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TOXIC RESPONSES OF THE BLOOD OF RATS EXPOSED TO AQUEOUS EXTRACT OF *DIALIUM GUINEENSE* STEM BARK

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ABSTRACT

Dialium guineense have been shown to possess medicinal properties and its parts are used to treat different ailments. The present study investigated the toxic responses of the blood of rats exposed to subchronic doses of aqueous extract of *Dialium guineense* stem bark. Thirty-five (35) rats of Wistar strain (160 to 180 g) were divided into seven groups of 5 rats each. Group I served as control, while rats in the other groups were administered varied doses of extract (200 - 5000 mg/kg body weight, bwt) orally for 28 days. Haematological indices of rat blood were analysed using haematological Swelab autocounter 920E+ (UK) system. The results showed that graded doses of aqueous extract of *D. guineense* stem bark did not significantly alter the concentrations of the measured haematological parameters ($p > 0.05$). These results indicate that aqueous extract of the medicinal plant has no deleterious effect on haematopoietic system of rats.

Keywords: Blood, *Dialium guineense*, Haematology, Haematotoxicity, Haematopoietic system

INTRODUCTION

Haematotoxicology refers to the study of adverse effects of chemicals on blood and blood-forming tissues. Due to the pivotal roles played by blood cells, the tissue is highly susceptible to intoxication (Jain, 1986). Apart from hepatorenal toxicity, haematotoxicity is a major consideration in screening of drugs (Jain, 1986). The blood comprises approximately 7 % of the body weight of an adult human. Some of its functions are: (1) delivery of oxygen to tissues; (2) maintenance of vascular integrity; and (3) immunity (Jain, 1986). Blood cells are produced at a rate of 1 to 3 million/s in a healthy adult. However, in hemolytic anemia or suppurative inflammation, the rate is greatly increased (Kaushansky, 2006). Drugs used to treat cancer, infection, and immune-mediated disorders are particularly toxic to the blood (Kane *et al.*, 1988). Similarly, substances that affect the supply of nutrients (for example, iron); clearance of toxicants and metabolites (for example, urea); or the synthesis of important growth factors, such as erythropoietin and granulocyte colony-stimulating factor (G-CSF) also produce adverse effect in the blood (Kane *et al.*, 1988).

The effects of haematotoxic substances (hypoxia, hemorrhage and infection) can be life-threatening. They could be subclinical (slowly progressive) or acute and fulminant (presenting dramatic clinical symptoms). In chemotherapy, most especially, haematotoxicity is assessed to evaluate risk as against benefit. It is used to define dosage in cancer, viral and thrombotic therapies (Collen and Lijnen, 1991). Unavoidable in the treatment of some serious illnesses, haematotoxicity may be regarded as primary or secondary (Krupp and Barnes, 1989; Weingand *et al.*, 1992).

Plants are utilized globally either as food or medicine (Stickel and Schuppan, 2007). At least one-quarter of sick individuals use plant-based products. The World Health Organization (WHO) estimated that 80 percent of the population of some Asian and African countries rely on herbal medicine (Luper, 1998; Thyagarajan *et al.*, 2002; Abu *et al.*, 2017).

Dialium guineense (Velvet Tamarind) is a medicinal plant used in folklore medicine for the treatment of diarrhea, severe cough, bronchitis, wound, stomachaches, malaria fever, jaundice, ulcer and hemorrhoids (Bero *et al.*, 2009). At present, little or nothing is known about the adverse effect of extracts of the plant on rat blood. The aim of this study was to investigate the toxic responses of the blood of rats exposed to aqueous extract of *D. guineense* stem bark.

MATERIALS AND METHODS

Chemicals

The chemicals and reagents used in this study were of analytical grade and they were bought from Sigma-Aldrich Ltd. (USA).

Collection of Plant Material

The authenticity of the stem barks of *D. guineense*, obtained from Auchi Town in Edo State, Nigeria, were verified at the Department of Plant Biology and Biotechnology, University of Benin, Benin City, Nigeria. The prepared plant specimen was deposited in the herbarium of same department (No. UBHD330).

Preparation of Plant Extract

The plant stem bark was washed and shade-dried at room temperature for two weeks and then ground into powder using a mechanical blender. Exactly 500 g of the pulverized stem bark was soaked in 5000 mL distilled water. The resultant aqueous extract was filtered with a muslin cloth and freeze dried using a lyophilizer (Abu *et al.*, 2015).

Experimental Rats

Male rats of Wistar strain (n = 35) weighing between 160 and 180 g (mean weight = 170 ± 10 g) were obtained from the Animal House of Anatomy Department, University of Benin, Benin City, Nigeria. The rats were housed in metal cages under standard laboratory conditions. They were allowed unrestricted access to rat feed and drinking water. The rats were acclimatized to the laboratory environment for one week prior to commencement of the study. Standard experimental protocol was followed for this study.

Experimental Design

The rats were assigned to 7 groups (5 rats per group). One group served as control, while rats in the treatment groups

received varied doses of the extract (200 - 5000 mg/kg bwt) for 28 days. Blood samples were collected for haematological analysis at the end of the treatment period.

Haematological Analysis

Haematological parameters of rat blood were analysed using hematological Swelab autocounter 920E+ (UK) system.

Statistical Analysis

Data are expressed as mean ± standard error of mean (SEM, n = 5). Statistical analysis was performed using SPSS (version 20). Groups were compared using Duncan multiple range test. Statistical significance was assumed at $p < 0.05$.

RESULTS

Effect of Aqueous Extract of *D. guineense* Stem Bark on Body Weight

As shown in Table 1, percentage increases in body weights of rats treated with aqueous extract of *D. guineense* stem bark were significantly reduced, relative to the control group ($p < 0.05$).

Table 1: Comparison of the Effect of Aqueous Extract of *D. guineense* Stem Bark on Body Weight

Groups	% Increase in weight
Control	61.35 ± 4.11
200 mg/kg bwt	49.09 ± 4.83[a]
500 mg/kg bwt	47.39 ± 3.09[a]
1000 mg/kg bwt	42.38 ± 2.61[a]
2000 mg/kg bwt	37.28 ± 3.94[a]
3500 mg/kg bwt	31.65 ± 2.83[b]
5000 mg/kg bwt	27.82 ± 0.40[b]

Data are percentage weight increases and are expressed as mean ± SEM (n = 3). [a]$p < 0.05$, when compared with control group; [b]$p < 0.05$, when compared with 200 mg/kg bwt group.

Concentrations of Haematological Parameters in Extract-Treated Rats

Graded doses of aqueous extract of *D. guineense* stem bark did not significantly alter the concentrations of the measured haematological parameters ($p > 0.05$; Tables 2 to 4).

Table 2: Concentrations of Haematological Parameters in Rats Treated with Aqueous Extract of *D. guineense* Stem Bark

Groups	Hg (g/100 mL)	PCV (%)	MCV (fi)	MCH (p.g)
Control	16.65 ± 1.85	49.95 ± 6.75	75.55 ± 1.45	22.15 ± 0.65
200 mg/kg bwt	15.40 ± 0.30	43.15 ± 1.35	71.40 ± 1.60	21.90 ± 0.30
500 mg/kg bwt	15.80 ± 0.10	48.70 ± 1.60	81.45 ± 2.85	23.70 ± 0.90
1000 mg/kg bwt	15.35 ± 1.65	46.40 ± 1.20	70.80 ± 1.00	21.70 ± 0.60
2000 mg/kg bwt	18.70 ± 2.00	54.0 ± 3.30	73.05 ± 0.65	22.60 ± 0.70
3500 mg/kg bwt	17.80 ± 0.10	50.55 ± 0.15	75.30 ± 2.70	23.55 ± 0.75
5000 mg/kg bwt	17.80 ± 0.10	47.50 ± 5.20	93-95 ± 8.95	23. 45 ± 0.55

Data are concentrations of haematological indices and are expressed as mean ± SEM (n = 3).
Hg = Haemoglobin; PCV = packed cell volume; MCV = mean cell volume; and MCH = mean corpuscular haemoglobin

Table 3: Concentrations of Some Haematological Parameters in Extract-Treated Rats

Groups	RBC (10^6/µL)	WBC (× 10^3/µL)	MCHC (g/dL)	RETICS (%)
Control	7.48 ± 0.61	7.75 ± 1.65	31.00 ± 1.60	0.90 ± 0.10
200 mg/kg bwt	7.02 ± 0.03	7.85 ± 0.50	30.65 ± 0.25	2.90 ± 0.30
500 mg/kg bwt	6.55 ± 0.22	6.35 ± 0.55	29.25 ± 0.05	2.65 ± 0.35
1000 mg/kg bwt	7.04 ± 0.57	6.05 ± 1.25	30.70 ± 0.40	2.65 ± 0.15
2000 mg/kg bwt	8.25 ± 0.63	10.40 ± 2.40	30.90 ± 1.20	2.05 ± 0.95
3500 mg/kg bwt	7.55 ± 0.20	12.00 ± 2.60	31.25 ± 0.15	2.55 ± 0.45
5000 mg/kg bwt	6.05 ± 0.97	5.40 ± 0.10	25.10 ± 1.80	3.00 ± 0.00

Data are concentrations of haematological indices and are expressed as mean ± SEM (n = 3).
RBC = red blood cells; WBC = white blood cells; MCHC = mean corpuscular haemoglobin concentration; RETICS = reticulocytes.

Table 4: Concentrations of monocytes and platelets in Extract-Treated Rats

Groups	NEUT (%)	LYMPH (%)	MO (%)	PLT (× 10^5/µL)
Control	49.0 ± 1.00	45.00 ± 1.00	6.0 ± 0.00	4.82 ± 0.44
200 mg/kg bwt	52.50 ± 1.50	40.00 ± 2.00	7.50 ± 0.50	5.58 ± 0.46
500 mg/kg bwt	54.50 ± 5.50	42.0 ± 5.00	3.50 ± 0.50	7.27 ± 0.55
1000 mg/kg bwt	51.50 ± 3.50	43.50 ± 1.50	5.0 ± 2.00	5.17 ± 1.23
2000 mg/kg bwt	53.0 ± 4.00	42.50 ± 2.50	4.50 ± 1.50	4.42 ± 0.45
3500 mg/kg bwt	54.0 ± 4.00	41.00 ± 6.00	5.0 ± 2.00	5.91 ± 1.30
5000 mg/kg bwt	53.50 ± 4.50	41.50 ± 4.50	5.0 ± 0.00	4.45 ± 1.31

Data are concentrations of haematological indices and are expressed as mean ± SEM (n = 3).
NEUT = neutrophils; LYMPH = lymphocytes; MO = monocytes; and PLT = platelets

DISCUSSION

Drugs can produce primary or secondary effects in blood cells. As a matter of necessity most preclinical and clinical safety studies include toxicological evaluation of the haematopoietic system. Although iatrogenic blood dyscrasias is primary, it is frequently secondary to other tissue toxicity. In the hierarchy of toxicity, primary haematotoxicity comes after liver and kidney toxicities (Kane *et al.,* 1988). Blood tissue is used in the assessment of systemic toxicity. The sole aim of preclinical and clinical safety studies is to diagnose clinical blood disorders (Collen and Lijnen, 1991).

Hematotoxicity is the study of blood and blood-forming tissues as target for drugs, chemicals; and factors such as stress, exercise, and ionizing radiation. The high vulnerability of blood to chemical-induced toxicity is due to the high mitotic rate of the tissue and the fact that the cells are directly exposed to all substances administered systemically. In normal individuals, red cells, platelets and neutrophils are synthesized at a rate approximately 1 – 3 million/s. Like other rapidly dividing tissue, such as intestine and gonads, bone marrow is particularly sensitive to certain classes of drugs and other nontherapeutic compounds. For example, cytopenia often accompany treatment regimens making use of anticancer and immunosupressive agents as well as radiotherapy. In addition, the marrow can be a therapeutic target for agents designed to stimulate the production of blood cells or protect against myelotoxicity (Jain, 1986; Kaushansky, 2006). The consequences of bone marrow impairment or direct damage to blood cells leading to cytopenia or dysfunction can be extensive and serious. The obvious sequellae include anoxia, infection/sepsis, and haemorrhage. These changes can be dramatic or subtle and present with a host of secondary and compensatory alterations in haematopoietic or extra-medullary tissues. Anticancer drugs account for 61 % of drug-induced haematotoxicity. With the exception of cancer patients and those suffering from chronic alcoholism, severe liver or renal disease (such as viral hepatitis), infectious mononucleosis, disorders requiring transfusions, familial conditions, or other conditions associated with haematopathology, only 1 in 100,000 come down with drug-induced haematotoxicity (Collen and Lijnen, 1991; Weingand *et al.,* 1992).

Haematological parameters (haematocrit, haemoglobin, erythrocytes and white blood cells) are used as indicators of toxicity. They have broad applications in environmental and occupational monitoring. The normal ranges of these parameters are altered by the ingestion of some toxic substances. It has been reported that alterations in haematological parameters by medicinal compounds could either be positive or negative (Islam *et al.,* 2004; Mmereole, 2008).

This study investigated the toxic responses of the blood of rats exposed to aqueous extract of *D. guineense* stem bark. The results showed that graded doses of aqueous extract of the medicinal plant stem bark did not significantly alter the concentrations of the measured hematological parameters, an indication that it may not be toxic to the blood and blood-forming tissues. The relative safety as well as the protective properties of extracts of the medicinal plant have reported (Abu *et al.*, 2022a,b,c,d,e). Extracts of *D. guineense* stem bark have been reported to possess different pharmacological and biological activities (Abu *et al.*, 2022f,g,h,i,j,k).

CONCLUSION

The results of this study have shown for the first time that aqueous extract of *D. guineense* stem bark does not produce any toxic response in rats blood. It has no deleterious effect on haematopoietic system of rats.

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