

The Effects of Active Fractions and Ethanolic Fruit Extract of *Raphia hookeri* on Aluminium Chloride-Induced Toxicity in Male Wistar Rats

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ABSTRACT

Aluminium (AL) is the third most abundant element in the earth's crust and constitutes about 8% of the total mineral components. The availability of AL has recently drawn more attention to its bio-toxicity. Hence the effects of aluminium chloride (AlCl₃) toxicity on haematological profile administered active fractions and ethanolic fruits extract of *Raphia hookeri* in male wistar rats were investigated.

Methodology: A total of 110 healthy male wistar rats weighing 180-200 g were grouped into 11 groups of 10 rats each. Group 1: Normal feed and water (normal control); Group 2: AlCl₃; Group 3: 200 mg/kg b.wt. of vitamin C; Group 4 and 5: N-hexane fraction at 10 and 20 mg/kg b. w; Group 6 and 7: Ethyl acetate fraction at 10 and 20 mg/kg b. w; Group 8 and 9: Aqueous fractions at 10 and 20 mg/kg b. w; Group 10 and 11: Ethanol extract at doses of 200 mg/kg b. w and 400 mg/kg b. w. The treatment lasted for 21 days.

Results: Results revealed a significant ($p \leq 0.05$) increase in all the treatment groups when compared with the negative control (2.71 ± 0.60). A significant ($p \leq 0.05$) increase of Hemoglobin (Hb) was observed when all the treatment groups were compared with the negative control (6.88 ± 0.48). Haematocrit (HCT) revealed a significant ($p \leq 0.05$) increase in all the treatment groups when compared with the negative control (25.82 ± 2.00). Mean Cellular Volume (MCV) revealed non-significant ($p \leq 0.05$) difference when AlCl₃+Eth 20 mg (73.04 ± 1.16), AlCl₃ + 10 mg aq (71.82 ± 0.81), AlCl₃+20 mg aq (72.95 ± 1.04), and AlCl₃+Crude 200 mg (72.70 ± 0.96) were compared with the negative control (73.38 ± 1.76). MCH also revealed a significant ($p \leq 0.05$) increase in all the treatment groups when compared with the negative control group (13.30 ± 1.70). Mean cellular Hemoglobin Concentration (MCHC) further revealed a significant ($p \leq 0.05$) increase when all the treatment groups were compared with the negative control (19.08 ± 3.42). There was significant ($p \leq 0.05$) decrease in WBC in all the treatment groups when compared with the negative control (13.10 ± 1.1). PLT revealed a significant ($p \leq 0.05$) decrease in all the treatment groups when compared with the negative control group (1020.00 ± 64.37). Lymphocyte (LYM) % revealed a non-significant ($p \leq 0.05$) difference in all the treatment groups except AlCl₃ + Crude 400 mg (73.02 ± 2.60), when compared with the negative control group (88.86 ± 3.6). LYM# revealed a significant ($p \leq 0.05$) decrease in all the treatment groups: AlCl₃+Vit. C (200 mg) (4.82 ± 1.36), AlCl₃+10 mg aq (5.82 ± 0.58), AlCl₃+n-h 20 mg (7.22 ± 0.72), AlCl₃+Eth 10 mg (8.86 ± 1.05), AlCl₃+10 mg aq (5.82 ± 0.58), AlCl₃+20 mg aq (7.25 ± 1.64), AlCl₃+ Crude 200 mg (7.66 ± 1.31), AlCl₃+Crude 400 mg (6.38 ± 0.97 when compared with the negative control.

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Conclusion: The ethanol fruit extract of *R. hookeri* (Rh) demonstrated augmenting effect on AlCl₃- induced haematotoxicity. These effects may be due to the presence of some phytochemicals which prevented the deleterious effects of AlCl₃ on RBCs membrane with subsequent stimulation of the hematopoietic activity in the bone marrow.

Keywords: Aluminium chloride; *Raphia hookeri*; Haematotoxicity; Blood cells

INTRODUCTION

Aluminium is the third most abundant element in the earth's crust and constitutes about 8% of the total mineral components [1]. It is widely used in the manufacture of cosmetics, cookware, and food additives. Industrial waste and particulate matter generated by cement producing factories contain high amounts of aluminum and individuals who reside around the vicinity are exposed to high levels of this metal [2]. Food sources of aluminium include corn, yellow cheese, salt, herbs, spices and tea [3,4]. Human exposure to aluminum is inevitable because of its presence in food, water, and pharmaceuticals [5]. The normal daily consumption rate of aluminum for adults is 1-10 mg [6]. It has been reported that aluminum is poorly absorbed after oral intake and in plasma 80%-90% of this element is transported bound to transferrin [7]. The Biological effects of Aluminium (Al) are linked to the development of many diseases. Many studies have shown that AlCl₃ induced toxic effects on the brain, bone, immune and hematopoietic systems [8]. The toxicity of aluminium was observed to be mediated by the generation of free radicals hence various antioxidant compounds and plant extracts are reported to play a role in ameliorating the toxic effects of this element [5,9,10]. However, there is certainly growing evidence that several fruits possess interesting pharmacological effects. Rh is one of the most economically useful plants in Africa. Leaves are used for shelter and stems produce palm sap which is drunk as a beverage. The fruits are oblong to ovoid and covered with glossy golden brown scales. They can be eaten once boiled, or used in traditional medicine for the preparation of laxatives and treatment of dysentery and haemorrhage [11]. The phytochemical evaluation of the mesocarp and peel of *Raphia* palm fruits showed that the mesocarp is rich in bioactive compounds such as vitamin E, niacin, alkaloids, saponins, flavonoid and phenols [12]. The effects of this fruit have been shown on exogenous testosterone and estradiol induced benign prostatic hyperplasia [13], and it leaf to modulate carbohydrate hydrolyzing enzymes linked to type-2 diabetes [14]. The active fractions contained in the ethanolic fruit extract of *Raphia hookeri* may have some beneficial effects on the hematopoietic system. This study therefore warrants investigation of the effects of aluminum chloride toxicity on some haematological formulations in male wistar rats administered active fractions and ethanolic fruit extract of *Raphia hookeri*.

MATERIALS AND METHODS

Plant materials

The fruits were obtained and identified by a plant taxonomist. It

was cleaned and air dried for extraction. After extraction the crude was further subjected to column chromatography using silica gel (60-120 mesh) with various solvent system ratios in their order of polarity (n-hexane, ethanol and water) as described by Mbaka, et al. [15]. The fractions were further screened and then 100% fractions were selected for haematological study [16].

Experimental animals

A total of 110 wistar rats were kept in cages under standard laboratory conditions (25°C), 12 h light/12 h dark cycle and had free access to grower mash, Vital Feeds Company Nigeria and clean tap water ad-libitum for two (2) weeks before the commencement of the experiment according to the guidelines of the Organisation for Economic Cooperation and Development [17]. The experimental animals were randomized into eleven (11) groups of ten (10) rats in each group.

Drugs and chemicals

Aluminum Chloride (AlCl₃) was obtained from Sigma-Aldrich Co. (USA). All other chemicals and kits were of highest analytical grade.

Experimental design

Total of 110 healthy male wistar rats weighing 180-200 g were grouped into 11 groups of 10 rats each. Aluminium chloride 4.2 mg/kg b.wt was administered intraperitoneally once to all the experimental animals except group 1. Group 1 normal control rats received normal feed and water. Group 2 AlCl₃ control received AlCl₃ 4.2 mg/kg b.wt intraperitoneally once without treatment. Group 3 received AlCl₃ 4.2+200 mg/kg b.wt of vitamin C. Groups 4 and 5 received AlCl₃ 4.2+n-hexane fraction at 10 and 20 mg/kg b.wt. Groups 6 and 7 received AlCl₃ 4.2+ethyl acetate fraction at 10 and 20 mg/kg b.wt. Group 8 and 9 received AlCl₃ 4.2+aqueous fractions at 10 and 20 mg/kg b.wt. While group 10 and 11 received AlCl₃ 4.2 +ethanolic extract at doses of 200 mg/kg b. w and 400 mg/kg b.wt. The experimental animals were treated with different fractions and crude extracts of *R. hookeri* where groups 4 and 5 received n-hexane fraction at 10 and 20 mg/kg b.wt. Groups 6 and 7 received ethyl acetate fraction at 10 and 20 mg/kg b.wt. Groups 8 and 9 received aqueous fractions at 10 and 20 mg/kg b.wt. While group 10 and 11 received ethanolic crude extract at doses of 200 mg/kg b.wt and 400 mg/kg b.wt respectively on a daily basis for 21 days. The negative control group received 200 mg/kg b.wt of vitamin C. 200 mg while the positive control was administered aluminum chloride without any treatment. After 24 hours of the last/final administration of

the fractions and extracts of *R. hookeri*, the experimental animals were starved overnight, anaesthetized with chloroform and sacrificed. Blood sample was collected by cardiac puncture, and was separated into EDTA for plasma and plain bottles for serum respectively.

Determination of haematological indices

The haematological indices selected includes; Haemoglobin (Hb), Red Blood Cells (RBC) count, Packed Cell Volume (PCV), White Blood Cells (WBC) count, Platelets (PLT), Lymphocytes (LYMP), Neutrophils (NEU), Monocytes (MID), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), and Mean Corpuscular Haemoglobin Concentration (MCHC). The whole blood samples were analyzed using Sysmex KX-21N automated machine (Sysmex Corporation, Kobe, Hyogo, Japan) following the manufacturer's instructions. Briefly, the sample was mixed and placed in contact with the sample probe for aspiration, when the buzzer sounded twice "beep beep" and the LCD screen displayed ANALYZING, the sample was removed. Following this, the unit executed an automated analysis, and the result was displayed on the LCD screen.

RESULTS

Effect of crude and active fractions of ethanolic fruits extract of *Raphia hookeri* on some haematological indices (RBC, Hb, HCT, MCV, MCH and MCHC)

Treatment with active fractions and crude ethanolic fruit extract of *Raphia hookeri* revealed a significant ($p \leq 0.05$) increase in RBC in all the treatment groups when compared with the negative control (2.71 ± 0.60). A significant ($p \leq 0.05$) increase of Hb was observed when all the treatment groups were compared with the negative control (6.88 ± 0.48). HCT revealed a significant ($p \leq 0.05$) increase in all the treatment groups when compared with the negative control (25.82 ± 2.00). MCV revealed non-significant ($p \leq 0.05$) difference when AlCl_3 +Eth 20 mg (73.04 ± 1.16), AlCl_3 +10 mg aq. (71.82 ± 0.81), AlCl_3 +20 mg aq. (72.95 ± 1.04), and AlCl_3 +Crude 200 mg (72.70 ± 0.96) were compared with the negative control (73.38 ± 1.76). MCH also revealed a significant ($p \leq 0.05$) increase in all the treatment groups when compared with the negative control group (13.30 ± 1.70). MCHC further revealed a significant ($p \leq 0.05$) increase when all the treatment groups were compared with the negative (19.08 ± 3.42) (Table 1).

Groups	RBC ($10^6/\mu\text{L}$)	Hb (g/dl)	HCT (%)	MCV	MCH (g/dL)	MCHC (g/dL)
Normal control	6.92 ± 0.21^{abc}	13.06 ± 0.64^c	53.02 ± 3.59^c	73.24 ± 1.66^b	18.98 ± 0.35^b	25.94 ± 0.26^b
Negative control (AlCl_3 only)	2.71 ± 0.60^a	6.88 ± 0.48^a	25.82 ± 2.00^a	73.38 ± 1.76^b	13.30 ± 1.70^a	19.08 ± 3.42^a
AlCl_3 +Vit. C (200 mg)	5.44 ± 0.54^b	10.50 ± 0.77^{bc}	48.06 ± 1.80^{bc}	69.26 ± 2.71^{ab}	18.94 ± 0.97^b	26.44 ± 0.58^b
AlCl_3 +n-h 10 mg	6.19 ± 1.30^{bc}	12.56 ± 1.10^c	49.18 ± 1.24^{bc}	67.30 ± 0.57^a	19.68 ± 1.06^b	28.18 ± 1.12^b
AlCl_3 +n-h 20 mg	6.60 ± 0.26^{bc}	12.40 ± 0.57^c	46.50 ± 2.06^{bc}	70.78 ± 0.31^{ab}	20.36 ± 0.75^b	28.78 ± 1.18^b
AlCl_3 +Eth 10 mg	6.84 ± 0.36^{bc}	11.56 ± 1.09^{bc}	47.80 ± 2.37^{bc}	69.90 ± 1.12^{ab}	19.08 ± 1.53^b	27.24 ± 2.02^b
AlCl_3 +Eth 20 mg	7.33 ± 0.16^c	11.14 ± 1.48^{bc}	51.42 ± 2.26^{bc}	73.04 ± 1.16^b	18.60 ± 0.29^b	25.40 ± 0.35^b
AlCl_3 + 10 mg aq	6.12 ± 0.81^{bc}	12.36 ± 0.20^c	44.02 ± 2.90^b	71.82 ± 0.81^b	18.58 ± 0.64^b	25.52 ± 1.05^b
AlCl_3 +20 mg aq	7.01 ± 0.31^{bc}	12.05 ± 0.89^{bc}	51.20 ± 2.77^{bc}	72.95 ± 1.04^b	19.00 ± 0.45^b	25.45 ± 0.25^b
AlCl_3 +Crude 200 mg	6.71 ± 0.28^{bc}	12.54 ± 0.88^c	48.88 ± 2.62^{bc}	72.70 ± 0.96^b	18.62 ± 0.59^b	25.42 ± 0.47^b
AlCl_3 +Crude 400 mg	5.37 ± 0.17^b	9.30 ± 0.86^{ab}	50.58 ± 4.01^{bc}	70.82 ± 0.27^{ab}	18.64 ± 0.34^b	24.62 ± 0.52^b

Note: Values are expressed as mean \pm Standard Error of Mean (S.E.M); N=5. Values with different superscripts down the column are considered statistically significant $P \leq 0.05$. Red Blood Cells (RBC); Mean Corpuscular Volume (MCV); Mean Corpuscular Haemoglobin (MCH); Mean Corpuscular Haemoglobin Concentration (MCHC).

Table 1: Effect on red blood cell formulations (RBC, Hb, HCT, MCV, MCH, MCHC) in AlCl_3 -induced toxic rats administered active fractions and ethanolic fruit extract of *R. hookeri*.

Effect of crude and active fractions of ethanolic fruits extract of *Raphia hookeri* on the white blood cells indices (WBC, PLT, LYM% and LYM

Treatment with crude and active fractions of ethanolic fruit extract of *Raphia hookeri* revealed a significant ($p \leq 0.05$) decrease in WBC in all the treatment groups when compared with the negative control (13.10 ± 1.1). PLT revealed a significant ($p \leq 0.05$) decrease in all the treatment groups when compared with the negative control group (1020.00 ± 64.37). LYM % revealed a non-significant ($p \leq 0.05$) difference in all the treatment groups except AlCl_3 +Crude 400 mg (73.02 ± 2.60), when compared with the negative control group (88.86 ± 3.6). LYM# revealed a significant ($p \leq 0.05$) decrease in all the treatment groups: AlCl_3 +Vit. C (200 mg) (4.82 ± 1.36), AlCl_3 +10 mg aq (5.82 ± 0.58), AlCl_3 +n-h 20 mg (7.22 ± 0.72), AlCl_3 +Eth 10 mg (8.86 ± 1.05), AlCl_3 +10 mg aq (5.82 ± 0.58), AlCl_3 +20 mg aq (7.25 ± 1.64), AlCl_3 +Crude 200 mg (7.66 ± 1.31), AlCl_3 +Crude 400 mg (6.38 ± 0.97) when compared with the negative control group (Table 2).

DISCUSSION

Induction of stress with aluminium chloride resulted in a significant decrease in red blood cell count with significant increase in haematocrit levels in the treatment animals. It can be explained by the fact that the oxidative stress caused by AlCl_3 increase production of free radicals and the erythrocyte ATP

concentration [18-20]. The significant decrease in haematocrit in the positive control group when compared to the treatment groups could be due to some of these deleterious effects of AlCl_3 on RBCs membrane increase in the rate of destruction or a reduction in the rate of formation of red blood cells. Bouasla, et al. [21], had reported that aluminium can disrupt erythropoiesis through its combined effect on mature erythrocytes and delayed cellular metabolism of progenitor erythrocytes. The administration in the active fractions and ethanolic fruit extract of *R. hookeri* caused a significant increase of these parameters. It is due to the presence of some metabolites in the extract which stimulate hematopoietic activity in the bone marrow [21].

Induction of toxicity with AlCl_3 also led to a significant increase in the level of white blood cells and absolute lymphocytes in the blood samples of the positive control group. Oxidative stress usually leads to the activation of the white blood cells that are lymphocytes and neutrophils which indicate the activation of the defence and immune system [22,23]. These results are in concordance with Emmanuel, et al. [24], who reported that the induction of fibrosis by carbon tetrachloride showed a significant increase in plasma white blood cell levels of rats. Also, Bouasla, et al. [21], observed a decrease in these parameters in rats which have induced hepatotoxicity with aluminium chloride. Moreover, the administration of the active fractions and ethanolic fruit extract of Rh resulted in a significant decrease in the rate of these parameters. This drop is due to the presence of macro and micronutrients in the fruit extract. The nutritional

Groups	WBC ($10^3/\mu\text{L}$)	PLT ($10^3/\mu\text{L}$)	LYM (%)	LYM (#)
Normal control	5.16 ± 0.40^a	696.60 ± 46.00^a	91.68 ± 0.98^b	9.10 ± 1.00^{bc}
Negative control (AlCl_3 only)	13.10 ± 1.18^b	1020.00 ± 64.37^b	88.86 ± 3.67^b	10.22 ± 1.72^c
AlCl_3 +Vit. C (200 mg)	5.38 ± 0.86^a	606.20 ± 35.22^a	85.86 ± 3.67^b	4.82 ± 1.36^a
AlCl_3 +n-h 10 mg	4.92 ± 0.46^a	655.80 ± 70.52^a	90.50 ± 2.55^b	6.76 ± 1.71^{abc}
AlCl_3 +n-h 20 mg	5.90 ± 0.85^a	659.20 ± 118.35^a	75.18 ± 5.12^a	7.22 ± 0.72^{abc}
AlCl_3 +Eth 10 mg	5.08 ± 0.52^a	496.60 ± 43.98^a	90.90 ± 1.27^b	8.86 ± 1.05^{abc}
AlCl_3 +Eth 20 mg	6.28 ± 1.49^a	619.60 ± 53.25^a	85.70 ± 1.80^b	8.40 ± 1.15^{abc}
AlCl_3 +10 mg aq	6.44 ± 0.66^a	572.60 ± 69.02^a	86.88 ± 0.56^b	5.82 ± 0.58^{ab}
AlCl_3 +20 mg aq	6.80 ± 1.01^a	602.00 ± 61.94^a	85.98 ± 1.90^b	7.25 ± 1.64^{abc}
AlCl_3 +Crude 200 mg	4.84 ± 0.90^a	625.40 ± 48.39^a	87.86 ± 1.51^b	7.66 ± 1.31^{abc}
AlCl_3 +Crude 400 mg	5.92 ± 1.22^a	630.80 ± 79.57^a	73.02 ± 2.60^a	6.38 ± 0.97^{abc}

Note: Values are expressed as mean \pm Standard Error of Mean (SEM); N=5. Values with different superscript down the column are considered statistically significant $P \leq 0.05$. White Blood Cells (WBC); Platelets (PLT).

Table 2: Effect on white blood cell formulations (WBC, PLT, LYM%, LYM#) in AlCl_3 -induced toxic rats administered active fractions and ethanolic fruit extract of *R. hookeri*.

values of *Raphia hookeri* have been reported [25,16]. In addition, the work of Cotoraci, et al. [26], showed natural antioxidants in anaemia treatment. These results agree with the work of Akpanyung, et al. [27], who observed a decrease in white blood cell count after inducing hepatic stress with carbon tetrachloride and administering crude and infused herbs in wistar rats. Other works on effect of aluminium chloride and protective effect of ginger extract on hematological profiles in male wistar rats have also been documented [28].

CONCLUSION

The present study has demonstrated augmenting effect of the active fractions and ethanolic fruit extract of *Raphia hookeri* against Aluminum Chloride (AlCl₃)-induced haematotoxicity in male wistar rats. These effects were in dose dependent manner. The results which were provided have experimental evidence for the ethanol medicinal use of the fruits of *Raphia hookeri* in the management of anaemia.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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