Evaluation of the Anti-Plasmodial and Toxicological Properties of *Moringa Oleifera* and *Annona Muricata* Leaves Extracts in Albino Rats

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***Abstract*- Malaria is the major cause of mortality and morbidity an infectious disease caused by Plasmodium species. In a bid to address the health problems posed by malaria especially in tropical regions, plants are progressively being resorted to. This study aimed at evaluating the anti-plasmodial and toxicological effects of *Moringa oleifera* and *Annona muricata* ethanolic leaves extracts in albino rats. The plant extracts were carried out using the modified soxhlet extraction method. The phyto-constituents of plants make them a source of therapeutic agents for the treatment of malaria. In this study, the experimental animals were all (except for the normal control) inoculated with 2 X 10^7/ml *Plasmodium berghei* infected erythrocytes as described by Ryles and Peters. The infection was confirmed by viewing the Giemsa – stain blood smear obtained from the tail of the infected mouse and studied under the microscope. This was established by the fourth day. The animals were treated with the plant extracts doses of 100, 300, 500, 800 and 1000mg/kg body weight and reference drug (combisunate 10mg/kg). curative effects and hematological investigations were carried out after five days of administration with blood samples obtained from the animals through the cardiac venous puncture. The results showed that there was reduction in the parasitemia level of the treated groups relative to the untreated control which was significant at $p<0.05$. Except for the groups treated with *Moringa* oleifera leaves. The hematological tests revealed a decrease in PCV, Hemoglobin concentration, Neutrophil and RBC and an increase in total WBC and Lymphocytes count of the treated groups compared with the normal control. This suggested that the pathological changes in the blood were corrected on treatment with the extracts. Hence, it can be inferred that *Moringa oleifera* has low or no anti-plasmodial effect, whereas *Annona muricata* showed moderate anti-plasmodial activity against *P. berghei* and when further researched on can serve as a base for new anti-malaria drug.**

Keywords: **Toxicological, antiplasmodial, *Moringaoleifera, Annonamuricata, Plasmodiumberghei***

I. INTRODUCTION

Malaria is a known life-threatening infection caused by Plasmodium parasites. It is transmitted to humans through the bites of an infected female anopheles' mosquitoes. The Plasmodium parasite in man is of five species, out of which two, *Plasmodiumfalciparum* and *Plasmodiumvivax*, pose the highest danger [1]. Malaria is still currently a major epidemic in sub-Saharan Africa, and it is reported that a child dies in Africa from Malaria every 60 seconds. This disease has been in existence for centuries and has a very low rate in the western world, but it is an infectious disease that still plagues the continent of Africa, in particular sub-Saharan countries [2].

Herbs or traditional medicines have been used to treat malaria for many centuries and are still the sources of the two main groups-artemisinin and quinine derivatives of modern antimalarial drugs. With the problems of increasing levels of drug resistance coupled with the difficulties in poor areas and the challenges of being able to afford and access effective antimalarial drugs, traditional medicines could be good alternative therapies [3].

Clinical investigations on traditional remedies are laudable and indeed helpful. A number of herbal remedies may be safe and beneficial for the treatment of malaria and other health disorders. Yet, better confirmation from several clinical trials is required before herbal medications can be recommended on a large-scale. Due to the expensive and time consuming nature of these trials, it is imperative to prioritise remedies for clinical inquiry particularly in line with available data from ethnobotanical, sociological, pharmacological, and preliminary clinical examinations. More so, in remote areas with meager income where present antimalarials are not readily accessible, research can make available indications for traditional medicine, to enlighten local treatment choices [3]. Based on these reasons has this research embarked on a quest for a natural, bioavailable and less affordable source of antiplasmodial Plants that can withstand strain resistance, as well as having, a wide spectrum for the prevention and cure of malaria infections. Two plants were investigated in the curse of this study and they include: *Moringa oleifera* and *Annona muricata*. The general properties of these plants will be explored alongside their nutritional and phytochemical abilities.

Fresh *Moringa oleifera* leaves are very rich in Vitamin C, 7 times more than orange juice. The malaria belt of the world (tropical regions) with rich sources of vitamin C constitutes

malaria endemic zones, where vitamin C rich food such as citrus fruits and green vegetables abound, a mutual relationship between the two appears to exist [4]. *Annona Muricata L.* has quite high nutritional value. The whita juicy pulp of the fruit is high in carbohydrates and sugars and fair amount of vitamin C, vitamin B, vitamin B_2, Potassium and dietary fibre, however, it is poor in vitamin A [5]. Recent studies have supported many of *Annonamuricata's* traditional medicinal uses and also showed that various parts of the tree contain acatogenins which have been shown to be responsible for its myriad arrays of its medicinal attributes. The presence of different major minerals such as K, Ca, Na, Cu, Fe and Mg suggest that regular consumption of the *A. muricata* fruit can help provide essential nutrients and elements to the human body [6].

1.1 Aim and Objectives of the Study

Aim

This study is aimed at evaluating the anti-plasmodial and toxicological properties of *Moringa oleifera* and *Annona muricata* leaves extracts in albino rats infected with *plasmodium berghei*.

Objectives

In this study, the following objectives were set to be accomplished:

I To determine the *Plasmodium* curative effect of the extracts in albino rats

II. To evaluate the action of the extracts on hematological indices in rat inoculated with *Plasmodium berghei*.

III. To evaluate the effect of dose variation of each extracts on the anti-plasmodial potency and their toxicological effects in albino rats.

II. MATERIALS AND METHODS

2.1 Preparation of Crude Extracts

The solid crude extract of *Moringa oleifera* and Sour sop (*Annona muricata*) leaves were prepared by a soxhlet (solid extraction) extraction method[7]with slight modifications. A known amount (500g) of the solid samples already grounded and shelved into fine powder were placed inside the thimble and the ethanol placed inside the reservoir. On application of heat from a heating mantle the liquid vaporized, condensed in the condenser and dropped into the thimble to extract components of the solid sample. The filtrates were then filtered using a filter paper and the filtrates were condensed in a rotary evaporator. A greenish residue weighing 43.45 and 30.56g respectively were obtained. The extracts were kept in air tight sample bottles in a refrigerator until needed.

2.2 Animal Care

Pathogen-free White male albino rats weighing about 120–150 g were used throughout this study. The rats were obtained from the Animal Housing Unit, university of Port Harcourt and allowed access to food (feeding pellets ad libitum) and water. Rats were handled with care especially when they are being transferred from the animal house to laboratory at least an hour prior to use, in order to reduce the effects of stress. They were kept under observation (Acclamatization) for about 7 days before the onset of the experiment. The chosen animals were housed in plastic well aerated cages at normal atmospheric temperature (25 ± 5 °C) and normal 12-hour light/dark cycle.

2.3 Determination of Median Lethal Dose (LD_{50}) of Moringa oleifera and Annona muricata leaves on Rat

The acute toxicity was determined by fixed dose procedure. A total of twelve rats with an average weight of 124g were put into four groups labeled 1-4, with each group having three (3) rats each and these groups were replicated in two places each representing the extracts of *Moringa oleifera* and *Annona muricata leaves* respectively. A single dose of 1000mg, 2000mg, 3000mg and 5000mg of extracts per kg body weight was administered to each rat in groups 1, 2, 3 and 4 respectively, using intubation canula. The animals were observed individually every 30 minutes after dosing during the first 24 hours. Special attention was given during the first 4 hours, and daily thereafter for a total of 7 days. Mortality and other physical factors like changes in skin and fur, eyes and somatomotor activity were monitored.

2.4 Evaluation of Curative Activity

Curative activity was determined using Rane curative test [8]. fifty-two (52) albino rat were selected and fourty-eight (48) of these were injected intraperitoneally with 0.5ml of blood infected with 1×10^7/ml *Plasmodium berghei* (NK65 strain) on the first day. The infection was confirmed by viewing the Giemsa – stain blood smear obtained from the tail of the infected mouse and studied under the microscope. This was established by the fourth day. After the confirmation, the animals were put into groups of four rat per group. Group 1 was uninoculated and treated with distilled water. Group 2 was inoculated and treated with 1ml/kg distilled water daily. Groups 3 (which were inoculated) received daily dose of 10mg/kg body weight of combisurnate[@]. Five different concentrations of 100mg/kg, 300mg/kg, 500mg/kg, 800mg/kg and 1000mg/kg body weight of *Moringa oleifera* and *Annona muricata leaves* extracts were administered to groups 4-8 and 9-13 respectively for five days. All administration was by oral route. Thin films stained with Geimsa stain, were prepared from the tail blood of each animal on the first, third and fifth day to monitor the parasitemia level.

Figure 1: Estimation of parasitemia levels of prepared slides

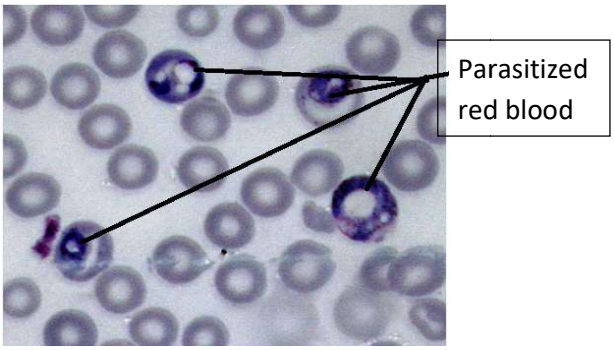

Figure 2a: Estimation of parasitemia levels of prepared slides thin film showing the parasitized red blood cells

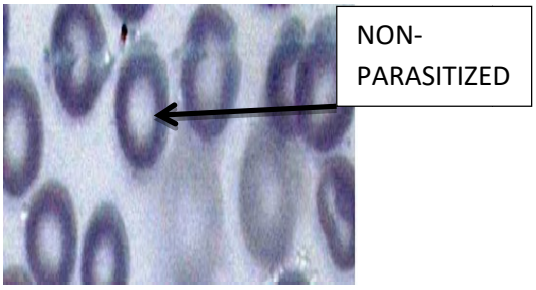

Figure 2b: Estimation of parasitemia levels of prepared slides thin film of giemsa-stain showing the non-parasitized red blood cells

2.5 Parasitaemia Measurement

To Measure the parasitaemia levels in the animals, thick and thin film smears were made on slides for microscopic viewing. A drop of blood through venesection of the tail from each malarial animal, onto the edge of a microscope slide (single, 76 x 26 mm thickness). The blood was drawn evenly across a second slide to make a thin blood film. The slides were fixed with methanol before staining with Giemsa stain. Slides were viewed under light microscopy with oil immersion (1000x magnification). Parasitaemia was calculated as follows:

% Parasitemia = No of parasitized RBC× 100/No of total RBC---------(1)

Figure 3: Thick and thin smear slide for qualitative and quantitative estimation of parasitemia

III. RESULT

3.1 Acute Toxicity

The results of the acute toxicity evaluation of *Moringa oleifera* and *Annona muricata leaves* extracts showed no remarkable behavioral changes in the administered rats. No mortality occurred within the observation period of 7 days. However, behavioral signs of toxicity were observed in rats given 5000 mg/kg which include paw licking, salivation, stretching and reduce activity. There was however no mortality at all the doses used.

3.2 Curative Effects of Moringa oleifera and Annona muricata Leaves Extracts against P. berghei (Curative Test)

The curative effect of the ethanolic laeves extracts of *Moringa oleifera* produced a significant ($p<0.05$) dose dependent increase in parasitaemia levels in the extract treated groups. The average parasitaemia of *Moringa oleifera* extract treated groups on day 5 were 14.45±1.01, 16.34±0.43, 20.93±1.73 and 16.46±0.65 for the 100, 300, 500 and 800 mg/kg/day of the extracts, respectively. The increase in parasitaemia is an indication that the *Moringa oleifera* leaves extracts have little or no anti-malarial property. The 1000mg/kg dose of the same extract showed 100% mortality rate on the third day of administration.

The ethanolic leaf extract of *Annona muricata* produced a dose dependent reduction in parasitaemia levels in the extract treated groups, with a similar reduction as in combisunate[@] treated group (positive control). While, we observed a daily increase in parasitaemia in the negative control group. In general, there was an average parasitaemia level of above 10% in all the infected groups in the first day (post inoculation). While a progressive reduction in the parasitaemia level was observed in the positive control and groups treated with *Annona muricata Leaves* extracts, the untreated group and the groups treated with *Moringa oleifera* had an increase in the parasiteamia level.

Table 1a: CURATIVE EFFECT OF *MORINGA OLEIFERA AGAINT P. berghei*

S/N	GROUP	Treatments	DAY 1	DAY 3	DAY 5
1	NORMAL CONTROL	Food and water only (no inoculation)	0.00±0.00^{bc}	0.00±0.00	0.00±0.00^{bc}
2	NEGATIVE CONTROL	Inoculated but not treated	10.85±1.54^{ac}	15.70±0.99^{ac}	23.19±2.49^{ac}
3	POSITIVE CONTROL	Inoculated + combisunate 10mg/kg	17.31±1.40^{ab}	1.75±0.22^{b}	0.36±0.03^{ab}
4	GA1	100mg/kg	9.21±0.99^{ac}	10.77±1.30^{bc}	14.45±1.01^{abc}
5	GA2	300mg/kg	6.23±0.30^{abc}	11.62±1.58^{abc}	16.34±0.43^{ac}
6	GA3	500mg/kg	13.14±0.984^{ac}	18.22±0.96^{abc}	20.93±1.73^{abc}
7	GA4	800mg/kg	10.77±0.65^{ac}	13.15±0.61^{abc}	16.46±0.65^{abc}
8	GA5	1000mg/kg	12.07±1.22^{ac}	40.35±6.39^{abc}	0.00±0.00^{abc}

Data are expressed as Mean ± SEM. n=4. Values found in a column with common superscript letter a, are significantly different ($p<0.05$) when compared to the normal control. Values with superscript b, are significantly different ($p<0.05$) relative to the negative control. While values with the superscript c, are significantly different ($p<0.05$) compared to the positive control.

Table 1b CURATIVE EFFECT OF *ANNONA MURICATA AGAINT P. berghei*

S/N	GROUP	Treatments	DAY 1	DAY 3	DAY 5
1	NORMAL CONTROL	Food and water only (no inoculation)	0.00±0.00^{bc}	0.00±0.00	0.00±0.00^{bc}
2	NEGATIVE CONTROL	Inoculated but not treated	10.85±1.54^{ac}	15.70±0.99^{ac}	23.19±2.49^{ac}
3	POSITIVE CONTROL	Inoculated + combisunate 10mg/kg	17.31±1.40^{ab}	1.75±0.22^{b}	0.36±0.03^{ab}
4	GB1	100mg/kg	16.38±1.30^{abc}	15.06±0.55^{ab}	11.57±0.68^{ab}
5	GB2	300mg/kg	13.85±0.50^{abc}	9.05±0.60^{abc}	3.14±0.27^{abc}
6	GB3	500mg/kg	16.04±0.58^{abc}	8.60±0.49^{bc}	2.05±0.13^{b}
7	GB4	800mg/kg	18.54±0.77^{abc}	7.32±0.88^{abc}	1.6±0.20^{ab}
8	GB5	1000mg/kg	13.21±0.57^{abc}	2.95±0.11^{abc}	0.70±0.08^{b}

Data are expressed as Mean ± SEM. n=4. Values found in a column with common superscript letter a, are significantly different ($p<0.05$) when compared to the normal control. Values with superscript b, are significantly different ($p<0.05$) relative to the negative control. While values with the superscript c, are significantly different ($p<0.05$) compared to the positive control.

3.3 Effects of Moringa oleifera and Annona muricata leaves extracts on hematological parameters

The result represented in table 2 indicated a general reduction in RBC in the treated group (ranging values of 0.00- 4.20) as compared to the normal control (uninfected group) which showed a value of 4.65±0.25. The untreated group (negative control) also had a reduction in RBC 2.17±0.18. the group treated with 800mg/kg *Moringaoleifera* had the least value of RBC 2.12±0.13 this group also recorded a mortality rate of 40% at the end of the third day of treatment. There was a 100% mortality rate in the group treated with 1000mg/kg of the same *Moringaoleifera* ethanolic leaf extract as a result, no result was displayed for this concentration. On a more general note, the total white blood count, absolute lymphocytes and monocytes were significantly higher in cases of the infected groups compared to the uninfected normal control ($p<0.05$) group. The results show a higher number of leukocytes, predominantly of the mononuclear cells, being a major feature in the malaria infected rats these are probably typical findings in malaria infection. However, the PCV, Hb, absolute neutrophils and RBC were significantly lower in the malaria infected groups than in the uninfected control ($p<0.05$) group. A lower PCV in the malaria infected patients may reflect anaemia which is often mainly due to mechanical destruction of parasitized red cells as well as spleenic clearance of parasitized and defected erythrocytes. Also it is most probably that relative neutropenic leukocytopenia develops subsequently in malaria infected rats with a relative increase in mononuclear cells as reflected by the significantly lower neutrophils and higher lymphocytes/monocytes in the infected rats.

TABLE 2a: EFFECT OF *MORINGA OLEIFERA,* EXTRACTS ON HEMATOLOGICAL PARAMETERS

S/N	GROUP	PCV	Hb	RBC	WBC	NEU	LYM	MONO
1	NORMAL CONTROL	40.75±2.09 ^{bc}	14.02±0.08 ^{bc}	4.65±0.25 ^{bc}	3.42±0.25 ^{bc}	72.50±1.70 ^{bc}	22.25±0.85 ^{b}	1.00±0.40 ^{bc}
2	NEGATIVE CONTROL	16.50±2.10 ^{ac}	5.82±0.49 ^{a}	2.17±0.18 ^{ac}	11.10±1.28 ^{ac}	60.75±2.56^{c}	31.50±1.84 ^{ac}	2.75±0.47 ^{ac}
3	POSITIVE CONTROL	34.50±1.84 ^{ab}	11.57±0.49 ^{ab}	4.02±0.13 ^{ab}	5.47±0.30 ^{b}	70.75±1.25 ^{ab}	22.25±0.47 ^{ab}	1.25±0.629 ^{a}
4	GA1	28.50±1.04 ^{abc}	10.27±0.25 ^{ac}	3.45±0.11 ^{ac}	8.12±0.49 ^{bc}	49.42±14.48 ^{ab}	28.00±1.47 ^{abc}	2.25±0.47 ^{abc}
5	GA2	22.50±2.02 ^{abc}	8.10±0.43 ^{abc}	2.75±0.19 ^{ab}	9.02±0.54 ^{ac}	62.00±1.58 ^{abc}	30.00±1.08 ^{abc}	2.25±0.62 ^{bc}
6	GA3	18.75±1.25 ^{ac}	6.80±0.54 ^{abc}	2.40±0.15 ^{abc}	10.10±0.55 ^{abc}	52.50±2.02 ^{bc}	39.25±2.32 ^{ab}	3.00±0.40 ^{bc}
7	GA4	14.75±1.49 ^{ac}	5.27±0.34 ^{abc}	2.12±0.13 ^{bc}	11.27±0.70 ^{ab}	51.00±4.63 ^{abc}	38.75±5.05 ^{ab}	2.00±0.40 ^{abc}
8	GA5	0.00±0.00 ^{abc}	0.00±0.00 ^{ab}	0.00±0.00 ^{ac}	0.00±0.00 ^{abc}	0.00±0.00 ^{abc}	0.00±0.00 ^{bc}	0.00±0.00 ^{abc}

Data are expressed as Mean ± SEM. n=4. Values found in a column with common superscript letter a, are significantly different ($p<0.05$) when compared to the normal control. Values with superscript b, are significantly different ($p<0.05$) relative to the negative control. While values with the superscript c, are significantly different ($p<0.05$) compared to the positive control.

TABLE 2b: EFFECT OF *ANNONA MURICATA* EXTRACT ON HEMATOLOGICAL PARAMETERS

S/N	GROUP	Treatment	PCV	Hb	RBC	WBC	NEU	LYM	MONO
9	GB1	100mg/kg	23.25±1.75 ^{abc}	8.15±0.43 ^{abc}	2.92±0.16 ^{abc}	6.97±0.24 ^{bc}	63.25±2.13 ^{ab}	27.50±1.70 ^{bc}	1.50±0.28 ^{abc}
10	GB2	300mg/kg	26.00±2.27 ^{abc}	8.77±0.69 ^{bc}	3.15±0.18 ^{ab}	6.77±0.62 ^{abc}	68.75±1.10 ^{ab}	23.75±2.25 ^{abc}	0.50±0.28 ^{ac}
11	GB3	500mg/kg	28.00±1.08 ^{ab}	9.67±0.37 ^{ac}	3.37±0.13 ^{abc}	5.32±0.30 ^{abc}	70.50±1.32 ^{bc}	19.50±0.64 ^{abc}	1.25±0.25 ^{ab}
12	GB4	800mg/kg	31.25±1.25 ^{abc}	10.30±0.27 ^{abc}	3.62±0.10 ^{bc}	5.05±0.10 ^{ab}	76.00±2.34 ^{bc}	18.25±1.31 ^{abc}	0.50±0.28 ^{abc}
13	GB5	1000mg/kg	36.00±1.29 ^{bc}	12.37±0.28 ^{ab}	4.20±0.13 ^{abc}	4.40±0.19 ^{ab}	77.00±1.77 ^{abc}	18.25±2.95 ^{ac}	0.25±0.25 ^{bc}

Data are expressed as Mean ± SEM. n=4. Values found in a column with common superscript letter a, are significantly different ($p<0.05$) when compared to the normal control. Values with superscript b, are significantly different ($p<0.05$) relative to the negative control. While values with the superscript c, are significantly different ($p<0.05$) compared to the positive control.

IV. DISCUSSION

From the result obtained it has been shown that except for the plant leaves of *Moringa Oleifera,* the plant *Annona Muricata Leaves* ethanolic extracts have anti-plasmodial activities. It has also been shown that *Moringa Oleifera* might be toxic to the body of malaria infected rats if the dosage is not regulated. *Annona Muricata Leaves* plant species possess Alkaloids which inhibit the growth and functioning of the Plasmodium in the system. Although, more research is needed to investigate the effectiveness and toxicity of these plants, it can be said that these species can be used in the cure and possible eradication of malaria. Moringa oleifera is commonly addressed as the "miracle tree", and has strong record for curing many diseases, but no concrete write-up has suggest its antimarial properties. This does not mean that there is no probably the presence in the plant of a few molecules which could demonstrate antiplasmodial properties. Dry leaves of the plant do not inhibit beta-hematin in the assay which is often used to screen for antimalarials.

Malaria is a major public health problem in Sub-Sahara Africa including Nigeria, where it accounts for more cases of infection and deaths than most other countries in the world. Haematological parameters as an investigating tool for cases of early malaria infections may help to detect early complications associated with serious malaria infection so as to help in the care for the patients and prevent death that may result from such complications. The haematological parameter changes in malaria infected blood sample have been reported. They reported that the infected patients tended to have significantly lower PCV, haemoglobin, and red blood cell counts, which is in agreement with the present study where the RBC counts in malaria infected blood were significantly lower than that of non-infected rats. The PCV level were also noted to be significantly lower in the untreated controls ($P<0.05$). The result in this study, which indicates significant increase in the white blood cell count of the malaria infected rats ($p<0.05$) when compared to the non-inoculated control, probably is as a result of an increase in the release of leukocytes at the early stage of the infection, to content and fight against the infection. Increase in WBC count in malaria rats in this study collaborate that reported [9]. The mean values of haematological parameters were examined between the malarial infected rats. Significantly lower PCV conforms to the report of [10] which showed parasitaemia and haematological alterations in malaria. The level of neutrophils in infected rats were found to be significantly lower than that in the normal control ($P<0.05$), which is in line with the report of [10]. The alteration in counts including relative lymphocytosis and decrease in packed cell volume were observed in this study just as reported by [11]. Although Kakoma also observed increase in the level of neutrophils

which is in contrast with this study where the neutrophils were seen reducing as infection progresses. This observation is in line with what was observed by Goldstein [12]. Haematological abnormalities are considered a hallmark of malaria and are reported to be most pronounced in P. falciparum infections. This study showed that P. berghei malaria infections can lead to significant changes of various blood cell parameters varying from infections with P. falciparum, which shows higher neutrophil and lower lymphocyte responses. This finding is found to be similar with that of a previous study which reported that malaria induced changes include a reduction in neutrophil levels [12]. The underlying mechanisms include the marginalization of neutrophils to the sites of inflammation, splenic localisation, serum lymphotoxic factors, and intercurrent bacterial infections [13].

V. CONCLUSION

Ethanolic extracts of *Annona muricata* leaves have significant positive effects as antiplasmodial agents against *P. berghei* parasitized rats and have showed no toxicological effect at the varied concentrations so selected for this research. Except for *moringa oleifera* which shows little or no antiplasmodial effects on rats infected with *P. berghei* after five days of treatment with varied concentrations of the ethanolic extracts. Results of groups treated with *moringa oleifera* also show significant toxicological effects as it tends to aid the parasites in synergy to reduce most of the blood hematological parameters beyond the normal range. Hence, consumption of *moringa oleifera* during malaria infection is deleterious as the "Miracle plant" tends to boast the production of the parasite instead of causing a healing effect. Haematological investigation is relatively inexpensive and a less technically sophisticated way for malaria parasite detection. Haematological parameters of malaria infected rats significantly differ from that of healthy uninfected ones.

VI. RECOMMENDATIONS

Research should be carried out on other physiological parameters other than the ones measured in this research so as to further ascertain their safety on other organs of the body. Since *Moringa* leaves extract deductively from this research is seen as not only been useful to the host (rat) but also to the parasite, its consumption during malaria infection should be limited. Reason is that, *Moringa oleifera* has mild toxicity effects and many families worldwide consume the leaves over varying periods of time, without knowing the possibility of causing organ toxicity. The methods used in this study are simpler in comparison to cell blood count with automatic analyzers which are even not readily available in many remote rural areas of the sub-Sahara Africa. Further researches should be carried out on some other health benefits of these leaves such as: Weight loss, relieving constipation, promoting heart health, reducing heart disease risk, Impotence, Pregnancy deliveries, preventing colon cancer e.t.c The mechanism via which these effects are introduced are unknown, hence, the need for further study. Dosage should be adjusted to view the effect of higher or lower concentrations. The leaves should be combined and researched on to ascertain their synergetic effect.

VII. CONTRIBUTION TO KNOWLEDGE

This research adopted a comparative study of the ethanolic extracts of two plants viz: *Moringa oleifera* and *Annona muricata* leaves with the efficacy of Combisunate[@]. The dosage concentrations adopted by this research varies from the usual dose used in previous researches (100-1000mg/kg). The duration of induction and treatment varies slightly from that of other researchers. The uniqueness of the ameliorative effects of the various extracts as indicated by the average parasitemia levels and haematological results. From this research, *Moringa oleifera* showed poor antimalarial property and high toxicity in the prevention and cure of malaria compared with *Annona muricata* leave extracts which showed moderate antimalaria properties. Hence, their ameliorating effects based on the dose range administered.

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