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Original article

EFFECTS OF *MANGIFERA INDICA* EXTRACT ON HAEMATOLOGICAL AND HISTOPATHOLOGICAL INDICES IN LABORATORY MICE

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ABSTRACT

Toxicological properties of crude leaf extract of *Mangifera indica* were carried out using standard procedures in laboratory mice. Forty Swiss albino mice grouped into four groups each for the acute and sub-acute toxicity study were administered doses of 100, 200, 300mg/kg and normal saline (control). The results of showed increased in weight from 21.54±0.95g to 29.53±0.48g, 21.45±0.84g to 29.16±3.33g, 21.23±0.90g to 23.81±1.28g for 300mg/kg, 200mg/kg and 100mg/kg respectively after 14 days of treatment. The mice treated with 300mg/kg progressively increased in weight from 18.52±0.48 to 26.93±0.74g after 21days (week 3), the 200mg/kg treated group increased from 19.14±0.98 to 30.76±0.56g in week 4 while the 100mg/kg treated group increased from 19.46±0.76 to 30.23±0.45 in week 3 respectively after 28 days of treatment. The haemoglobin counts were 10.15±0.35g/dl, 10.78±0.50g/dl, 9.78±0.33g/dl and 10.12±0.32g/dl for 300, 200, 100mg/kg and control groups respectively. The packed cell volume (PCV) increased from 28.00±2.09% control group to 28.80±0.97%, 32.50±1.85% and 29.25±2.14% for 100, 200 and 300mg/kg respectively. Furthermore, the red blood cell (RBC) counts also increased from 3.82±0.29x10^{12}/L to 4.33±0.35 x 10^{12}/L for 200mg/kg. There was a general increase in the white blood cell (WBC) levels 5.36±1.03 x 10^{9}/L, 6.21±0.78 x 10^{9}/L, and 5.84±1.13 x 10^{9}/L for 100, 200 and 300mg/kg compared to the control 3.98±0.55 x 10^{9}/L. The mean corpuscular volume (MCV) revealed an increase that is dose dependent 7.56±0.84, 8.05±1.00 and 8.12±0.79cuμ for 100, 200 and 300mg/kg respectively while the mean corpuscular haemoglobin (MCH) 2.57±0.30, 2.56±0.28 and 2.84±0.29pg did not follow this pattern and the mean corpuscular haemoglobin concentration (MCHC) 34.04±0.32, 33.23±0.81 and 33.04±1.01% for 100, 200 and 300mg/kg decreased respectively. The histophatological defects observed were enlargement of nuclei on the liver and necrosis of the glomeruli of the kidney administered with higher doses of the kidney.

Keywords: *Mangifera indica*, haematological indices, histopathological, albino mice.

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INTRODUCTION

Medicinal plant usage have cut across different spheres of medicine ranging from herbal medicine to pharmaceutical processing [1]. Plants have been of immense use for both the treatment and management of human diseases [2]. These plants have been confirmed to possess active ingredients like flavonoids, phenolics and alkaloids among many others which are good precursors for chemo-pharmaceutical [3].

Mangifera indica Linn. (family: Anacardiaceae) commonly known as mango (English), Mangoro (Yoruba - Western Nigeria), Mangwaro (Hausa - Northern Nigeria), Mangolo (Igbo - Eastern Nigeria) is widely grown in different parts of Africa, especially the Southern part of Nigeria, where it is valued for its edible fruit [4]. *M. indica* is a large evergreen tree that can reach 15 to 30 m tall, anchored by a long unbranched taproot that can descend to a depth of 6-8 m. It bears green leaves (red or yellow at first) which are about 29-30 cm long with tiny red or yellowish– green flowers. The fruits vary in size, shape and colour [4].

M. indica have been confirmed to have bioactive properties like; antidiarrhoeal [1], antibacterial [5], antihyperlipidemic [6] and antiulcerogenic [7].

The plant extracts was evaluated against rodent malaria parasite *Plasmodium berghei* in laboratory mice and gave a dose dependent reduction in parasitaemia [8]. It is against this backdrop that the purpose of this study was to evaluate the haematological and histopathological changes in the liver, kidney, lungs, heart and the intestine of mice.

MATERIALS AND METHODS

Study area

The research was carried out in the Haematology laboratory of the College of Veterinary and Medical Laboratory Technology while the histopathological studies were carried out in the Central Diagnostic Laboratory all in the National Verterinary Research Institute (NVRI) Vom, near Jos, Plateau state.

Collection and Preparation of Plant Materials

The plants used for the experiment *Mangifera indica* Anacardiaceae (Mango leaves) were obtained from the School of Forestry Jos. The leaves were randomly picked and put inside clean polythene bags and immediately transported to the laboratory. The leaves were spread thinly on a flat clean tray and allowed to air dry at room temperature (25^0C) for seven days to prevent spoilage due to moisture condensation and then reduced to coarse powder using a wooden pestle and mortar [9].

Extraction of Plant Materials

The methods described by Expendu *et al*. (2000) were adopted. One hundred grams (100g) each of coarse powder of *M. indica* leaf were transferred into conical flasks and macerated in 300mls each of distilled water. The mixtures was allowed to stand overnight then later shaken for 3 hours using a mechanical shaker. Filtration of the extracts was carried out through a Buckner flask using a suction or vacuum pump. The filtrates obtained were evaporated to dryness using a rotary evaporator. The weight of each extract was taken before storage in the refrigerator.

Acute Toxicity

Twenty Swiss albino mice all males weighing 16-24g were divided into fourgroups. Groups A-C was treated with the extract 100mg/kg, 200mg/kg and 300mg/kg of *M. indica* respectively. Group D received normal saline for fourteen (14) days. All animals were observed daily for mortality and any

apparent toxicity during the first 24 hours and up to 14 days. ([10]; [11]; [12]).

Sub-Acute Toxicity

Twenty Swiss albino mice all males weighing 16-24g were divided into fourgroups. Groups A-C was treated with the extract 100mg/kg, 200mg/kg and 300mg/kg of *M. indica* respectively for 30 days. Group D received normal saline. Thereafter, the animals were sacrificed, blood collected and vital organs examined microscopically.

Haematological Test

Blood samples were collected after all animals surviving toxicity studies were killed by anaesthetizing with chloroform in a dessicator and laid on a dissecting board on its back then dissected using a scissors. Incision was created on the jugular vein around the shoulder and blood was collected using syringes and transferred into EDTA bottles to prevent clotting [12]. The red blood cells, white blood cells, platelets counts, haemoglobin content, PCV and differential counts were determined in the Haematology laboratory of the College of Veterinary and Medical Laboratory Technology Vom using standard procedures [13].

Tissue Histology

The mice surviving the sub-acute toxicity test were killed by anaesthetizing with chloroform in a dessicator and laid on a dissecting board on its back then dissected using a scissors and the vital organs including the heart, lungs, liver, spleen, kidney and intestine were carefully dissected out and fixed in 10% formalin. The organs were transported in sample bottles to the Histopathology unit of the Central Diagnostic Laboratory NVRI Vom for further processing and sectioning using standard techniques [14]. Tissue slice of 3 to 4cm thick were cut and put in the automatic tissue processor where they were further fixed in 10% formalin-saline solution for 2 hours. They were then dehydrated for 2 hours in each of the following ascending grades of alcohol: 85%, 90%, and 100% v/v. the dehydrated tissues were then cleared in toluene for 2 hours, after which the tissue slice were embedded in paraffin wax and were left to cool. The blocks were trimmed at 5 microns. The ribbons of sections were dewaxed in xylene and rehydrated in the following descending grades of alcohol: 100%, 90%, and 70% v/v. They were then stained in haematoxylin for about 5 minutes, differentiated in 1% acid alcohol, blued in scoff's tap water and stained in eosin for 3 minutes. They were later rinsed, dehydrated in ascending grades of alcohol: 70%, 90% and 100% v/v finally cleared in xylene and mounted in a box. The slides were then examined microspically for pathological lesions.

Data Analysis

Results are expressed as mean $\pm$ standard error of mean (SEM). The student t-test was used to compare the mean of each treated group with the control for any significant difference in mice treated with leaf extracts using S.P.S.S version 11.0.

RESULTS

Table 1 showed that the crude water extract of *M. indica* produced an increase in the body weight of mice from day 1 to day 14. The mice in control group increased in weights from 22.79$\pm$0.58g on day 1 to 30.36$\pm$0.92g on day 14. The 300mg/kg treated group increased from 21.54$\pm$0.95g to 29.53$\pm$0.48g while the 200mg/kg group increased from 21.45$\pm$0.84g to 29.16$\pm$3.33g on day seven but decreased to 27.94$\pm$2.82g on day 14. The 100mg/kg group increased from 21.23$\pm$0.90g on day 1 to 23.81$\pm$1.28g on day 7 and 24.61$\pm$1.38g

on day 14 respectively. The result generally indicated a dose dependent increase in body weights.

Table 1: Effect of daily administration of the aqueous extracts of *M. indica* on body weight of mice for a period of 14 days (acute toxicity)

Treatment	Body weight (g) Day 1	Day 7	Day 14
300mg/kg	21.54±0.95	24.52±1.32	29.53±0.48
200mg/kg	21.45±0.84	29.16±3.33	27.94±2.82
100mg/kg	21.23±0.90	23.81±1.28	24.61±1.38
Control	22.79±0.58	27.33±0.85	30.36±0.92

n=5, Data presented as mean ± SEM P≥0.05 (no significant difference in weight).

Table 2 shows the results of the haematological indices following administration with *M. indica* extracts. The haemoglobin counts were 10.15±0.35g/dl, 10.78±0.50g/dl, 9.78±0.33g/dl and 10.12±0.32g/dl for 300, 200, 100mg/kg and control groups respectively. The packed cell volume (PCV) increased from 28.00±2.09% control group to 28.80±0.97%, 32.50±1.85% and 29.25±2.14% for 100, 200 and 300mg/kg respectively. Furthermore, the red blood cell (RBC) counts also increased from $3.82\pm0.29x10^{12}$/L to $4.33\pm0.35 \times 10^{12}$/L for 200mg/kg and lowered to $3.75\pm0.60 \times 10^{12}$/L for 300mg/kg. There was a general increase in the white blood cell (WBC) levels $5.36\pm1.03 \times 10^{9}$/L, $6.21\pm0.78 \times 10^{9}$/L, and $5.84\pm1.13 \times 10^{9}$/L for 100, 200 and 300mg/kg compared to the control $3.98\pm0.55 \times 10^{9}$/L. The mean corpuscular volume (MCV) revealed an increase that is dose dependent 7.56±0.84, 8.05±1.00 and 8.12±0.79 cuμ for 100, 200 and 300mg/kg respectively while the mean corpuscular haemoglobin (MCH) 2.57±0.30, 2.56±0.28 and 2.84±0.29pg and the mean corpuscular haemoglobin concentration (MCHC) 34.04±0.32, 33.23±0.81 and 33.04±1.01% for 100, 200 and 300mg/kg respectively showed reduction in values as the dose increases when compared with the control.

Table 2: Effect of daily administration of the aqueous extracts of *Mangifera indica* on haematological indices in mice after 14 days.

Treatment	Haematological Indices Hb g/dl	PCV (%)	RBC $\times10^{12}$/L	WBC $\times10^{9}$/L	MCV	MCH	MCHC
300mg/kg	10.15±0.35	29.25±2.14	3.75±0.60	5.84±1.13	8.12±0.79	2.84±0.29	33.04±1.01
200mg/kg	10.78±0.50	32.50±1.85	4.33±0.35	6.21±0.78	8.05±1.00	2.56±0.28	33.23±0.81
100mg/kg	9.78±0.33	28.80±0.97	3.98±0.45	5.36±1.03	7.56±0.84	2.57±0.30	34.04±0.32
Control	10.12±0.32	28.00±2.09	3.82±0.29	3.98±0.55	7.38±0.51	2.68±0.13	36.73±2.02

n=5, Data presented as mean ±SEM. P≥0.05, compared to control; student-t test for all values

The results of the WBC differential counts after administration of crude water extracts of *M. indica* showed that the neutrophil counts in the treated group were dose dependent; 34.75±10.27, 43.50±4.17, 47.80±3.58 for 300, 200 and 100mg/kg when compared with the control 33.60±6.77. The lymphocytes counts 52.00±8.92, 46.50±6.03, 38.60±3.61 for 300, 200 and 100mg/kg reduced considerablly compared to the control 58.20±7.07. The monocytes, esinophils and basophils showed an increase that is not consistent with increase in dose level observed when compared to the control.

Table 3: Effect of daily administration of the aqueous extract of *Mangifera indica* on WBC differential counts in mice after 14 days.

Treatment	Neutrophils	Lymphocytes	Monocytes	Esinophils	Basophils
300mg/kg	34.75±10.27	52.00±8.92	13.00±2.12	3.33±2.47	0.25±0.13
200mg/kg	43.50±4.17	46.50±6.03	9.00±2.97	1.25±0.63	0
100mg/kg	47.80±3.58	38.60±3.61	11.40±3.39	1.40±0.24	0.40±0.40
Control	33.60±6.77	58.20±7.07	7.00±1.48	0.60±0.40	0.20±0.20

n=5, Data presented as mean ±SEM, P ≥ 0.05, compared to control, student-t test for all values

Table 4 shows the effect of daily administration of crude water extracts of *M. indica* on body weights of mice for 28days. The mice treated with 300mg/kg progressively increased in weight from 18.52±0.48 at initiation of treatment to 26.93±0.74g after 21days (week 3) and decreased to 26.82±2.21g in week 4. Similarly, the 200mg/kg treated group increased in a linear fashion from 19.14±0.98 to 30.76±0.56g in week 4 while the 100mg/kg treated group also increased from 19.46±0.76 to 30.23±0.45 in week 3 and then reduced to28.67±1.35g after week four. The mice administered normal saline (control) increased in weights from 20.36±0.83 to 28.46±0.52 week 3 and decreased to 27.82±0.78g on termination of treatment.

Table 4: Effects of daily administration of the aqueous extracts of *M. indica* on body weight of mice over a period of 28days (subacute toxicity).

Treatment	Weeks					
	Day 0	1	2	3	4	
300mg/kg	18.52±0.48	21.26±0.63	25.61±0.84	26.93±0.74	26.82±2.21	NSD
200mg/kg	19.14±0.98	20.97±1.18	26.94±0.85	28.12±0.40	30.76±0.56	SD
100mg/kg	19.46±0.76	22.24±0.85	28.94±1.06	30.23±0.45	28.67±1.35	SD
Control	20.36±0.83	23.11±0.94	27.59±0.56	28.46±0.52	27.82±0.78	

n=5, mean ±SEM, NSD (no significant difference, p ≥ 0.05), SD (significant difference, p ≤ 0.05).

Table 5 shows effect of daily administration of crude water extracts of *M. indica* on haematological indices in mice after 28days. The result revealed that the haemoglobin counts reduced from 18.40±0.98g/dl control to 18.07±0.47g/dl for 100mg/kg, 17.10±1.10g/dl for 200mg/kg and increased to 19.45±0.78g/dl for 300mg/kg. The PCV increased from 33.00±3.39% control group to 34.00±2.08% for 100mg/kg, 38.00±2.52% for 200mg/kg and reduced to 31.25±4.89% for 300mg/kg. The RBC counts increased from 2.06±0.14 x 10^{12}/L control to 2.11±0.22 x 10^{12}/L for 100mg/kg but reduced to 1.83±0.03 x10^{12}/L for 200mg/kg and 3.03±0.30 x 10^{12}/L for 300mg/kg. The WBC counts increased from 0.80±0.07 to 0.83±0.43 and 1.13±0.11 x 10^{9}/L for 100 and 300mg/kg but reduced to 0.70±0.06 x 10^{9}/L for 200mg/kg respectively. The erythrocyte sedimentation rate (ESR) reduced to 3.67±0.33 and 3.67±0.67 for 100 and 200mg/kg but unchanged 4.25±0.63mm/hr for 300mg/kg when compared with 4.25±0.63mm/hr of the control group. The MCV values were inconsistent 16.50±2.22, 20.77±1.11 and 10.54±1.91cuμ for 100, 200 and 300mg/kg compared to the control 16.24±2.01 cuμ. Similarly, the MCH and MCHC values also showed inconsistency for the different doses of treatment 8.80±1.11, 9.37±0.61, 6.54±0.39pg and 53.54±3.60, 45.51±4.74, 66.39±9.11% for 100, 200 and 300mg/kg when compared to the control group 8.98±0.23pg and 57.59±6.45% respectively.

Table 5: Effect of daily administration of the aqueous extract of *M. indica* on haematological indices in mice after 28 days (Sub-acute toxicity).

Treatment	Hb (g/dl)	PCV (%)	RBC (×10^{12}/L)	WBC (×10^{9}/L)	ESR mm/hr	MCV cuμ	MCH pg	MCHC %
300mg/kg	19.45±0.78	31.25±4.89	3.03±0.30	1.13±0.11	4.25±0.63	10.54±1.91	6.54±0.39	66.39±9.11
200mg/kg	17.10±1.10	38.00±2.52	1.83±0.03	0.70±0.06	3.67±0.67	20.77±1.11	9.37±0.61	45.51±4.74
100mg/kg	18.07±0.47	34.00±2.08	2.11±0.22	0.83±0.43	3.67±0.33	16.50±2.22	8.80±1.11	53.54±3.60
Control	18.40±0.98	33.00±3.39	2.06±0.14	0.80±0.07	4.25±0.48	16.24±2.01	8.98±0.23	57.59±6.45

n=5, Data presented as mean ±SEM. P ≥ 0.05

Table 6 showed that all the organs (heart, lungs, liver and the intestines) observed after 28 days of administration of *M. indica* extracts; were apparently normal in all the dose levels except that there was an enlargement of nuclei observed on the liver of mice that was administered 300mg/kg. Conversely, the kidneys of 200mg/kg had enlarged glomeruli without opening while that of the 300mg/kg was characterized by necrosis of glomeruli and diffuse nuclei within a collection duct without a normal opening. However, the kidney of 100mg/kg was normal

Table 6: Histopathological observation of tissue of mice administered with aqueous extract of *M. indica* after 28 days of administration.

	Treatment			
Organs	**300mg/kg**	**200mg/kg**	**100mg/kg**	**Control**
Heart	Normal	Normal	Normal	Normal
Kidney	Necrosis of glomeruli	Enlarged glomeruli	Normal	Normal
Liver	Enlarged nuclei	Normal	Normal	Normal
Lungs	Normal	Normal	Normal	Normal
Intestine	Normal	Normal	Normal	Normal

DISCUSSION

The LD_{50} of *M. indica* had been reported to be 794.33mg/kg [8] which is close to that of > 1000mg/kg earlier reported by [5].

The toxicity of the extract could be attributed to the presence of terpeniods which are reported to have toxic effects on mice ([16]; [11]).

The result generally indicated a dose dependent increase in body weights. Body weight changes serves as sensitive indication of the general health status of test animals. Any rapid loss in body weight may signal the onset of intoxication or disease [17].

The haematological indices were generally normal and within the normal limits relative to the control group, for mice administered crude extracts of *M. indica* with no significant difference ($p > 0.05$). The results of the WBC differential counts after administration of crude water extracts of *M. indica* for 14days showed that the neutrophil counts in the treated group were dose dependent when compared with the control. The lymphocytes counts reduced considerable compared to the control while the monocytes, esinophils and basophils showed an increase that is not consistent with increase in dose level when compared to the control.

The results of the WBC differential counts of the mice administered with crude extracts *M. indica* for 28 days showed a significant change ($p < 0.05$) with 300mg/kg dose producing a significant change in the number of monocytes and esinophils respectively.

Chronic toxicity studies indicated that mice gained weights significantly ($p < 0.05$) with administration of 100 and 200mg/kg crude extracts of *M. indica* respectively, but a general decline in week four for all the mice treated with 300mg/kg. The probably reason may be due to the absence of nutrients and immunomodulatory substances in addition to the extracts possessing some anti-appetite properties [18].

The haematological indices after 28 days of extract administration revealed a decrease in haemoglobin, packed cell volume and red blood cell counts but increase in the white blood cell counts that is dose-dependent with no significant changes ($p > 0.05$). Earlier studies by some researchers showed that PCV reduces with increased range of doses ([18]; [19]) which in line with the current study.

The vital organs macroscopically observed were normal after 28 days of

continuous administration of extract of *M. indica* for lower doses, except the kidney of the mice given 200mg/kg and 300mg/kg had enlarged glomeruli and necrosis respectively. The kidney is the chief organ responsible for excretion and maintenance of body fluid homeostasis. The lesions observed may have resulted from accumulation of the extracts to a toxic concentration and adversely affecting the renal function of drug clearance. The progressive deterioration of renal function associated with chronic tubulo-intertitial nephropathy has been reported on chronic use of analgesic agents [20].

CONCLUSION

The values obtained from haematological indices are within the normal limits relative to the control group, these suggest that the extracts have no harmful effects on the blood indices such as haemaglobin (Hb), packed cell volume (PCV) count, white blood cell (WBC) count, mean cell volume (MCV), mean cell haemoglobin (MCH), mean cell haemoglobin concentration (MCHC), white blood cell differential counts at the doses tested. The vital organs did not show any major histological changes except with higher dose of 300mg/kg indicating that the plant extracts are relatively safe for human consumption when treating malaria in West Africa.

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