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ACUTE TOXICITY AND HAEMATOLOGICAL EFFECTS OF ETHANOL BARK EXTRACTS OF *Entandrophragma utile* (DAWE & SPRAGUE) SPRAGUE AND *E. angolense* (WELW.) C.D.C. IN MALE MICE

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ABSTRACT

Background: *Entandrophragma utile* and *E. angolense* are traditionally used medicinal plants in Africa, yet their acute toxicity profiles remain underexplored.
Objectives: This study investigated the acute toxicity and haematological and histopathological effects of ethanol bark extracts of *E. utile* and *E. angolense* in male mice.
Method: Fifty adult male mice were allocated into five groups per extract. While the control group received normal saline, treatment groups were orally administered increasing doses (200–1600 mg/kg) of each plant extract for 14 days. Parameters assessed included body weight, haematology, liver histology, and mortality to calculate the median lethal dose (LD_{50}).
Results: The LD_{50} values were 2754.23 mg/kg for *E. utile* and 1862.1 mg/kg for *E. angolense*, indicating a higher toxicity potential for the latter. Haematological analysis revealed dose-dependent reductions in packed cell volume (PCV) and haemoglobin (Hb), particularly with *E. angolense*. Liver histology showed mild changes at low doses but significant hepatic congestion and necrosis at higher concentrations, especially in *E. angolense*-treated groups.
Conclusion: Both extracts exhibited dose-dependent haematological and hepatic effects. While relatively safe at low doses, high concentrations pose hepatotoxic risks, emphasizing the need for controlled therapeutic use.

Keywords: Acute toxicity, *Entandrophragma utile*, *Entandrophragma angolense*, haematology, histopathology, mice

INTRODUCTION

Entandrophragma angolense and *E. utile*, commonly known as African mahogany, are tropical hardwood tree species in the Meliaceae family. These valuable timber species are renowned for their commercial significance in the timber industry due to their high-quality wood with desirable properties such as durability, strength, and aesthetic appeal. Beyond their economic importance, these trees play crucial ecological roles in tropical forests, contributing to biodiversity conservation and ecosystem stability (Orwa *et al.,* 2009; CABI International, 2022a, 2022b).

Widely distributed across tropical regions of Africa, these tree species have been traditionally employed for their alleged therapeutic benefits, including anti-inflammatory, antimicrobial, and anticancer activities (Orisadipe *et al.,* 2005; John *et al.,* 2012; Trinh *et al.,* 2021; Youn *et al.*, 2022;Kola-Mustapha *et al.,* 2023;).While the timber attributes of *E. angolense* and *E. utile* have been studied, limited research has focused on their potential toxicological effects on biological their safety and possible risks to human health and the environment, especially in regions where they are extensively utilised (Subramanian *et al.,* 2018; Atanasov *et al.,*2021; Chaachouay and Zidane, 2024; Miranda, 2021).

In this context, conducting a comparative toxicological analysis of *E. angolense* and *E. utile* is imperative to evaluate their potential impact on living organisms. Mice, as common mammalian models in toxicological studies, provide valuable insights into the effects of various substances on biological systems (Bryda, 2013; Mukherjee *et al.,* 2022; Domínguez-Oliva *et al.,* 2023).

Given the increasing reliance on plant-based treatments, understanding potential toxic effects is essential to prevent adverse outcomes and to promote safe usage (Mensah *et al.,* 2019; Van Wyk and Prinsloo, 2020). By subjecting mice to extracts or components derived from these tree species, we can assess their haematological parameters, histological changes, and overall toxicological effects.

This study aims to elucidate the toxicological, haematological, and histological responses of mice exposed to *E. angolense* and *E. utile* extracts. By evaluating these profiles and comparing the effects of the two closely related species, we seek to provide a comprehensive understanding of their safety and potential health impacts as well as identify possible differences in toxicity profiles. The findings from this study will not only contribute to the existing knowledge on the toxicological properties of African mahogany species but also validate the traditional uses of these plants and ensure their safe incorporation into modern pharmacotherapy.

METHODOLOGY

Collection of plant material

The bark of Entandrophragma utile and E. angolense was collected from the Forestry Research Institute of Nigeria. The plant materials were identified and authenticated by a taxonomist with voucher numbers FHI-113968 and FHI-113969, respectively, in the Forest Herbarium, Ibadan. The bark was then oven-dried at 40°C in the laboratory, ground into a powder using a hammer mill, and sieved to ensure uniformity.

Extraction process of plant material

The extraction of the ethanol extract from the bark was performed using the cold maceration method. Five hundred grams (500 g) of each powdered bark of E. utile and E. angolense were soaked separately in 1 litre of 70% and 100% ethanol for 72 hours to obtain the ethanol extract. The content of each extract was filtered through a Whatman filter paper-lined funnel into a conical flask. The filtrates of each extract were concentrated using a rotary evaporator at 40°C, followed by gentle evaporation to dryness at room temperature (28°C). The extracts were then stored in separate clean, dry bottles and kept in the refrigerator at 4°C. Dilutions to the desired concentrations were prepared for each extract as needed.

Experimental design

This study was meticulously designed with a robust experimental framework to evaluate the acute toxicity of ethanol extracts of E. utile and E. angolense bark. The experiment involved fifty adult male mice, divided into five distinct groups for each extract. Each group comprised five mice, ensuring a robust sample size for reliable results. This design permitted a comprehensive analysis of the effects of varying concentrations of the extracts on the subjects.

Experimental animals and their management

A total of fifty adult male mice, each weighing between 40-45 g, were procured from the well-maintained Animal House of the Department of Physiology, University of Ibadan, Nigeria. Before the experiment, the mice were acclimatised for two weeks under standard conditions (12 h light and 12 h dark cycle). This was done in well-ventilated, pathogen-free cages at room temperature (28°C) in the animal house of the Department of Biomedicinal Research Centre, Forestry Research Institute of Nigeria (FRIN). They were fed with standard mouse pellets and had ad libitum access to water, ensuring their well-being throughout the experiment. This careful management of the experimental animals ensured their health and minimised any external factors that could influence the results.

Procedure for LD_{50} test

The LD_{50} test was conducted following the method of Nath and Yadav (2015) with some modifications. This method was chosen for its reliability in determining the percentage of death of the animals 14 days after the daily oral dose. After the two weeks of acclimatisation, each extract was diluted as required and administered once orally to the mice at 9.00 am daily for the period of the test (14 days). This was done after the animals had been starved for 12 h before the onset of the treatment, ensuring consistent absorption of the extracts. The groups were constituted as follows for each extract:

For the *E. utile* bark extracts, Group 1 (Control group) was given only normal saline, while Groups 2-5 were administered with increasing doses (200, 400, 800 and 1600 mg/kg) of the dissolved ethanol bark extract of *E utile* in 1ml of normal saline. For the *E. angolense* bark extracts, Group 1 (Control group) was given only normal saline, while Groups 2-5 were administered with increasing doses (200, 400, 800 and

1600 mg/kg) of the dissolved ethanol bark extract of *E angolense* in 1ml of normal saline.

This detailed procedure ensured a comprehensive evaluation of the acute toxicity of the ethanol extracts of *E. utile* and *E. angolense* bark. The use of a control group and multiple test groups allowed for a thorough comparison of the effects of different concentrations of the extracts.

Procedure for weight change, haematology, and histology

Throughout the 14-day experimental period, a systematic record was maintained for each mouse, documenting any changes in behaviour, weight, and mortality. This was done to study the lethal toxicity of each dose and the lethality of each extract. The data were subjected to rigorous statistical analysis using Probits in Excel 2019 and GraphPad 2019, ensuring a comprehensive evaluation of the data.

After the 14-day treatment period with the extracts, blood samples were collected from each surviving mouse. This was done using the tail vein puncture method, a standard procedure that ensures minimal discomfort to the animal. The collected blood samples were placed in heparinised tubes, which were gently rocked to ensure proper mixing of the blood with the anticoagulants. These samples were then labelled appropriately for subsequent haematological analysis (Ofem *et al.,* 2012; Enenebeaku *et al.,* 2021;).

Following the methods described by Singh *et al.* (2013) with some modifications, the mice were humanely sacrificed after 14 days. The liver samples of the mice were harvested from the various groups. These samples were bottled dry and fixed in 10% formaldehyde (pH 7.2 to 7.4) in preparation for histological analysis.

Data analysis methods

The data collected from the study were subjected to rigorous statistical analysis. Probits analysis in Excel 2019 and GraphPad 2019 were used to determine the lethal toxicity of each dose and lethality of each extract. The *haematological* data were analysed and interpreted to understand the impact of the extracts on the health of the mice. The histological analysis of the liver samples provided insights into the potential tissue damage or changes caused by the extracts. This comprehensive data analysis ensured a thorough understanding of the acute toxicity of the ethanol extracts of *E. utile* and *E. angolense* bark.

RESULTS AND DISCUSSION

Lethal dose (LD_{50}) concentration test of *Entandrophragma* species

Entandrophragma utile

The lethal dose (LD_{50}) concentration of the ethanol bark extract of *Entandrophragma utile* was determined using a range of dosages (Table 1). The control group (Group A) and groups administered with dosages up to 400 mg/kg (Groups B and C) experienced no mortalities. Specifically, the log doses for Groups A, B, and C were 0, 2.30103, and 2.60205999 respectively, all yielding a 0% mortality rate. A slight increase in mortality was observed in the group administered with 800 mg/kg (Group D). This group reported one mortality, resulting in a 20% mortality rate. This was the first instance where positive mortality was noted, aligning with a log dose of 2.90308999. After this, the 1600 mg/kg group (Group E) reported one mortality out of the test subjects, translating to a 20% mortality rate. Despite the relatively higher dose, mortality remained low. This dosage corresponds to a log dose of 3.20422998 and a probit value of 4.16. As observed in Figure 1, the LD_{50} of the ethanol bark extract of *E. utile*, using probit analysis, is approximately 2754.23 mg/kg, which correlates with a log dose value of 3.44.

Table 1: Determination of the assay of the ethanol bark extract of *Entandrophragma utile*

Group	Logdose	Total mortality	% mortality	Probit
A (Control group)	0	0	0	0
B (200mg/kg)	2.30103	0	0	0
C (400mg/kg)	2.60205999	0	0	0
D (800mg/kg)	2.90308999	1	20	4.16
E (1600mg/kg)	3.20411998	1	20	4.16

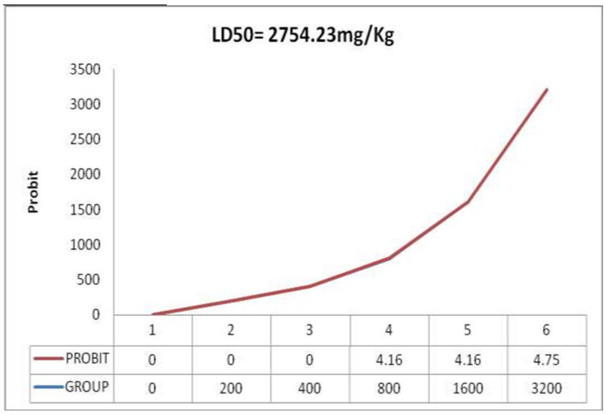

Figure 1. Graph of probit against log doses of *Entandrophragma utile* ethanol bark extract

Table 2: Determination of assay of the ethanol bark extract of *Entandrophragma angolense*

Group	Logdose	Total Mortality	% Mortality	Probit
A (Control group)	0	0	0	0
B (200mg/kg)	2.30103	0	0	0
C (400mg/kg)	2.60205999	1	20	4.16
D (800mg/kg)	2.90308999	1	20	4.16
E (1600mg/k)	3.20411998	2	40	4.75

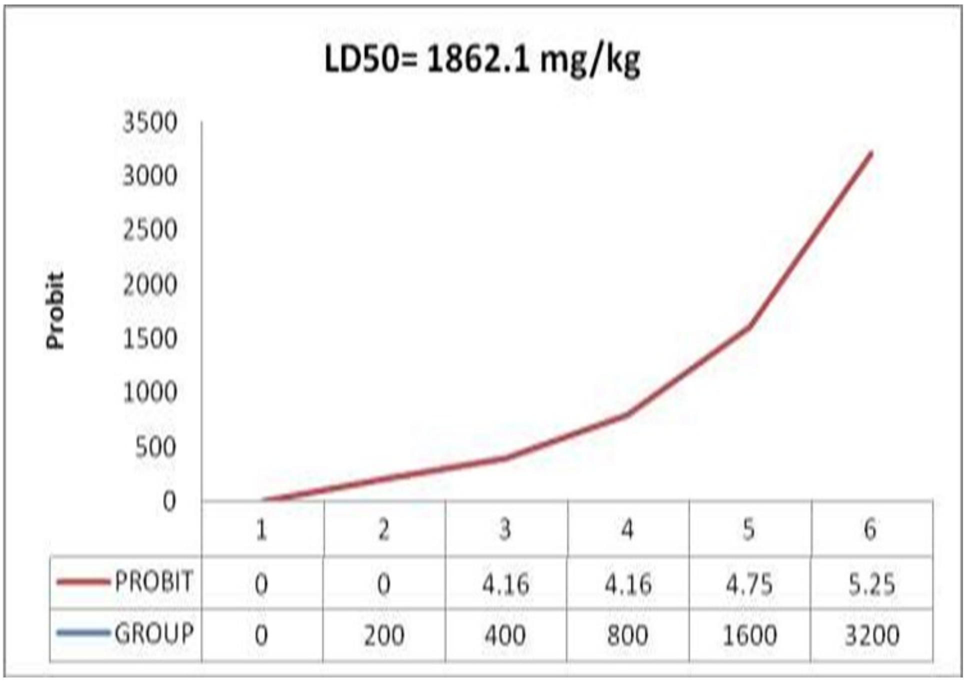

Figure 2. Graph of probit against log doses of *Entandrophragma angolense* ethanol bark extract

Table 3: Weight changes of the mice during assay of the ethanol extract of *Entandrophragma utile*

Groups	Mean Body Weight (g)		
	Initial	Final	Weight changes (%)
A (Control group)	44.46±0.2	47.80±1.1	3.34±1.1††
B (200mg/kg)	43.30±2.4	45.20±1.4	2.1±0.8††
C (400mg/kg)	45.00±0.2	49.10±1.6	4.0±2.4††
D (800mg/kg)	44.70±1.0	48.90±1.4	4.2±0.7††
E (1600mg/kg)	42.50±0.2	45.10±1.6	3.6±0.3††

Key: Weight gain = ††

Entandrophragma angolense

The determination of the lethal dose concentration of the ethanol bark extract of *E. angolense* was carried out using different dosage groups (A-E), and the results are summarized in Table 2. In the control group (Group A), which received no ethanol bark extract, there was no mortality recorded, corresponding to a 0% mortality rate. Similarly, in Group B, which was administered a dose of 200 mg/kg (log dose 2.30103), no mortality was observed, maintaining a 0% mortality rate with a probit value of 0. Exposure to a higher dose of 400 mg/kg (log dose 2.60205999) in Group C resulted in a single mortality case out of the total group, translating to a 20% mortality rate and a corresponding probit of 4.16. This same mortality rate and probit value were observed in Group D, which received a dose of 800 mg/kg (log dose 2.90308999). An increase in the dosage to 1600 mg/kg (log dose 3.20411998) for Group E resulted in 2 mortalities, which corresponded to a 40% mortality rate and a probit value of 4.75. The data were used to calculate the lethal dose (LD_{50}) concentration using probit analysis. The resulting LD_{50} value for the ethanol bark extract of *E. angolense* was determined to be $10^{3.27}$, equivalent to 1862.1 mg/kg as shown in Figure 2.

The investigation into the lethal dose (LD_{50}) of ethanol bark extracts from *Entandrophragma utile* and *E. angolense* revealed valuable insights into their toxicity profiles (Tables 1 and 2). In the study on *E. utile*, escalating dosages up to 1600 mg/kg demonstrated a progressive relationship between dose levels and mortality rates (Table 1). Mortality commenced at 800 mg/kg, with a peak mortality rate of 20% at the highest dose, indicating a relatively low toxicity threshold. Probit analysis estimated the LD_{50} at approximately 2754.23 mg/kg, suggesting a high tolerance limit for the extract and implying potential safety at lower concentrations (Figure 1). This aligns with the findings of John and Onabanjo (1990), who observed slight toxicity with maximum possible doses considerably higher than those evaluated for pharmacological efficacy. Both studies indicate that *E. utile* extracts possess a relatively high margin of safety at lower concentrations, reinforcing their potential for therapeutic applications with controlled dosing. Contrary to *E. utile*, the examination of *E. angolense* showcased a dose-dependent toxicity pattern (Table 2). Lower doses (up to 200 mg/kg) and the control group exhibited no mortalities, indicating the safety of these concentrations. However, mortality rates increased with higher doses, reaching 40% at 1600 mg/kg. The LD_{50} value of 1862.1 mg/kg derived from probit analysis underscored the quantifiable toxicity of the extract, emphasizing the importance of dose considerations in its pharmacological applications (Figure 2). This observation agrees to some extent with the findings reported by Degaulle *et al.* (2018), wherein *E. angolense* extracts exhibited slight toxicity but at much higher maximum tolerable doses 500 g/kg in oral administration.

These findings highlight the distinct toxicity profiles of ethanol bark extracts from *E. utile* and *E. angolense*. While *E. utile* demonstrated a higher LD_{50} and lower overall mortality rates, *E. angolense* exhibited a lower LD_{50} and a more pronounced dose-dependent lethality. Understanding these differences is crucial for guiding the safe use and toxicological assessment of these extracts in future research and potential therapeutic endeavours (Tsatsakis *et al.*, 2018. Borgert *et al.,* 2021; Jităreanu *et al.,* 2023).

Weight changes of mice during ethanol extract assay of *Entandrophragma* species

The effects of the ethanol extract of *Entandrophragma utile* on the body weight of mice were evaluated across different dosage groups and compared to a control group as illustrated in Table 3. Initially, the mean body weight of mice in the control group (Group A) was recorded at 44.46±0.2g. By the end of the assay period, these mice had a mean body weight of 47.80±1.1g, reflecting a weight gain of 3.34±1.1%. In Group B, which received a 200mg/kg dose of the extract, the initial mean body weight was 43.30±2.4g. This increased to 45.20±1.4g, corresponding to a weight gain of 2.1±0.8%. The mice in Group C, administered 400mg/kg of the extract, had an initial mean body weight of 45.00±0.2g. By the conclusion of the study, their mean body weight rose to 49.10±1.6g, marking a significant weight gain of 4.0±2.4%. For Group D, with an 800mg/kg dose, initial and final mean body weights were noted as 44.70±1.0g and 48.90±1.4g respectively. This group exhibited the highest percentage weight gain among the tested groups, at 4.2±0.7%. Finally, Group E, which was administered the highest dose at 1600mg/kg, had its mean body weight change from 42.50±0.2g to 45.10±1.6g. This group experienced a weight gain of 3.6±0.3%.

Table 4 reveals the mean body weight of mice across different treatment groups to evaluate the effects of varying doses of the ethanol extract of *Entandrophragma angolense*. The changes in body weight percentages were subsequently recorded. In the control group (Group A), the initial mean body weight was 44.32±1.5 g, which increased to 49.80±0.5 g by the end of the assay period. This group exhibited a weight gain of 9.48±2.1%. Group B, which received 200 mg/kg of the ethanol extract, started with a mean body weight of 41.31±2.1 g, increasing to 46.20±1.0 g. This represented a weight gain of 8.89±1.7%. For Group C, administered with 400 mg/kg of the extract, the initial mean body weight was 43.38±1.0 g. However, by the end of the study period, the mean body weight

Table 4: Weight changes of the mice during assay of the ethanol extract of *Entandrophragma angolense*

Groups	Mean Body Weight (g)		
	Initial	Final	Weight changes (%)
A (Control group)	44.32±1.5	49.80±0.5	9.48±2.1††
B (200mg/kg)	41.31±2.1	46.20±1.0	8.89±1.7††
C (400mg/kg)	43.38±1.0	42.10±0.3	3.72±0.5†
D (800mg/kg)	41.70±0.4	40.90±1.0	3.2±1.1†
E (1600mg/kg)	43.38±1.0	42.10±0.3	2.72±1.0†

Key: Weight gain = ††; Weight loss = †

Table 5: Haematological parameters of ethanol bark extract of *Entandrophragma utile* in experimental mice

Parameters	Group A (Control group)	Group B (200 mg/kg)	Group C (400 mg/kg)	Group D (800 mg/kg)	Group E (1600 mg/kg)
PCV (%)	26.00±2.00[c]	22.01±0.58[d]	21.33±0.58[d]	20.34±0.58[d]	22.33±0.58[d]
Hb (g/dl)	15.23±0.82[d]	14.88±0.06[c]	14.43±0.06[c]	13.44±0.06[c]	14.66±0.06[c]
RBC (cell/L)	7.92±0.35[d]	7.99±0.08[d]	7.77±0.08[d]	7.78±0.08[d]	7.77±0.08[d]
WBC (x103 cell/L)	6.5±0.46[b]	5.33±0.30[ab]	5.33±0.20[ab]	6.33±0.10[ab]	6.43±0.20[ab]
PLATELET (x105 cell/L)	1.31±0.20[a]	1.48±0.40[a]	1.47±0.40[a]	1.56±0.40[a]	1.57±0.40[a]
LYM (%)	44.0±3.0[c]	47.0±1.0[b]	46.0±1.0[b]	45.2±1.0[b]	46.0±2.0[b]
NEUT (%)	32.3±3.5[c]	20.0±1.0[b]	21.0±1.0[b]	23.2±1.0[b]	22.0±2.0[b]
MONO (%)	1.7±0.6[bc]	1.7±0.1[c]	1.5±0.3[c]	1.5±0.0[c]	1.6±0.3[c]
EO (%)	2.0±1.0[b]	1.6±0.3[ab]	1.5±0.0[ab]	1.6±0.0[ab]	1.5±0.0[ab]
MCV (*fl*)	58.1±1.2[c]	59.9±0.3[a]	59.8±0.2[a]	59.8±0.2[a]	59.9±1.2[a]
MCH (*pg*/cell)	19.2±0.2[d]	19.8±0.2[a]	19.7±0.3[a]	19.6±0.1[a]	19.7±0.3[a]

Values are Means ± S.D, n < 4; Mean with similar superscript on the same column are not significantly difference (P<0.05)

Table 6: Haematological parameters of ethanol bark extract of *Entandrophragma angolense* in experimental mice

Parameters	Group A (Control group)	Group B (200 mg/kg)	Group C (400 mg/kg)	Group D (800 mg/kg)	Group E (1600 mg/kg)
PCV (%)	24.00±2.00[c]	12.56±3.62[a]	13.66±3.60[a]	12.56±3.62[a]	12.56±3.62[a]
Hb (g/dl)	14.23±0.82[d]	7.24±0.95[ab]	8.26±0.95[ab]	9.24±0.95[ab]	10.28±0.95[ab]
RBC (cell/L)	9.92±0.35[d]	14.29±0.9 [b]	15.30±1.9 [b]	15.22±0.3[b]	15.25±0.5 [b]
WBC (x10^3 cell/L)	35.5±0.46[b]	37.95±2.17[b]	38.95±2.17[b]	39.55±2.17[b]	39.65±2.17[b]
PLATELET (x10^5 cell/L)	51.11±0.20[a]	51.84±2.67[a]	51.84±2.33[a]	51.84±2.57[a]	51.84±2.57[a]
LYM (%)	19.0±3.0[c]	19.23±1.31[ab]	19.23±2.11[ab]	19.23±5.11[ab]	19.23±7.33[ab]
NEUT (%)	30.3±3.5[c]	35.25±0.43[a]	35.75±0.43[a]	36.75±3.03[b]	36.77±0.43[b]
MONO (%)	41.6±0.6[bc]	43.00±10.75[b]	43.17±10.75[b]	43.25±10.7[b]	43.22±0.25[b]
EO (%)	2.2±1.0[b]	1.5±0.3[ab]	1.5±0.4[ab]	1.5±1.5[ab]	1.5±1.3[ab]
MCV (*fl*)	51.1±1.2[c]	49.9±0.3[a]	49.9±1.3[a]	49.9±1.6[a]	49.8±0.6[a]
MCH (*pg*/cell)	10.2±0.2[b]	10.8±2.2[a]	10.8±2.3[a]	10.8±2.2[a]	10.8±3.2[d]

Values are Means ± S.D, n < 4; Mean with similar superscript on the same column are not significantly difference (P<0.05) slightly decreased to 42.10±0.3 g, reflecting a weight loss of 3.72±0.5%. In Group D, treated with 800 mg/kg, the initial mean body weight was 41.70±0.4 g, which decreased to 40.90±1.0 g. This group experienced a weight loss of 3.2±1.1%. Group E, administered with the highest dose of 1600 mg/kg, showed a slight decrease in mean body weight from 43.38±1.0 g to 42.10±0.3 g, resulting in a weight loss of 2.72±1.0%.

Overall, it was observed that mice in the control and low-dose groups (Groups A and B) experienced weight gain, while those in the higher-dose groups (Groups C to E) showed varying degrees of weight loss. The extent of weight loss appeared to correlate with the increasing doses of the ethanol extract.

The study evaluated the impact of ethanol extracts from Entandrophragma utile and E. angolense on the body weight of mice, revealing distinct dose-dependent effects (Tables 3 and 4). In E. utile, varying dosages demonstrated different influences on weight gain. Groups administered lower doses exhibited minimal changes in weight, while intermediate doses (400-800mg/kg) resulted in significant weight gains, suggesting a dose-response relationship. Interestingly, the highest dosage (1600mg/kg) resulted in modest weight gain, hinting at a potential inhibitory effect at very high concentrations (Table 3). Conversely, E. angolense displayed contrasting effects on body weight. Lower doses (up to 200mg/kg) had minimal impact on weight gain, similar to the control group. However, higher doses (400mg/kg and above) induced weight loss, with significant reductions observed at 400mg/kg and increasing at higher concentrations. These findings suggest a dose-dependent negative impact on body weight, particularly notable at doses of 400mg/kg and beyond (Table 4).

These results underscore the importance of dosage considerations in assessing the potential therapeutic applications and adverse effects of these extracts on body weight regulation (Pittler *et al.,* 2005; York *et al.,* 2007). Further research is warranted to elucidate the underlying mechanisms driving these dose-dependent responses and to optimize the safe and effective use of these extracts in potential therapeutic interventions.

Haematological analysis of *Entandrophragma* species

The haematological analysis of experimental mice administered ethanol bark extract of *Entandrophragma utile* at various dosages (200, 400, 800, 1600 mg/kg) demonstrated noticeable trends in the primary blood parameters compared to the control group (Table 5). The control group (A) exhibited a packed cell volume (PCV) of 26.00 ± 2.00%. In contrast, all treatment groups showed a decrease in PCV values, ranging from 22.01 ± 0.58% in group B (200 mg/kg) to 22.33 ± 0.58% in group E (1600 mg/kg), with the lowest PCV observed in group D (20.34 ± 0.58%). The haemoglobin (Hb) content in the control group was 15.23 ± 0.82 g/dl. Following treatment, a marginal reduction in Hb levels was noted across all dosages. Group D (800 mg/kg) recorded the lowest Hb level (13.44 ± 0.06 g/dl), while the highest treated group, E (1600 mg/kg), exhibited Hb values close to those of group B (14.88 ± 0.06 g/dl).

The red blood cell (RBC) count of the control group was 7.92 ± 0.35 x 10^{12}/l. The RBC levels showed slight variation among the treated groups, with group B (200 mg/kg) at 7.99 ± 0.08 x 10^{12}/l and group E (1600 mg/kg) at 7.77 ± 0.08 x 10^{12}/l. The control group had a white blood cell (WBC) count of 6.5 ± 0.46 x 10^{9}/l. Variations were observed in the treated groups, remaining relatively consistent, with values ranging from 5.33 ± 0.30 x 10^{9}/l in group B to 6.43 ± 0.20 x 10^{3}/l in group E. Platelet counts were similar across all groups, with the control group recording 1.31 ± 0.20 x 10^{11}/l and the treated groups showing minimal variation, ranging from 1.47 ± 0.40 x 10^{11}/l (Group C) to 1.57 ± 0.40 x 10^{11}/l (Group E).

Lymphocytes (LYM) percentages increased slightly in treated groups, with the control group at 44.0 ± 3.0% and group E at 46.0 ± 2.0%. Neutrophil (NEUT) percentages were lower in treated groups (20.0 ± 1.0% to 22.0 ± 2.0%) compared to the control (32.3 ± 3.5%). Monocyte (MONO) and eosinophil (EO) percentages remained relatively stable across all groups. The control group had a mean corpuscular volume (MCV) of 58.1 ± 1.2 fl, which increased slightly in treated groups (59.8 ± 0.2 fl to 59.9 ± 1.2 fl). Similarly, the control had a mean corpuscular haemoglobin (MCH) of 19.2 ± 0.2 pg/cell, with treated groups showing slight increases ranging from 19.6 ± 0.1 pg/cell to 19.8 ± 0.2 pg/cell.

However, Table 6 reveals the haematological parameters of experimental mice treated with various doses of ethanol bark extract of *Entandrophragma angolense* are summarized.

The control group (A) exhibited a mean packed cell volume (PCV) of 24.00±2.00%. In comparison, all treated groups (B to E) showed a notable reduction in PCV, ranging from 12.56±3.62% to 13.66±3.60%, with no significant differences between the treated groups ($P<0.05$). The control mice presented a haemoglobin (Hb) concentration of 14.23±0.82 g/dl. The groups treated with ethanol extract saw a significant decrease, with levels ranging from 7.24±0.95 g/dl in group B to 10.28±0.95 g/dl in group E. While all treated groups showed reduced Hb levels compared to the control, there were no significant differences among the treated groups ($P<0.05$).

Red blood cell (RBC) counts exhibited an inverse trend to PCV and Hb. The control group (A) showed a mean RBC count of 9.92±0.35 $x10^{12}$ cell/L, whereas treated groups (B to E) displayed significantly higher RBC counts ranging from 14.29±0.9 to 15.30±1.9 $x10^{12}$ cell/L ($P<0.05$). The control group had a white blood cell (WBC) count of 35.5±0.46 $x10^{3}$ cells/L. Treatment with ethanol extract resulted in a slight increase in WBC counts, with values from 37.95±2.17 to 39.65±2.17 $x10^{3}$ cell/L across groups B to E. However, these changes were not significantly different from the control group ($P<0.05$). The mean platelet counts showed no significant differences amongst all groups, including the control, with counts remaining steady at approximately 51.11±0.20 $x10^{5}$ cell/L in the control and hovering between 51.84±2.33 and 51.84±2.67 $x10^{5}$ cell/L in the treated groups ($P<0.05$).

Lymphocyte (LYM) percentages remained consistent across all treated groups, similar to the control (19.0±3.0%), with minor variations ranging from 19.23±1.31% to 19.23±7.33% ($P<0.05$). Neutrophil (NEUT) percentages increased in all treated groups compared to the control. The control group had a percentage of 30.3±3.5%, while treated groups ranged from 35.25±0.43% to 36.77±0.43% ($P<0.05$). Monocyte (MONO) levels remained fairly stable across groups, with the control group at 41.6±0.6% and treated groups ranging from 43.00±10.75% to 43.25±10.7% ($P<0.05$). Eosinophil (EO) percentages decreased slightly in treated groups as compared to the control. The control group had a percentage of 2.2±1.0%, whereas treated groups displayed values from 1.5±0.3% to 1.5±1.5% ($P<0.05$). Mean corpuscular volume (MCV) in the control group was 51.1±1.2 fl. The treated groups showed a slight decrease, ranging from 49.8±0.6 to 49.9±1.6 fl ($P<0.05$). The mean corpuscular haemoglobin (MCH) values were higher in the treated groups (10.8±2.2 to 10.8±3.2 pg/cell) compared to the control group (10.2±0.2 pg/cell), although these differences were not significant ($P<0.05$).

The *haematological* analysis of mice treated with varying dosages of ethanol extracts from *Entandrophragma utile* and *E. angolense* revealed distinct impacts on key blood parameters compared to control groups (Tables 5 and 6). In *E. utile*-treated mice, decreased packed cell volume (PCV) and haemoglobin (Hb) levels were observed, with the lowest values recorded in the 800 mg/kg dosage group. Red blood cell (RBC) counts showed minor variations, while white blood cell (WBC) counts remained relatively stable. Platelet counts were consistent across all groups. Lymphocyte percentages exhibited slight increases, while neutrophil percentages were lower compared to controls. Monocyte and eosinophil percentages remained constant, and mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) values showed slight elevations in treated groups (Table 5). Conversely, mice treated with ethanol bark extract from *E. angolense* displayed significant alterations in *haematological* parameters. Reductions in PCV and Hb levels were notable, accompanied by a significant increase in RBC counts. WBC counts showed a slight rise, with no significant changes in platelet counts. Variations in lymphocyte, neutrophil, monocyte, and eosinophil percentages were observed among treated groups, along with slight changes in MCV and MCH values (Table 6). These findings suggest that both extracts can impact *haematological* parameters in mice, influencing erythropoiesis and immune cell dynamics (Adeyemo-Salami and Ewuola, 2015; Muriithi *et al.,* 2015;Kang *et al.,* 2022; Nurhayati, 2023; Shokan *et al.,* 2024).

The differential effects of *E. utile* and *E. angolense* on *haematological* parameters underscore the need for further investigation into the underlying mechanisms driving these alterations. Understanding the *haematological* effects of these extracts is crucial for evaluating their safety and potential therapeutic applications, particularly in the context of erythropoiesis and immune function. Further research is warranted to elucidate the specific pathways through which these extracts influence blood parameters and to assess their suitability for clinical use.

E. angolense *E. utile*

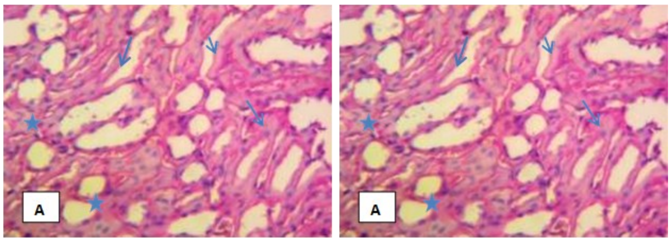

Plate 1 | Group A: Control group administered with normal saline

E. angolense *E. utile*

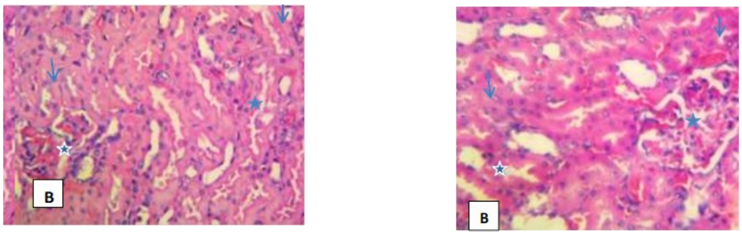

Plate 2 | Group Badministered with 200mg/kg of the dissolved ethanol bark extract of *Entandrophragma species* in 1ml of normal saline

E. angolense E. utile

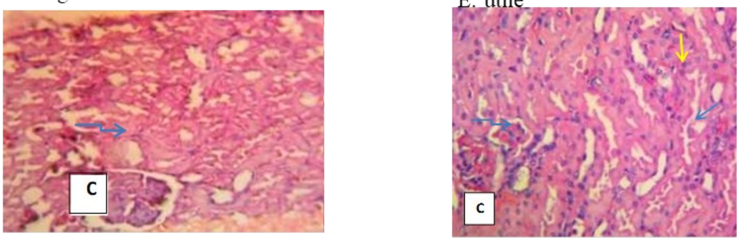

Plate 3 | Group Cadministered with 400mg/kg of the dissolved ethanol bark extract of *Entandrophragma species* in 1ml of normal saline

E. angolense *E. utile*

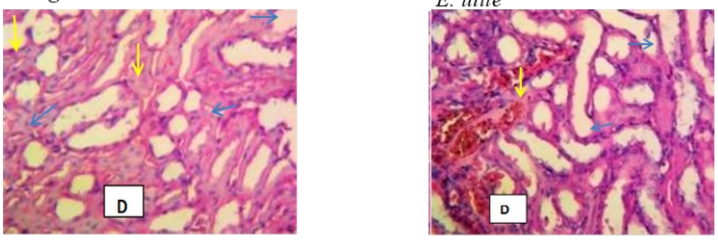

Plate 4 | Group Dadministered with 800mg/kg of the dissolved ethanol bark extract of *Entandrophragma species* in 1ml of normal saline

E. angolense *E. utile*

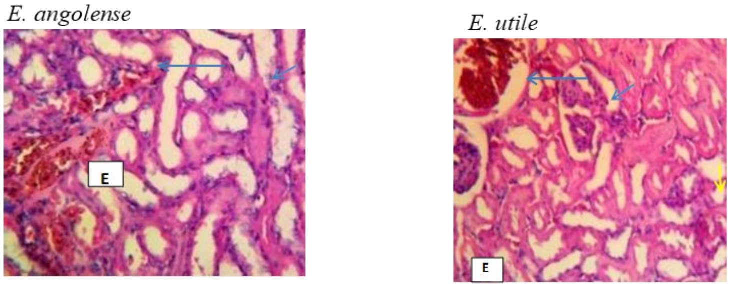

Plate 5 | Group Eadministered with 1600mg/kg of the dissolved ethanol bark extract of *Entandrophragma species* in 1ml of normal saline

Histological analysis of the ethanol bark extract of *Entandrophragma utile*

The comparative histological responses to the single daily doses of ethanol bark extracts of *Entandrophragma* species were assessed using light microscopy at x400 magnification. The results, illustrated in Plates 1-5, indicate variations in liver pathology among the different treatment groups.

The control group (Group A) exhibited normal histological architecture with no significant pathological alterations. The liver tissue displayed healthy hepatocytes, well-organised lobular structures, and a lack of noticeable congestion or necrosis. Mice in the low-dose groups (Groups B and C) also showed minimal histological changes. The liver tissues from these groups were largely comparable to those of the control group. In the medium dose group (Group D), some histological changes began to manifest. The liver tissues showed minimal congestion and scattered foci of necrosis. Mild infiltration by mononuclear cells was observed, indicating an incipient inflammatory response. Despite these changes, the hepatocytes largely maintained their normal appearance, although peri-vascular lymphocytosis was more evident compared to the control and low-dose groups. Major histological changes were prominent in the high dose groups (Groups D and E). These included conspicuous congestion and scattered foci of necrosis throughout the liver parenchyma. Mononuclear cell infiltration was more pronounced, suggesting a more robust inflammatory response. Although the hepatocytes remained structurally unchanged, peri-vascular lymphocytosis was markedly increased.

Histological analysis of the ethanol bark extract of *Entandrophragma angolense*

The control group (Group A) showed normal liver histology, with no signs of congestion, focal necrosis, or abnormal cell infiltration. The hepatocytes and vascular structures were intact and well-preserved. Liver sections from the low -dose groups (Groups B and C) exhibited no pathological changes. The tissues showed compact mononuclear cell infiltration and normal hepatocyte morphology, consistent with findings from non-treated or minimally treated groups. Group D displayed minimal congestion with scattered foci of necrosis. The mononuclear cell infiltration was sparse, and hepatocytes remained largely normal, although peri-vascular lymphocytosis was visibly increased. Significant congestion and widespread necrotic lesions were observed in the high-dose group (Group E). These sections also showed scattered mononuclear cell infiltration and heightened perivascular lymphocytosis, indicating severe inflammatory and pathological responses.

The histological evaluation of liver tissue in mice treated with ethanolic bark extracts of *Entandrophragma utile* and *E. angolense* revealed dose-dependent effects on hepatic Histopathology (Plates 1-5). In the case of *E. utile*, low doses (Groups B and C) did not induce significant histopathological changes. This implies that such dosages are likely safe for hepatic function and structure, maintaining normal hepatocyte architecture and lacking congestion or necrosis (Aronson, 2006; Crawford *et al.,* 2018; Mao *et al.,* 2024). However, medium doses (Group D) led to minor hepatic alterations, including congestion, scattered necrotic foci, and mild mononuclear cell infiltration, indicating an early inflammatory response. High dose (Group E) resulted in pronounced congestion, increased necrotic foci, and robust mononuclear cell infiltration, highlighting significant liver tissue damage and inflammatory responses (Thoolen *et al.,* 2010; Zhang *et al.,* 2011; Wang *et al.,* 2020). Similarly, treatment with ethanolic bark extracts of *E. angolense* demonstrated varying effects on liver tissue in mice. Low doses (Groups B and C) did not induce histological changes, maintaining cellular integrity and normal function. Slightly higher doses (Group D) led to minimal congestion and mild inflammatory responses, with hepatocytes largely unaffected. In contrast, high dose (Group E) caused significant histopathological distress, including congestion, widespread necrotic lesions, and heightened inflammatory responses, indicating severe liver tissue damage.

These findings underscore a clear dose-dependent relationship between extract concentration and liver tissue damage for both *E. utile* and *E. angolense*. While low to moderate doses appeared to have minimal impact on liver histology, high doses precipitated significant histological changes, emphasizing the hepatotoxic potential of elevated extract concentrations. Understanding these dose-dependent effects is crucial for assessing the safety and potential risks associated with the use of these ethanolic bark extracts in clinical or therapeutic settings. Further research is warranted to elucidate the underlying mechanisms driving these histopathological alterations and to determine the optimal dosage range for safe administration.

CONCLUSION

This study demonstrated that ethanol bark extracts of *Entandrophragma utile* and *E. angolense* exhibit dose-dependent toxicological effects in male mice. *E. utile* showed a higher LD_{50}, indicating a relatively lower acute toxicity profile compared to *E. angolense*. While low-dose administration of both extracts resulted in minimal haematological and histological changes, higher doses led to significant reductions in PCV and Hb, and histopathological signs of liver injury, including congestion and mononuclear cell infiltration.

These findings support the potential use of these extracts in traditional medicine, but also highlight the importance of strict dosage regulation to avoid adverse effects. Future studies should explore the chronic toxicity, mechanisms of action, and isolate bioactive compounds responsible for the observed effects to establish a comprehensive safety profile.

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