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

Muhammed Muazu¹*, Karderam Bukar Dikwa², Deborah Madi Dibal², Muhammed Danjuma³, Gideon Obaje Sunday⁴ and Yahaya Junaidu⁵

¹Pharmacology Laboratory, College of Health Sciences, Kogi State University, Anyigba, Nigeria.
²Department of Biological Sciences, Nigerian Defense Academy Kaduna, Nigeria.
³Department of Applied Biology, Federal Polytechnic of Oil and Gas, P. M. B 5027, Bonny Island, Rivers State, Nigeria.
⁴Department of Medical Biochemistry, College of Health Sciences, Kogi State University, Anyigba, Nigeria.
⁵Department of Human Physiology, College of Health Sciences, Kogi State University, Anyigba, Nigeria.

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.

Article Information

DOI: 10.9734/JAMB/2021/v21i530348

Editor(s): (1) Dr. Foluso O. Osunsanmi, University of Zululand, South Africa.

Reviewer(s): (1) Rohit Chaudhary, University of Malaya, Malaysia.
(2) Welligton Luciano Braguini, Midwestern Paraná State University, Brazil.

Complete Peer review History: http://www.sdiarticle4.com/review-history/68681

Received 10 March 2021
Accepted 16 May 2021
Published 22 May 2021

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...
(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 1x10³ 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 hepatoprotective 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 antimalarial potentials is important as a result of development of resistance. Hence, the need to study the antimalarial 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 groups: 1 (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 ± 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 5 days 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 5 days 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 *Daniella 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
showed increased value of packed cell volume.

**Haematological Analysis**

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

| Doses | POSITIVE CTRL (GROUP 1) | NEGATIVE CTRL (GROUP 2) | NORMAL CTRL (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)
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 ± 0.88a   | 62.33 ± 0.88a    | 0.37 ± 0.03c  | 21.63 ± 0.03a | 0.53 ± 0.03a  | 33.00 ± 0.58a  | 21.33 ± 0.88a | 11.50 ± 0.06a | 13.60 ± 0.06a |
| 2     | 391.33 ± 1.86f   | 92.00 ± 1.53f    | 0.43 ± 0.07   | 25.60 ± 0.06a | 0.63 ± 0.03f  | 73.00 ± 0.58e  | 21.33 ± 32.67 | 0.33bc       | 14.53 ± 0.09e | 16.07 ± 0.03f |
| 3     | 156.33 ± 1.45a   | 63.33 ± 1.76ab   | 0.27 ± 0.03a  | 19.27 ± 0.09a | 0.60 ± 0.06a  | 40.67 ± 0.33c  | 21.00 ± 0.58a | 12.13 ± 0.09b | 12.83 ± 0.03d |
| 4     | 303.00 ± 2.08e   | 77.67 ± 0.33e    | 0.37 ± 0.03c  | 23.03 ± 0.03d | 0.53 ± 0.03c  | 37.67 ± 0.88b  | 24.00 ± 0.58d | 13.33 ± 0.03c | 11.40 ± 0.2c  |
| 5     | 267.33 ± 0.88d   | 64.67 ± 1.45d    | 0.30 ± 0.06b  | 22.23 ± 0.12bc | 0.50 ± 0.06b  | 43.00 ± 0.58d  | 32.33 ± 0.88b | 13.47 ± 0.03cd | 10.40 ± 0.21ab |
| 6     | 255.00 ± 1.53c   | 63.67 ± 1.76abc  | 0.27 ± 0.03a  | 22.33 ± 0.18bc | 0.43 ± 0.03a  | 43.33 ± 0.88d  | 32.67 ± 1.2bc  | 13.33 ± 0.09c | 10.10 ± 0.1a  |

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       | RBC X10^6 ML | WBC X10^3 ML | PLATELET | %LYMPH | %NEUT | %MONO | %EOSIN |
|-----|---------------|---------------|--------------|--------------|-----------|--------|-------|-------|--------|
| 1   | 46.00 ± 0.58^a| 14.30 ± 0.06^a| 7.48 ± 0.01^a| 3906.67 ± 3.33^a| 96016.67 ± 8.82^a| 72.33 ± 0.33^a| 25.33 ± 0.88^a| 1.33 ± 0.33^a| 1.33 ± 0.33^a|
| 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^a| 1.33 ± 0.33^a| 2.33 ± 0.33^c|
| 3   | 52.33 ± 1.2^a | 16.47 ± 0.12^f| 8.74 ± 0.01^f| 7321.67 ± 14.81^d| 58026.67 ± 14.63^a| 74.67 ± 1.2^b| 26.33 ± 0.88^c| 1.33 ± 0.33^a| 1.33 ± 0.33^b|
| 4   | 34.33 ± 1.76^a| 11.37 ± 0.03^a| 5.33 ± 0.01^b | 3111.67 ± 9.28^a| 77016.67 ± 12.02^b| 68.00 ± 0.58^bc| 28.00 ± 0.58^a| 4.67 ± 3.67^d| 2.33 ± 0.33^c|
| 5   | 43.33 ± 1.76^a| 13.13 ± 0.09^b| 6.66 ± 0.01^c | 4206.00 ± 3.06^ci| 86023.33 ± 12.02^c| 67.00 ± 1.0^c| 26.67 ± 1.2^b| 1.67 ± 0.33^a| 0.00    |
| 6   | 44.67 ± 0.88^cd| 14.40 ± 0.2^cd| 6.84 ± 0.01^cd| 7812.67 ± 7.22^a| 98016.67 ± 8.12^a| 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 + 0.2mL 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

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)
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

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

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

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.
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 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 anemia as indicated in the similar findings by [20] that, malaria is a major cause of anemia 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 *Daniella 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.

REFERENCES

1. Kethamakka SRP, Meena DS. Jayanti veda (tridax procumbens): Unnoticed medicinal plant by ayurveda. Journal of Indian System of Medicine. 2014;2:6-22.
2. Fulong L. Discovery of Artemisinin (Qinghaosu). Molecules. 2009;14(12): 5362–5366.
3. Temitope OO, Fasusi OA, Ogunmodede AF, Thonda AO, Oladejo BO, Yusuf-Babatunde AM, Ige OO. Phytochemical Composition and Antimicrobial Activity of *Daniella oliveri* Extracts on Selected Clinical Microorganisms. International Journal of Biochemistry Research and Review. 2016;14(1):1-13.
4. Gilbert M. Medicinal importance of Copaiba oil. J. Pharmaco
c. 2000;4:1159-1164.
5. Al-Harrasi A, Al-Rawahi A, Hussain J, Rehman N, Ali L, Hussain H. Proximate analysis of the resins and leaves of Boswellia sacra. J Med Plants. Res. 2012;6(16):3098-3104.
6. Ahmdau AA, Haruna AK, Garba M, Yaro AH. Antispasmodic Actions of the leaves of *Daniella oliveri*. Nigerian Journal Natural Product and Medicine. 2003;7:13–15.
7. Muhammad MI. A pharmacognostical efficacy of five plants traditionally used for the treatment of cancer in Northern Nigeria; 2017. Retrieved March 15, 2020. Available:http://docs.edu.tr/library/6502099512
8. Muhammad M, Dada EO, Alo AA. Antibacterial property of ethanolic leaf extract of eucalyptus citriodora hook on clinical and typed isolates of escherichia coli. South Asian Journal of Microbiology. 2018;2(1):1-8.
9. Dada EO, Muhammad D. Effect of ethanolic leaf extract of eucalyptus citriodora hook on haematological parameters of swiss albino mice infected with plasmodium berghei NK 65. South Asian Journal of Parasitology. 2018;1(2):1-8.
10. Dada EO, Oloruntola DA. In vivo Antiplasmodial Activity of Ethanolic Leaf Extract of *Tithonia diversifolia* (Hemsl.) A. Gray Against *P. berghei* NK65 in Infected Swiss Albino Mice. Journal of Applied Life Science International. 2016; 8(3):1-8.
11. Alo AA, Dada EO, Muhammed D. Phytochemical Screening and Antiplasmodial Activity of Ethanolic Bark Extract of *Khaya grandifolioia*in Swiss Albino Mice Infected with Plasmodium bergheri NK 65. South Asian Journal of Parasitology. 2018;1(4):1-8.
12. Omeiza Favour O, Ademowo George O, Funmilola A Ayeni. Research Evaluation of in vivo anti-malarial potential of *omidun* obtained from fermented maize in Ibadan, Nigeria, Malaria Journal. 2020;19:414.
13. Kahn ME, Amupitan JO, Oyewale AO, Nduke IG. Evaluation of the Invivo Antiplasmodial activity of the methanolic leaf extract of Nepatacateria, Research in Pharmaceutical Biotechnology. 2015;6(12): 8-15.
14. Ogundolie OO, Dada EO, Osho IB, Oloruntola DA. Effect of Raw Ethanol Seed Extract of *Tetracarpidium conophorum* on Heamatological Parameters in Swiss Albino Mice Infected with *P. berghei*. Journal of Applied Life Sciences International. 2017;12(2):1103-234.
15. Sowunmi A, Gbotosho GO, Adedeji AA, Fateye BA, Sabitu MF and HappiCT. Res. Effects of acute Plasmodium falciparum
malaria on body weight in children in an endemic area. Parasitol. 2007;101:343–49. PMID: 17323138.

16. Basir R, Rahimna SF, Hasballah K. P. berghei ANKA Infection in ICR Mice as a Model of Cerebral Malaria. Iran Journal of Parasitology. 2012;7(4):62-74.

17. Okunade SA, Olafadehan OA, Isah OA. Fodder potential and Acceptability of selected tree leaves by goats. Animal Nutrition and Feed Technology. 2014; 14(3):489-498.

18. Craig Steven, David D Kuhn. Understanding Fish Nutrition, Feeds, and Feeding, Virginia Corporate Extention. 2019;420-256. Available:https://fisheries.tamu.edu/files/2019/01/FST-269.pdf. 420-256.

19. Naria Mohandas, Xiuli An. Malaria and Human Red Blood Cells. Medical Microbiol Immunol 2012;(4):593-598.

20. White NJ. Anaemia and malaria. Malaria Journal. 2018;17:371.

21. Adelakun Ayodele A, Adediji Isaac O, Motayo Babatunde, Akinwande Kazeeem. Biochemical indices of liver functions in infected malaria patients in Nigeria. International Journal of Biomedical Research. 2015;6(03):177-180.

22. Akanbi OM. Antiplasmodial Activity of Methanolic Leaf Extract of Anogeisus leioicarpus and its Effect on Heart and Liver of Mice Infected with Plasmodium berghei. Pharmaceutica Analytica Acta. 2015; 6(2):330-335.

23. Onoja SO, Madubuike GK, Ezeja, ML. Hepatoprotective and antioxidant activity of hydromethanolic extract of Daniellia oliveri leaves in carbon tetrachloride-induced hepatotoxicity in rats. Journal of Basic and Clinical Physiology and Pharmacology, 2015;26(5):465-470.

24. Uraku AJ. Hepatoprotective Effects of Plasmodium berghei Infected Swiss Mice Treated with some Plant Extracts. Journal of Pharmacy and Allied Health Sciences. 2016;6:1-7.

25. Lateef Adegboyega Sulaimon, Efere Martin Obuotor, Lukman Abubakar Rabiu, Amina Abubakar Shehu, Mukhtar Aliyu, Maryam Qaseem Shiro. Antioxidant and hepatoprotective potentials of ethanol stem bark extract of Daniela oliveri (Rolfe) Hutch and Dalz (Caesalpinaceae), Synergy. 2020;11:100067. ISSN 2213-7130.

26. Oloruntola DA, Dada EO, Osho IB, Ogundolie OO. Effects of Hydro-ethanolic Leaf Extract of Tithonia diversifolia on parasitaemia level, serum metabolites and histopathology of organs in swiss albino mice infected with plasmodium berghei NK 65. Asian Journal of Medicine and Health. 2017;6(2):1-11.

27. Olafadehan OA, Oluwafemi RA, Alagbe JO. Performance, haemato-biochemical parameters of broiler chicks administered Rolfe (Daniellia oliveri) leaf extract as an antibiotic alternative. Drug Discovery. 2020;14(33):135-145.

28. Zaki HY, Abdalla BE, Hayder B. Biochemical profiles of Children with Severe Plasmodium falciparum malaria in central Sudan: A case control study. Al Neelain Med.J. 2013;3:15-23.

29. Salazar Josh A. Overview of Urea and Creatinine, Laboratory Medicine. 2014; 45(1):19-20.

30. Cheeke PR. Actual and potential applications of Yucca schidigera and Quillaja saponaria in human and animal nutrition. Journal of Animal Science; 2000.

31. Sriwiphat S, Nakhinchat S, Chachiyo S, Srichairatanakool S, Uthaipibull C, Somsak Sriwiphat S, Nakhinchat S, Chachiyo S, Srichairatanakool S, Uthaipibull C, Somsak. Modulation of total cholesterol and triglyceride in Plasmodium berghei infected mice by aqueous crude extract of Andrographis paniculata. J. Health Res. 2015;29(2):109-14.

32. Olarewaju M Oluba, Augustine O Olusola, George O Eidangbe, Leye J Babatola, Echukwu Onyeneke. Modulation of Lipoprotein Cholesterol Levels in Plasmodium berghei Malarial Infection by Crude Aqueous Extract of Ganoderma lucidum. Hindawi; 2012. DOI: 10.1155/2012/536396

33. Murithi NJ, Maina GS, Mugendi NM, Maina MB and Kiambi MJ. Determination of Hematological Effects of Methanolic Leaf Extract of S. incanum in Normal Mice. Pharm Anal Acta 2015;6:429. DOI: 10.4172/21532435.1000429

34. Manas Kolepui, Duangjai Piwkham, Bhukdee Phun Phuech, NuoolPhiwklam, Chaowanee Chupeerah, of Plasmodium berghei Infected Mice Treated with Ethanol Extract and Fractions of Nauclea latifolia Roots.Int.J.Curr.Microbiol.App.Sci.2017;61 2):25462556. DOI:https://doi.org/10.20546/ijcmas.2017.6 12.295
35. Balogun EA, Akinloye OA, Lasisi AA, Adeyi OE. Biochemical and Histological Changes Associated with Treatment of Malaria and Diabetes mellitus in Mice with Extracts of Mormodia ccharantia. An International Journal of the Nigerian Society for Experimental Biology. 2012; 24(1):38–47.
36. Asangha EE, Igile GO, Iwara IA, Ebong PE, Eseyin OA. Haematological Indices of Plasmodium berghei Infected Mice Treated with Ethanol Extract and Fractions of Nauclea latifolia Roots. International Journal of Current Microbiology and Applied Sciences. 2017;6(12):2546-2556.
37. Aitken Elizabeth H, Agersew Alemu, Stephen J Rogerson. Neutrophils and Malaria, Frontiers in Immunology. 2018;9:3005.
38. Waters LS, Taverne J, Tai P-C, Spry CJF, Targett GAT, Playfair JHL. Killing of Plasmodium falciparum by eosinophil secretory products. Infect Immun. 1987;55:877–81.
39. Faizi S, Khan, RA, Azher S, Khan SA, Tauseef S, Ahmad A. New antimicrobial alkaloids from the roots of Polyalthia longifolia. Planta Med. 2003;69:350-355.
40. Amaya Ortega-Pajares, Stephen J Rogerson. The Rough Guide to Monocytes in Malaria Infection, Frontiers in Immunology. 2018;9:2888.

© 2021 Muazu et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/68681