



Effects of Methanolic Leaf Extracts of *Daniella oliveri* on Biochemical and Haematological Parameters of Albino Mice Infected with *Plasmodium berghei* NK 65

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Authors' contributions

This work was carried out in collaboration among all authors. Authors MM and KBD designed the study. Author GOS performed the statistical analysis. Authors MM, KBD and DMD wrote the protocol, and wrote the first draft of the manuscript. Authors KBD and DMD managed the analyses of the study. Authors MM, MD and YJ managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

The rapid emergence and spread of *Plasmodium falciparum* resistance to Artemisinin derivatives and all the conventional antimalarial drugs necessitates the importance of ethnobotany, resulting in need to study the antiplasmodial potentials and the resultant effects of the methanolic leaf extract of *Daniella oliveri* (*D.oliveri*) on the biochemical and haematological parameters of the infected and treated albino mice. A total of 30 mice were randomized to six groups; 1 (positive control), 2

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(negative control), 3 (normal control), 4, 5 and 6 (treatment groups) of five mice per group, body weights of mice were measured before and after infection and treatments, the mice were infected intravenously with 0.2 ml of 1×10^7 standard inoculum of chloroquine sensitive *Plasmodium berghei* infected erythrocytes on the first day (day 0), treatment commence 72 hours later (day 3), continued for 5 days to terminate on day 7. On day 8, the Swiss Albino mice used for antiplasmodial activity were subjected to euthanasia under chloroform, aseptically dissected and blood was collected through cardiac puncture in lithium heparin bottle for biochemical assays and in an ethylene diamine tetra- acetic acid (EDTA) bottles for haematological assays. All mice in the treatment group showed decrease in body weight except for normal control group that showed increase in body weight. Methanolic leaf extract of *D. oliveri* contains some secondary metabolites that are hepato-protective in nature with no significant effects on the biochemical and hematological parameters of the malaria infected and treated albino mice.

Keywords: Biochemical; haematological; parameters; antiplasmodial; methanolic; leaf; extract.

1. INTRODUCTION

The rapid emergence and spread of *Plasmodium falciparum* resistance to Artemisinin derivatives and all the conventional antimalarial drugs necessitates the importance of ethnobotany recognized as an effective way of discovering future medicines from barks, seeds, fruit bodies, leaves and other parts of plants. About 80% of the world's population, especially millions of people in the rural areas of developing countries and more than 65% of the global population use traditional medicine for their basic health care needs [1]. Artemisinin was the most effective antimalarial preparation, obtained from the leaves of a medicinal plant called *Artemisia annua* L., discovered in China by You-You Tu in the early 1970s [2]. There have been documented cases of resistance to artemisinin derivatives and her partner drugs, therefore, sourcing for more medicinal plants with folkloric evidence of antiplasmodial potentials is important as a result of development of resistance. Hence, the need to study the antiplasmodial potentials and the resultant effects of methanolic extract of *Daniella oliveri* on the biochemical and haematological parameters of the albino mice. *D. oliveri* is a medium sized deciduous tree that may reach a height of 100 feet and trunk diameter of 4 feet [3]. *Daniella oliveri* produces liquid oleoresin used in folk medicine for more than four hundred years [4]. The oleoresin is produced in the tree's stem, trunk and leaves [5]. The liquid oleoresin consists of large but varying amounts of volatile oils (primarily composed of sesquiterpene hydrocarbons, usually including caryophyllene) [3]. The leaves are traditionally used in Nigeria to treat diabetes, gastro-intestinal disturbances, yellow fever, and as diuretic and aphrodisiac [6]. *Daniella oliveri*, as reviewed by [7], have shown to be of great medicinal values, and

scientifically studied by different researchers to possess several pharmacological activities; including cardiovascular activity, cytotoxic activities, anti-diabetic activity, anti-diarrheal activity, anti-helminthic activities, hepatoprotective activity, anti-inflammatory activities, anti-microbial activities, anti-nociceptive activities, anti-oxidant/anti-radical activities, anti-spasmodic activity and anti-ulcer activity. With these promising pharmacological activities of the methanolic leaf extracts of *D. oliveri*, there is need to evaluate the biochemical and haematological parameters of all the *plasmodium berghei* infected and treated albino mice.

2. MATERIALS AND METHODS

2.1 Preparation of Methanolic Leaf Extract's Dosage

The dosages of the extract were prepared by dissolving 0.4 g, 0.8 g and 1.6 g of the extract in 20 ml of distilled water each in sterile universal bottle based on the body weight and total number of mice per group to obtain 200, 400 and 800 mg/kg body weight respectively [8].

2.2 Assemblage of Experimental Mice

A total of 30 Swiss albino mice of body weight between 18-25g were obtained from the Animal House, Institute for Advance Medical Research and Training (IMRAT), University College Hospital, University of Ibadan, Nigeria. The mice were kept in cages underlaid with saw dust at room temperature, fed with standard diet (Grand cereal) and water *ad libitum* and left to acclimatize for 7 days in the animal's house at IMRAT. Donor mouse containing *Plasmodium berghei* NK65 was acquired from IMRAT.

2.3 Grouping of Animals

The method adopted by [9] was used to group the experimental mice. A total of 30 mice were randomized to six groups¹ (positive control), 2 (negative control), 3 (normal control), 4, 5 and 6 (treatment groups) of five mice per group for antiplasmodial activity prior to biochemical and haematological analysis.

2.4 Determination of Body Weight of the Mice

The body weights of each mouse in all groups were measured before and after infection and treatments using sensitive digital weighing balance [10].

2.5 Preparation of Inoculum, Mice Inoculation and Determination of Chemo-Suppression

The donor mouse of 20% parasitaemia was anaesthetized with chloroform, by cardiac puncture, 0.2 ml of the blood containing *P. berghei* infected erythrocytes was withdrawn from the infected mouse and serially diluted with sterile 4.8 ml of normal saline to obtain 1×10^7 *P. berghei* infected erythrocyte and used to infect the mice immediately [11]. The Parasitemia level was determined daily starting from day three post infection to day seven in accordance with the method of [12] and the method of [13] was used to calculate the average chemo-suppression.

2.6 Collection of Blood Samples for Biochemical and Haematological Assays

On the eighth day, the Swiss Albino mice used for antiplasmodial activity were subjected to euthanasia under chloroform, aseptically dissected and blood was collected through cardiac puncture in lithium heparin bottle for biochemical assays and in an ethylene diamine tetra- acetic acid (EDTA) bottles for haematological assays.

2.7 Biochemical Assay

Aspartate transaminase (AST), Alanine transaminase (ALT), , total bilirubin, creatinine, blood urea nitrogen (BUN), cholesterol, triacylglycerol, high density lipoprotein (HDL) and low density lipoprotein (LDL) were determined using Spectrophotometer (SM23A, China).

2.8 Haematological Analysis

Haematological analysis was carried out to know the effects of leaf extract and *P. berghei* on the haematological parameters. Red blood cell (RBC), white blood cells (WBC), platelet (PLT), packed cell volume (PCV), haemoglobin concentration (Hb), mean cell haemoglobin concentration (MCHC), mean cell corpuscular volume (MCV), mean cell haemoglobin (MCH), lymphocyte, neutrophil, monocyte and eosinophil were analyzed using Abacus 380 haematology analyzer, Hungary [14].

2.9 Statistical Analysis

Data are expressed as Mean \pm SEM. Data were subjected to analyses using Microsoft Excel, SPSS, GraphPad and SAS 9.12 software. One – way analysis of variance (ANOVA) was used to detect the treatment effects. Pearson correlation was used to evaluate relationship between measured parameters. The means were separated by Duncan multiple range test (DMRT) and a probability value less than 0.05 was considered statistically significant.

3. RESULTS

3.1 Body Weight of Mice Before and After Infection and Treatment

Mice infected and treated with 5mg/kg chloroquine (Group 1) lost the greatest weight. Mice infected and not treated (Group 2) and those infected treated with 200mg/kg body weight of extract (group 4) showed decrease of body weight after 5days of treatments. However, the mice treated with 400mg/kg and 800mg/kg (Groups 5 and 6) and those treated with 5mg/kg chloroquine (Group 1) also showed decrease body weight after 5days of treatment, but not as that of infected-treated with 5mg/kg chloroquine (Group 1) mice and infected treated with 800mg/kg body weight of *D. oliveri* leaf extracts. Mice of not infected and not treated (Group 3) experienced increase body weight (Table 1).

3.2 Biochemical Assay

Table 2 showed the result of biochemical assay of all animals administered with different doses of the methanol extract of *Daniella oliveri* leaf. Significant difference ($P < 0.05$) exists in the level of AST in mice of all groups. The observed values of AST in groups 1, 3, 4, 5 and 6 was

Table 1. Body weight of mice before and after infection and treatment

Doses	POSITIVE CRTL (GROUP1)	NEGATIVE CRTL (GROUP 2)	NORMAL CRTL (GROUP 3)	200mg/kg (GROUP 4)	400mg/kg (GROUP 5)	800mg/kg (GROUP 6)
Before	20.36 ± 1.06	18.64 ± 0.11	18.08 ± 0.08	18.08 ± 0.09	23.04 ± 0.18	23.2 ± 0.23
After	18.14 ± 0.17	17.56 ± 0.15	21.00 ± 0.07	16.78 ± 0.13	22.3 ± 0.16	21.6 ± 0.14

Data are presented as Mean ± S.E (n=3)

Legend: Group 1: *P. berghei* + 5 mg/kg body weight Chloroquine. Group 2: *P. berghei* + 0.2mL normal saline. Group 3: 0.2 mL normal saline. Group 4: *P. berghei* + 200 mg/kg body weight leaf extract. Group 5: *P. berghei* + 400 mg/kg body weight leaf extract. Group 6: *P. berghei* + 800 mg/kg body weight leaf extract. Control= (CRTL)

Lower than the values seen in mice of group 2. With ALT and total bilirubin levels, similar trend was also observed. The level of AST, ALT and total bilirubin in groups treated with methanol leaf extracts of *D. oliveri* significantly increased ($P < 0.05$), this is in comparison with the animals in groups 1 and 3. However, of all animals treated with methanol leaf extracts of *D. oliveri*, it was observed that, there was lower values of AST, ALT and total bilirubin in group treated with 800mg/kg compared with groups treated with 200mg/kg and 400mg/kg. There was no difference between the values of total bilirubin in mice of group 1 and group 4. Also, there was no difference between the level of total bilirubin in animals of group 3 and group 6. The amount of BUN and creatinine in group 2 animals was higher as compared with groups 1, 3, 4, 5 and 6. The values of BUN in animals of group 5 and group 6 showed no significant difference. There was no difference between the values of creatinine in groups 1 (infected and treated with 5 mg/kg of chloroquine) and group 4 (infected and treated with 200mg/kg of extract). The higher quantity of cholesterol and triacylglycerol in group 2 animals differs from the values in mice of groups 1, 3, 4, 5 and 6. However, the amount of cholesterol and triacylglycerol in the groups treated with extracts was comparatively lower than values obtained in group 4. Level of cholesterol in animals treated with 400mg/kg body weight and 800mg/kg body weight showed no difference. There was no difference in levels of triacylglycerol between animals of groups 1 and 3 as seen with groups 3 and 4. Also, there was no difference in levels of triacylglycerol in animals of groups 2 and 6. The values of HDL and LDL in group 2 was significantly different ($P < 0.05$) from the values of groups 1, 3, 4, 5 and 6. Mice of the treatment groups 4 and 6 do not show any difference in the values of HDL.

3.3 Haematological Analysis

Haematological analysis (Tables 3 and 4) showed increased value of packed cell volume

(PCV), haemoglobin (HB), red blood cell (RBC), White blood cell (WBC) and platelet (PLT) in mice of groups 4, 5 and 6 (infected treated with 200, 400 and 800mg/kg body weight extract). These values were significantly different ($P < 0.05$) from mice of group 2 (infected but not treated). Mice of group 2 had the lowest values of PCV, HB, RBC, WBC and group 3 (not infected and not treated) showed the lowest value of PLT. Mice of group 3 (not infected and not treated) had the highest values of PCV, HB, RBC and least value of PLT. Group 6 showed the highest value for WBC. The mean corpuscular volume (MCV) values in mice of groups 4, 5 and 6 increased after treatment with extract, compared with mice of group 2. The values of mean cell haemoglobin concentration (MCHC) and mean cell haemoglobin (MCH) in mice of groups 1 reduced after treatment. These values were not different from mice in groups 5. Mice in group 2 showed lowest values of HB and RBC. Mice in group 1 showed lowest values of MCV, MCHC. Mice in groups 2, 3 and 5 showed lowest values of PCV, PLT, and MCH respectively. The white Blood Cell (WBCs) in animals of groups 1, 2, 4 and 5 reduced significantly ($P < 0.05$) compared with groups 3, however, the highest WBC counts occur in group 6. There was no difference between the observed values of WBC in groups 2 and 4. Lymphocyte count in mice of groups 2, 4, 5 and 6 decreased significantly ($P < 0.05$) compared with mice of groups 1 and 3. The mice in group 2 showed low counts compared with mice of extract treated groups (groups 4, 5 and 6.). The observed values of monocyte counts showed no significant difference between mice of groups 1, 2 and 3. The observed values of eosinophil count showed no significant difference between mice of groups 1 and 3, groups 2 and 4. There was increase counts in values of neutrophil in animals of groups 2, 4 and 5 and decrease in values of neutrophil in groups 1 and 6 when compared with group 3. There was no significant difference between neutrophil counts of groups 3 and 5.

Table 2. Biochemical parameters of the infected and treated mice

GRP	AST (UL)	ALT (UL)	T-BIL (mg/dL)	BUN (mg/dL)	CREAT (mg/dL)	T.CHOL (mg/dL)	TRIG (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
1	224.33 ± 0.88 ^b	62.33 ± 0.88 ^a	0.37 ± 0.03 ^c	21.63 ± 0.03 ^b	0.53 ± 0.03 ^c	33.00 ± 0.58 ^a	21.33 ± 0.88 ^a	11.50 ± 0.06 ^a	13.60 ± 0.06 ^e
2	391.33 ± 1.86 ^f	92.00 ± 1.53 ^f	0.43 ± 0.07	25.60 ± 0.06 ^e	0.63 ± 0.03 ^f	73.00 ± 0.58 ^e	32.67 ± 0.33 ^{bc}	14.53 ± 0.09 ^e	16.07 ± 0.03 ^f
3	156.33 ± 1.45 ^a	63.33 ± 1.76 ^{ab}	0.27 ± 0.03 ^a	19.27 ± 0.09 ^a	0.60 ± 0.06 ^e	40.67 ± 0.33 ^c	21.00 ± 0.58 ^a	12.13 ± 0.09 ^b	12.83 ± 0.03 ^d
4	303.00 ± 2.08 ^e	77.67 ± 0.33 ^e	0.37 ± 0.03 ^c	23.03 ± 0.03 ^d	0.53 ± 0.03 ^c	37.67 ± 0.88 ^b	24.00 ± 0.58 ^d	13.33 ± 0.03 ^c	11.40 ± 0.2 ^c
5	267.33 ± 0.88 ^d	64.67 ± 1.45 ^d	0.30 ± 0.06 ^b	22.23 ± 0.12 ^{bc}	0.50 ± 0.06 ^b	43.00 ± 0.58 ^d	32.33 ± 0.88 ^b	13.47 ± 0.03 ^{cd}	10.40 ± 0.2 ^{1ab}
6	255.00 ± 1.53 ^c	63.67 ± 1.76 ^{abc}	0.27 ± 0.03 ^a	22.33 ± 0.18 ^{bc}	0.43 ± 0.03 ^a	43.33 ± 0.88 ^d	32.67 ± 1.2 ^{bc}	13.33 ± 0.09 ^c	10.10 ± 0.1 ^a

Data are presented as Mean ± S.E (n=3). Values with the same superscript letter(s) along the same column are not significantly different (P<0.05)

Legend: Group 1: *P. berghei* + 5 mg/kg body weight Chloroquine. Group 2: *P. berghei* + 0.2 ml normal saline. Group 3: 0.2 ml normal saline. Group 4: *P. berghei*+ 200 mg/kg body weight leaf extract. Group 5: *P. berghei* + 400 mg/kg body weight leaf extract. Group 6: *P. berghei* + 800 mg/kg body weight leaf extract
Aspartate Transaminase (AST), Alanine Transaminase (ALT), Total bilirubin (T. Bil.), Blood Urea Nitrogen (BUN), Creatinine (Creat.), Cholesterol (Chol), Triacylglycerol (TRIG), High Density Lipoprotein (HDL) and Low-Density Lipoprotein (LDL)

Table 3. Haematological parameters of the infected and treated mice

GRP	PCV %	HB g/dl	RBCX10 ⁶ ML	WBC X10 ³ ML	PLATELET	%LYMPH	%NEUT	%MONO	%EOSIN
1	46.00 ± 0.58 ^f	14.30 ± 0.06 ^{cde}	7.48 ± 0.01 ^e	3906.67 ± 3.33 ^b	96016.67 ± 8.82 ^e	72.33 ± 0.33 ^d	25.33 ± 0.88 ^b	1.33 ± 0.33 ^a	1.33 ± 0.33 ^b
2	27.00 ± 0.56 ^a	8.67 ± 0.12 ^a	4.37 ± 0.00 ^a	3110.00 ± 5.77 ^a	87016.67 ± 8.82 ^d	63.33 ± 1.76 ^a	36.00 ± 0.58 ^e	1.33 ± 0.33 ^a	2.33 ± 0.33 ^c
3	52.33 ± 1.2 ^e	16.47 ± 0.12 ^f	8.74 ± 0.01 ^f	7321.67 ± 14.81 ^d	58026.67 ± 14.63 ^a	74.67 ± 1.2 ^e	26.33 ± 0.88 ^c	1.33 ± 0.33 ^a	1.33 ± 0.33 ^b
4	34.33 ± 1.76 ^b	11.37 ± 0.03 ^b	5.33 ± 0.01 ^b	3111.67 ± 9.28 ^a	77016.67 ± 12.02 ^b	68.00 ± 0.58 ^{bc}	28.00 ± 0.58 ^d	4.67 ± 3.67 ^d	2.33 ± 0.33 ^c
5	43.33 ± 1.76 ^c	13.13 ± 0.09 ^c	6.66 ± 0.01 ^c	4206.00 ± 3.06 ^c	86023.33 ± 12.02 ^c	67.00 ± 1.0 ^b	26.67 ± 1.2 ^c	1.67 ± 0.33 ^b	0.00
6	44.67 ± 0.88 ^{cd}	14.40 ± 0.2 ^{cd}	6.84 ± 0.01 ^{cd}	7812.67 ± 7.22 ^e	98016.67 ± 8.12 ^f	71.67 ± 0.33 ^c	23.67 ± 0.33 ^a	3.33 ± 0.33 ^c	3.33 ± 0.33 ^d

Data are presented as Mean ± S.E (n=3)

Values with the same superscript letter(s) along the same column are not significantly different (P<0.05)

Legend: Group 1: *P. berghei* + 5 mg/kg body weight Chloroquine. Group 2: *P. berghei* + 0.2mLnormal saline. Group 3: 0. 2 mLnormal saline. Group 4: *P. berghei*+ 200 mg/kg body weight leaf extract. Group 5: *P. berghei* + 400 mg/kg body weight leaf extract. Group 6: *P. berghei* + 800mg/kg body weight leaf extract

Red blood cells (RBC), White blood cells (WBC), Platelet, Packed Cell Volume (PCV) and haemoglobin concentration (Hb), Mean Corpuscular Volume (MCV), Mean Cell Haemoglobin Concentration (MCHC) and Mean Cell Haemoglobin (MCH), Lymphocyte, Neutrophil, Monocyte and Eosinophil (EOS)

Table 4. Haematological parameters of the infected and treated mice

GRP	MCV	MCHC	MCH
1	161.52 ± 0.75 ^b	31.09 ± 0.26 ^b	3.11 ± 0.03 ^b
2	261.74 ± 1.36 ^{bc}	32.10 ± 0.71 ^c	3.21 ± 0.07 ^c
3	359.86 ± 1.38 ^a	31.46 ± 0.64 ^{bc}	3.15 ± 0.06 ^{bc}
4	464.38 ± 3.25 ^d	33.11 ± 1.79 ^d	3.31 ± 0.18 ^d
5	565.10 ± 2.55 ^e	30.31 ± 1.16 ^a	3.03 ± 0.12 ^a
6	665.30 ± 1.23 ^f	32.24 ± 0.26 ^{cd}	3.22 ± 0.03 ^c

Data are presented as Mean ± S.E (n=3)

Values with the same superscript letter(s) along the same column are not significantly different (P<0.05)

Legend: Group 1: *P. berghei* + 5mg/kg body weight Chloroquine. Group 2: *P. berghei* + 0.2ml normal saline.

Group 3: 0. 2ml normal saline. Group 4: *P. berghei*+ 200mg/kg body weight leaf extract. Group 5: *P. berghei* + 400mg/kg body weight leaf extract. Group 6: *P. berghei* + 800mg/kg body weight leaf extract

Mean Corpuscular Volume (MCV), Mean Cell Haemoglobin Concentration (MCHC) and Mean Cell Haemoglobin (MCH),

4. DISCUSSIONS

Loss in body weight observed in infected not treated and infected treated mice compared with normal control mice, could be due to resultant decrease in food intake resulting from loss of appetite, increase in the metabolic rate and feed conversion efficiency, as reported by [15] that malaria have shown to contribute to weight reduction and suboptimal growth as advanced by [16]. Decreased body weight in mice could be due to hypoglycemia associated with malaria. The body weight of mice in normal control group before and after infection and treatment increased. This agrees with [17] that, *D. oliveri* serve as source of protein and energy to animal body as expected because, the mice were having normal feeding *ad libitum* with good feed conversion efficiency and are healthy. This agrees with [18] that, dietary nutrients are essential for the construction of living tissues and are source of stored energy for digestion, absorption, growth, reproduction, and other life processes.

The decreased values of PCV in animals of groups Infected treated and infected not treated compared with animals in group 3 is expected and could be due to anaemia as a result of increased destruction of both infected and uninfected red cells due to membrane alterations and destruction by *Plasmodium* [19]. This agrees with the reasons advanced by [20], that Malaria infection causes haemolysis of infected and uninfected erythrocytes and bone marrow dyserythropoiesis.

The increase in values of AST and ALT in group 2 (negative control) could be attributed to reasons provided by [21] that, the liver enzymes increase in malaria parasitaemia to a level

proportionate to the degree of parasitaemia due to the involvement of liver in the pathophysiology of malaria [22]. [21] equally claimed that, it is an indication of *P. berghei* infection and leakage from hepatic cell that were damaged by the immune response. Also, the significant increase in values of AST and ALT in extract treated groups compared with positive and normal controls agree with [23], who stated that increase in AST and ALT in mice of extract treated groups might be as a result of concentration dependent antioxidant activity and accumulation of free radical generated by the extract used to treat the mice, which may also be responsible for the destruction of the parasite. The lowest values of AST and ALT was obtained in mice of group 6 is comparable with other extract treated groups, this agrees with findings of [24], who stated that, there was a dose dependent reductions in the activities of AST, ALT and ALP in parasitized treated mice. The reduced values of AST and ALT in mice of extract treated groups agree with [25], who reported that *Daniella oliveri* stem bark has a potent hepatoprotective effect that may be linked to its antioxidant potential and validates its use in the traditional management of liver diseases or it might be due to the relatively lower concentration or short-term administration of the extract. Increased level of total bilirubin in mice of group 2 might be attributed to hemolysis of both parasitized and nonparasitized erythrocytes and partly due to liver damage resulting from malaria infection, this is in line with the similar report of [26]. The observed insignificant difference (P<0.05) between the values of total bilirubin in mice of group 1, 4, 5 and 6 compared with group 2 and 3 agree with [27], who concluded that feeding with *Daniella oliveri* enhanced the overall performance and does not have any deleterious effect on the animal. Urea and creatinine are indicators of renal functions. The observed

increase in level of urea in mice of group 2, might be due to the pathological effect of malaria infection, this agrees with [22]. Similarly, the observed increase in level of creatinine in mice of group 2 (negative control), could be a result of sequestration of the parasite into the renal microvasculature bed which may have led to ischemia, this agrees with [28]. The observed decrease in creatinine in extract treated groups compared with negative control mice, is in line with the report of [29], who discussed that Creatine is synthesized in the liver, pancreas, and kidneys, this agree with [25], who reported that *Daniella oliveri* has a potent hepatoprotective effects and also supports the findings of [28], that, the sequestration of the parasite into the renal microvasculature bed which may have led to ischemia that may have resulted in renal failure have been averted by the antiplasmodial effects of *Daniella oliveri* extracts. [30] reported the beneficial effects of saponins on blood cholesterol levels and stimulation of the immune system. The increase level of cholesterol in mice of group 2 compared with other groups agrees with the report of [31], he attributed the promotion of cholesterol and triacylglycerol synthesis to increased lipolysis induced by threshold of Parasitemia. Elevation in total cholesterol and triacylglycerol may also be due to decrease uptake by the infected erythrocytes as a result of increased levels of parasitemia. The increase in values of cholesterol, triacylglycerol, HDL- cholesterol and LDL- cholesterol in mice of group 2 (negative control) agrees with [32] that Serum lipids primarily bound to lipoproteins, this contribute to hyperlipidemia that is often produced by some pathological changes. The increase in values of cholesterol, triacylglycerol, HDL- cholesterol and LDL- cholesterol in mice of groups 5 and 6 compared to normal control (group 3) suggests that Lipids have been implicated in the production of immunity against diseases as seen in percentage parasitemia and percentage chemosuppression in group 5 and 6 of this experiment. This agrees with Results obtained by [32], in a similar studies which showed significant increases in serum and liver total, LDL, VLDL, and HDL cholesterol in mice infected with *Plasmodium berghei*.

The observed increase of RBCs and its indices (Hb, PCV, MCV, MCH and MCHC and PLT) in mice of groups 4, 5 and 6 (mice treated with extract at different concentrations) compared with group 2 (infected and not treated), agrees with [33], who concluded that extract possess erythropoietin promoting activity and

phytochemicals that slow down the natural process of oxidative breakdown of erythrocyte. This concur with [27] that, the main hematological parameters such as RBC, Hb, PCV, MCV, MCH and MCHC including eosinophils, monocytes, lymphocytes and heterophils were higher in animals fed with *Daniella oliveri* extracts compared with control. The decrease values of RBC, PCV, MCH, MCV and MCHC in mice of group 2 is expected and could probably be explained as due to anaemia as indicated in the similar findings by [20] that, malaria is a major cause of anaemia as malaria infection causes haemolysis of infected and uninfected erythrocytes and bone marrow dyserythropoiesis, this agrees with [34] that hemoglobin is significantly reduced in high parasitemia. Also, decrease Hb observed in mice of negative control (group 2) agrees with reason advanced by [35], that the malaria parasite growing in the erythrocytes degrades haemoglobin. The decrease in MCH and MCHC observed in mice of negative control (group 2) are expected and these two parameters were not measured directly but calculated from RBC, HB and MCV, this is in consistent with [36]. The increase in WBC counts for extract treated groups and chloroquine treated group are expected and could be probably due to immune boosting of the extract to fight the malaria parasite, this concur with the findings of [33] that, significant increase in white blood cells and the differential leukocytes counts in the test animal shows that the methanolic extracts of *Solanum incanum* (Linn) may have immune boosting properties. Likewise, increased platelet counts for extract treated groups compared with normal control, agrees with [33], that extract may have stimulatory effects on platelet production causing a significant increase in platelet probably by enhancing thrombopoietin's secretion. The increased neutrophil in negative control revealed that, neutrophils are activated and are capable of clearing malaria parasites by phagocytosis and it could be associated with responses to stress or excitement caused by malaria. This agrees with [37] that, neutrophil play a role in the activation and regulation of the immune response. In this study, eosinophils count was insignificant for all group, this is because eosinophils did not participate majorly in infection by *P. berghei*. Eosinophils may play a role in protection against malaria by induction of parasite killing. This agreed with [38]. The increased monocyte in the extract treated groups could be probably due to the stimulatory and immune boosting property of *Daniella oliveri*

extract. These agrees with [39] that the presence of alkaloids in significant amounts in *Daniellia oliveri* implies that it can be as analgesics, anti-malaria and stimulants. Also, [40], concur that monocytes control parasite burden and contribute to host protection.

5. CONCLUSION

Methanolic leaf extract of *D. oliveri* contains some secondary metabolites that are hepato-protective in nature with no significant effects on the biochemical and hematological parameters of the malaria infected and treated albino mice at the highest treatment dose (800 mg/kg).

ETHICAL APPROVAL

The experimental management, Animal handling and care were approved by the Research and Ethics Committee of the Department of Biological Sciences, Nigerian Defense Academy Kaduna.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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