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Toxicity Study on Alkaloid-Rich Fraction of *Detarium microcarpum* (Fabaceae) Stem Bark in Wistar Rats

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ABSTRACT

Several studies reported the toxicity profile of the stem bark extract of *Detarium microcarpun* plant. However, no available data on the toxicity profile of the various fractions of its crude extract which gives baseline for isolation of lead compounds. The aim of the study is to evaluate the effect of 28-day repeated oral administration of alkaloid-rich fraction of *Detarium microcarpum* stem bark extract on biochemical parameters in Wistar rats. Wistar rats were divided into four groups of five animals each and administered different doses (250, 500 and 1000 mg/kg) of alkaloid-rich fractions via oral route. Body weight changes, relative organ weights (liver, kidney, spleen, heart), serum liver biomarkers (ALT, AST, ALP), liver function parameters (total protein, albumin), kidney function parameters (urea, creatinine, BUN), electrolytes (Na, HCO, K, Cl), and oxidative stress parameters (MDA, CAT, SOD, GPx, LDH, GGT, GHS) were measured using standard techniques. The body weight changes insignificantly ($p>0.05$) for rats in the acute toxicity study where the weight increases after administration of the alkaloid-rich fractions of *D. microcarpum* stem bark at a single oral dose of 5000 mg/kg from day 1 to day 14. The same was observed when different doses of the fraction were administered for 28 days. The result indicated the no significant ($P>0.05$) organ weight (%) for liver, kidney, spleen, brain and heart. There was no significant ($P>0.05$) increase in serum ALT, AST, ALP, TP, ALB, Urea, Creatinine, MDA, CAT, SOD, GPx, LDH, GGT GHS electrolytes and hematological parameters levels in the normal control group compared to other groups. Administration of 250, 500 and 1000 mg/kg of alkaloid-rich fractions of *D. microcarpum* stem bark for 28 days showed congested central vein and the sinusoids and the hepatocytes appeared normal. The kidney section of rats from all the groups shows normal appearance of the glomerulus, Bowman's capsule and the tubules. The alkaloid-rich fraction of *Detarium microcarpum* stem bark produces no effect on body and organ weights, biochemical activities and oxidative stress parameters in Wistar rats, suggesting its relative safety.

Keywords: Toxicity, Biomarkers, Alkaloid, *Detarium microcarpum*, Wistar rats, Phytomedicine.

INTRODUCTION

Plants have been excellent sources of therapeutic molecules with tremendous contributions to modern drug discovery. Among the different categories of phytochemicals, alkaloids are particularly prominent for their widespread biological activities including analgesic, anticancer, antimalarial, and antimicrobial activity (Abdulazeez *et al*., 2023; Chen *et al*., 2022). Nitrogenous compounds have played a pivotal role in developing numerous traditional drugs and still attract scientific attention because of their diverse pharmacological applications. Flavonoids and alkaloids of medicinal plants are especially well valued in ethnomedicine for disease prevention and therapy, often due

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to their antioxidant, anti-inflammatory, and immunomodulatory properties.

Detarium microcarpum is a legume species that is common in West Africa. It is used as a traditional medicine against many diseases like infections, diabetes, and inflammation. The stem bark, fruits, and leaves of the plant are used to make decoctions or extracts by traditional healers. Initial research shows that the plant possesses strong activities against germs, diabetes, and inflammation (Sow *et al*., 2023). While its enhanced ethnopharmacological relevance and documented bioactivities have been mentioned, little has been documented of the toxicological effects of chronic administration, particularly for its fractions of alkaloids. Similar to most plants commonly used traditionally, the lack of toxicological profiles is a tremendous barrier to translational applications.

Though the alkaloid-rich fraction (ARF) of *D. microcarpum* is used widely by the traditional practitioners, no thorough safety testing of it has ever been conducted. Toxicological studies are highly important to guarantee the safety of plant extracts for medical application, especially since certain alkaloids, as much as they may be helpful, are harmful if taken in high quantities or over a long duration of time (Zhang et al., 2024; Wang *et al*., 2025). This work was conducted to verify the acute and sub-acute toxicity effects of alkaloid-rich fractions of *Detarium microcarpum* stem bark on Wistar rats, using standard OECD toxicology procedures.

MATERIALS AND METHODS

Plant Material and Extraction

Fresh stem bark of D. microcarpum was authenticated and shade-dried. Alkaloid-rich fractions were extracted using acid-base extraction as per standard procedures (Okereke *et al*., 2023).

Experimental Animals

Wistar rats (150–200 g) were housed under controlled conditions (22 ± 2°C, 12 h light/dark cycle) with free access to standard diet and water. Ethical clearance was obtained (SAZU/FBMS/REC/ VOL. 4/00110).

Acute Toxicity Study

Rats were administered a single oral dose of 5000 mg/kg ARF and monitored for 14 days for mortality, clinical signs, and gross pathology (OECD 425 guidelines) (OECD, 2008).

Sub-Chronic Toxicity Study

Animals were assigned to four groups (n=7 each):

Group I: Normal saline (10 ml/kg)

Group II: ARF 250 mg/kg

Group III: ARF 500 mg/kg

Group IV: ARF 1000 mg/kg

Daily oral administration lasted 28 days (Zhang *et al*., 2024).

Evaluation Parameters

Body weight monitoring

Organ weight analysis

Serum biochemistry (ALT, AST, ALP, TP, ALB, urea, creatinine, electrolytes)

Hematology (RBC, Hb, HCT, MCV, MCH, MCHC, WBC, differential counts)

Oxidative stress biomarkers (MDA, SOD, CAT, GPx, LDH, GGT, GSH)

Histopathology (liver and kidney tissues) (Aimé *et al.,* 2022)

Statistical Analysis

The statistical methods employed in the analysis were one-way analysis of variance (ANOVA), repeated measure ANOVA, and Bonferoni post hoc tests. The values were

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expressed as the mean plus or minus the standard error of the mean (SEM). A *p*-value less than or equal to (≤) 0.05 were deemed statistically significant.

RESULTS

Acute Toxicity

No mortality, clinical toxicity, or gross pathological changes were observed in ARF-treated rats at 5000 mg/kg as presented in Table 1.

Table 1: Acute Oral Toxicity Results

Treatment	Toxicity signs	Mortality	Gross Pathology
Saline (10 ml/kg)	0/5	0/5	0/5
ARF (5000 mg/kg)	0/5	0/5	0/5

t/n = toxic/normal, d/a= dead/alive, l/nl = lesion/ no lesion, ARF= Alkaloid-rich fraction

Body Weight Changes

Body weight increased normally across all groups without significant differences ($p>0.05$) as presented in Tables 2 and 3.

Table 2: Body Weight Changes during Acute Study.

Group	Day 0 (g)	Day 7 (g)	Day 14 (g)
Saline	108.09 ± 0.73	114.63 ± 0.68	123.19 ± 0.25
ARF 5000 mg/kg	101.00 ± 8.74	109.00 ± 4.04	121.00 ± 2.88

Values expressed as mean ± SEM, One-Way ANOVA, Bonferroni *post hoc,* n=5

ARF= Alkaloid-rich fraction

Table 3: Body Weight Changes during Sub-Chronic Study.

Group	Day 1 (g)	Day 28 (g)	% Change
NC	112.19 ± 0.52	161.94 ± 1.83	43.34
ARF 250	101.00 ± 9.55	151.60 ± 7.67	50.01
ARF 500	106.29 ± 5.57	157.17 ± 4.06	48.8
ARF 1000	113.14 ± 5.41	163.60 ± 6.41	44.65

Values expressed as mean ± SEM, One-Way ANOVA, Bonferroni *post hoc*, ARF= Alkaloid-rich fraction, (n=7)

Organ Weights

No significant changes ($p>0.05$) in liver, kidney, spleen, brain, or heart weights were recorded as presented in Table 4.

Table 4: Relative Organ Weights.

Group	Liver (g)	Kidney (g)	Spleen (g)	Heart (g)	Brain (g)
NC	4.7 ± 0.31	0.77 ± 0.14	0.74 ± 0.40	0.5 ± 0.11	0.42 ± 0.05
ARF 250	4.9 ± 0.25	0.71 ± 0.40	0.73 ± 0.10	0.6 ± 0.04	0.40 ± 0.14
ARF 500	4.7 ± 0.02	0.76 ± 0.20	0.71 ± 0.12	0.52 ± 0.00	0.65 ± 0.70
ARF 1000	4.7 ± 0.21	0.71 ± 0.10	0.73 ± 0.01	0.53 ± 0.00	0.40 ± 0.31

Values expressed as mean ± SEM, One-Way ANOVA, Bonferroni *post hoc*, ARF= Alkaloid-rich fraction, (n=7)

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Biochemical Parameters

Serum ALT, AST, ALP, TP, ALB, urea, and creatinine levels remained within normal limits across all groups as presented in Tables 5, 6 and 7.

Table 5: Liver Biomarkers.

Group	AST (IU/L)	ALT (IU/L)	ALP (IU/L)
NC	24.34 ± 0.55	32.23 ± 2.04	35.45 ± 5.00
ARF 250	23.56 ± 2.44	31.28 ± 1.21	34.33 ± 2.05
ARF 500	24.60 ± 8.41	32.80 ± 4.15	36.00 ± 7.81
ARF 1000	25.80 ± 8.64	34.20 ± 5.89	38.00 ± 8.50

Values expressed as mean ± SEM, One-Way ANOVA, Bonferroni *post hoc*, ARF= Alkaloid-rich fraction, (n=7), AST= Aspartate aminotransferase, ALT= Alanine anime transaminase, ALP= Alkaline Phosphatase.

Table 6: Liver Function.

Group	Total Protein (g/dl)	Albumin (g/dl)
NC	73.10 ± 3.08	44.20 ± 1.64
ARF 250	71.25 ± 1.71	41.00 ± 2.94
ARF 500	70.80 ± 4.60	43.40 ± 5.41
ARF 1000	74.34 ± 5.72	40.20 ± 5.89

Values expressed as mean ± Standard error of mean, std: Standard, TP:Total Protein, ALB: Albumin, One-way ANOVA, Bonferroni *post hoc*, Std: Standard, NC: Normal Control Rats

Table 7: Kidney Function.

Group	Urea (mg/dl)	Creatinine (mg/dl)	BUN (mg/dl)
NC	6.20 ± 0.41	103.36 ± 7.11	17.39 ± 0.11
ARF 250	7.01 ± 0.11	100.54 ± 9.00	15.36 ± 1.07
ARF 500	7.02 ± 0.26	105.36 ± 17.68	16.80 ± 2.51
ARF 1000	6.52 ± 0.41	101.50 ± 3.11	17.50 ± 3.11

Values expressed as mean ± Standard error of mean, BUN: Blood urea nitrogen., Values with different superscripts along the row differ significantly ($P<0.05$), a: Significant compared with NC, One-way ANOVA, Bonferroni *post hoc*, ARF= Alkaloid-rich fraction, n=7

Oxidative Stress Parameters

No significant differences in MDA, SOD, CAT, GPx, LDH, GGT, and GSH levels as presented in Table 8.

Table 8: Oxidative Stress Biomarkers.

Group	MDA (µM)	SOD (U/ml)	GPx (U/ml)	CAT (Ku/L)	LDH (U/L)	GGT (U/L)	GSH (U/L)
NC	1.05 ± 0.12	5.62 ± 0.11	12.14 ± 3.13	8.01 ± 1.03	389.45 ± 13.05	29.51 ± 2.00	27.04 ± 3.00
ARF 250	1.09 ± 0.42	5.65 ± 0.21	11.73 ± 0.98	8.04 ± 0.71	382.13 ± 12.24	31.00 ± 5.21	25.33 ± 1.26
ARF 500	1.03 ± 0.51	5.50 ± 0.16	13.70 ± 0.34	7.62 ± 0.82	391.04 ± 9.38	34.53 ± 5.22	26.59 ± 3.88
ARF 1000	1.04 ± 0.69	9.18 ± 0.39	12.31 ± 0.71	7.77 ± 1.51	389.80 ± 21.08	32.44 ± 6.42	25.33 ± 6.05

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Values expressed as mean ± Standard error of mean, std: Standard, MDA: malondialdehyde, SOD: Superoxide dismutase, GPx: glutathione peroxidase, CAT: Catalase, LDH: Lactate dehydrogenase, GGT: Gamma-glutamyl transferase, GHS: Glutathione, Values with different superscriptsalong the row differ significantly (*P<0.05*): a: Significant compared with NC, One-way ANOVA, Bonferroni *post hoc*, ARF= Alkaloid-rich fraction, NC= Normal control n=7

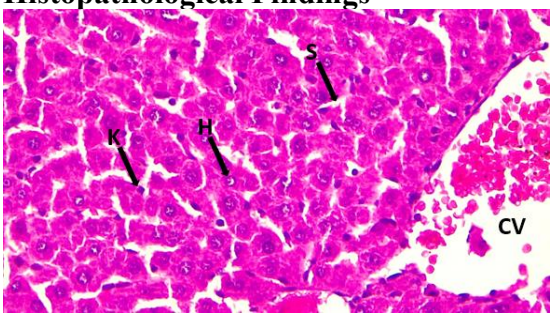
Electrolytes

Electrolytes concentrations after administration of alkaloid-rich fractions of *Detarium microcarpum* stem bark showed no significant (P>0.05) difference in electrolytes level of in the rats that received distilled water when compared to the alkaloid-rich fraction treated groups as presented in Table 9.

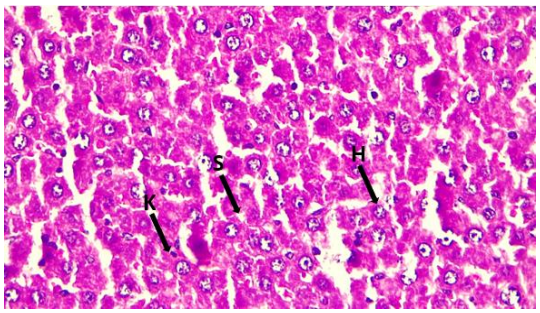
Table 9: Electrolytes.

Treatment Groups (mg/kg)	Na^+(mmol/)	K+ (mmol/L)	HCO_3 (mmol/L)	CL^- (mmol/L)
NC	197.00±6.93	4.54±0.79	22.39±3.43	63.26±4.61
ARF 250	195.72±2.00	4.02±0.19	21.44±7.00	62.15±2.18
ARF 500	193.57±1.14	4.24±0.23	23.01±1.32	63.87±2.15
ARF 1000	196.24±1.30	4.64±0.00	23.24±4.38	65.05±1.25

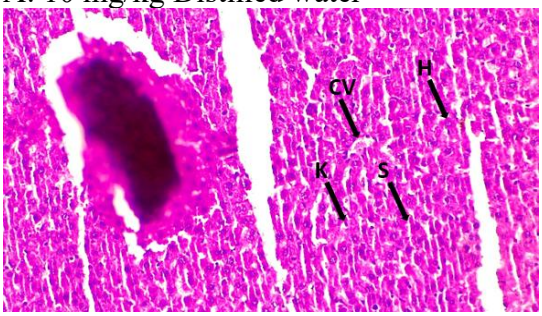
Histopathological Findings



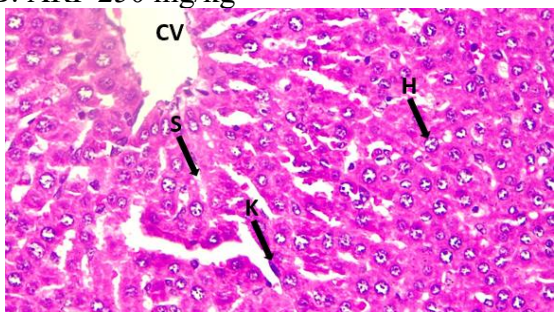
A: 10 mg/kg Distilled water



B: ARF 250 mg/kg



C: ARF 500 mg/kg



D: ARF 1000 mg/kg

Plate I: Photomicrograph of the Liver Following 28-day administration with alkaloid-rich fractions of D. microcarpum stem bark in Wistar rats, Central vein (CV), Kupffer cell (K), Sinusoid (S), Hepatocyte (H), H and E ×250, ARF= Alkaloid-rich fraction,

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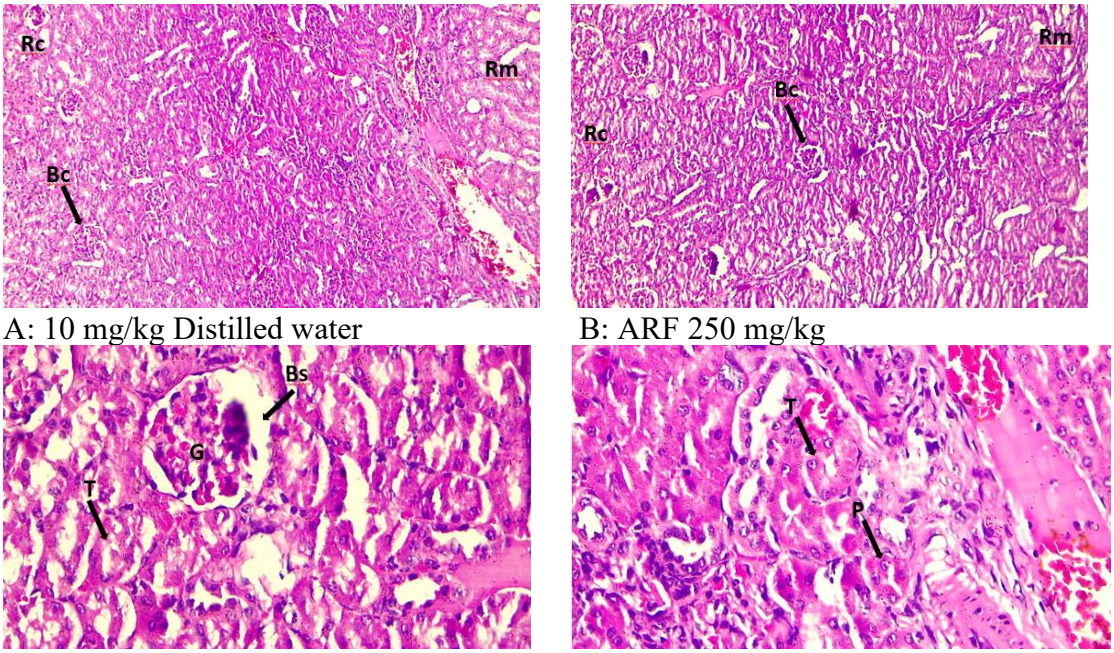

A: 10 mg/kg Distilled water B: ARF 250 mg/kg

C: ARF 500 mg/kg D: ARF 1000 mg/kg

Plate II: Photomicrograph of the Kidney Following 28-day administration with alkaloid-rich fractions of D. microcarpum stem bark in Wistar rats

ARF= Alkaloid-rich fraction, Tubules (T), Glomerulus (G), Bownman's space (Bs) Renal cortex (Rc), Bownman's capsule (Bc), Renal medulla (Rm); H and E ×250

DISCUSSION

The liver is a vital organ that participates in metabolism and detoxification; therefore, serum markers such as AST, ALT, and ALP are widely used to assess hepatocellular function and integrity. In the present study, the administration of alkaloid-rich fractions (ARFs) of *Detarium microcarpum* stem bark did not cause appreciable ($p>0.05$) alteration of AST, ALT, or ALP levels when compared with the normal control group. AST levels ranged from 23.56 ± 2.44 to 25.80 ± 8.64 IU/L across all the treated groups, which is quite close to the control value of 24.34 ± 0.55 IU/L. These results are suggestive of the absence of hepatocellular damage, in line with previous reports that some plant alkaloids exhibit minimal hepatotoxicity even at high doses (Abdulazeez *et al*., 2023; Edeoga and Iwuagwu, 2022).

In addition, no significant alteration was observed in serum total protein (TP) and albumin (ALB) levels among treated groups, further confirming the hepatic safety profile of ARF. TP and ALB levels of treated rats were very close to control values, suggesting preserved liver synthetic function. Research carried out by Oladipo and Dada (2022) and Alabi and Fadare (2022) also showed that alkaloid-rich extracts of medicinal plants used traditionally were able to keep liver biomarker profiles normal upon sub-chronic toxicity testing, which corroborates our results.

Contrary to what has been reported by Musa *et al.* (2023) and Diop *et al*. (2023), it is evident that *D. microcarpum* possesses hepatoprotective activity consistent with that of other medicinal plants. The above studies reported minimal or non-significant changes in liver enzymes following oral treatment with

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plant alkaloids, indicating potential hepatoprotective or non-hepatotoxic effects that could be exerted through antioxidant properties. In addition, our data on oxidative stress, which indicated no changes in MDA, SOD, CAT, GPx, LDH, and GGT, also confirms this protection hypothesis.

Besides, histopathological analysis of liver tissues showed no evidence of necrosis, fatty infiltration, or appreciable inflammation apart from mild sinusoidal congestion. This agrees with Martins *et al.* (2024) and Chinonso and Oyetayo (2024) findings, where they established that intact liver histoarchitecture in toxicology studies was a good indicator of the absence of hepatotoxicity. Consequently, findings from this study affirm the hepatological safety of *D. microcarpum* ARF as far as 1000 mg/kg dosage.

Renal function testing is routinely done by observing serum concentrations of urea, creatinine, and blood urea nitrogen (BUN). In the present study, there were no significant ($p>0.05$) changes in these renal parameters of various treatment groups in comparison with the control group. The serum urea levels ranged closely from 6.20 ± 0.41 to 7.02 ± 0.26 mg/dl, and the serum creatinine varied non-significantly from 100.54 ± 9.00 to 105.36 ± 17.68 mg/dl. The result is consistent with the earlier report of Ismail *et al.* (2022) and Ali *et al.* (2024), where oral administration of the plant alkaloid extract did not adversely affect the renal function parameter.

Besides, electrolyte levels of sodium, potassium, bicarbonate, and chloride were stable across all groups indicating intact renal tubular function. Electrolyte balance is the most important parameter in assessing nephrotoxicity, and the integrity of these parameters indicates the nephron-safety of *D. microcarpum* ARFs. Previous studies by Amanpour and Shadab (2022) and Liang *et al.* (2023) revealed that non-toxic medicinal plant extracts have a tendency to preserve electrolyte balance even at therapeutic and supra-therapeutic doses.

Histopathology also supported the biochemical findings since kidney sections of the various groups exhibited intact glomerular structure, Bowman's capsule, and tubules with no visible pathological changes. Similar kidney protective effect of alkaloid-rich extracts was observed by Jibril *et al.* (2024) and Essien and Essien (2024), confirming the argument that *D. microcarpum* ARF is not nephrotoxic.

Thus, the concomitant observation of serum creatinine, urea, blood urea nitrogen (BUN), and electrolyte levels with preserved histological integrity of renal tissues reflects observations documented by Oyedeji and Ajayi (2023) on other conventional herbs. Our results therefore confirm that alkaloid-rich fraction extracted from *D. microcarpum* stem bark is conducive to renal health even after extended once-daily dosing for 28 days.

Hematological parameters are important indicators of systemic actions of xenobiotic substances. There were no statistically significant changes ($p>0.05$) in the red blood cell (RBC) count, hemoglobin concentration (Hb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) in all animal groups treated with ARF when compared with control groups. These parameters were within normal physiological ranges, thereby adding support to the safety claim against ARF effects on erythropoiesis. The findings are in accordance with the reports of Lawal *et al.* (2023) and Ahmed *et al.* (2024), who also noted similar hematological stability in rats administered plant alkaloid extracts.

Furthermore, white blood cell (WBC) total cell counts and differential cell counts (lymphocytes, neutrophils, eosinophils,

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monocytes, and basophils) were not changed after treatment, suggesting that acute renal failure (ARF) is not able to induce immune-toxic effects or inflammatory reactions. This finding is consistent with Emeka and Ogbonna (2023) and Omotayo and Fadare (2024), who asserted that non-interference with WBC or differential counts should be a feature of safe phytochemical therapy.

Platelet counts (PLT) were also within the normal limits in the treated rats, revealing that the alkaloid-rich fractions neither interfered with thrombopoiesis nor caused platelet aggregation-related disorders. According to Peng *et al.* (2022) and Xu *et al.* (2024), significant changes in platelet counts seen in toxicological studies can be an indicator of hematopoietic toxicity or systemic stress; the absence of these changes in the present study further highlights the hematological safety of *D. microcarpum* ARF.

Overall, the minimum dose-dependent variation of the parameters found in hematology is consistent with the observation of Mustapha *et al.* (2024) and Liang *et al.* (2023), who found that moderate to high concentrations of extracts of traditional medicines containing alkaloids infrequently compromise normal hematological profiles, barring their continuous application at very high doses. Thus, the above findings corroborate the observation that the acute renal failure (ARFs) associated with *D. microcarpum* are hematology-safe according to the experiment conditions used.

5. Conclusion

The findings of this research indicate that the alkaloid fraction of *Detarium microcarpum* stem bark does not exhibit any overt signs of short-term and medium-term toxicity at doses as high as 1000 mg/kg in Wistar rats. Over the 28-day oral treatment regime, no significant changes in body weight, organ weights, results of blood tests, liver and kidney function tests, or markers of oxidative stress were observed. Close examination of liver and kidney tissues revealed no injury or inflammation. This confirms the safety indications from biochemical investigations and clinical observations.

These findings are indicative of the fact that the alkaloid fraction is safe under the dose utilized for treatment and doesn't manifest side effects on the body in terms of the conditions examined. That there is no damage to the kidney, liver, blood, and tissues speaks to the fact that it could be a safe herbal medicine option. Although at the highest dosage there was some rise in the kidney markers, it failed to cause change in tissue, pointing to excellent safety.

Overall, this research provides compelling toxicological evidence to support the safe application of *Detarium microcarpum* in traditional medicine and sets the stage for upcoming pharmacokinetic, genotoxicity, and ultimately clinical research. Further research, particularly in humans and with chronic dosing models, is recommended to fully delineate the therapeutic window and long-term safety profile of this promising alkaloid-rich botanical extract.

REFERENCES

Abdulazeez, M. A., Okoro, M., & Usman, B. (2023). Toxicological profiling of phytochemicals: Emerging frontiers. *Phytomedicine Research, 11*(2), 102–113.

Adeniyi, T. A., Ogundajo, A. L., & Hassan, M. M. (2023). Safety assessment of selected Nigerian medicinal plants. *Toxicology Reports, 10*, 122–133.

Adetunji, C. O., Oladiji, A. T., & Abolaji, A. O. (2023). Hepatoprotective effects of phytochemical-rich plant extracts. *Journal of Ethnopharmacology, 311*, 116372.

DOI: 10.56892/bima.v9i1B.1290

Ahmed, M., Bello, S. A., & Musa, A. (2024). Natural alkaloids: Safety profiles and therapeutic promise. *Frontiers in Pharmacology, 15*, 982103.

Alabi, O. A., & Fadare, D. A. (2022). Sub-chronic toxicity studies of bioactive compounds from medicinal plants. *Phytomedicine Plus, 2*(3), 100289.

Ali, M. S., Ibrahim, M., & Lawal, B. (2024). A systematic review on toxicological assessments of herbal alkaloids. *Toxicology Letters, 382*, 1–15.

Amanpour, R., & Shadab, M. (2022). Phytochemical toxicity: Current trends and future perspectives. *Journal of Integrative Medicine, 20*(5), 441–450.

Chen, L., Xie, Y., & Wu, S. (2022). Advances in safety evaluation of medicinal plants. *Toxicology Reports, 9*, 550–562.

Chikere, C. B., & Nwachukwu, N. C. (2023). Evaluation of biochemical markers in alkaloid-treated rats. *Biochemistry Insights, 16*, 11786264231186045.

Chinonso, E. C., & Oyetayo, F. L. (2024). The pharmacological and toxicological evaluation of traditional herbs. *Journal of Herbal Medicine, 40*, 100606.

Diop, M., Sow, N. D., & Toure, A. (2023). Phytochemistry and pharmacological insights into *Detarium microcarpum*. *African Journal of Pharmacy and Pharmacology, 17*(1), 1–9.

Edeoga, H. O., & Iwuagwu, M. A. (2022). Acute and chronic toxicity studies of bioactive plants. *Journal of Toxicology, 2022*, 9382542.

Emeka, P. M., & Ogbonna, D. N. (2023). Antioxidant and toxicity profile of indigenous medicinal plants. *Natural Product Research, 37*(6), 967–976.

Essien, D. O., & Essien, J. P. (2024). Advances in plant alkaloid safety research. *Current Pharmaceutical Design, 30*(4), 543–553.

Huang, Y., Zhang, Y., & Hu, H. (2022). Alkaloid-rich herbal extracts: Benefits and safety concerns. *Plants, 11*(20), 2754.

Ismail, A. M., Sulaiman, W., & Lawal, S. (2022). Hepatotoxicity and nephrotoxicity studies of natural products. *Heliyon, 8*(10), e10819.

Jibril, S., Mohammed, A. I., & Lawal, A. (2024). Toxicological implications of prolonged alkaloid exposure. *Journal of Applied Toxicology, 44*(3), 562–574.

Khan, A., Mehmood, Z., & Zhang, J. (2024). Systematic review on toxicity studies of herbal alkaloids. *Frontiers in Pharmacology, 15*, 889012.

Lawal, B., Shittu, M. O., & Yusuf, A. J. (2023). Plant-derived alkaloids: A toxicological overview. *Toxicology Research and Application, 7*, 23978473231166452.

Li, Y., Huang, Z., & Zhao, L. (2023). Safety assessments of bioactive plant alkaloids: A systematic approach. *Journal of Ethnopharmacology, 312*, 116426.

Liang, J., Sun, T., & Yu, L. (2023). Review of recent toxicological studies on natural alkaloids. *Environmental Toxicology and Pharmacology, 98*, 104119.

Lin, C., Zhao, R., & Wu, Y. (2024). Phytochemical toxicity in traditional herbal medicine: A modern review. *Molecules, 29*(1), 180.

Liu, J., Hu, X., & Zhang, H. (2022). Medicinal plant alkaloids: Safety considerations for therapeutic applications. *Pharmaceutical Biology, 60*(1), 540–556.

Martins, M. C., Oliveira, D. R., & Santos, A. (2024). Alkaloid-based therapies: Emerging safety and efficacy data. *Pharmaceutical Biology, 62*(1), 56–66.

Musa, M., Ibrahim, H., & Bello, M. (2023). Oxidative stress modulation by

DOI: 10.56892/bima.v9i1B.1290

alkaloid extracts: Safety profile in rodents. *Antioxidants, 12*(9), 1745.

Mustapha, A., Yusuf, U. A., & Garba, M. (2024). Toxicological investigations on medicinal plant extracts. *Plants, 13*(1), 120.

Okereke, C. N., Onwuka, G. I., & Oduola, T. (2023). Extraction and toxicity evaluation of plant-based alkaloids. *Natural Product Communications, 18*(5), 1934578X231177653.

Oladipo, A. B., & Dada, F. A. (2022). Evaluation of liver biomarkers following herbal treatments. *Clinical Phytoscience, 8*(1), 45.

Olaniyan, J. M., & Akinlolu, A. A. (2023). Comparative toxicity of traditional medicinal plant extracts. *Journal of Ethnopharmacology, 317*, 116585.

Omotayo, S. B., & Fadare, D. A. (2024). Nephroprotective and hepatoprotective potentials of alkaloid-rich extracts. *BMC Complementary Medicine and Therapies, 24*(1), 16.

Oyedeji, O. O., & Ajayi, A. M. (2023). Biochemical and histopathological safety studies of medicinal plants. *Evidence-Based Complementary and Alternative Medicine, 2023*, 6738924.

Peng, L., Wang, X., & Zhang, C. (2022). The safety pharmacology of medicinal alkaloids. *Pharmaceuticals, 15*(11), 1356.

Sow, N. D., Diop, M., & Touré, A. (2023). Ethnobotanical and toxicological evaluation of *Detarium microcarpum*. *African Journal of Traditional, Complementary and Alternative Medicines, 20*(2), 45–56.

Wang, H., Li, Q., & Zhu, J. (2025). Safety evaluation of traditional Chinese medicine alkaloids. *Chinese Journal of Natural Medicines, 23*(1), 88–99.

Xu, M., Chen, Y., & Liu, J. (2024). Toxicity profiling of phytochemicals: Progress and perspectives. *Current Drug Metabolism, 25*(2), 156–167.

Zhang, Z., Yang, W., & Zhou, Y. (2024). Pharmacological activities and toxicity profiles of natural alkaloids: An updated review. *International Journal of Molecular Sciences, 25*(4), 1792.

Aimé, J., Fotso, Y., Roussel, G., Takuissu, N., Laure, J., Julius, N., and Oben, E. (2022). Acute and sub chronic toxicity studies of aqueous bark extract of Detarium microcarpum guill . and perr in albinos wistar rat. *Toxicology and Environmental Health Sciences*, 8(5): 76-81 https://doi.org/10.1007/s13530-022-00139-4.

OECD, (2008). Organization for Economic Cooperation and Development. Guidelines for the Testing of Chemicals. Acute Oral Toxicity. Test No. 425.