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TOXICITY EVALUATION OF AQUEOUS STEM EXTRACTS OF *Euphobia lateriflora* (SCHUM AND THONN) IN SOME ALBINO RATS

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ABSTRACT

The effect of administration of graduated dose of an aqueous stem extract of *Euphorbia lateriflora* on alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), bilirubin, total protein, creatinine and urea in rats were determined to ascertain the toxic effects on the liver and kidney. There was a significant increase ($p< 0.05$) in ALT activity and significant decreases in urea level in the group administered with 100mg/kg aqueous stem extract of *Euphorbia lateriflora* compared to the control. In groups administered with 250mg/kg, there was a significant increase ($p < 0.05$) in ALT, AST activities and bilirubin level than the control. The result suggests a possible hepatotoxic effect of root extract of *Euphorbia lateriflora* after administration of 100 mg/kg and 250 mg/kg. There was no possible kidney malfunction. The result of the oral acute toxicity study shown that *Euphorbia lateriflora* have oral LD_{50} above 5000 mg/kg.

Keywords: Toxicity, Liver, Kidney, Function

INTRODUCTION

Since ancient times, medicinal plants have been used to cure or improve infections or disturbances in both humans and animals (Jamil *et al.*, 2022). Since time immemorial, people search for drugs in nature for rescue of their disease. The use of traditional plants could lead to the discovery of new powerful botanical agents for the treatment of several ailments (Eddouks *et al.*, 2014). Medicinal plants may contain secondary metabolites such as alkaloids, glycosides, steroids and other classes of compounds with noticeable pharmaceutical activity as anticancer, antidiabetic, antidysentric antimalarial and (Biradar, 2015). In Nigeria ethnomedicine, *Euphorbia lateriflora* is well known and used for the treatment of skin mucosae, cutaneous and subcutaneous parasitic infections. It is also used in the treatment of venereal diseases as well as in the remedy for head lice (Elufioye and Olaifa, 2015). *Euphorbia lateriflora* is a popular traditional herb whose leaves are used in Africa, particularly in Nigeria, to treat wounds and many diseases (Falana and Nurudeen, 2022). The liver plays a fundamental role in the body's overall metabolic activities, harmful metabolic byproduct clearance and xenobiotics (foreign substances) detoxification (Wierling, 2014). The strategic localization of liver, its blood flow and eminent role it play in xenobiotics metabolism make that organ susceptible to chemical injury to which are exposed (Gu and Manautou, 2012). The functions of Kidney include getting rid of the body's waste substances that are either ingested, produced via metabolism or due to of detoxification by the liver. These and other roles of the kidney, can be tempered as a results of toxic metabolites or chemicals accumulation leading to renal ailment (Usman *et al*., 2014).

Euphorbia lateriflora belongs to the family Euphorbiaceae, it is a shrub reaching a height

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of 1.70m with near-vertical, smooth-glaucous succulent branches (Obi, 2011). The used of *E. lateriflora* locally for the treatment of sexually transmitted disease such as candiditis, Gonorrhea and syphilis was reported in Ibadan. The dried stem (peel) of *Euphorbia lateriflora* powdered was used as Concoction for the remedy of gonorrhea, syphilis and candiditis (Gbadamosi, 2014). Extract from *Euphorbia lateriflora* was found to demonstrate antiviral activity using the measles virus on human epidermoid carcinoma cell line (Obi *et al*., 2006). Numerous scientific report indicated that, the leave extract of *Euphorbia lateriflora* exhibited potential against chickenpox (Falana and Nurudeen, 2022). It has been reported that an extract from *Euphorbia lateriflora* displayed antibacterial activity against antibiotic resistant bacteria (Coker et al., 2021). Despite widespread use of *Euphorbia lateriflora* as medicinal plant in Nigeria and other parts of Africa, data on the toxicity evaluation of *Euphorbia lateriflora* is scarce.

MATERIALS AND METHODS

Sample Collection

Fourty (40) albino rats with body weight ranging from 100 to 162g (of both sexes) were procured from National Veterinary Research Institute Vom, Jos, Nigeria. The rats were kept in cages in the animal house of the Department of Biological Sciences, Gombe State University and the animals were allowed access to normal diet (Growers marsh, Vital feeds Ltd) and water

Extracts Preparation

The stem of the plant was collected from around Galinja village in Madobi Local Government Area, Kano State. The stem collected was dried under shade and ground to powder using pestle and mortar. For subacute toxicity testing, 40g of stem was dissolved in $500cm^3$ of distilled water followed by filtration after 24 hours, the residue was dried by evaporation. The concentration of the extract was determined as a difference between the original weight and the dried residue. The filtrates were concentrated to $300cm^3$ using oven drier (Genlab Limited UK). The concentration of stem extract was $6.8g/300cm^3$. For acute toxicity test, the stem powder was dissolved in water and filtered after 24 hours. The filtrate was evaporated to dryness in an oven. The dried extracts were weighed and dissolved in distilled water to a concentration of $4.8g/40cm^3$ stem.

Subacute Toxicity

For subacute toxicity studies twelve rats were used. The animals were placed into 3 groups of 4 rats per group. Groups I and II, were the study groups. The animals in groups I and II (test groups) were administered orally with 100 mg/kg and 250 mg/kg of aqueous stem extracts of *Euphorbia lateriflora* respectively while group III, control group were administered with distilled water. The oral administration of aqueous stem extracts was carried out once every 24 hours for the duration of three weeks.

Acute Toxicity

For acute toxicity studies, sixteen rats were used. Four groups of rats with 4 animals in each group were given orally different doses (2000, 3000, 4000 and 5000 mg/kg) of the stem extracts. The deaths in each group were recorded within 24 hours.

Collection and Preparation of Blood Samples

Animals were sacrificed by decapitation at the end of third week of oral administration of stem. Blood samples were collected into clean centrifuge tubes using Pasteur pipette. After clotting of the blood at room temperature for 5 minutes the clot blood was carefully loosen by using applicator stick. The blood was then

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centrifuged at 2500 rpm for 10 minutes. The serum was carefully collected into a clean labeled specimen bottle. The activities of alanine aminotransferase, aspartate aminotransferase were determined as described by (Reitman and Frankel, 1957), alkaline phosphatase (Rec, 1972) and the concentrations of bilirubin (Jendrassik & Grof, 1938) in the presence of caffeine which releases albumin bound bilirubin, total protein (Weichselbaum, 1946) by interaction with an alkaline medium, creatinine (Rartels & Böhmer, 1971) and urea (Weatherburn, 1967) via hydrolysis by the action of urease.

RESULTS

The results of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), bilirubin, total protein, creatinine and urea are shown in Table 2. Data were expressed as mean ± standard deviation. Statistical analysis was carried out by the student t – test distribution for comparison. In Table 2, there was a significant increase ($p< 0.05$) in ALT activity and significant decreases in urea level in group administered with 100mg/kg aqueous stem extract of *Euphorbia lateriflora* compared to the control. In groups administered with 250mg/kg, there was a significant increase ($p < 0.05$) in ALT, AST activities and bilirubin level than the control.The result of the oral acute toxicity shown no mortality recorded in any groups administered with 2000, 3000, 4000 and 5000mg/kg aqueous stem extracts of *Euphorbia lateriflora*. However, the treated animals showed signs of depression. In groups administered orally with 2000, 3000, 4000 and 5000mg/kg aqueous root extract of *Euphorbia lateriflora*, two deaths were recorded. According to the toxicity scale of Hodge and Sterner, any compound with an oral LD_{50} above 5000mg/kg should be considered practically non-toxic (Gujbama and Usman, 2022).

Table 1: Mortality recorded for oral acute toxicity

Concentration of extract (mg/kg	Mortality
2000	No
3000	No
4000	No
5000	No

Table 2: Effects of the aqueous stem extract of *Euphorbia lateriflora* on serum ALT, AST, ALP, bilirubin, total protein creatinine and urea.

Group	ALT (U/dm^3)	AST (U/dm^3)	ALP (U/dm^3)	Bilirubin (µmol/dm^3)	Total protein (g/dm^3)	Creatinine (µmol/dm^3)	Urea (mmol/dm^3)
100mg/kg	13.05±0.65^a	22.85±1.82	83.33± 9.47	8.33 ± 1.07	73.35±2.32	59..68±0.41	9.10 ±1.16^a
250mg/kg	12.48±1.17^a	23.33±0.66^a	95.70± 10.44	10.85± 1.59^a	70.07± 8.05	59.80± 1.83	10.57± 1.83
Control	9.40 ± 0.68	21.38± 0.41	80.85± 11.27	8.33 ± 1.07	73.80± 5.32	59.75± 0.27	11.10± 1.58

Values with superscript a are significantly different from control values at $p<0.05$
Values represent mean ± SD (n = 4)

DISCUSSION

From Table 2, the serum activity of ALT was found to be significantly higher ($P<0.05$) than the control in both groups administered with 100mg/kg and 250mg/kg aqueous stem extract of *Euphorbia lateriflora*. This signifies that oral administration of aqueous stem extract of *Euphorbia lateriflora* could have possible mild hepatotoxic effect. This could be linked to the fact that liver necrosis is among the causes of elevated levels of serum ALT (Mwakalila *et al*., 2022). Levels of ALT enzyme in the blood increase above normal ranges as a result of liver damage. The

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enzyme usually affected include ALT among others. Liver toxicity is determined if ALT level increase three times the level at the start of study (Hosein, 2001). However, the ALT activities in groups administered with 100mg/kg and 250mg/kg aqueous stem extract of *Euphorbia laterflora* were not up to three times higher than in control group.

There was a significantly higher ($P<0.05$) in the activity of AST in group administered with 250mg/kg of stem extract of *Euphorbia lateriflora* compared to the control as shown in Table 2. There was no significant difference ($P>0.05$) in the activity of AST in group administered with 100mg/kg of stem extract of *Euphorbia lateriflora.* The increase in the activity of AST could be linked to the fact that, AST increase in the serum a suggestive of cellular damages and loss of functional reliability of the hepatocyte membrane leading to their leakage into the serum (Jassim *et al*., 1987). However, concurrent increase in ALT and AST is a suggestive of mild necrosis. This could be linked to the fact that liver toxicity is ascertained if there is increase in ALT three times it level at the start study as reported by (Hosein, 2001). However, the ALT activities of groups administered with 100mg/kg and 250mg/kg aqueous stem extract were not up to three times as that of control.

From Table 2, it was found that, there was no significant difference ($p > 0.05$) in the activity of ALP compared to the control in groups administered orally with 100mg/kg and 250mg/kg stem extract of *Euphorbia lateriflora*. Liver ALP is a non-plasma specific enzyme that is secreted from the sinusoidal surface of the liver cell and thus is present in the serum at low levels in the absence of liver damage (Prince and Stevens, 1989). From Table 2, it was observed that the serum level of bilirubin was significantly higher in group administered with 250mg/kg stem extract of *Euphorbia lateriflora* compared to the control. The increased could be linked to the fact that hyperbillirubinemia is caused by such factors such as extra-hepatic effect of the drug/substances, like hemolysis, or its interference with a specific aspect of bilirubin disposition (Sane *et al*., 2014). The plasma bilirubin concentration reaches the upper limit when the normal load of bilirubin cannot be conjugated and/or extracted by damage liver cells (Kwo *et al*., 2017). However, increased plasma level in this study was not up to twice the control value as shown in Table 2.

From Table 2, it was observed that, there was no significantly difference ($P > 0.05$) in serum total protein compared to the control in the groups administered with 100mg/kg and 250mg/kg aqueous stem extract of *Euphorbia lateriflora*. From Table 2, there was no significant difference ($P > 0.05$) in serum total creatinine compared to the control in groups administered with 100mg/kg and 250mg/kg aqueous stem extract of *Euphorbia lateriflora.* This shows there was no possible kidney malfunction. Creatinine is removed from the plasma by glomerular filtration and is then excreted in the urine without being reabsorbed by the tubules to any significant extent. In addition, when plasma creatinine level increased above the normal, the kidney can also excrete it through the tubules. Consequently, serum of blood creatinine levels in renal disease generally do not increase until renal function is substantially impaired (Faulkner and King, 1982).

From Table 2, it was observed that serum urea level was significantly lower than the control in group administered with 100mg/kg. The significantly lower urea level seen is contrary to the fact that urea concentration is raised in renal disease (Lin *et al*., 2022),the decrease

could be due to the fact that urea concentration is influenced by diet (Lin *et al*., 2022). In addition all rats were fed with a protein rich diet and rats administered with aqueous extract had less appetite than the control, which could lead to lower urea level Alldredge (Alldredge, 1993). The reduced feed intake in animals fed tannin containing diet can be attributed to the strong astringent property of tannins and induction of internal malaise in mammals, which may contribute to reduce feed intake.

CONCLUSION

It was found that oral administration of 100mg/kg and 250mg/kg stem extracts of *Euphorbia lateriflora* could lead to possible hepatotoxic effect with groups administered with 250mg/kg having a higher possible hepatotoxic effect. It was also found that, there was no possible kidney malfunction after oral administration of aqueous stem extract of *Euphorbia lateriflora* for 3 weeks. In line with the result of this work, there is need for more research to be carried on its toxicity and implications.

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