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Acute toxicity profile of crude methanolic stem bark extract of *Parkia biglobosa* in West African Dwarf (WAD) goats

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ABSTRACT: Despite the high demand for herbal medicines for treatment of health disorder, there are still concerns associated with not only their use, but their safety. This study was aimed at providing information on the potential toxicity profile of the stem bark extracts of *P. biglobosa* in goats. For this purpose, the stem bark parts of *P. biglobosa* were collected and processed. The acute toxicity, biochemical and histopathological analysis in goats were determined. The results of phytochemical constituents revealed the presence of alkaloids, anthraquinones, cardiac glycosides, glycosides, oils, phlobatannins, reducing sugar, saponins and tannins (condensed and hydrolysable). The results of acute toxicity studies showed no mortality with up to 5000 mg/ kg of the body weight. The blood collected revealed that, CMSBE has no significant ($p>0.05$) effect on biochemical parameters of WAD goats. However, there were slight changes in glucose concentration, cholesterol and triglyceride level, though they were no statistically significant ($p>0.05$). The extracts did not also have deleterious effect on morphology of the tissues observed during histopathology. The study has scientifically established that, stem bark extract of *P. biglobosa have* LD_{50} that is greater than 5,000 mg/kg and it can be inferred that the plant might have a wide margin of safety typical of treatment of some diseases. It is therefore recommended that despite the non-toxicity as demonstrated in this present study, detailed toxic and pharmacological effects of the extracts of *P. biglobosa* stem bark in other animals should be investigated.

Keywords: Biochemical profile, doses, histopathology, medicinal plant, phytochemicals.

INTRODUCTION

Medicinal plants are plants in which one or more of their parts contain substances that can be used for therapeutic purposes or which are precursors for the synthesis of therapeutic agents (Sofowora, 2008). Presently, focus on plant research as anthelmintic is on the increase globally and substantial evidence has been collected to show the immense potentials of medicinal plants used in various traditional systems (Adamu *et al.,* 2009).

The use of medicinal plants, as a normative basis for the maintenance of good health, has been widely observed in most developing countries and world at large (Jordan *et al*., 2010). A survey conducted by the World Health Organization (WHO) indicated that about 70-80% of the world populations rely on non-conventional medicine mainly of herbal sources in their primary healthcare (WHO, 2003).

Despite the high demand for herbal medicines for treatment of health disorder, there are still concerns associated with not only their use, but their safety. It is a common belief that the phytotherapeutic or nutraceutical options, as well as other "natural" products, are safer than synthetic drugs (Athanasiadou *et al*., 2007). This statement is incorrect because, in fact, many plant secondary metabolites with anthelmintic effects may also have negative effects on the hosts. For example, tannins may affect diet digestibility (Méndez-Ortíz *et al*., 2012).

Over the last two decades, different retrospective studies done indicated that the incidence of deaths occurring due to exposure to plants ranged from 1.5 to 7.2% in different countries of the world (Gaillard and Pepin, 1999). However, the total number of deaths due to exposure to plants throughout the world is very difficult to establish and must certainly be underestimated since all cases of such deaths were from analytical and forensic points of view, not always well documented and thus, rarely published (Bent and Ko, 2007).

One of the basic criteria set by WHO for the use of herbs as medicines is that they should be indicate to be non-toxic (WHO, 2011). Toxicity testing of herbal drugs has also been found to have a lot of benefits (OECD, 2008). Notably, it is easy to identify the toxic effects and thus determine the limit of exposure levels especially to sensitive population.

Plants such as *Parkia biglobosa* which grow naturally in West Africa are one of the most important economic trees in the Northern part of Nigeria. It has been used in Nigeria and other West African rural communities to treat a variety of diseases (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 (Shao, 2002; Grønhaug *et al*., 2008; Tijani *et al*., 2009).

So far, most of the claims of efficacy of the extracts of stem bark of *P biglobosa* have been scientifically established, however, little or no information exist on the potential toxicity profile of the stem bark extract of *P. biglobosa* in goats. Therefore, the aim of this study is to provide information on adverse effects of extract of stem bark of *P biglobosa* on goats and to determine the extent at which such effects occur. This would then give us the information about the safety of the plant because of its widespread use in the management of various disorders.

MATERIAL AND METHODS

Collection, processing and extraction of plant materials

The fresh stem bark of *P. biglobosa* was collected in Kwara State, Nigeria. The identification and authentication of plant sample was done by a taxonomist in the Department of Botany, Ahmadu Bello University Zaria, Kaduna State, Nigeria. This plant sample was given a Voucher number ABU/7064 which was deposited in the herbarium in the same department for reference purposes. The plant sample was processed using the method of Soetan *et al.* (2011) and Meraiyebu *et al*. (2013).

The stem bark of *P. biglobosa* (100 g at a time) was extracted with 600 mL of methanol in a Soxhlet's apparatus for 4 hours using the methods of Asuzu and Onu (1994) and Builders *et al. (*2012). Another 100 g was weighed again with sensitive weighing balance and the same procedures above were followed until 25 kg was exhausted. All the filtrate was evaporated using water bath at 65°C. The weight by weight (w/w) yield of the extract was stored in an airtight container at 4°C until use. The determination of percentage yield of extract was calculated using the formula of Ezekwe *et al.* (2013) as follows:

$$\% \text{ Yield} = \frac{\text{Weight of the extract}}{\text{W. of pulverized stem bark of } P.\ biglobosa} \text{ x } 100$$

Qualitative phytochemical screening of stem bark extract of *P. biglobosa*

The phytochemical screening of the extract was carried out to identify the constituents using standard phytochemical methods**.** The crude methanol extract of stem bark was screened to determine the possible presence of alkaloids, flavonoids, saponins, tannins, terpenoids, anthraquinones, glycosides, cardiac glycoside/ cardenolides, phlobatannins, sterols and steroids, carbohydrates, starch, proteins and oils **(**Evans, 2002).

Determination of maximum convenient concentrations (MCCs), maximum convenient doses (MCDs) and LD_{50} of extract used in toxicity studies

The maximum convenient doses were calculated, due to lack of information on the actual doses of the plant extracts. The MCCs of the stem bark of *P. biglobosa* extract was prepared using the methods of Lorke (1983) and Ibrahim (1984). One gramme (1 g) of each extract was thoroughly mixed with 1 mL of distilled water (0.05 mL at a time) until the solution could be delivered through a needle at room temperature. The MCCs of extract in g/mL were determined from the volume of the solvent used. The maximum convenient volume (MCV) that could be administered to the goat by the oral route (gavage) is 5 mL/kg (Loomis, 1978; Lorke, 1983; Ibrahim, 1984). The MCDs (g/kg) was calculated by multiplying the MCCs (g/mL) by the MCV (mL/kg) (Kimani *et al.,* 2014).

$$\text{Volume (ml)} = \frac{\text{Dose rate mg/kg) b. w XBody weight (kg)}}{\text{Concentration (mg mL)}}$$

The established MCD was then used as the basis for the administration of the plant extracts in acute toxicity studies.

Acute toxicity studies

LD_{50} experiment was done with modification using the methods of Bruce (1985), OECD (2001, 2008), Deora *et al*. (2010) and Chinedu *et al.* (2013). The test extract was administered generally in a single dose by gavage to goats fasted 24 hours prior to dosing and was administered to five groups. Firstly, a lower dose of 1000 mg/kg was administered to single goat at a time within interval of 24 hours. After 24 hours of the administration of the first dose, the next dose was determined by the outcome of the first dose administered. If the animal survives the first dose, the dose is adjusted upward, but if mortality is recorded at first dose, it is adjusted downward. The adjustment of dose either upward or downward was by a constant factor. Each animal was observed for 1 or 2 days before dosing the next animal. Surviving animals monitored for delayed death for a total of 7 days. Testing was terminated when the upper limit (5000 mg/kg) has been reached without mortality or when the LD_{50} has been established from the test.

$LD_{50} = (M_0 + M_1)/2$

Where: M_0 = Highest dose of test substance that gave no mortality, and M_1 = Lowest dose of test substance that gave mortality.

Immediately after oral administration of the CMSBE of *P. biglobosa*, the goats were critically examined for survival time, behavioral changes and clinical signs of toxicity.

Biochemical analysis of serum

Blood samples (2 mL) for serum analysis were collected from each goat per group during pre-administration and post-administration via jugular venipuncture using a 5 mL syringe into non heparinized tubes. This was allowed to coagulate at room temperature and then centrifuged for 10 minutes at 1500 x g. The serum was separated and 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, chloride and potassium ions) levels using the method of Henry (1991). The change in glucose/serum lipids was evaluated as follow.

$$\%\ \text{Change in glucose/serum lipid conc.} = \frac{Final\ Conc.}{Base\ line\ conc.}\ x\ 100$$

Post mortem examination of animals in the LD_{50} experiment

Post mortem examination was performed on the goats that died within 24 hours after dosing with extracts. All goats with prolonged signs of toxicity and showing no signs of recovery at 48 hours were also euthanized and post mortem examination were performed. Histopathological investigation of the liver and kidney were carried out according to the method of Pieme *et al.* (2006).

Ethical consideration

This research work was conducted in accordance with the ethical rules on animals' experimentation as approved by the Ethical Committee of Federal University of Technology (FUT), Minna.

Data analysis

The data were computed in tables. The percentage yields of the extracts were calculated. Biochemical parameters were expressed as mean±SEM. They were further subjected to t-test and one-way analysis of variance (ANOVA) followed by Turkey's post hoc test where necessary. Value of $p<0.05$ was considered significant. GraphPad Instat version 3.05 Windows from Graphpad Software (2000), San Diego, California USA (www.graphpad.com) was used to analyze the data.

RESULTS

The results of qualitative phytochemical screening are shown in Table 1. The results revealed the presence of alkaloids, anthraquinones, cardiac glycosides, glycosides, oils, phlobatannins, reducing sugar, saponins and tannins (condensed and hydrolysable). However, the extract tested negative for protein and triterpenoid. The level of availability of these phytochemical constituents varied. Alkaloids, glycosides, saponins and condensed tannins are present in higher amount.

The percentage yield of the methanol extraction of pulverized stem bark of *P. biglobosa* are shown in Table 2. The CMSBE of *P. biglobosa* was readily soluble in water. One (1 g) of extract was conveniently dissolved (pass through 18 G needle at room temperature) in 1.25 mL of distilled water to obtain its MCC (g/mL). The MCDs (g/kg) was obtained by multiplying MCCs (g/mL) by MCV (5 mL/kg). Therefore, the MCC (g/mL) and MCD (g/kg) of

Table 1. Qualitative phytochemical screening of methanol stem bark extracts of *P. biglobosa.*

Chemical constituents	Test methods	Methanol extract
Alkaloids	Mayer's test	+++
	Wagner's test	+++
Anthraquinones	Bontrager's test	+++
Cardiac Glycosides	Keller-Kiliani test	+
Flavonoids	NaoH test	++
Glycosides	Benedict's test,	+++
	Ferric chloride	+++
Oil	Filter paper test	++
Protein	Millon reagent test,	–
	Biuret test	–
Phlobatannins	Hcl test	++
Reducing Sugar	Fehling test	++
Saponins	Frothing test	+++
Starch	Iodine test	–
Sterols and Steroids	Conc H_2So_4 test	++
Tannin (Condensed)	Ferric chloride test	+++
Tannin (Hydrolysable)	Ferric chloride test	++
Terpenoid	Salkowski test	++
Triterpenoids	Salkowski test	–

Key= - Absent, + Present, ++ Very present, +++ much present.

Table 2. Percentage yield of methanol extracts from pulverized stem bark of *Parkia biglobosa.*

Components of *P. biglobosa*	Initial weight of Pulverized bark (g)	Final weight of the extracts(g)	Percentage yield (%)
Stem bark	3000	753.56	25.12

Table 3. Solubility, Maximum Convenient Concentrations (MCCs) (g/mL) and Maximum Convenient Doses (MCDs) (g/kg) of stem bark extract of P*. biglobosa.*

Parkia biglobosa	MCC (g/mL)	MCD (g/kg)
Crude methanol stem bark extract (CMSBE)	0.8	4

the extract were 0.8 and 4 respectively and is shown in Table 3.

The result of acute toxicity studies is shown in Table 4. Varying doses of CMSBE of *P. biglobosa* were given to five groups of goats at different time and there was no mortality in all the animals administered with up to 5000 mg/kg of their body weight. The absence of death at this higher dose showed that the LD_{50} of the extracts (CMSBE) is greater than 5000 mg/kg of body weight of the animal. The only signs of toxicity such as dullness were showed in group 4 and dullness, enlargement of abdomen, dizziness and anorexia were showed in group 5 (Table 4). All these signs disappeared within 24 hours of extracts administration and all the groups were observed for seven days before postmortem.

There were no significant ($p>0.05$) changes in bilirubin, serum urea, $Na^{+,}$ K^+ Cl^- and uric acid in all groups of WAD goats administered with CMSBE of *P. biglobosa* including the control (Table 5). But glucose concentration differed significantly ($p<0.05$) in groups B and E with respect to pre-administration and post-administration. More also groups (A, D and E) of creatiine including control were not significantly different ($p>0.05$) as shown in Table 5

On the other hand, the CMSBE of *P. biglobosa* administered produced no significant change ($p>0.05$) in the cholesterol, triglyceride, total protein levels as well as aspartate aminotransferase (AST), alanine aminotransferase (ALT and alkaline phosphate (ALP) levels of WAD

Table 4. Result of acute toxicity studies of crude methanol extract of stem bark of *P. biglobosa* administered to WAD goats.

Group	Dosage (mg/Kg)	Survived	Dead	Clinical sign(s) or behavioural changes
1	1000	1	0	No signs
2	2000	1	0	No sign
3	3000	1	0	No sign
4	4000	1	0	Dullness
5	5000	1	0	Dullness, enlargement of abdomen, dizziness and anorexia

Table 5. Changes in the biochemical parameters of WAD goats administered with CMSBE of *P. biglobosa*.

Biochemical Parameters	Experimental groups (mg/ml)	Pre-administration day	Post - administration day
Bilirubin (umol/l)	Control	0.33±1.46^{a}	0.25±0.05^{a}
	A	0.57±0.03^{a}	0.50±0.12^{a}
	B	0.60±0.00^{a}	0.60±0.00^{a}
	C	0.60±0.00^{a}	0.40±0.12^{a}
	D	0.60±0.00^{a}	0.63±0.03^{a}
	E	0.50±0.10^{a}	0.63±0.03^{a}
Glu Est. (mmol/l)	Control	2.63±0.03^{a}	2.40±0.30^{a}
	A	2.60±0.06^{a}	2.67±0.07^{a}
	B	2.50±0.06^{a}	2.97±0.18^{b}
	C	2.60±0.12^{a}	2.70±0.06^{a}
	D	2.60±0.15^{a}	2.73±0.09^{a}
	E	2.27±0.33^{a}	2.73±0.03^{b}
Urea (mmol/l)	Control	2.63±0.48^{a}	3.10±0.00^{a}
	A	6.23±0.03^{a}	5.23±1.02^{a}
	B	5.90±0.35^{a}	4.87±0.84^{a}
	C	5.23±0.03^{a}	3.30±0.06^{a}
	D	5.07±0.53^{a}	3.77±0.38^{a}
	E	4.50±1.12^{a}	3.37±0.12^{a}
Na^{+} (mmol/l)	Control	49.67±6.81^{a}	49.50±5.50^{a}
	A	64.67±1.33^{a}	61.67±0.33^{a}
	B	65.00±1.53^{a}	59.00±2.19^{a}
	C	62.33±0.33^{a}	57.67±2.96^{a}
	D	58.00±2.00^{a}	59.67±1.86^{a}
	E	58.00±2.00^{a}	58.67±1.76^{a}
K^{+} (mmol/l)	Control	0.57±0.13^{a}	0.55±0.05^{a}
	A	0.83±0.03^{a}	0.67±0.03^{a}
	B	0.80±0.06^{a}	0.60±0.06^{a}
	C	0.83±0.03^{a}	0.63±0.03^{a}
	D	0.57±0.03^{a}	0.67±0.09^{a}
	E	0.70±0.06^{a}	0.73±0.07^{a}
Cl^{-} (mmol/l)	Control	46.00±0.0^{a}	45.50±2.50^{a}
	A	43.67±1.20^{a}	44.67±1.33^{a}
	B	42.00±0.58^{a}	43.33±1.33^{a}
	C	43.33±0.88^{a}	41.33±0.33^{a}
	D	41.00±0.00^{a}	43.33±1.33^{a}
	E	42.00±0.58^{a}	42.00±0.00^{a}

Table 5. Contd.

Creatine (mmol/l)	**Control**	**59.67±7.13[a]**	**55.50±7.50[a]**
	A	68.33±3.67[a]	62.67±5.49[a]
	B	70.00±2.00[a]	55.00±7.02[b]
	C	71.33±0.33a	62.00±0.58[b]
	D	66.00±0.33[a]	65.67±0.67[a]
	E	63.67±1.67[a]	64.00±0.58[a]
Uric acid (u/l)	Control	3.33±1.33[a]	3.00±0.00[a]
	A	5.67±0.33[a]	6.00±0.00[a]
	B	6.33±0.33[a]	5.00±0.00[a]
	C	6.33±0.33[a]	4.67±1.20[a]
	D	5.33±0.33[a]	6.00±0.00[a]
	E	5.00±1.00[a]	5.00±0.58[a]

Each value is mean±SEM for three goats in each group. There were no significant (p>0.05) difference between the pre-administration and post-administration group.

goats. The total protein for group B differs significantly (p<0.05) (Table 6). The percentage change in glucose concentration of WAD goats administered with CMSBE of *P. biglobosa* are shown in Table 7. Elevated glucose concentration was observed in all the groups except in control group that showed reduced glucose concentration. The percentage increases in the cholesterol levels was evident compared to control group and group B that had reduced cholesterol. No change was observed in the cholesterol levels of WAD goat in group 4 (Table 8). Over all reduction of triglycerides was observed among the experimental groups and the reduction was not significant (p<0.05) (Table 8).

The histopathological studies of liver and kidney of goats administered with CMSBE of *P. biglobosa* are presented in Figures 1 and 2. In all the treatment groups including controls, there were no structural changes or abnormalities in the liver and kidney. The liver hepatocytes were preserved in all groups as well as prominent present of central vein. But group C, D and E showed passive congestion of central vein and infiltration of eosinophils around the portal vein (Figure 1). The architectural morphology of kidney showed no observable lesion in the group examined (Figure 2).

DISCUSSION

Medicinal plants offered great prospect for the development of novel chemotherapeutic agents that are essential for the management of various diseases in food animals and human (Sofowora *et al.*, 2013). In this study, the results of qualitative phytochemicals screening showed that alkaloids, anthraquinones, cardiac glycosides, glycosides, flavonoides, oil, protein, phlobatannins, reducing sugar, saponins, sterols/steroids, tannin (condensed and hydrolysable) and terpenoids were present.

The results in this study were similar to that of Ezekwe *et al*. (2013) and Josiah *et al*. (2022) in methanol extracts of stem bark of *P. biglobosa*. Millogo-Kone *et al.* (2006) also reported the presence of saponins, glycosides, tannins and other phenolics with trace quantity of alkaloids while Banwo *et al.* (2004) confirmed the same. However, the report of Builders *et al*. (2012) differed slightly from this result and the previous findings of Banwo *et al.* (2004) and Millogo-Kone *et al.* (2006) due to absence of alkaloids from the methanol stem bark extracts of *P. biglobosa.* Thus, the absence may not be a minus for the medicinal efficacy of stem bark of *P. biglobosa* but could be the methods of processing and geographical location of this plant that might have led to differences in phytochemical constituents in this work and the work of Builders *et al*. (2012).

Different methods exist for the extraction and separation of plant materials for pharmacological and medicinal uses. In this study, the extract (CMSBE) yielded 25.12%, which is higher than that of Salit *et al*. (2014) who reported 4.0% yield extracts of stem bark of *P. biglobosa*. This is an indication that the method used in this study would be the best method of extracting phytochemical constituent of plant materials for toxicity studies. The CMSBE of *P. biglobosa* was readily soluble in water, with MCC and MCD of 0.8 g/mL and 4 g/kg, respectively. These findings are quite similar to those obtained by Oshadu (2014) in his MCC and MCD determination of different portions of *Acanthus montanus* leaves where he reported MCCs (g/ml) of 0.8 and MCDs (g/kg) of 4, for crude ethanol extract of *Acanthus montanus* leaves.

The acute toxicity study of CMSBE *P. biglobosa* showed no any obvious signs of toxicity or change of demeanour at doses ranging from 1000 to 4000 mg/kg. However,

Table 6. Changes in the biochemical parameters (coronary, heart and liver determination) of WAD goats administered with CMSBE of *P. biglobosa*.

Parameters	Group	Pre- treatment- day	Post treatment- day 15
Cholesterol mmol/l	Control	0.57±0.13^{a}	0.50±0.10^{a}
	A	0.57±0.03^{a}	0.60±0.00^{a}
	B	0.63±0.03^{a}	0.50±0.06^{a}
	C	0.67±0.03^{a}	0.70±0.06^{a}
	D	0.67±0.07^{a}	0.67±0.07^{a}
	E	0.50±0.10^{a}	0.57±0.03^{a}
Triglyceride mmol/l	Control	0.77±0.09^{a}	0.75±0.07^{a}
	A	0.83±0.03^{a}	0.77±0.12^{a}
	B	0.90±3.83^{a}	0.77±0.15^{a}
	C	0.87±0.03^{a}	0.77±0.15^{a}
	D	0.93±0.13^{a}	0.83±0.06^{a}
	E	0.87±0.03^{a}	0.80±0.00^{a}
Total protein g/ml	Control	2.77±0.15^{a}	2.80±0.00^{a}
	A	2.80±0.10^{a}	2.60±0.00^{a}
	B	2.93±0.06^{a}	2.43±0.21^{b}
	C	2.87±0.06^{a}	2.80±0.10^{a}
	D	2.67±0.12^{a}	2.57±0.06^{a}
	E	2.80±0.10^{a}	2.70±0.17^{a}
Aspartate aminotransferase (ASP)(u/l)	Control	14.00±1.53	14.50±1.50^{a}
	A	15.00±0.00^{a}	16.00±0.00^{a}
	B	16.00±0.00^{a}	16.00±0.00^{a}
	C	15.67±0.58^{a}	16.33±1.20^{a}
	D	16.00±0.00^{a}	16.00±0.00^{a}
	E	16.33±0.58^{a}	16.00±0.00^{a}
Alanine aminotransferase ALT) (u/l)	Control	9.67±1.86^{a}	11.00±0.00^{a}
	A	11.33±0.33^{a}	11.00±0.00^{a}
	B	11.00±0.58^{a}	11.33±0.33^{a}
	C	11.67±0.33^{a}	12.33±0.88^{a}
	D	11.00±0.00^{a}	11.33±0.33^{a}
	E	10.67±0.33^{a}	11.33±0.33^{a}
Alkaline phosphate (ALP))(u/l	Control	21.67±2.96^{a}	22.00±1.00^{a}
	A	25.67±0.33^{a}	25.00±1.00^{a}
	B	25.67±0.33^{a}	24.33±1.67^{a}
	C	26.00±0.00^{a}	26.33±0.33^{aaa}
	D	26.00±0.58^{a}	25.67±0.33^{a}
	E	24.33±1.20^{a}	25.67±0.67^{a}

Each value is mean±SEM for three goats in each group. The mean for each parameter with different superscript alphabet in the same row are statistically significant different ($p<0.05$).

dullness, dizziness, enlargement of abdomen and anorexia were observed at 5000 mg/kg but disappeared within 24 hours without mortality. This result suggested that CMSBE of *P. biglobosa* had an oral LD_{50} greater than 5000 mg/kg. The high LD_{50} value implies a remote risk of acute intoxication and high degree of relative safety when extract is administered orally. Though *P. biglobosa has* been used by Traditional Medical Practitioners (TMPs) without report of any mortality due to toxicity, this claim has been authenticated by the lack of death in oral treatment

Table 7. Percentage change in glucose concentration of WAD Goats administered with CMSBE of *P biglobosa*.

Experimental groups (mg/mL)	%change of glucose conc.	Mode of change
Contro1	-8.75	Decrease
A	+2.69	Increase
B	+18.8	Increase
C	+3.85	Increase
D	+5.0	Increase
E	+20.26	Increase

Key: Control = distilled water (DW) 5ml/kg; A = CMSBE of P. biglobosa (1000mg/kg); B= CMSBE of P. biglobosa (2000mg/kg); C = CMSBE of P. biglobosa (3000mg/kg)7; D = CMSBE of P. biglobosa (4000mg/kg); E = CMSBE of *P. biglobosa* (5000mg/kg).

Table 8. Percentage change in serum lipid concentration of WAD Goats administered with different dosage of CMSBE of *P biglobosa.*

Group	% change of cholesterol	Mode of change	% change of Triglyceride	Mode of change
Control	-12.28	Decrease	-2.6	Decrease
A	+5.26	Increase	-7.23	Decrease
B	-20.63	Decrease	-14.44	Decrease
C	+4.48	Increase	-12.5	Decrease
D	0	The same	-10.75	Decrease
E	+14	Increase	-8.05	Decrease

of WAD goats at the dose rate of 5000 mg/kg body weight. These finding agreed with the work of Tijani *et al.* (2009), Udobi and Onaolapo (2009) and Builders *et al.* (2012) who reported LD_{50} greater than 5000 mg/kg body weight of rat administered with CMSBE of *P. biglobosa.* The low toxicity obtained may have been responsible for its widespread use in different ethnotherapeutic interventions and it is therefore considered practically non-toxic (Schorderet, 1992). However, this result contradicted the report of Ezekwe *et al.* (2013) who opined that LD_{50} of CMSBE of *P. biglobosa* was 400 mg/kg body weight of albino rat. The differences in acute oral LD_{50} values observed could be attributed to possible differences between species in drug metabolism and susceptibility to toxic effects as reported by Salawu *et al.* (2008).

Attempts to grade dose-toxicity relationships of toxic substances under experimental conditions have been made by a number of researchers. One of such grading according to Loomis (1978), Mutschler *et al.* (2008) and Wink and van Wyk (2008) defined <1 mg/kg as extremely toxic, 1-50 mg/kg as highly toxic, 50-500 mg/kg as moderately toxic, 500-5000 mg/kg slightly toxic, 5000 - 15,000 mg/kg as practically non-toxic and > 15,000 mg/kg as relatively harmless. In this study, the extract tested in goat is therefore regarded as practically non-toxic, since the LD_{50} fall within the range 5000 -15,000 mg/kg. Femi-Ola *et al. (*2008) also reported that *P. biglobosa* plant is non-toxic to humans and that is why African countries use *P. biglobosa* as herbal medications. But the bark and the pods of the same plant contain parkine and equally have piscicidal property (Abalaka and Auta, 2010).

In this study, CMSBE of *P. biglobosa* has no effect on biochemical parameters of WAD goats. There was no significant ($p>0.05$) increase in serum creatinine, urea, uric acid, sodium, potassium and chloride ions. These results were in contrast with the results of Ezekwe *et al. (*2013) who recorded increase in the level of creatinine and urea when methanol extract of *P. biglobosa* stem bark was administered to albino rats. Also increase in serum creatinine, urea, uric acid, sodium and potassium ions were recorded by Njidda *et al.* (2013) in Kano Brown and Red Sokoto breed of goats fed on natural grazing range land of Northern Nigeria. However, this result coincides with the finding of Builders *et al.* (2012) who administered extract of *P. biglobosa* stem bark to albino rats without increase in serum creatinine, urea, uric acid, sodium and potassium ions. The normal levels of serum creatinine, urea, uric acid, sodium, potassium and chloride ions shows that the CMSBE of *P. biglobosa* did not affect the renal function and that the integrity of renal was preserved (Kaneko, 1989).

Research findings have shown that, terpenoid coumarin,

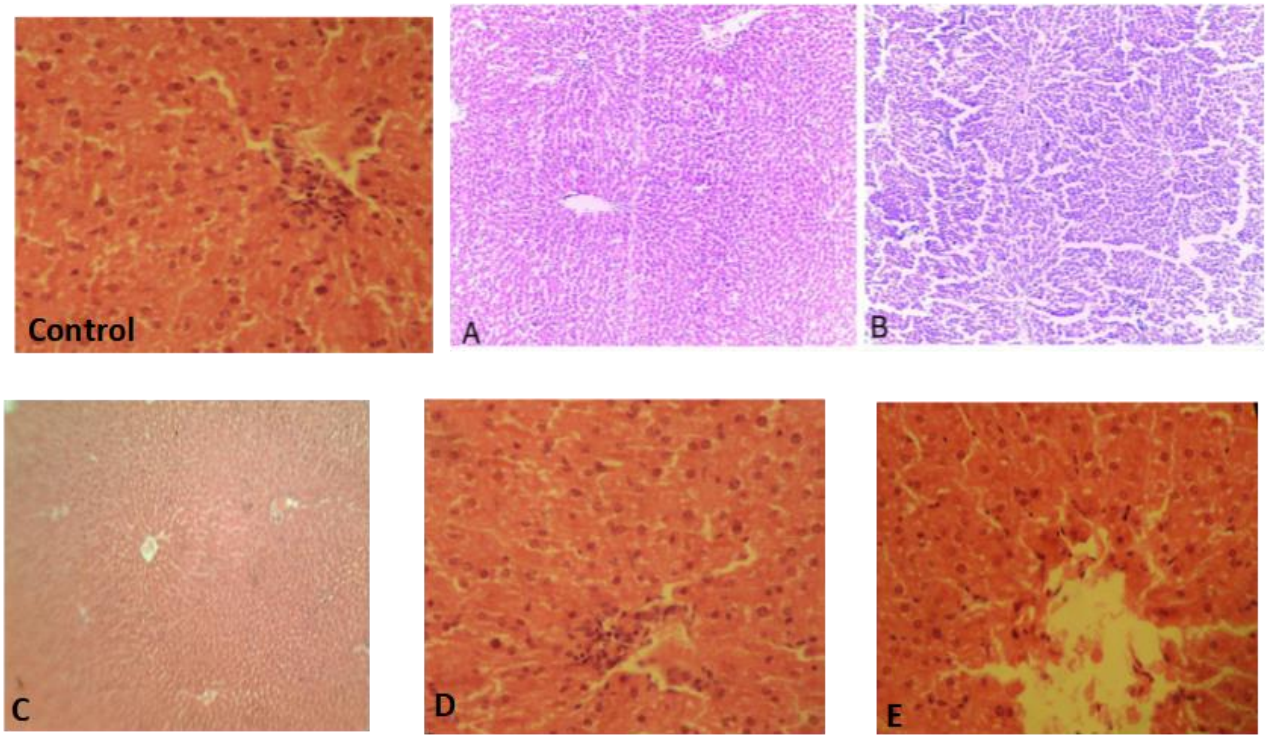

Figure 1. Comparative Photomicrographs of Section of Goat Liver Exposed to Different dosage of *CMESB of Parkia biglobosa.* No Observable Microscopic Difference Between Control and the dosage. **Key: Control =** Liver of goat exposed to 5 ml/kg of distilled water (control) (H & E, 100). The black arrow showed central vein and red arrow showed normal hepatocytes; **A =** Liver of goats administered with 1000mg/kg of CMESB of *P. biglobosa* (H & E, ×100). Passive congestion of the central vein and dilated sinusoids as well as normal hepatocytes; **B =** Liver of goats administered with 2000mg/kg of CMESB of *P. biglobosa* (H & E, ×400). Central vein and normal hepatocyte; **C =** Liver of goat administered with 3000mg/kg of CMESB of *P. biglobosa* (H & E, ×400). Infiltration of eosinophils around the central vein and slight dilation of sinusoid; **D =** Liver of goat treated with 4000mg/kg of CMESB of *P. biglobosa* (H & E, ×400). Infiltration of eosinophils around the central vein and slight dilation of sinusoid; **E =** Liver of goat treated with 5000mg/kg of CMESB of *P. biglobosa* (H & E, ×400). Infiltration of eosinophils around the central vein and slight dilation of sinusoid.

flavonoid and a host of other secondary plant metabolites such as glutamic acids and arginine posses' hypoglycemic effects in various experimental animals model (Akah and Okafor, 1992). However, this hypothesis stipulated that plants which contain flavonoids and/or terpenoid possess hypoglycemic activities in diabetic and normal mammals. 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). In this study, despite the presence of flavonoid and terpenoid, there was no significant hypoglycemic activity exhibited by CMSBE of *P. biglobosa.* However, the flavonoid present in CMSBE would have been responsible for regulation of glucose level to some extent. Certain drugs and other substances are known to affect and influence circulating bilirubin. Increase in bilirubin suggests increase in hemolysis (Orisakwe *et al*., 2003). The CMSBE of *P. biglobosa* did not alter the bilirubin level of the treated goats when compared to the control.

The CMSBE of *P. biglobosa* did not interfere with total protein since there was not significant difference between the groups except group B. This result disagreed with the result of Sachin and Sahni (2010) who reported increase in total protein when extract of *Nigella sativa, Swertia chirata* and *Piper longum* were used for deworming goats. The reasons for these discrepancies are not known but may be due to immune response of animals during administration of CMSBE of *P. biglobosa.*

The serum enzymes (AST, ALT and ALP) as well as bilirubin are conventionally used as indicator of hepatic damage (Adama *et al*., 2011). The serum concentration of these constituents was within the reference values of goats and there was no difference between the administered groups. Therefore, CMSBE of *P. biglobosa* show possibly no negative effect on liver function. This result agreed with that of Raghuvansi *et al*. (2007). The study also agreed with the finding of Builders *et al.* (2012)

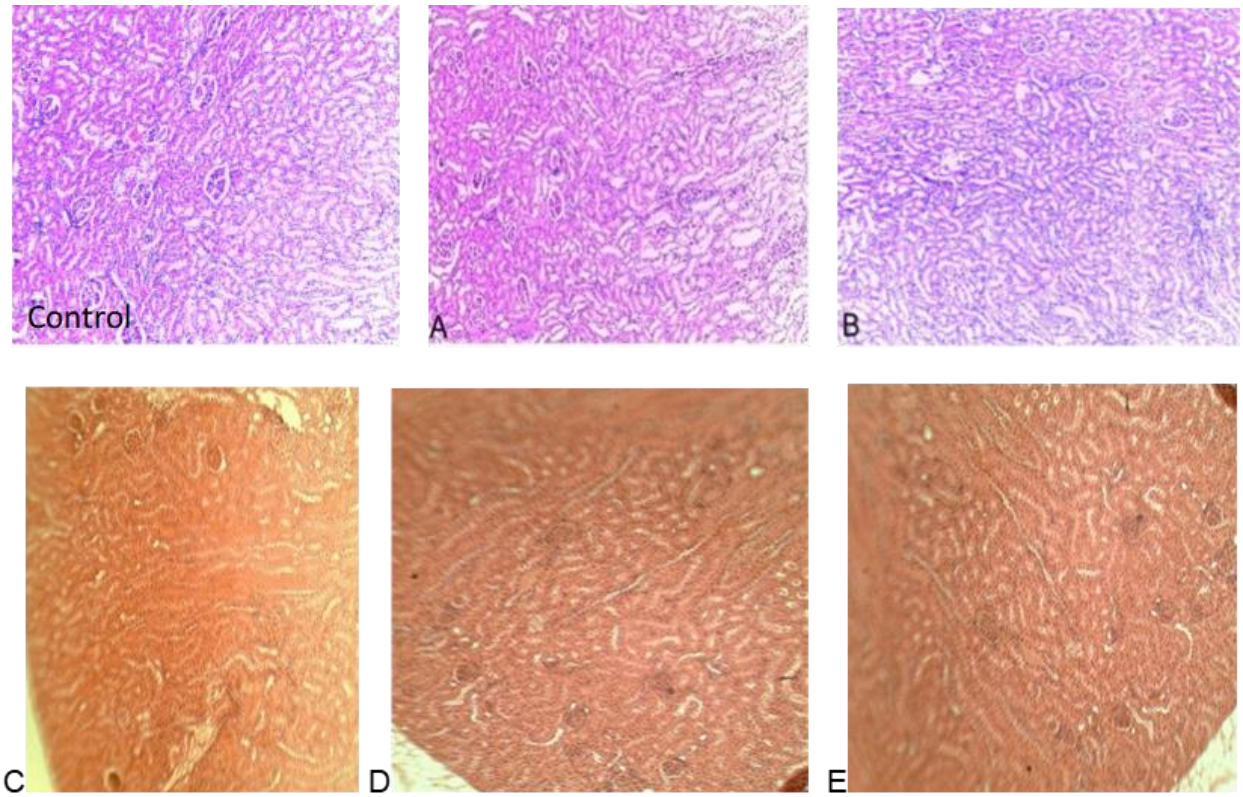

Figure 2. Comparative Photomicrographs of Section of Goats Kidney Exposed to Different dosage of CMESB of *P. biglobosa.* No Observable Microscopic Lesions in the dosage and Control group. **Keys: Control** = Kidney of goat administered with 5 ml/kg of distilled water (control).Bowman's capsule and the glomerulus are intact (H & E, ×100); **A =** Kidney of goat administered 1000mg/kg of CMESB of *P. Biglobosa* Bowman's capsule and the glomerulus are intact (H & E, ×100); **B =** Kidney of goat administered with 2000mg/kg of CMSBE of *P. biglobosa.* Bowman's capsule and the glomerulus are intact (H & E, ×100); **C =** Kidney of goat administered 3000mg/kg og CMESB of *P. Biglobosa* Bowman's capsule and the glomerulus are intact (H & E, ×100); **D =** Kidney of goat administered 4000mg/kg og CMESB of *P. Biglobosa* Bowman's capsule and the glomerulus are intact (H & E, ×100); **E =** Kidney of goat administered 5000mg/kg of CMESB of *P. Biglobosa.* Slight haemorrhage in Bowman's capsule and the glomerulus (H & E, ×100).

and Ezekwe *et al.* (2013) who reported decrease in serum alkaline phosphatase level with respect to control when they investigated the toxicity of the stem bark extract of *P. biglobosa* in albino rats. A rise in alkaline phosphatase is usually a characteristics found in cholestatic liver disease. As such, the significant reduction in ALP shows that no possible cholestasis occurred at the dose levels tested (Kaneko, 1989).

Glucose is relatively a good indicator of energy balance. The reduction in glucose level in animals, result in gross reduction in weight gain and milk yield and in change in the fatty acid composition of the milk (Zapta *et al.,* 2003). The slight change in the glucose concentration in the current study is an indication that infection was responsible for reduction despite the feeds that was provided. In this study, all groups showed slight increase in glucose level except the control group. This indicate that CMSBE of *P. biglobosa* can provide energy. The result agreed with that of Builders *et al.* (2012) who reported increase in serum glucose level of rat treated with aqueous extract of *P. biglobosa.*

The finding in this research showed reduction in triglyceride and cholesterol. The reduction in triglyceride and cholesterol indicates that the CMSBE of *P. biglobosa* may have lipid some beneficial effects on the cardiovascular risk factors by lowering the lipid activity (Dixit *et al.,* 1992). The reduction may be as a result of presence of flavonoid (Viana *et al*., 2004; Sharma *et al.,* 2008; Zhou *et al.,* 2009). Several research findings indicated that many plant sterols reduce serum cholesterol absorption (Sushruta *et al.,* 2006). Therefore, the lowering property of these extracts may be the synergistic interaction of polyphenol that is present (Uma, 2010).

The histopathological results revealed no effect of CMSBE on liver and kidney tissues since there was no structural changes or abnormalities of these organs when

compared with controls. The normal hepatocytes displayed by the liver tissue without any enlargement in central vein, sinusoidal vein and portal triad in all administered groups and control agreed with the finding of Builders *et al.* (2012), when 5000 mg/kg of methanol extract of stem bark of *P. biglobosa* was administered to albino rats. Similar findings were reported by Roy *et al.* (2016) without structural changes in liver tissues when extract of *Senna alata* leaf of varying dosages of 1000 to 3000 mg/kg were administered to Swiss Albino mice. Bello *et al*. (2016) also reported the same findings when methanolic extract of *Alstonia scholaris* stem bark was administered to albino rats. However, this result contradicts that of Builders *et al*. (2012), where they administered 5000 mg/kg of aqueous extract of stem bark of *P. biglobosa* to albino rats; there was fatty degeneration of liver cells.

Kidney micrograph revealed normal architecture of glomerulus and Bowman's capsules with no tubular degeneration and dilation of glomerular capillaries. The normal architecture of kidney in this study agreed with the finding of Builders *et al.* (2012) who administered 5000 mg/kg of methanol extract of stem bark of *P. biglobosa* to albino rats without abnormalities but 5000 mg/kg of water extract of stem bark of *P. biglobosa* showed tubular degeneration and dilation of glomerular capillaries. Other researchers such as Ping *et al.* (2013) and Nabukenya *et al.* (2014) also reported normal architectural of kidney when *Euphorbia hirta* L. methanol extract and aqueous extracts of *Tephrosia vogelii*, *Vernonia amygdalina* and *Senna occidentalis* extracts were administered to albino rats, respectively.

Thus, the histopathological evaluation during the administration of CMSBE of *P. biglobosa* administration protocol indicated that the extracts did not have any deleterious effect on morphology of the tissues observed. These findings supported the biochemical results observed in this study since the extracts used did not produce any toxic effect in WAD goats.

Conclusion

In conclusion, the CMSBE of *P. biglobosa* seemed to be blood, liver and kidney friendly as none of these parameters were altered during biochemical and histopathological analyses. This study has scientifically established that the LD_{50} of CMSBE of *P. biglobosa* is greater than 5,000 mg/kg and it can be inferred that the plant might have a wide margin of safety typical of anthelmintics and treatment of other diseases. It is therefore recommended that despite the non-toxicity as demonstrated in this present study, detailed toxic and pharmacological effects of the extracts of *P. biglobosa* stem bark should be investigated in other animals.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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