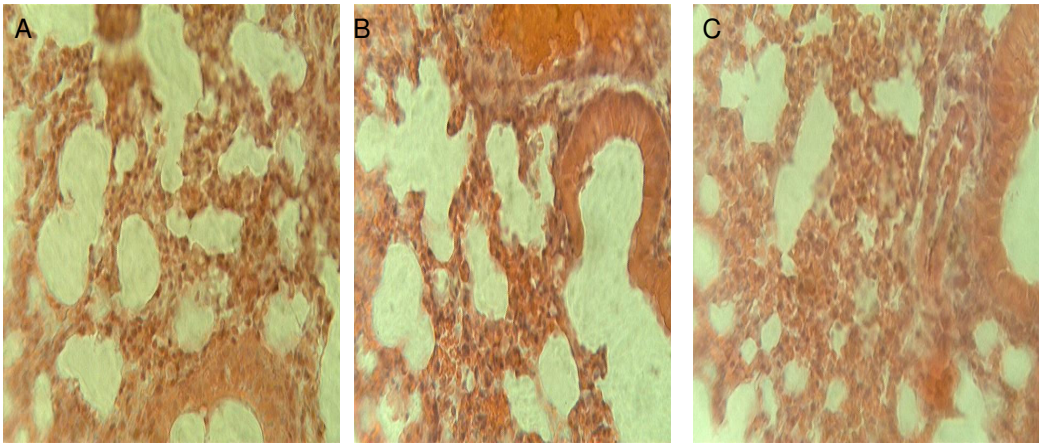


Figure 3. Photomicrograph of lung tissue treated rat.
All sections were stained with hematoxylin and eosin.
A: Section of control rat showing normal histological appearance of lung.
B: Section of rat treated with 5000mg/kg of water extract of P. biglobosa showing normal architecture.
C: Section of rat treated with 5000mg/kg of methanol extract of P. biglobosa showing normal architecture. (X 40 magnifications)

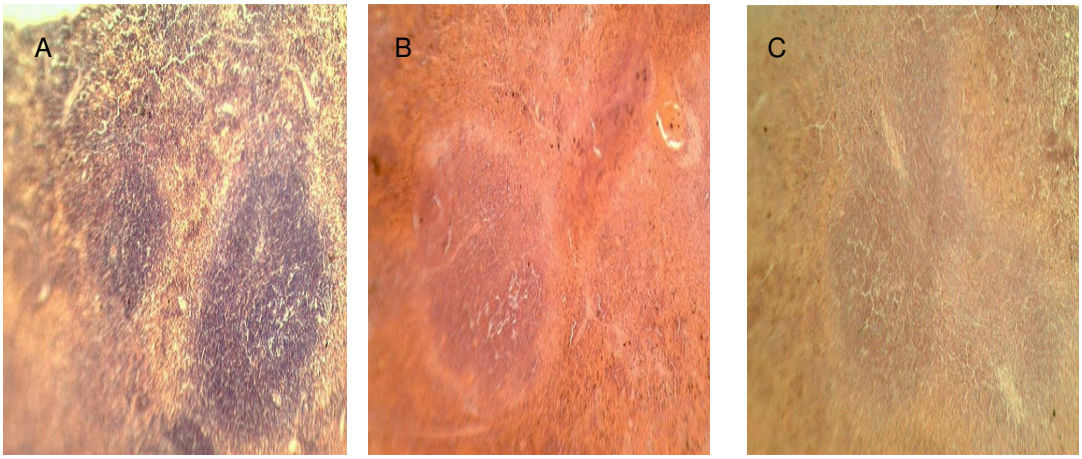


Figure 4. Photomicrographs of spleen tissue rat.
All sections were stained with hematoxylin and eosin.
A: Section of control rat showing normal histological appearance of spleen.
B: Section of rat treated with 5000mg/kg of water extract of P. biglobosa showing normal architecture.
C: Section of rat treated with 5000mg/kg of methanol extract of P. biglobosa showing normal architecture. (X40 magnifications)

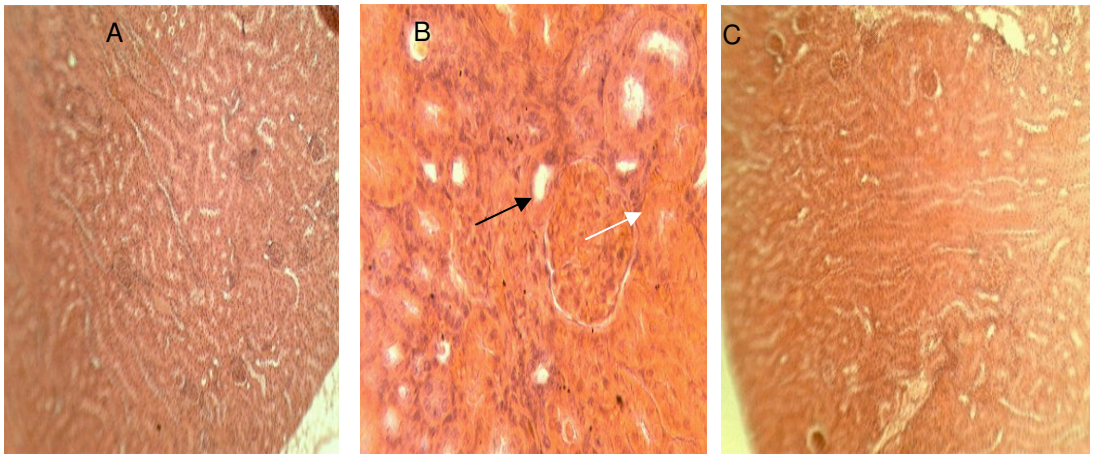


Figure 5. Photomicrographs of Kidney tissue of treated rat.
All sections were stained with hematoxylin and eosin.
A: Section of control rat showing normal histological appearance of kidney.
B: Section of rat treated with 5000mg/kg of water extract of P. biglobosa showing tubular degeneration (black arrow) and dilation of glomerular capillaries (white arrow).
C: Section of rat treated with 5000mg/kg of methanol extract of P. biglobosa showing normal architecture. (X40 magnifications).

3.5 Hematology

There were no significant changes in packed cell volume, hemoglobin, mean Corpuscular hemoglobin, mean corpuscular hemoglobin concentration, monocytes and eosinophils, total leukocyte count, differential leukocyte count, erythrocyte, leukocyte and platelet of all the treated groups.

3.6 Effects on Hepatic Function Indices

The water extract produced no significant changes in the levels of AST, ALT and ALP. But we observed significant reduction in the level of ALP with methanol extract treated groups in relation to the control (Fig. 6). A significant dose dependent increase in serum glucose level was observed for all the animals treated with water extract with maximum change of 10.8% while significant dose dependent reduction was noted with the methanol extract treated groups compared to the control groups with maximum change of 13.8% (Fig. 7).

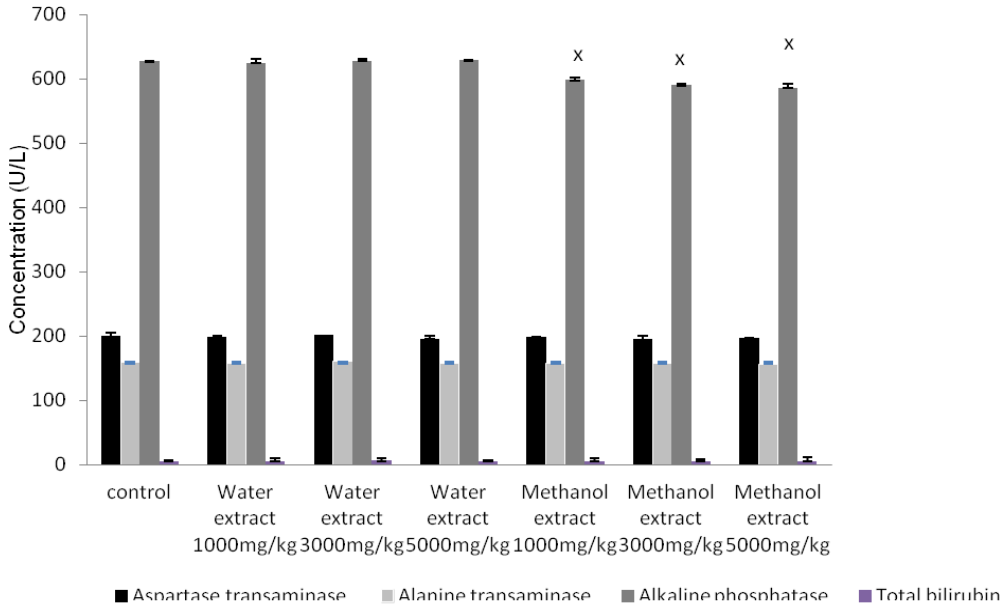
3.7 Effects on Renal Function

No significant changes were observed in sodium, chloride and potassium ions for all the treated rats. There was no significant alteration in the blood urea, creatinine and uric acid of all the treated animals in relation to the control group.

3.8 Effects on the Serum Lipid Profile

A significant dose dependent increase in serum triglycerides concentration and total cholesterol levels were noted with the water extract treated rats with maximum changes of

50.3% and 27.0% while significant dose dependent reduction was observed with the groups administered methanol extract in relation to the control groups with maximum changes of 51.4% and27.0% (Fig. 8).



F igure 6. Effects of the extract of *P. biglobosa* on liver enzymes level

Note: values represent the mean ± SEM (n=6);
^{x} p<0.05. Significantly different from controls.

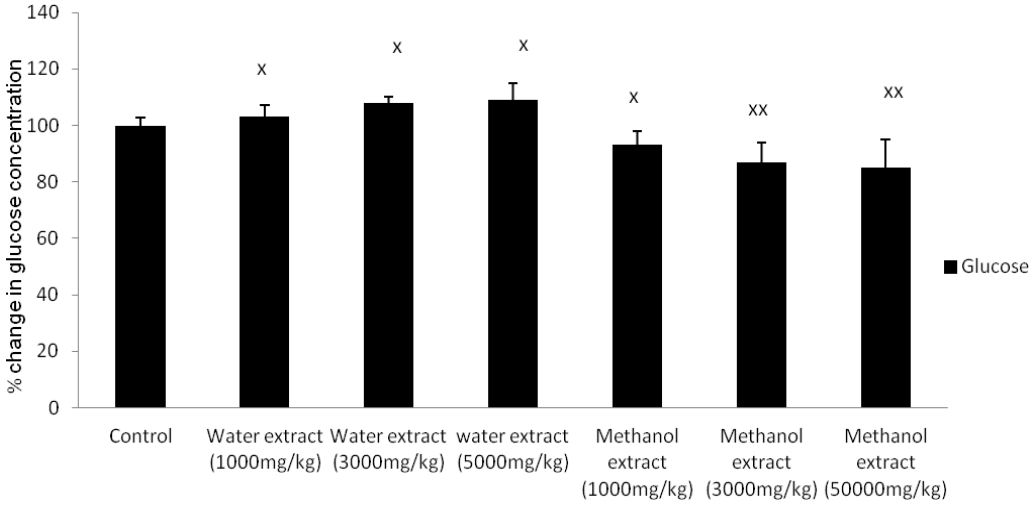


Figure 7. Effects of the extract of *P. biglobosa* on the plasma glucose in rats

Note: values represent the mean ± SEM (n=6); ^{x} p<0.05. Significantly different from controls; ^{xx} p<0.01. Very significantly different from controls.

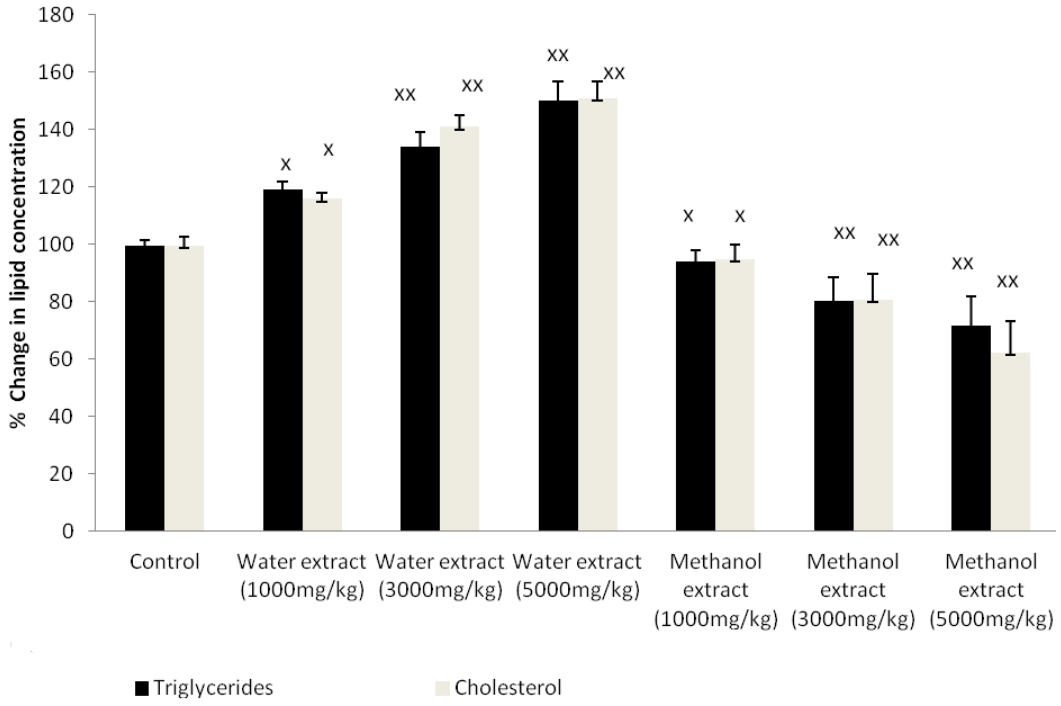


Figure 8. Effects of the extract of *P. biglobosa* on lipid serum profile

Note: values represent the mean ± SEM (n=6); ^{x} p<0.05. Significantly different from controls; ^{xx} p<0.01. Very significantly different from controls.

4. DISCUSSION

The plant kingdom represents an enormous reservoir of biologically active compounds with various chemical structures and protective /disease preventive properties (phytochemicals). These phytochemicals, often secondary metabolites present in smaller quantities in higher plants, include the alkaloids, steroids, flavonoids, terpenoids, tannins, and many others. The active principles of many drugs found in plants are secondary metabolites (Ghani, 1990; Dobelis, 1993). Therefore, basic phytochemical investigation of these extracts for their major phytoconstituents is also vital.

The acute toxicity of *P. biglobosa* has been investigated to determine any adverse effect that may arise as a result of a short time animal exposure to the extracts within 24 h period. Though P *.biglobosa has* been used by TMPs without report of any mortality due to toxicity, this claim has been authenticated by the lack of death at oral treatment of over 5000 mg/kg body weight of the extract, however these finding agreed with the work of (Tijani et al., 2009; Udobi and Onaolapo, 2009). The results thus suggest that the extract *P. biglobosa* has low toxicity (Schorderet, 1992), since the LD_{50} was greater than 5000mg/kg body weight. The low toxicity obtained may have been responsible for its widespread use in different ethno-therapeutic interventions.

Rats treated with various doses of the extract (1000, 3000 and 5000mg/kg) showed no significant increase in body weights in relation to the control animals, indicating that *P.*

biglobosa did not have any adverse effects on the body weight, which is used to assess the response to therapy of drugs and to indicate adverse effects of drugs (Teo et al., 2002).

No significant differences existed in the relative weights of the isolated organs of the methanol treated and control animals, suggesting that methanol extract of *P. biglobosa* did not induce any toxic effect on any of the organs. Furthermore, the histopathological results indicated it was not toxic to the heart, kidneys, lung, liver and spleen since they all exhibited normal architecture. The groups treated with 5000mg/kg of water extract revealed a significant increase in the relative weight of the kidneys and severe histopathological changes in kidney and liver.

The histopathological findings revealed tubular degeneration, dilation of glomerular capillaries in the kidneys. The glomerulus is the primary site of action of several chemicals and it may be injured by any toxic, metabolic and immunologic mechanism (Himri et al., 2004). The toxic irritant substances brought to the kidney by circulatory blood cause degenerative changes in the kidney tissues according to Varely (1987).

The fatty degeneration of the liver in groups treated with 5000mg/kg of water extract is in agreement with the research conducted by Fafioye et al., (2004), who observed histopathological changes in the liver of fish treated with barks of *P. biglobosa.* In the early phase of fatty degeneration, vacuoles appear in the cytoplasm around the nucleus, because their lipid content is dissolved in the course of embedding. The vacuoles appear empty. As the damage to the cells progresses, the hepatocytes become swollen and a single large vacuole will occupy their entire cytoplasm, pushing aside the nucleus and making the hepatocyte signet-ring shaped. The degenerated hepatocytes form wide trabeculae which compress and narrow the lumen of the sinusoids (Himri et al., 2011).

Research conducted by Onyenyili *et al*., (1998), showed that anemia is as a result of hemolytic phenomenon and or inhibition of blood cell synthesis by active constituents of the extract and decrease in hematological parameters has been associated with anemia. The active constituents of *P. biglobosa* did not cause lysis of blood cells and or inhibition in blood cells synthesis, since there was no reduction in hematological parameters.

Ordinarily, liver cell damage is characterized by a rise in plasma enzymes (AST, ALT, LDH etc); therefore *P. biglobosa* did not induce hepatocellular changes. A rise in plasma alkaline phosphatase (ALP) level is usually a characteristic finding in cholestatic liver disease (Kaneko, 1989), the significant reduction in ALP levels by the methanol extract of *P. biglobosa* shows that no possible cholestasis occurred at the dose levels tested. Certain drugs and other substances are known to affect and influence circulating bilirubin. Elevation of bilirubin suggests increase in hemolysis (Orisakwe et al., 2003). The extracts of *P. biglobosa* did not alter the bilirubin level of the treated rats, as well as the albumin and the total protein compared to the control.

The water extract treated rats exhibited increase in serum glucose level while the methanol extract treated groups showed reduction in serum glucose level; this suggests that the methanol extract could produce some hypoglycemic effects. A number of investigators have shown that coumarin, flavonoid, terpenoid and a host of other secondary plant metabolites including arginine and glutamic acids posses' hypoglycemic effects in various experimental animals model (Akah and Okafor, 1992; Marles and Farnsworth, 1995). However, this hypothesis stipulates that plant which contain terpenoid and/or flavonoids posses hypoglycemic activities in diabetic and normal mammal. Therefore the hypoglycemic activity

of the methanol extract of stem bark of *P. biglobosa* may probably be due to terpenoid present, which appears to be involved in the stimulation of the ß-cells of the pancreas and the subsequent secretion of preformed insulin. One or more of the other chemical constituents of the plant especially flavonoid is also likely to have played a crucial role in the hypoglycemic action of the plant extract (Goji et al., 2009; Aragao et al., 2010; Valcheva-Kuzmanova et al., 2007) .

The normal levels of serum urea, creatinine, uric acid, sodium, potassium and chloride ions indicate that *P. biglobosa* did not interfere with renal function and that the renal integrity was preserved (Kaneko, 1989).

The water extract demonstrated increase in the triglyceride and cholesterol levels while the methanol extract exhibited reduction in the triglyceride and cholesterol levels , this shows that the methanol extract of *P. biglobosa* possesses lipid lowering activity and also some beneficial effects on the cardiovascular risk factors (Dixit et al.,1992).

The lipid lowering effect of the methanol extract may be as a result of presence of flavonoids; these have shown to have numerous health benefits, which include lowering of tissue lipids (Zhou et al., 2009; Sharma et al., 2008; Viana et al., 2004). Several researches conducted had indicated that many plant sterols reduce serum cholesterol absorption (Sushruta et al., 2006).

Therefore the synergistic interaction of the polyphenol found in this extract may be responsible for lipid lowering property (Uma, 2010).

The toxic effect of water extract of *P. biglobosa* on the kidneys and liver may be due to any one or more of the phytochemicals present in the extract. Furthermore the phytochemical screening of the water extract of *P. biglobosa* indicated presence of appreciable amount of tannins. Study conducted by Yamasaki et al. (2002), Bajaj (1988), showed that a large intake of tannins may cause kidney and liver damage.

5. CONCLUSION

This study has shown the diversity in toxicity as well as the chemical constituent of the stem barks of *P. biglobosa* in relation to the extraction solvent. However this study provides the basis for further study on the detailed toxic and pharmacological effects of the extracts of *P. biglobosa* stem bark and their active component(s).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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