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Comparative Evaluation of Anti-malarial activities of Methanol Leaf Extracts of *Dialium guineense* and *Morinda lucida* in *Plasmodium berghei* – Infected Mice

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ABSTRACT: Malaria, a serious global health issue, has become increasingly difficult to treat due to drug resistance. As a result, researchers are focusing on finding new treatments, including those derived from medicinal plants. The pathogenesis of malaria involves significant changes in hematological and biochemical parameters. This study aims to compare the effectiveness of methanol leaf extracts from Dialium guineense and Morinda lucida in treating malaria in mice infected with Plasmodium berghei. The methanol leaf extracts were subjected to Gas Chromatography and Mass Spectrometry for the determination of bioactive compounds. Different doses of the extracts and Artesunate (20 mg/kg) were administered orally to the infected mice for five days, thereafter parasitaemia was monitored. The livers were collected for weighing and histological studies. The GC-MS results indicated the presence of large quantities of alpha tocopherol, squalene, linolenic acid and moderate levels of lupeol and other pharmacologically active compounds. At P< 0.05, there was significant suppression of parasitaemia in the groups of mice infected and treated with rated doses of the extracts and Artesunate. The infection induced significant hepatomegaly in the infected and untreated animals which were significantly ameliorated in the groups of infected mice treated with the rated doses of the extracts and Artesunate. Both extracts were effective in protecting against hepatomegaly and severe lesions in the histoarchitecture; validating their experiential use as remedies for malaria. However, when compared with the infected and untreated groups, the methanol leaf extract of M. lucida had a greater preventive effect in this study.

Keywords: Anti-malarial, Dialium guineense, Morinda lucida, Plasmodium berghei, leaf extracts, infected mice

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INTRODUCTION

Malaria is one of the world's most important parasitic infection that poses major public health challenges (Tanner *et al.*, 2015) and a major cause of morbidity in the world (WHO, 2010). It is an acute and chronic vector borne infectious disease caused by obligate intracellular eukaryotic protist of the genus *Plasmodium* transmitted between individuals through the bite of a female Anopheles mosquito that is infected with one of the four species of *Plasmodium*: *Plasmodium ovale*, *Plasmodium falciparum*, *Plasmodium vivax and Plasmodium malariae* (Akinleye, 2009). Malaria can also be transmitted from a mother to her unborn baby (congenitally) and through blood transmission. In pregnancy, it is a recognized risk factor for maternal and fetal complications, particularly with *P. falciparum* infestation (Elbadawi *et al.,* 2011). The resultant effect of resistance of malaria parasites to current anti-malaria drugs necessitates research into potent antimalaria drugs from numerous sources.

Although synthetic pharmaceutical agents continue to dominate research, natural products are of considerable interest in this quest. Herbal remedies are often more available and affordable than conventional anti-malarial drugs (Olasehinde *et* al., 2014).

The use of traditional and herbal remedies seems to be the alternative choice of treatment in countries where malaria is endemic. Several pharmacologically active anti-malarial compounds have been in development from West African medicinal plants (Madara *et al.,* 2012). Numerous medicinal plants have been used locally to treat malaria infection. Frantic efforts are now geared towards discovery and development of new, chemically diverse anti-malarial agents (Elujoba *et al*., 2005).

Morinda lucida (LBO) is a medicinal plant growing in many African countries and widely used as a medicine. It is used as ingredients of fever teas taken for the traditional treatment of malaria. Decoctions and infusions or plasters of root, bark and leaves are recognized remedies against different types of fever, including yellow fever, malaria and trypanosomiasis (Trampuz *et al*., 2003). In some cases, the plant is used for the treatment of diabetes, hypertension, cerebral congestion, dysentery, ulcers, and gonorrhea (Lawal *et al*., 2012).

This study is aimed at profiling the active principles in the selected plants and to evaluate comparatively the antimalarial potential of the methanol leaf extracts of *Dialium guineense* (DGA) and *Morinda lucida* in mice infected with *Plasmodiumberghei*.

MATERIALS AND METHODS

Collection of plant materials and extracts preparation

The leaves of *D. guineense and M. lucida* were collected from a farm in Olowa in Dekina Local Government Area of Kogi State, Nigeria. They were air-dried at room temperature. The dry leaves were ground to powdered form. A portion of the powdered samples were each dissolved in absolute methanol for 72 hours for extraction of their phyto-constituents after which the mixture was filtered. The filterate was evaporated to dryness and the recovered paste was stored until use. The crude methanol leaf extracts obtained from samples were subjected to Gas Chromatography and Mass Spectrometry (GCMS) for the determination of bioactive volatile compounds.

Experimental animals/ animal groupings

Thirty adult albino mice of both sexes weighing (20 – 32) g obtained from the Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria were used for the study. The animals were housed under standard animal house conditions in accordance with the recommendations of the National Institute of Health Guide for the Care and Use of Laboratory Animals. The mice were given standard pellet diet and water *ad libitum* during the entire period of experimentation. The mice were divided into 10 groups. The treatment for each group is as follows:

Group 1 was inoculated with *P. berghei* without treatment (Negative control).
Group 2 was inoculated with *P. berghei* and treated with 200mg/kg body weight of *M. lucida* methanol leaf extract.
Group 3 was inoculated with *P. berghei* and treated with 400mg/kg body weight of *M. lucida* methanol leaf extract.
Group 4 was inoculated with *P. berghei* and treated with 600 mg/kg body weight of *M. lucida* methanol leaf extract.
Group 5was inoculated with *P. berghei* and treated with 200 mg/kg body weight of *D. guineense* methanol leaf extract.
Group 6was inoculated with *P. berghei* and treated with 400 mg/kg body weight of *D. guineense* methanol leaf extract.
Group 7 was inoculated with *P. berghei* and treated with 600 mg/kg body weight of *D. guineense* methanol leaf extract.
Group 8 was inoculated with *P. berghei* and treated with20mg/kg body weight of Artesunate (positive control).
Group 9 was uninfected naive control.
Group 10 was inoculated with *P. berghei* and treated with an equivalent volume of vehicle.

The parasite strain

The anti-malarial activity of the plant extracts was tested using infected mice with *Plasmodium berghei* NK-65 obtained from the Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria and maintained by successive serial blood passages (every 5 days) in mice. Blood samples were collected from the jugular puncture of infected mice. The experimental mice were each intraperitoneally infected. Each mouse received 0.2 ml of the infected blood. Estimation of parasitaemia was done by microscopic examination of blood smears made on slides.

Evaluation of schizonticidal activity in established infection (Curative test)

Evaluation of schizonticidal activity in established infection (Curative test) was done by the method described by Ryley and Peters (1970) as applied by Suruse *et al.* (2015). Thin films which were prepared from the tail venepuncture of each mouse were stained with Giemsa stain and viewed microscopically to monitor the parasitaemia level.

Histological studies

The histological examination of the tissues of the liver of malaria infected animals was done using the Paraffin method of Drury *et al.,* (1967).

Statistical analysis

Results were expressed as mean ± standard error of mean. One way analysis of variance (ANOVA) and Duncan Post Hoc test were used to analyze data and to compare the results at a 95% confidence level using SPSS version 20.

RESULTS

Phytochemical screening of plant extracts

The results obtained from the Phytochemical screening of the extracts by Gas chromatography and Mass spectrometry (GC-MS) are presented in (Tables 1 and 2). From this result, (Table 3) weights of the liver of the infected and untreated groups were significantly ($p< 0.05$) higher than the groups that were treated either with extracts or standard drug.

Effect of methanol leaf extracts of *M. lucida* and *D. guineense* on parasitaemia level

The percentage parasitaemia in all the treated groups significantly decreased ($p<0.05$) compared to the values for the percentage parasitaemia of mice in groups 1 and 10 (negative control) as the days progress (Figure 1).

Chemosupressive effect of methanol leaf extracts of *D. guineense* and *M. lucida*

The percentage parasitaemia in all the treated groups significantly decreased ($p<0.05$) compared to the values for the percentage parasitaemia of mice in group 1 and 10 (negative control) as the days progress. Days 8 and 14 reveal reduction in parasitaemia levels in infected mice. Day 21 showed significant ($p<0.05$) suppression and clearance of the parasitaemia in the treated groups compared to the values of the percentage parasitaemia in groups 1 and 10 (Figure 2).

DISCUSSION

Malaria is a serious health problem globally and treatment has been compromised by drug resistance (Mebrahtu *et al*., 2013). In view of this, indigenous plants play an important role in malaria treatment.Traditional medicinal plants have contributed significantly to current treatment of malaria. From (Tables 1 and 2), the GC-MS chromatogram of the methanol leaf extracts of *M. lucida* shows 34 peaks indicating presence of thirty four Phytoconstituents while that of *D. guineense* reveals 27 peaks. GC-MS results indicated the presence of large quantities of alpha tocopherol, squalene, mome inositol, linolenic acid as well as moderate levels of lupeol and other highly pharmacologically active compounds like4H-pyran-4-one, 2, 3-dihydro-3, 5-dihydroxy-6-methyl; 2(4H)-Benzofuranone, 5, 6, 7, 7- α -tetrahydro-4, 4, 7 - α-Trimethyl-, (R)-; 2-methoxy-4-vinylphenol;benzoic acid, 2-hydroxy, phenylmethyl ester; 9,12-octadecadienoic acid, methyl ester; 9, 12, 15-octadecatrienoic acid, methyl ester (ZZZ); 2-Hexadecen-1-ol, 3, 7, 11, 15-tetramethyl-, [R-[R*, R*-(E)]]-; octadecanoic acid. Alpha-bisabolol has anti-microbial, anti-cancer, anti-oxidant and anti-inflammatory activities (Kamatou and Viljoen, 2009). Benzoic acid; 2, 3-dihydro-benzofuran; benzoic acid, 4-hydroxy, hydride and 4, 5-dihydro-2-phenyl-1-methyl ethyl ester have fungicidal activity (Ilani *et al*., 2016). Significant antioxidant and molluscidal activities of *D. guineense* exhibited have also been reported (Lamien-Meda *et al*., 2008). Results from documented phytochemical analysis of medicinal herbs and dietary plants reveal the presence of phenolic compounds including flavonoids, alkaloids, tannins and saponin which play important roles in health. The antibacterial activities of both the aqueous and ethanolic leaf and bark extracts of *D. guineense* have been evaluated. Also, the methanolic crude leaf extract of *D. guineense* was found by Akinpelu *et al*. (2011) to possess bioactivity against fourteen out of eighteen environmental strains of *Vibrio* species. *Morinda lucida* extracts showed anti-inflammatory effects in tests with rats and promoted gastric emptying and intestinal motility (Aduloju, 2012). Leaf extracts showed *in vitro* antimalarial activity against *Plasmodiumfalciparum* while in several other tests antidiabetic properties were confirmed (Aduloju, 2012). In this study, the results obtained from the pharmacological properties of the phyto-compounds present in *D. guineense and M. lucida* revealed the medicinal potential of these plants and substantiates the antiplasmodial activity of these plants which can be potential sources of new chemotherapeutic and/or chemoprophylactic compounds and it aligns with previous works done on the antimalaria potentials of plants (Ebiloma *et al*., 2011).

The liver is an important organ involved during the pre erythrocytic phase of the malaria parasite's life cycle, where malaria sporozoites develop into merozoites (Viriyavejakul *et al*., 2014). The results obtained from this study showed that the weights of the liver of the mice in the negative control and the group of infected mice administered distilled water were significantly higher when compared with those in the positive control (group 8), those infected and treated with the graded doses of the extracts (groups 2,3,4,5,6,7) and the naïve control

Table 1: Bioactive compounds obtained from GC-MS analysis of methanol extract of *Morinda lucida.*

Peak#	R.Time	Area	MF	Name	Pharmacologic activity
1	7.308	3247542	$C_6H_8O_4$	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-	sympathetic nerve activity, anti-inflammatory,antimicrobial, anticancer (antiproliferative)effects
2	9.832	1224651	$C_9H_{10}O_2$	2-Methoxy-4-vinylphenol	anti-inflammatory and anti-arthritic
3	12.148	274863	$C_{22}H_{34}F_2O_2$	2,5-Difluorobenzoic acid, 5-pentadecyl ester	
4	12.572	984401	$C_6H_{10}O_5$	.beta.-D-Glucopyranose, 1,6-anhydro-	
5	14.458	3234652	$C_8H_9NO_3$	3-Methyl-2-Nitrobenzyl alcohol	
6	15.019	1237434	$C_{10}H_{16}O_2$	Limonene dioxide 3	Anti-oxidant and anti-cancer activities.
7	15.174	1654171	$C_{14}H_{28}O_2$	Tetradecanoic acid	Antioxidant, cancer preventive, hypocholestrolemic, nematicide, lubricant
8	15.565	966423	$C_{11}H_{16}O_3$	2(4H)-Benzofuranone, 5,6,7,7A-tetrahydro-6-H	Antifungal, antialgal, antioxidant, antibacterial
9	15.866	1530996	$C_{20}H_{38}$	2,6,10- Trimethyl,14-Ethylene-14-pentadecne	
10	16.314	674052	$C_{20}H_{40}O$	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	
11	16.769	1876116	$C_{17}H_{34}O_2$	Pentadecanoic acid, 14-Methyl-, Methyl ester	
12	17.252	24028778	$C_{16}H_{32}O_2$	n- Hexadecanoic acid	
13	17.682	2592688	$C_9H_{12}O$	7-Methylene-9-oxabicyclo[6.1.0]non-2-ene	
14	18.059	2631785	$C_{11}H_{16}O$	Tricyclo[7.1.0.0[1,3]]decane-2-carbaldehyde	
15	18.422	3998306	$C_{11}H_{16}O$	Tricyclo[7.1.0.0[1,3]]decane-2-carbaldehyde	
16	18.639	122012427	$C_{20}H_{40}O$	2-Hexadecen-1-ol, 3,7,11,15-Tetramethyl-, [R-[R*,	
17	18.867	484465	$C_{18}H_{32}O_2$	9,12-Octadecadienoic acid (Z,Z)-	Anti inflammatory, hypocholestrolemic, antihistaminic, antiandrogenic, antiacne, cancer preventive, hepato protective, nematicide, anticrornary, antiecezemic,
18	18.941	677720	$C_{18}H_{30}O_2$	9,12,15-Octadecatrienoic acid, (Z,Z,Z)-	
19	19.078	121931	$C_{18}H_{36}O_2$	Octadecanoic acid	Antifungal, antitumor, antibacterial, hypocholesterolemic, antioxidant
20	20.961	407495	$C_{16}H_{32}O_2$	Decanoic acid, hexyl ester	
21	22.606	256905	$C_{19}H_{38}O_4$	5,5 Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	
22	23.078	192618	$C_{24}H_{38}O_4$	4,1 Di-n-octyl phthalate	
23	27.172	20433283	$C_{30}H_{50}$	Squalene	Anti-bacterial, anti-oxidant, anti-tumor, cancer preventive,immune stimulant, chemo preventive, lypoxylgenase inhibitor, diuretic
24	28.302	88501	$C_{20}H_{34}O$	Geranyl linalool isomer b	Sedative effect inducer, glutamatergic neurons inhibitor,anti-inflammatory, anticarcinogenic, antiseptic, hypocholesterolemic,
25	28.446	717161	$C_{20}H_{34}O$	Geranyl linalool isomer B	Sedative effect inducer, glutamatergic neurons inhibitor,anti-inflammatory, anticarcinogenic, antiseptic, hypocholesterolemic,
26	28.596	645315	$C_{20}H_{34}O$	Geranyl linalool isomer B	Sedative effect inducer, glutamatergic neurons inhibitor,anti-inflammatory, anticarcinogenic, antiseptic, hypocholesterolemic,
27	29.299	217867	$C_{15}H_{26}O$	2,6,10- Dodecatrien-1-ol, 3,7,11-trimethyl-	
28	29.415	329187	$C_{20}H_{34}O$	1,6,10,14-Hexadecatetraen-3-ol, 3,7,11,15-tetramethyl-, (E,E)-	
29	30.069	7201013	$C_{28}H_{48}O_2$	.gamma.-Tocopherol	
30	31.449	49207870	$C_{29}H_{50}O_2$	Vitamin E	Antioxidant,
31	33.351	4166075	$C_{28}H_{48}O$	5-Cholestene-3-ol, 24-methyl-	
32	34.010	3009196	$C_{29}H_{48}O$	Stigmasterol	Anti-asthma,anti-inflammatory, diuretic, anti-arthritic
33	35.364	4703540	:$C_{29}H_{50}O$	.gamma.-Sitosterol	Antioxidant, antibacterial and prophylactic activities
34	35.776	2344155	$C_{20}H_{40}O$	2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, [R-R	Modulation of transcription, anticonvulsant, anti-inflammatory, antioxidant

Table 2: Bioactive compounds obtained from GC-MS analysis of methanol extract of *Dialium guineense.*

Peak #	R. Time	Area	MF	Name	Pharmacologic activity
1	9.832	1224651	$C_9H_{10}O_2$	2-Methoxy-4-vinylphenol	anti-inflammatory and anti-arthritic, antimicrobial, antioxidant
2	3.084	1919135	$C_9H_8O_4$	6-Methoxycoumaran-7-ol-3-one	
3	15.000	20837403	$C_7H_{14}O_6$	Mome inositol	Antiseizures
4	15.872	6244869	$C_{20}H_{38}$	2,6,10-Trimethyl,14-ethylene-14-pentadecne	
5	16.320	985317	$C_{20}H_{40}O$	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	
6	16.776	5237455	$C_{17}H_{34}O_2$	Hexadecanoic acid, methyl ester	
7	16.975	22824915	$C_7H_{14}O_6$	Mome inositol	Antiseizures
8	17.249	16575927	$C_{16}H_{32}O_2$	n-Hexadecanoic acid	Antioxidant hypocholestrolemic, nematicide, antiandrogenic, hemolytic
9	18.500	2746051	$C_{19}H_{32}O_2$	9,12,15-Octadecatrienoic acid, methyl ester, (Z,Z,Z)-	Anti-inflammatory, hypocholesterolemic, cancer preventive, hepatoprotective, nematicide, antihistaminic, antieczimic, antiacne, anticoronary, antiandrogenic, antiarthritic
10	18.984	37983122	$C_{18}H_{30}O_2$	9,12,15-Octadecatrienoic acid, (Z,Z,Z)-	
11	19.107	6192056	$C_{18}H_{36}O_2$	Octadecanoic acid	Antifungal, antitumor, antibacterial ,hypochlesterolemic, antioxidant
12	22.619	1834752	$C_{19}H_{38}O_4$	Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	
13	23.085	1027142	$C_{24}H_{38}O_4$	Di-n-octyl phthalate	Antivenom
14	23.175	178653	C11H18	1- Cyclohexyl-1-pentyne	
15	27.180	205219305	$C_{30}H_{50}$	Squalene	Anti-bacterial, anti- oxidant, anti-tumor, cancer preventive,immune stimulant, chemo preventive, lypoxygenase inhibitor, diuretic
16	27.356	2684621	$C_{20}H_{34}O$	1,6,10,14-Hexadecatetraen-3-ol, 3,7,11,15-tetramethyl-, (E,E)-	Sedative effect inducer, glutamatergic neurons inhibitor,anti-inflammatory, anticarcinogenic, antiseptic, hypocholesterolemic,
17	27.770	507526	$C_{28}H_{58}$	Octacosane	
18	28.315	2370615	$C_{20}H_{34}O$	Geranyl linalool isomer b	Sedative effect inducer, glutamatergic neurons inhibitor,anti-inflammatory, anticarcinogenic, antiseptic,hypocholesterolemic,
19	29.184	1229221	$C_{15}H_{26}O$	Farnesol isomer a	Antiseizures, anticarcinogenic, antibacterial,
20	29.316	785307	$C_{15}H_{26}O$	2,6,10-Dodecatrien-1-ol, 3,7,11-trimethyl-	
21	29.428	1906707	$C_{20}H_{34}O$	Geranyl linalool isomer b	Sedative effect inducer, glutamatergic neurons inhibitor,anti-inflammatory, anticarcinogenic, antiseptic, hypocholesterolemic,
22	30.069	1146544	$C_{28}H_{48}O_2$	gamma.-Tocopherol	Anti-inflammatory, anticancer, chemopreventiveb ,gene regulatory
23	31.514	85317688	$C_{29}H_{50}O_2$	dl-.alpha.-Tocopherol	Antioxidant
24	35.422	6501675	$C_{29}H_{50}O$	beta.-Sitosterol	Anti- inflammatory,modulation of immune response, antiallergenic, antiproliferative, antiarthritic, anticancer
25	35.826	1909233	$C_{30}H_{50}O_2$	Lup-20(29)-ene-3,28-diol, (3.beta.)-	Analgesic, anti-inflammatory, antiviral, antineoplastic,antiHIV, antioxidant, antiallergen, hepatoprotective, cytotoxic, hypolipemic, antihypoxic, immune modulator, detoxicant
26	36.426	1391494	$C_{30}H_{50}O_2$	Lup-20(29)-ene-3,28-diol, (3.beta.)-	Analgesic, anti-inflammatory, antiviral, antineoplastic,antiHIV, antioxidant, antiallergen, hepatoprotective, cytotoxic, hypolipemic, antihypoxic, immune modulator, detoxicant
27	37.520	8600259	$C_{30}H_{50}O$	Lupeol	Antiasthma, anti-inflammatory, diuretic, anti-cancer, anti-arthritic, antivenom

respectively. Although both extracts prevented hepatomegaly in the treated groups, the methanol leaf extract of *M. lucida* had a greater preventive effect on the liver. In the evaluation of schizontocidal activity of the extracts in established infection (curative or Rane test), the results show a continuous increase in the parasitaemia level of the infected and untreated (negative) control group.

Table 3: Effect of methanol leaf extracts of *M. lucida* and D. *guineense* on organ weight.

GROUP	TREATMENT	WT OF LIVER(g)
1	Neg. Control	2.16 ± 0.24^{e}
2	200mg/kg LBO	1.40 ± 0.09^{cd}
3	400mg/kg LBO	1.31 ±0.15^{bcd}
4	600mg/kg LBO	1.13 ± 0.11^{abc}
5	200mg/kg DGA	1.12 ± 0.54^{ab}
6	400mg/kg DGA	1.57 ± 0.46^{d}
7	600mg/kg DGA	1.01 ± 0.58^{ab}
8	Pos. control	0.96 ± 0.67^{ab}
9	Naïve control	0.89 ± 0.21^{a}
10	Distilled (Dd)water	1.46 ± 0.41^{cd}

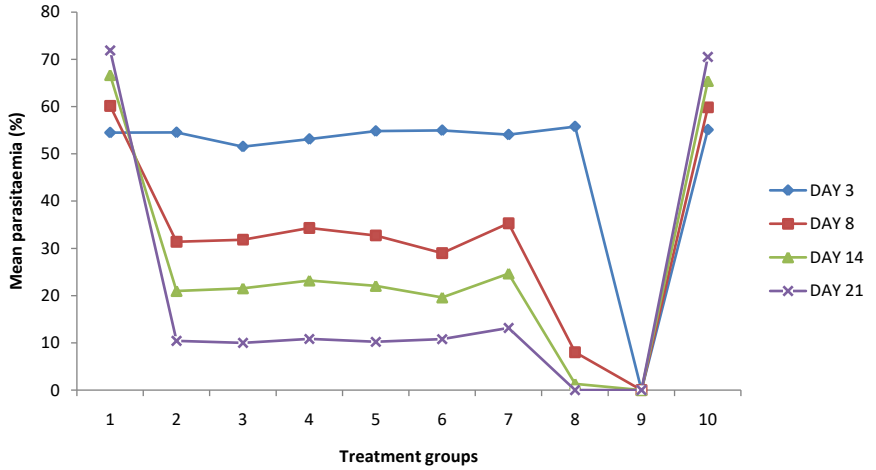

Figure 1: Effect of methanol leaf extracts of *M. lucida* and *D. guineense* on Parasitaemia level.

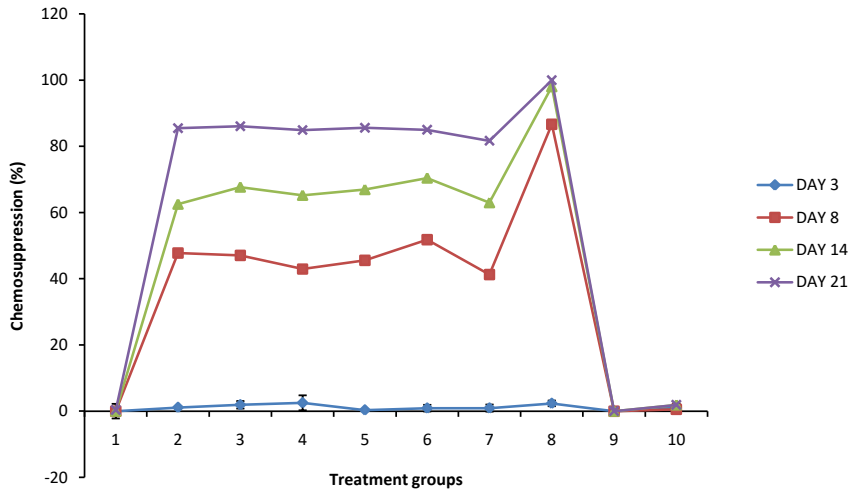

Figure2: Chemosuppressive effect of methanol leaf extracts of *M. lucida* and *D. guineense* on Parasitaemia level.

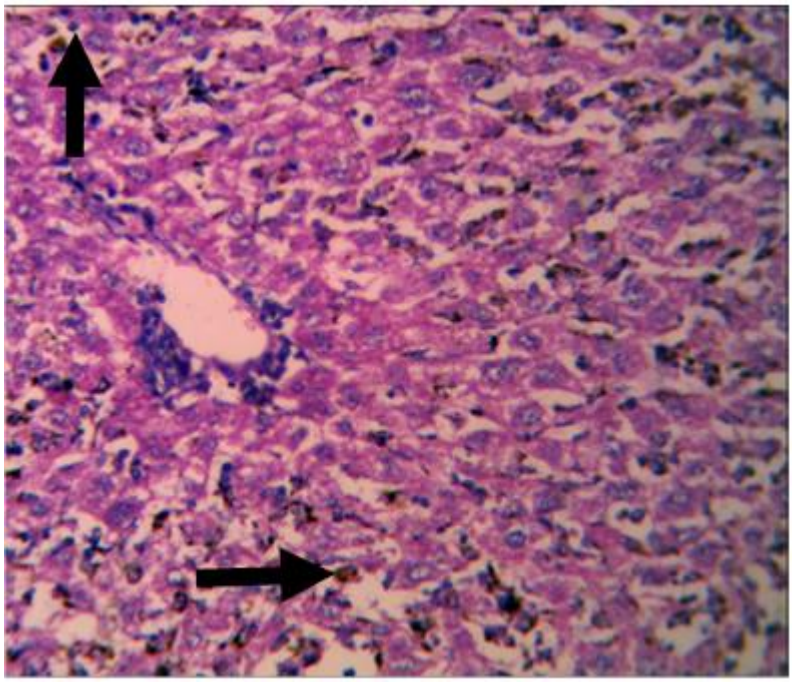

Plate 1: Photomicrograph of the liver of *Plasmodiumberghei* - infected mice in group 1: showing distorted hepatic architecture, necrosis, and widespread haemosiderosis seen as brown deposits indicated by the arrow. (HandE,Mg. X250).

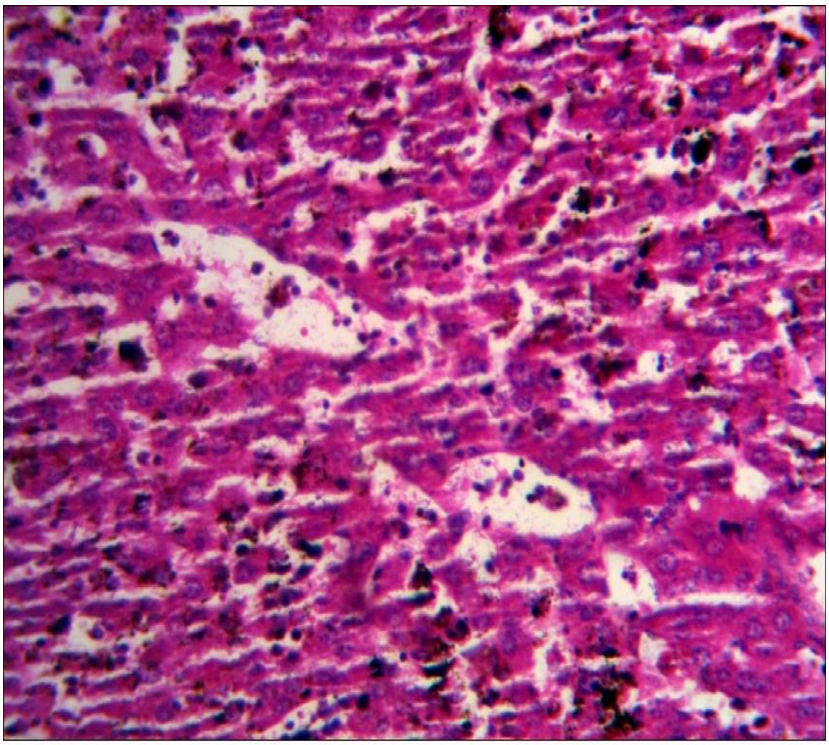

Plate 2: Photomicrograph of the liver of *Plasmodiumberghei* - infected mice in group 2 treated with 200mg/kg b.w of*M.lucida*showing perivascular cuffing and less severe haemosiderosis. (HandE, Mg. X250).

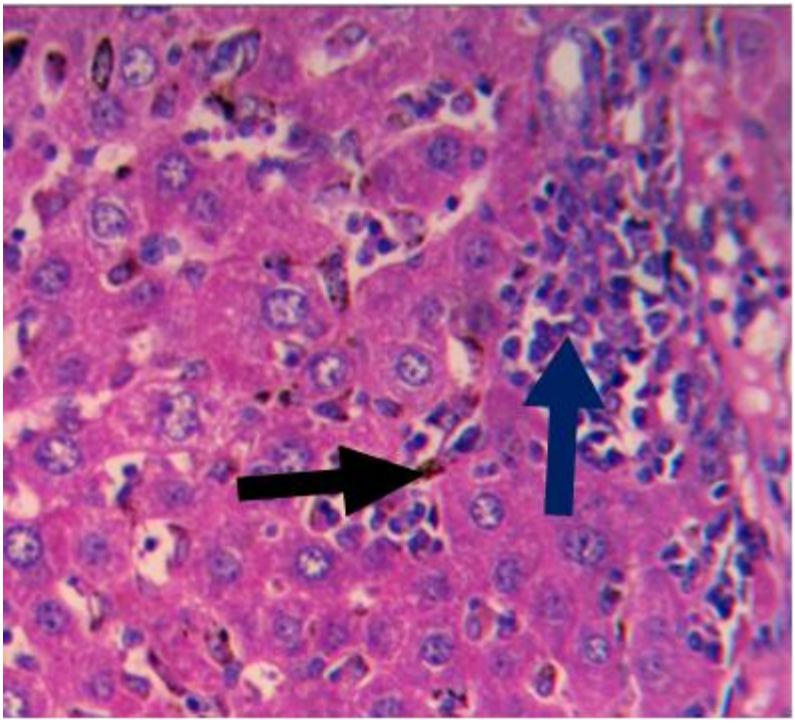

Plate 3: Photomicrograph of the liver of *Plasmodiumberghei* - infected mice in group 3 treated with 400mg/kg b.w of *M*. *Lucida* showing largely reduced deposition of Haemosiderin (black arrow) with mononuclear cell infiltration (blue arrow) with prominent kupffer cells (red arrow).(HandE, Mg. X250).

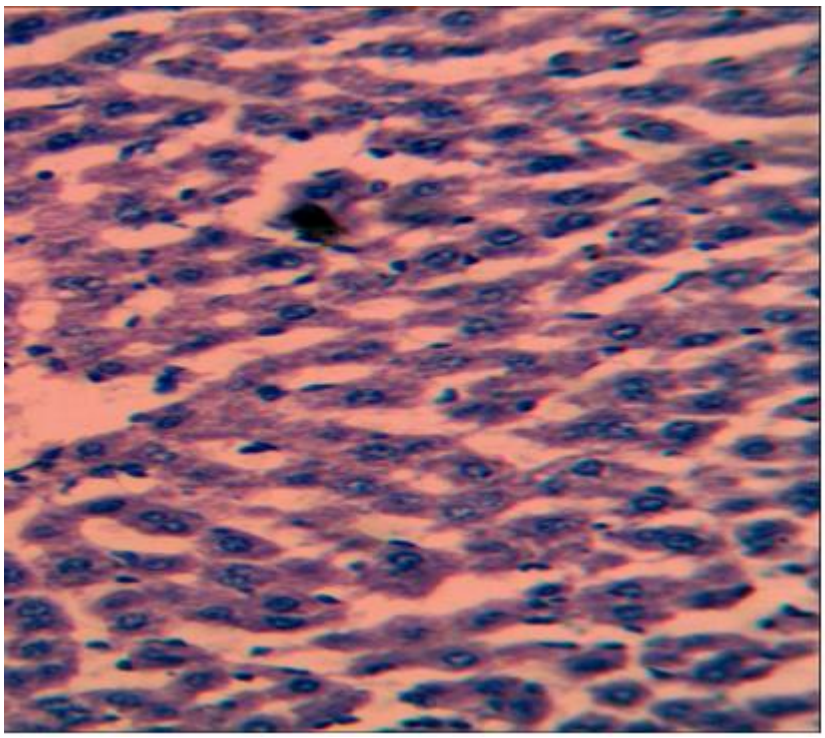

Plate 4: Photomicrograph of the liver of *Plasmodiumberghei* - infected mice in group 4 treated with 600mg/kg b.w of *M*. *lucida*:No significant observable findings.(HandE, Mg. X250).

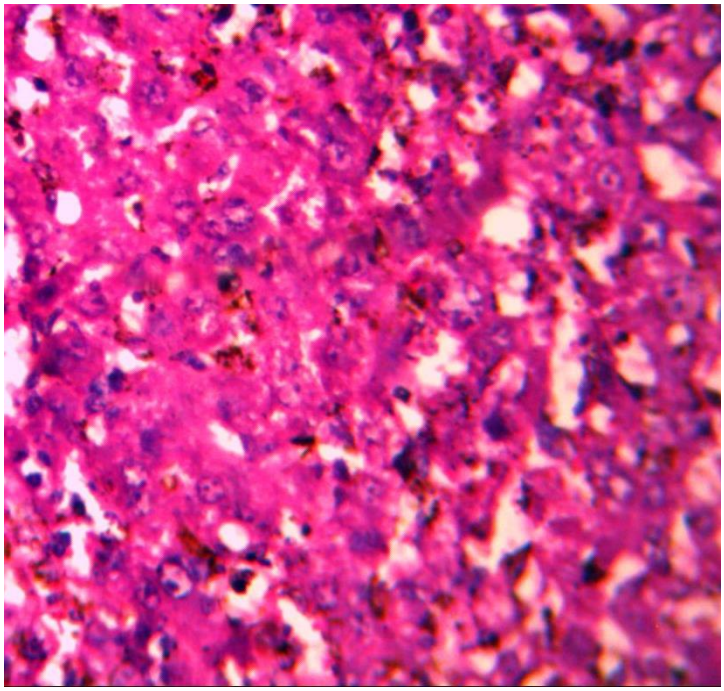

Plate 5: Photomicrograph of the liver of *Plasmodiumberghei* - infected mice in group 5 treated with 200mg/kg b.w of *D. guineense*: Distorted hepatic cords, vacoulation of hepatocytes, necrosis and moderate haemosiderosis displayed. (HandE, Mg. X250).

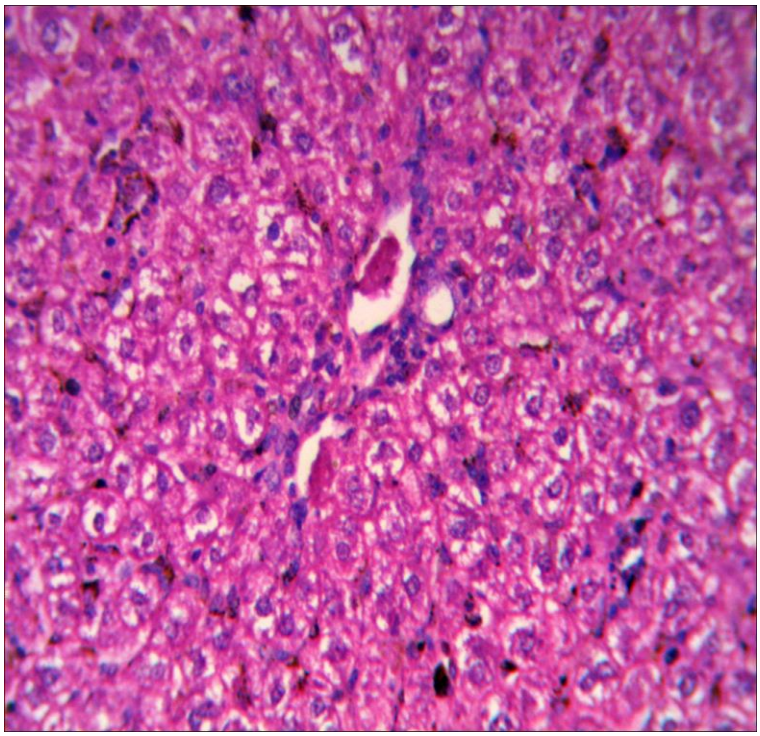

Plate 6: Photomicrograph of the liver of *Plasmodiumberghei* - infected mice in group 6 treated with 400mg/kg b.w of *D. guineense* showing vacoulation of hepatocytes and distorted hepatic cords.(HandE, Mg. X250).

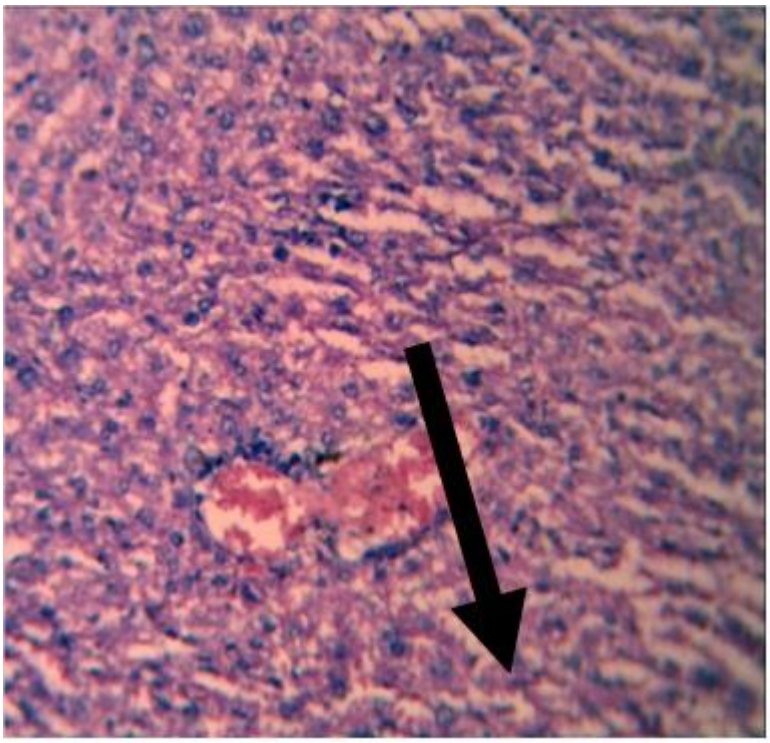

Plate 7: Photomicrograph of the liver of *Plasmodiumberghei* - infected mice in group 7 treated with 600 mg/kg b.w of *D*. guineense: observed to have congested central vein (HandE, Mg. X250).

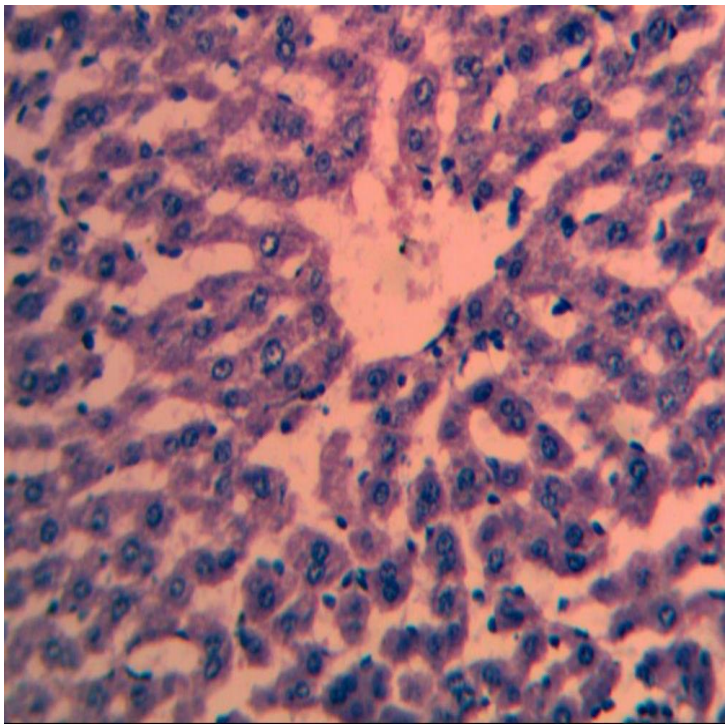

Plate 8: Photomicrograph of the liver of *Plasmodiumberghei* - infected mice in group 8 treated with 20 mg/kg b.w of Artesunate: No significant observable findings in the liver of mice tested in group 8 (HandE, Mg. X250).

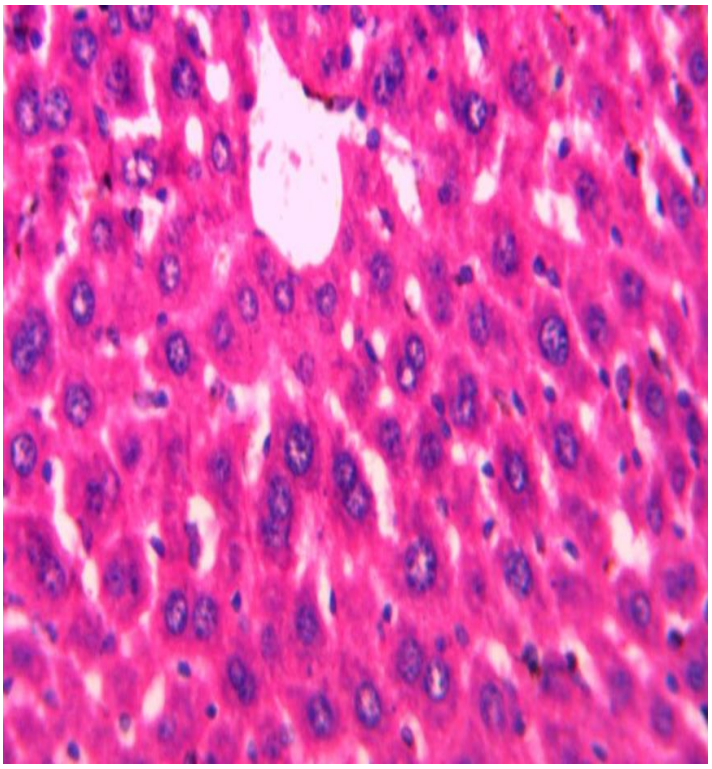

Plate 9: Photomicrograph of the liver of naïve mice in group 9. No significant observable findings were made in the liver of mice examined in group 9 (Naïve mice). (HandE, Mg. X250).

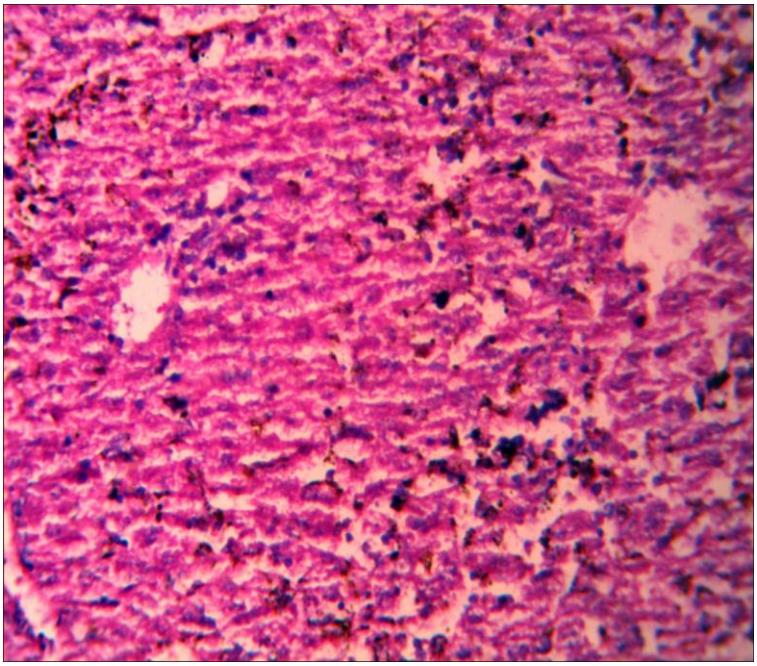

Plate 10: Photomicrograph of the liver of *Plasmodiumberghei* - infected mice in group 10 treated with distilled water; showing extensive necrosis of hepatocytes, distorted histoarchitecture and presence of haemosiderin deposits (HandE, Mg. X250).

There was statistically significant ($p < 0.05$) parasitaemia suppression of 86.06 ± 1.69 % and 85.63 ± 0.93 by 400mg/kg body weight of *M. lucida* and 200mg/kg body weight of *D. guineense* respectively. Present findings are consistent with earlier reports by Idowu *et al*.(2010) and Ebiloma *et al*. (2011) substantiating the curative potentials of Nigeria medicinal plants against established plasmodial infections. The pathologic process of malaria infection and its complications involves cytoadherenece and sequestration in microcirculation of vital organs of the body interfering with micro-circulatory flow and host tissue metabolism. The results obtained from the histology (Plates 1-10) of the tissues examined showed that the liver of the infected and untreated mice in groups 1 and 10 respectively displayed significant hepatic damage from physical observation and characterized by distorted hepatic architecture, mononuclear cell aggregation, necrosis and widespread deposition of haemosiderin. The consequences of microcirculatory obstruction are activation of the vascular endothelial cells and reduced oxygen (Ekaidem and Akpan, 2016). An ultra structural study reported an association between high PRBC load in the livers of malaria patients with hepatomegaly (Viriyavejakul *et al*., 2014). The immune response in the liver to PRBCs primarily involves the activation of Kupffer cells. In the histological evaluation, the severe lesions induced on the liver tissues of the untreated groups were greatly reduced close to normalcy by the extracts and standard drug when compared with the naïve mice examined.

Conclusion

The methanol leaf extracts of *Dialium guineense* and *Morinda lucida* exhibited comparatively similar and great antimalarial activity in *Plasmodiumberghei* infected mice as observed in their ability to reduce parasitaemia levels, as well as having protective effect on the liver by restoring their histoarchitecture, establishing the pharmacological basis for their ethnomedicinal use as remedies for malaria. In view of the pharmacological activities and ethnomedical use of *Morinda lucida* and *D. guineense,* thereis no doubt that they are very potent medicinal plants and in combination with other potential anti-malarial plants may therefore be resourceful for discovery of new chemotherapeutic agents.

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