Antiplasmodial and Toxicological Effects of Ethanolic Extracts of Mango (*Mangiferaindica*) Leaves and Bitter Cola (*Garcinia kola*) Seeds in Albino Rats

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Abstract: **Malaria is one of the most important diseases in the world. The choice for the treatment is highly limited due to drug resistance. Hence, finding the new compounds to treat malaria is urgently needed. The present study aim at investigating the toxicological and anti-plasmodial effects of extracts of *Mangiferaindica* and *Garcinia kola* on Albino rat infected with *Plasmodium berghei*. For efficacy test in vivo, standard 5-day curative test was carried out. Rats were inoculated with $1x10^7$/ml parasitized erythrocytes of *Plasmodium berghei* by intraperitoneal injection. The extracts (100,300, 500, 800, and 1000 mg/kg) of each plants were given separately to each group and orally once a day for 5 consecutive days. Average Percentage parasiemia and hemaological indices were estimated. Combisunate (10 mg/kg) was given to infected rats as reference control while untreated control was given only distilled water. It was found that ethanolic extracts of *Mangiferaindica* and *Garcinia kola* at different doses showed dose dependent parasitemia inhibitionbuthavenocurative effects. Therefore, *Mangiferaindica* and *Garcinia kola* exact significant anti-plasmodial activity and prolonged survival time with no toxicity.**

Keywords: **Toxicological, antiplasmodial, *Mangiferaindica*, *Garcinia kola*, *Plasmodium berghei***

I. INTRODUCTION

Plants provide nutrition for human based on their primary products of photosynthesis while the conventional pharmaceutical drugs, herbs, ethno medicines, essential oils and cosmetics are derived from secondary products of plants metabolism such as alkaloids, terpenoids and flavonoids [1]. These are the characteristics of medicinal plants, possession of pathological niche which revolved to a path genomic structure makes herbs being used for different ailments with respect to their actions/activities in the physiology of human.

Mango scientifically called *Mangiferaindica*, is a species of flowering plant in the family of Anacadiaceae, it has varieties approximately about 69 species spread in diversity exists in tropical and subtropical continents of the world. Importance of the mango cannot be over emphasized. The fruits are eaten and used in the production of juice and wineApplication of *Mangiferaindica* in traditional medical practice for the treatment of malaria infection had been reported by [2]. Hence the extracts of the mango leave are used and have an in vitro activity against plasmodium.

Garcinia kola (Heckeler), a member of the Guttiferae family of plants commonly called Bitter cola (English). It is a perennial plant that usually grows in the forest area of West and central Africa countries of Cameroon, Ghana, Sierra Leone, including Nigeria, where almost all ethnic groups have a medicinal value of *Garcinia kola*. The nut of the *Garcinia kola*is chewed to release its masticatory bitter content of which is valued for its varied medicinal content, reported in the literature which includes antiplasmodial, antimicrobial, anti-inflammatory, purgative, remedy for guinea-worm infection and for treatment for gastroenteritis, rheumatism, throat infections, bronchitis, and liver disorder [3]-[5]. The documented literature contents of phytochemicals obtained from the plant *Garcinia kola* includes Xanthones, coumarine, Biflavonoids, Kolanone, 24-methylene-cyclartenol, [6]. The plant is also used as antidiabetic, antioxidant, chemoprevention of aflotoxin B1 and antihepatotoxic activities [7]-[12].

Malaria is not only a disease commonly associated with poverty but also a major cause of poverty and a main hindrance to economic development. Malaria has infected humans for over 50,000, years and plasmodium may have been a human pathogen for the total history of the species [13]. The four rodent malaria parasites are principally parasites of thicket rats. Among may thousands of Normads examined in Africa, only few have been found to be infected. *Plasmodium berghei* has been isolated from three different species of thicket rats [14]. Which all others (sub) species parasites have been found in Tharmonysrutilans.the parasites have been shown to have a wide range of infectivity [15],[16]. The range of hosts experimentally infected by the inoculation of sporozoites of *Plasmodium berghei* and P. yoelii are among others, white mice, laboratory rats and hamsters.

1.1 Aim and Objectives

Aim: The Aim of this study is to investigate the toxicological and antiplasmodial effects of extracts of Mango (*Magiferaindica)* leaves and Bitter cola (*Garcinia kola)* seed on Albino rat infected with *Plasmodium berghei.*

Specific Objectives:

1. To determine the toxicological effect of extracts of Mango (*Mangiferaindica) leave*and Bitter cola (*Garcinia kola*) on Albino rats
2. To determine the Antiplasmodialcurative effects of extracts of Mango (*Mangiferaindica) leaveand* Bitter cola (*Garcinia kola*) on Albino rats infected with *Plasmodium berghei.*
3. To assess the antiplasmodialand effects of Mango leafand seeds of Bitter cola using hematological lindices as marker.
4. To determine the effective doses of the above mentioned plant extracts.

1.2 Justification of the Study

Previous researchers had works on antimicrobial activities of extracts of plants and plants products. We intend to investigate the antiplasmodial activities and toxicological properties of leaf of Mango (*Mangiferaindica)*and seeds of Bitter cola *(Garcinia kola*) on Malaria parasite of animal genus *Plasmodium berghei.* This study will provide the essential information about the medicinal properties and the potency of these plants with respect to antiplasmodial treatment. The cytotoxicity studies will also draw attention to the toxicological perspective of these plants.

II. MATERIALS AND METHODS

2.1 Plant Sample Collection and Identification

Fresh leaves of *Mangiferaindica* were obtained from the Botanical Garden of the Department of Plant Science and Biotechnology, University of Port Harcourt. While the fresh seeds of *Garcinia kola* were obtained from the Oil Mill Market in Port Harcourt. The plants parts were all identified by the Departmental Herbarium.

2.2 Ethanolic Extracts of Leaves of Mangiferaindicaand Seeds of Garcinia kola

The fresh leaves of *Mangiferaindica* and seeds of *Garcina kola* were all dried. The dried samples were ground into powdered form using grounding machine and the extractions were carried out using the soxhlet extraction method [17]with slight modification. The powders (0.5 kg) were placed separately in a thimble of a soxhlet extractor apparatus where they were extracted using absolute ethanol (99.9%) for 72 hours until the extraction process is complete. The filtrates were then filtered using a filter paper and the filtrates were condensed in a rotary evaporator under decreased pressure at 35°C. A greenish residue were obtained. The extracts were kept in air tight sample bottles in a refrigerator and maintained at 4°C, away from light until needed.

2.3 Screening of Phytochemical Components of the Extracts.

The assay of the bioactive or phytochemical constituents of the plants was done and referencing appropriately for Terpenoids, Saponins, Tannins, Alkaloids, Biflavonoides Glycosides, Polyphenols and Reducing Sugars.

2.4 Median Lethal Dose Test

In this study, acute toxicity study for *Mangiferaindica* and *Garcinia kola*ethanolic extracts were carried out using modified Lorke's method [18]. Twelve (12) male wistar rats were randomized into 4 groups of three rats each and were then given oral dose of extracts of 500, 1000, 2000, and 4000 mg/kg accordingly. The rats were observed for signs of toxicity, behavioural assessment such as paw licking, salivation, stretching of the entire body, weakness, sleep, respiratory distress, coma, and death in the first four hours and subsequently daily for 7 days.

2.5 Experimental Design

The animals were divided into thirteen groups of four animals each. The Control Group (normal control) received water and a balanced diet ad libitum but was not inoculated. The Negative Control Group (-ve ctrl) were inoculated but not treated. The positive control Group (+ve ctrl) received 10mg/kg of combisunate after inoculation with 2×10^7/ml infected erythrocytes in saline suspensions of 0.5 ml. Five different concentrations of 100mg/kg, 300mg/kg, 500mg/kg, 800mg/kg and 1000mg/kg body weight of *Mangiferaindica* and *Garcinia kola*ethanolic extracts were administered to groups 4-8 and 9-13 respectively for five days. On the first, third and fifth day, blood samples were collected from the caudal vein and thin blood smears were prepared. After Giemsa staining, the air dried prepared slides underwent microscopic examination. The parasitemia detected in the infected control and test animals were recorded at each dose and the average parasitemia was computed based on the obtained values.

TABLE 1a: EXPERIMENTAL DESIGN FOR ANTIPLASMODIAL EFFECT OF *Mangiferaindica* and *Garcinia kola*(CONTROL GROUPS)

S/N	GROUP	No. of rat	Food+water only	Parasite induction	Treatment	100 mg/kg	300 mg/kg	500 mg/kg	800 mg/kg	1000 mg/kg	10mg/kg combisunate[@]
1	NORMAL CONTROL	4	YES	NO	NO						
2	NEGATIVE CONTROL	4	YES	YES	NO						
3	POSITIVE CONTROL	4	YES	YES	YES						YES

Key: Normal control = non-inoculated and untreated group; Negative control = inoculated but untreated; Positive control = inoculate and treated with 10mg/kg combisunate[@]

TABLE 1b: EXPERIMENTAL DESIGN FOR ANTIPLASMODIAL EFFECT OF *Mangiferaindica*

S/N	GROUP	No. of rat	Food+water only	Parasite induction	Treatment	100mg/kg	300mg/kg	500mg/kg	800 mg/kg	1000 mg/kg	10mg/kg combisunate@
4	GA1	4	YES	YES	YES	YES					
5	GA2	4	YES	YES	YES		YES				
6	GA3	4	YES	YES	YES			YES			
7	GA4	4	YES	YES	YES				YES		
8	GA5	4	YES	YES	YES					YES	

KEY: GA1-GA5 represents the administration of ethanolic extracts doses: 100, 300, 500, 800 and 1000 in mg/kg of *Mangiferaindica*

TABLE 1c: EXPERIMENTAL DESIGN FOR ANTIPLASMODIAL EFFECT OF*Garcinia kola*

S/N	GROUP	No. of rat	Food+water only	Parasite induction	Treatment	100mg/kg	300mg/kg	500mg/kg	800 mg/kg	1000 mg/kg	10mg/kg combisunate@
9	GB1	4	YES	YES	YES	YES					
10	GB2	4	YES	YES	YES		YES				
11	GB3	4	YES	YES	YES			YES			
12	GB4	4	YES	YES	YES				YES		
13	GB5	4	YES	YES	YES					YES	

KEY: GB1-GB5 represents the administration of ethanolic extracts doses: 100, 300, 500, 800 and 1000 in mg/kg of *Garcinia kola*

2.6 Infection of Wistar Rats by Intraperitoneal (I.P) Injection of Infected Erythrocytes

In this study, *Plasmodium berghei* ANKA 65 strain was used. Frozen parasites from stock were passed at least once through albino rats before experiments.

When the parasitemia showed 15–20%, infected rat blood was then collected by cardiac puncture and suspended in phosphate buffer saline. Infection for experiments was carried out by intraperitoneal (IP) injection of approximately 2 x 10^7/ml parasitized erythrocytes. Tail blood from an infected rat with a parasitemia between 10 to 15% was collected and injected 2 x 10^5 to 10^8i.p into naive animals. About 10% of i.p. injected parasites will survive and enter the blood stream. Since *Plasmodium berghei* (ANKA strain) in laboratory mice/rats has a multiplication rate of about 10x per 24 hour during the first phase of blood stage infection. In these animals the parasitemia reaches levels of 5-10% on day 5 after infection, indicating an average of a 10x multiplication rate per 24h. This multiplication rate is a very stable feature of the parasites in the cloning procedure. Parasitemia was daily monitored by microscopy of Giemsa stained thin blood smear. The percentage of parasitemia (% parasitemia) was calculated using the formula:

$$\% \text{ Parasitemia} = \frac{\text{No of parasitized RBC} \times 100}{\text{No of total RBC}}$$

2.7 Curative Test

The standard 4-day suppressive test against *Plasmodium berghei* (ANKA strain) infection in rat was employed [19]. Naive rats were inoculated by IP injection of 2 x 10^7/ml parasitized erythrocytes. The infected rats were randomly divided into 18 groups of 4 mice per group and treated for 4 consecutive days with 100, 300, 500, 800 and 1000 mg/kg of ethanolic extract of *Mangiferaindica* and *Garcinia kola* accordingly and orally. Two control groups were used: the positive control was treated daily with 10 mg/kg of Combisunate@ while the untreated group was given Distilled Water. Parasitemia On day 1, 3 and 5 of experiment was monitored by microscopy of Giemsa stained thin blood smear. The percentage of parasitemia (% parasitemia) was calculated using the formula:

$$\% \text{ Parasitemia} = \frac{\text{No of parasitized RBC} \times 100}{\text{No of total RBC}}$$

The result of the test was used to determine the curative effects.

2.8 Blood Collection

On the fifth day, at the end of administration, each rat was withdrawn from the cage for sacrifice. The rats were anesthetized using chloroform. The thoracic region was opened up to reveal the heart and blood was collected by cardiac puncture. The blood was collected in well labeled sample bottles (EDTA bottles) and were used for some hematological assays.

2.9 Hematological Investigations

EDTA bottles were used to collect blood samples and were used to determine the hematological indices immediately. The percentage packed cell volume was determined using haematocrit method. White blood cell count (WBCs) were estimated using haemocytometer. The method described by [20] was used to carry out differential white cell count. The erythrocyte count as well as the haemoglobin concentration was also estimated.

2.10 Data Analysis and Interpretation

The SPSS version 23 was used. The one-way ANOVA was used to analyze and compare the results at a 95% confidence. Values of $p < 0.05$ were considered significant. Results were expressed as mean ± standard error of mean (SEM)

III. RESULT

3.1 Acute Toxicity

The results of the acute toxicity evaluation of *Mangiferaindica* and *Garcinia kola* 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 4000 mg/kg which include paw licking, salivation, stretching and reduce activity. There was however no mortality at all the doses used.

3.2 Qualitative Phytochemical Result of Mangiferaindica and Garcinia kolaextracts

The qualitative phytochemical screening of the ethanolic extracts of *Mangiferaindica* and *Garcinia kola* were conducted indicating the fact that flavonoids, tannins, saponins and alkaloid are highly present in *Garcinia kola*whereas, glycosides, steroids and terpenoids are seen to be moderately present. Anthroquinone is seen to be low. *Mangiferaindica* contains more of flavonoid and moderate composition of tannin, saponin, steroid, terpenoids and alkaloids. *Mangiferaindica* contains high glycoside and does not contain anthroquinone.

3.3 Curative activity of Mangiferaindica and Garcinia kola

The result of the effect of the treatment with different concentrations of plant extracts on parasitemia density in rat is presented in Table below. The parasitemia density for the non-treated group progressively increased for the five days' period, showing the mean number of the percentage parasitized red cells as 9.03±0.61 on the first day post inoculation and 18.81±0.79 by the fifth day. Treatment with the doses of the plant extracts (1000mg/kg) showed a significant parasitemia reduction ($p<0.05$) when compared to the non-treated group. The reduction in parasitemia level in one of the dose was similar to that observed for the reference drug. The highest parasitemia reduction was seen in Combisunate[@] followed by 1000mg/kg ethanoics extract of *Garcinia kola*on the fifth day. The 10mg/kg dose combisunate[@] showed a significant reduction of parasitemia from 10.56±0.34 on the first day to 0.10±0.03 on the fifth day. The parasitemia density for the treated groups progressively decreased for the five days' period, showing the mean number of the percentage parasitized red cells as 12.40±0.86 and11.40±0.90 on the first day post inoculation and 0.34±0.03 and 0.14±0.03 for *Mangiferaindica* and *Garcinia kola* respectively by the fifth day. This trend is also observed in the 100, 300, 500 and 800mg/kg ethanol extracts of the two experimented plants.

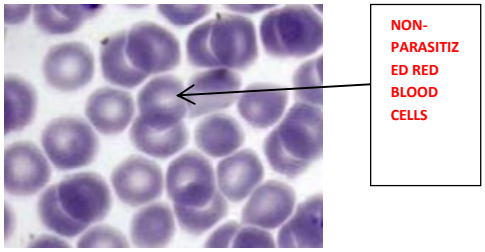

Figure 1a: slide showing non-parasitized red blood cells

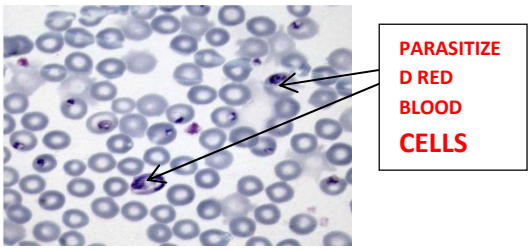

Figure 1b: slide showing parasitized red blood cells

Table 2a Curative Activity of Ethanolic Extracts of *Mangiferaindica* and *Garcinia kolaonPlasmodium berghei*(control groups)

Five-day treatment with Combisunate showed no curative effect as seen in the table below. A value of 0.10±0.03 was recorded. Though, this value was the average mean value of four rats, its indicates that if four persons were to be placed on five days combisunate therapy, chances are that one or two individual among them might not have total cure.

S/N	GROUP	DAY 1	DAY 3	DAY 5
1	NORMAL CONTROL	0.00 ± 0.00^{abc}	0.00 ± 0.00^{abc}	0.00 ± 0.00^{abc}
2	NEGATIVE CONTROL	9.03 ± 0.61^{abc}	13.50 ± 0.31^{abc}	18.81 ± 0.79^{abc}
3	POSITIVE CONTROL	10.56 ± 0.34^{abc}	0.94 ± 0.11^{abc}	0.10 ± 0.03^{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. **Key: Normal control = non-inoculated and untreated group; Negative control = inoculated but untreated; Positive control = inoculate and treated with 10mg/kg combisunate[@]**

Table 2b Curative Activity of Ethanolic Extracts of *Mangiferaindica on Plasmodium berghei*

In general, *Mangiferaindica* did not possess curative ability. It can only suppress the plasmodium parasite at all levels of treatment observed in this research.

S/N	GROUP	DAY 1	DAY 3	DAY 5
4	GA1	9.16 ± 0.73^{abc}	5.38 ± 0.33^{abc}	2.09 ± 0.12^{abc}
5	GA2	11.42 ± 0.40^{abc}	4.86 ± 0.09^{abc}	2.10 ± 0.19^{abc}
6	GA3	10.47 ± 0.16^{abc}	3.14 ± 0.15^{abc}	1.77 ± 0.11^{abc}
7	GA4	8.09 ± 1.50^{abc}	2.12 ± 0.13^{abc}	0.76 ± 0.09^{abc}
8	GA5	12.40 ± 0.86^{abc}	1.03 ± 0.07^{abc}	0.34 ± 0.03^{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.

KEY: GA1-GA5 represents the administration of ethanolic extracts doses: 100, 300, 500, 800 and 1000 in mg/kg of *Mangiferaindica*

Table 2c Curative Activity of Ethanolic Extracts of*Garcinia kola on Plasmodium berghei*

In general, *Garcinia kola* did not possess curative ability. It can only suppress the plasmodium parasite at all levels of treatment observed in this research.

S/N	GROUP	DAY 1	DAY 3	DAY 5
9	GB1	10.76±0.23^{abc}	4.25±0.26^{abc}	1.32±0.07^{abc}
10	GB2	13.50±0.38^{abc}	5.26±0.36^{abc}	1.13±0.16^{abc}
11	GB3	9.64±0.65^{abc}	3.04±0.06^{abc}	0.97±0.08^{abc}
12	GB4	16.09±0.86^{abc}	3.08±0.17^{abc}	0.43±0.03^{abc}
13	GB5	11.40±0.90^{abc}	2.27±0.30^{abc}	0.14±0.03^{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.

KEY: GB1-GB5 represents the administration of ethanolic extracts doses: 100, 300, 500, 800 and 1000 in mg/kg of *Garcinia kola*

Table 3a Effect of Ethanolic Extracts of *Mangiferaindica* and*Garcinia kola* on some hematological Parameters (Control Groups)

S/N	GROUP	PCV	Hb	RBC	WBC	NEU	LYM	MONO
1	NORMAL CONTROL	51.00±1.68^{abc}	15.10±0.07^{abc}	5.67±0.20^{abc}	6.17±0.16^{abc}	77.75±1.25^{abc}	19.25±0.85^{abc}	0.25±0.25^{abc}
2	NEGATIVE CONTROL	25.75±1.88^{abc}	9.52±0.41^{abc}	3.17±0.18^{abc}	12.25±0.76^{abc}	59.50±2.98^{abc}	38.00±1.87^{abc}	2.50±0.28^{abc}
3	POSITIVE CONTROL	40.25±2.01^{abc}	13.57±0.77^{abc}	4.55±0.21^{abc}	6.57±0.13^{abc}	75.50±2.17^{abc}	22.00±1.08^{abc}	0.50±0.28^{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.Key: Normal control = non-inoculated and untreated group; Negative control = inoculated but untreated; Positive control = inoculate and treated with 10mg/kg combisunate$^{@}$

3.4 Effect of Ethanolic Extracts of Mangiferaindica on some hematological Parameters

From the hematological values displayed for *Mangiferaindica,* it can be deduced that values of Red Blood Cells-RBC, Packed Cell Volume-PCV, Haemoglobin concentration-Hb, Neutrophils-NEU are observed to have increased with increase in concentration of the extracts. This infers that the extracts has anti-plasmodial and anti-hemolytic potencies.

Table 3b Effect of Ethanolic Extracts of *Mangiferaindica* on some hematological Parameters

S/N	GROUP	PCV	Hb	RBC	WBC	NEU	LYM	MONO
4	GA1	27.00±1.47^{abc}	9.45±0.55^{abc}	3.25±0.13^{abc}	10.70±0.19^{abc}	66.25±1.54^{abc}	26.00±0.91^{abc}	2.00±0.40^{abc}
5	GA2	31.25±1.31^{abc}	10.70±0.33^{abc}	3.70±0.10^{abc}	10.05±0.10^{abc}	70.00±0.40^{abc}	21.25±0.62^{abc}	0.75±0.25^{abc}
6	GA3	36.50±1.65^{abc}	12.70±0.33^{abc}	4.15±0.20^{abc}	9.20±0.15^{abc}	71.50±0.64^{abc}	19.25±0.85^{abc}	0.25±0.25^{abc}
7	GA4	39.50±1.32^{abc}	12.80±0.20^{abc}	4.47±0.11^{abc}	8.55±0.17^{abc}	73.00±0.40^{abc}	18.00±0.91^{abc}	0.25±0.25^{abc}
8	GA5	41.25±1.37^{abc}	14.02±0.28^{abc}	4.62±0.15^{abc}	7.95±0.25^{abc}	74.00±0.70^{abc}	17.25±1.25^{abc}	0.25±0.25^{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.

KEY: GA1-GA5 represents the administration of ethanolic extracts doses: 100, 300, 500, 800 and 1000 in mg/kg of *Mangiferaindica*

3.5 Effect of Ethanolic Extracts of Garcinia kolaon some hematological Parameters

From the hematological values displayed for *Garcinia kola,* it can be deduced that values of total White Blood Cells- WBC were found returning to its normal state in a dose dependent pattern (9.72±0.14, 8.47±0.08, 7.22±0.17, 6.35±0.12 and 5.20±0.18 respectively) as compared with the negative control (12.25±0.76). Red Blood Cells-RBC, Packed Cell Volume-PCV, Haemoglobin concentration-Hb, Neutrophils-NEU are observed to have increased with increase in concentration of the extracts. This infers that the extracts has anti-plasmodial and anti-hemolytic potencies

Table 3c Effect of Ethanolic Extracts of*Garcinia kola*on some hematological Parameters

S/N	GROUP	PCV	Hb	RBC	WBC	NEU	LYM	MONO
9	GB1	31.00±0.91^{abc}	10.95±0.29^{abc}	3.65±0.08^{abc}	9.72±0.14^{abc}	59.25±1.31^{abc}	30.25±1.25^{abc}	2.00±0.40^{abc}
10	GB2	35.25±1.88^{abc}	11.82±0.58^{abc}	4.05±0.19^{abc}	8.47±0.08^{abc}	61.00±0.91^{abc}	27.75±1.10^{abc}	2.00±0.40^{abc}
11	GB3	39.50±0.64^{abc}	13.55±0.17^{abc}	4.45±0.09^{abc}	7.22±0.17^{abc}	66.50±1.19^{abc}	25.75±1.31^{abc}	1.25±0.25^{abc}
12	GB4	42.75±2.39^{abc}	14.60±0.25^{abc}	22.32±17.45^{abc}	6.35±0.12^{abc}	69.75±0.64^{abc}	22.75±0.47^{abc}	0.50±0.28^{abc}
13	GB5	47.00±1.77^{abc}	14.72±0.21^{abc}	5.20±0.17^{abc}	5.20±0.18^{abc}	72.75±0.64^{abc}	19.00±1.58^{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.

KEY:GB1-GB5 represents the administration of ethanolic extracts doses: 100, 300, 500, 800 and 1000 in mg/kg of *Garcinia kola*

3.6 Discussion

Flavonoids have been detected in the Artemisia species and have been reported to show significant anti-malarial activity against *P.falciparium*[21]. These set of compounds (alkaloids and flavonoids) were identified in these two species of plant extracts, hence the allusion that the presence of these secondary metabolites could be the reason for the plant's therapeutic action. Meanwhile, the results partly corroborate claims made in traditional medicine of the anti-malarial efficacy of these plants [4],[5]. The results of this study support the botanical use of these plants in the treatment of malaria illness. Plants are a major pool of potential antiparasitic and antimicrobial compounds of pharmaceutical needs, [23]The results of this study showed that the ethanolic extracts of *Mangiferaindica* and *Garcinia kola* possess anti-malarial property.Data in this study indicated that combisunate[@] treatment during the infection almost completely abolished the parasites (0.10±0.03 on the fifth day). Physical signs of illness (diarrhea, lethargy, piloerection, reduced locomotor activity etc.) normally seen in malaria-infected rats were absent in combisunate-treated malarial rats and they appeared healthy after five days' post treatment. Results with combisunate indicate that the malarial model used in this study is sensitive to antimalarial agent (artemether and lumefantrine) and therefore justify its use in screening of antimalarial properties from other sources. Among the ethanolic extracts of *Mangiferaindica* and*Garcinia kola* tested against malaria infection in this study, *Garcinia kola* exhibited the most potent antimalarial activity. parasitaemia reached almost 1.32±0.07on the fifth day as against 10.76±0.23parasitemia recorded on the first day even at the lowest dose of 100mg/kg. A previous study revealed that flavonoid content of the seed plant was thought to be responsible for its antimalarial property [21]-[22]. From the acute toxicity carried out in this study via oral route administration of doses of the ethanolic extracts of *Mangiferaindica* and *Garcinia kola* ranging from 1000 up to 5000mg/kg showed that there are no toxic effects produced by a single exposure of these extracts as no sign of toxicity and death was recorded in the first four hours. Also, no toxic effects produced by multiple exposures of these extracts as no sign of toxicity and death was recorded in the subsequently daily administration of these extracts for 7 days. Acute toxicity of *Mangiferaindica* and *Garcinia kola*ethanolic extracts were carried out using modified Lorke's method [18]This is an indication that even up to 5000mg/kg, the ethanolic extracts of *Mangiferaindica*and*Garcinia kola*are still within physiologically tolerable range. The physiological state of the rats treated with *Mangiferaindica* and *Garcinia kola*were seen returning back to normal from the altered state it went after inoculation with the parasite. From the hematological values displayed for *Mangiferaindica* and *Garcinia kola it* can be deduced that values of Red Blood Cells-RBC, Packed Cell Volume-PCV, Haemoglobin concentration-Hb, Neutrophils-NEU are observed to have increased with increase in concentration of the extracts. This infers that the extracts have anti-plasmodial and anti-hemolytic potencies. Total White Blood Cells- WBC was found returning to its normal state in a dose dependent pattern. The Lymphocytes and the Monocytes were found reducing in a dose dependent pattern.One sensitive target in the human system to toxic compound is the hematopoietic system, it is also an important index of physiological and pathological status in both animal and man. Hematological status is important in the diagnosis of root causes of diseases, the disorder indicate abnormal blood parameter profile due to changes in metabolism, leading to altered cellular integrity, cell membrane permeability all due to exposure to toxic chemical compounds.

IV. CONCLUSIONS

Based on these findings, it is clear to us that the oral administration of ethanolic extracts of *Mangiferaindica and Garcinia kola* of range within the dose (100–1000 mg/kg) to rats for 4 days significantly suppressed parasitemia of *Plasmodium berghei* in experimental rats with nontoxicity but have no curative effects. The implication of this finding is that the ethanoic extracts of *Mangiferaindica* and *Garcinia kola* possess antimalarial effects and may therefore serve as potential sources of safe, effective, and affordable antimalarial drugs. They displayed high in vivo antimalarial properties and lack of toxic effect render *Magiferaindica* and *Garcinia kola* a candidate for future isolation of compounds which could develop into new lead structures and candidates for drug development programs against human malaria.

4.1 Contribution to Knowledge

The outcome of the study is expected to contribute to the knowledge of pharmacology. The availability of natural products like medicinal plants and plant products will greatly help to solve the healthcare problems of rural communities.

- The plant extracts showed moderate antimalarial property.
- Looking at the dose administered and its effect on the hematological markers, it can be deduced that *Mangiferaindica* and *Garcinia kola* have ameliorating effects based on the dose range administered.

4.2 Recommendations

On the basis of the findings of this research, the following are recommended:

1. Further work should be done to ascertain the use of the plant extracts in preventive malarial therapy.
2. The plants should be used in combination with other plant products with known antimalarial activity to understand how this synergy can boost the antimalarial property of such plants.
3. Other models for investigating antioxidant properties should be adopted to further establish the plant's antioxidant property and possibly elucidate its mechanism of action.
4. Attempts should be made to isolate the active substance responsible for specific therapeutic action.

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