Histomorphological And Biochemical Evaluation Of Herbal Cocktail Used In Treating Malaria On Kidneys Of Adult Wistar Rats.

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Abstract: Malaria continues to constitute a menace to Africa and the world at large and it remains a major problem in Nigeria with pregnant women and children mostly affected by this disease. This study investigates the histomorphology and biochemical activity of a herbal cocktail and its constituent extract on the kidneys of Plasmodium berghei infected Wistar rats. Thirty-five Wistar rats weighing an average of 200 g were divided into seven groups. Each group consisting of five rats were used in this study. The cocktail and aqueous extracts of Mangifera indica, Carica papaya, and Citrus limon were orally administered to the infected Wistar rats at a dose of 100 mg/kg/day for seven days while the aqueous leaf extract of Azadirachta indica was administered at a dose of 10 mg/kg/day. Blood was collected into anticoagulated bottles for biochemical assays for renal function tests while the kidneys were immediately excised and transferred into neutral buffered formalin for histological processing. Findings in this study showed that the aqueous extract of C. papaya and the cocktail were the most effective as no pathological lesions associated with malaria were observed in the kidneys, however extracts of M. indica was observed to be the least potent. Variations were observed in the electrolyte values obtained in different groups. Blood Urea values were observed to be normal among all groups with the exception of the group administered with aqueous leaf extract of C. papaya on comparison with the uninfected control group ($p<0.03$). Creatinine values were within the normal range among the various test groups on comparison with the uninfected control group ($p>0.05$). In conclusion, plants used in this study have potential antiplasmodial activities which could be exploited in malaria therapy.

Keywords: Cocktail, Creatinine, Electrolytes, Malaria, Plasmodium berghei, Urea,

INTRODUCTION

Malaria is an endemic disease of public health concern common in the tropics including the Sub- Saharan Africa [1]. It is caused by parasites of the genus Plasmodium and it is one of the leading infectious diseases in many tropical regions, including Nigeria. Five species are known to be pathogenic to man and they include *Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, Plasmodium knowlesi* and *Plasmodium falciparum*, with the latter being the most predominant in Africa and deadliest [2]. Until now, malaria is still a health problem worldwide, especially in tropical countries like Africa and Asia and about 3.3 billion people worldwide are at risk of malaria [3]. In 2017 an estimate of $2.2 billion out of the $3.1 billion allocated for the control and elimination of malaria was spent in the WHO African region [4]. A total of 219 million estimated cases of malaria were reported in 2017 with about 92% occurring in the WHO African region; 435,000 malaria associated death occurred globally with children under the age of five accounting for about 61% (266,000) of all malaria death worldwide. Eighty percent of the global death associated with malaria were concentrated in 17 countries with seven of the countries accounting for 53% of the global malaria death in 2017; Nigeria (19%), Democratic Republic of the Congo (11%), Burkina Faso (6%), United Republic of Tanzania (5%), Sierra Leone (4%), Niger (4%) and India (4%) [4]. Many Nigerians especially the rural dwellers are at risk of contracting malaria each year, making them dependent on the usage of traditional malaria remedies in the treatment of malaria. The menace of malaria remains evident in Africa with Nigeria largely imparted by this disease as it continually causes morbidity and mortality with children under the age of five and pregnant women being the most vulnerable [4]. The use of plant remedies has steadily increased worldwide in recent years, as well as the search for new phytochemicals that potentially could be developed as useful drugs for the treatment of malaria and other infectious diseases [5]. With Nigeria having a rich flora diversity, various plant with antiplamodial potential could be harnessed in combating malaria. Previous studies have shown that more than 1200 medicinal plants from 160 families are used worldwide to treat malaria or fever [6]. and traditional herbal medicines have been reportedly used in treating malaria for thousands of years in various regions of the world [7]. Although

effective anti-malarial drugs are available, the disease remains a threat to people living in endemic areas who have no proper and prompt access to effective drugs, access to pharmacies and health facilities, as well as drug costs, are major obstacles [8]. *Azadirachta indica, Mangifera indica, Carica papaya* and *Citrus limon* have been reported to possess antiplasmodial potentials [9], [10]. The Neem tree, *Azadirachta indica* (Meliaceae) is native to Southeast Asia and grows in many countries throughout the world [11],[12]. *Carica papaya*, also traditionally known as pawpaw or papaya, is a tree-like herbaceous plant belonging to the family of Caricaceae [13],[14]. *C. papaya* is widely cultivated in several tropical, sub-tropical and temperate regions, including Australia, Brazil, China, Hawaii, Malaysia and India [15]. Different parts of the plant (fruits, leaves, barks, roots, flowers, seeds, and latex) as well as some of their extracts have been traditionally used worldwide in folk medicine to treat a wide range of ailments in humans [16],[17]. The leaf and stem are acclaimed to be one of the most used medicinal plants in traditional practice [18]. Various traditional herbs have been tested and used in the prevention and treatment of malaria including, leaves of *C. papaya, A. indica* popularly called Dongoyaro in Nigeria, *M. indica* and *C. limon* [19],[10]. This study evaluates the histomorphology and biochemical activity of the cocktail and its constituent extracts in *P. berghei* infected Wistar rats.

METHODOLOGY

Experimental animals

This experiment was conducted at the University of Benin, Benin City, Nigeria. Adult Wistar rats weighing an average of 200 g, obtained from the Anatomy department of the University of Benin animal house were used as experimental animals for this study. The animals were kept in ventilated cages and were fed with growers mash obtained from Edo Feeds and Flour Mill Limited, Ewu, Edo State, Nigeria throughout the duration of this study.

Parasite and infection

The rodent malaria parasite used for infection was the chloroquine-sensitive Plasmodium berghei (NK 65 strain) obtained from the Institute of Advance Medical Research and Training (IMRAT), University of Ibadan, Nigeria. Thirty-five adult Wistar rats weighing an average of 200 g were divided into seven groups consisting of five rats each. The first group (Group I) is the uninfected control group that was administered with distilled water only while the second group labelled (Group II) were the infected untreated group consisting of adult Wistar rats infected with P. berghei and administered with distilled water only. The third group labelled (Group III) were infected with P. berghei and treated with the herbal cocktail while the fourth group (Group IV) consisted of infected rat administered with aqueous leaf extract of A. indica. The infected rats in the fifth group (Group V) were administered with aqueous leaf extracts of M. indica while the infected rats in the sixth group (Group 6) were treated with extracts of C. papaya. The last group (Group 7) consist of infected rats administered with aqueous juice extract of C. limon. Administration of the cocktail and the constituent extract spanned a period of seven days.

Inoculation procedure

Plasmodium berghei infected blood was obtained from donor mice with rising parasitemia of ≥25% and diluted with phosphate buffer saline to 10^8parasitized erythrocytes/ml. Healthy Wistar rats were inoculated intraperitoneally with preparation of the parasitized red blood cell preparation [20].

Percentage parasitaemia determination

Thin blood films were made from the blood collected from the tails of the infected Wistar rats and were stained with Giemsa stain and viewed with oil immersion objectives. The percentage parasitaemia was determined for each infected rat as described by Innocent et al, (2017) [21]. Rats with parasitaemia of ≥25%, were treated with the cocktail or individual extracts on the seventh post-infection day.

Cocktail and individual extract

Plant samples were collected and identified by a plant Taxonomist from Plant Biology and Biotechnology Department of the University of Benin, Benin City, Nigeria as A. indica (family Meliaceae), M. indica (family Anacardiaceae), C. papaya (family Caricaceae), and C. limon (family Rutaceae) [9]. The cocktail, C. limon fruit extract and aqueous leaf extracts of M. indica and C. papaya were administered to respective groups at a dose of 100 mg/kg/body weight, while aqueous leaf extract of A. indica was administered at 10 mg/kg/body. Samples obtained upon necropsy were histologically assessed while selected renal markers were assayed from the plasma obtained.

Histopathology studies

The Kidneys were fixed in 10% neutral buffered formalin and processed for light microscopic study using an automatic tissue processor machine (Shandon 2000, Frankfurt, Germany), and were examined microscopically using the Olympus microscope at magnifications of X100 and X400 respectively [22].

Biochemical studies

Biochemical markers associated with renal functions were determined using the plasma obtained from the Wistar rats upon necropsy after seven days of treatment. Sodium (Na^+), Potassium (K^+), Chloride (CL^-), Bicarbonate (HCO_3^-), Urea and Creatinine were assessed using Cobas C 111 Chemistry auto-analyser.

Statistical Analysis

Data obtained were analysed using statistical package for social sciences (SPSS) version 19.0 and were expressed as mean ± SD. Test of significance was calculated using paired Student's t-test. $p<0.05$ was considered to be significant.

HISTOPATHOLOGICAL STUDIES

Findings in this study indicated that the aqueous leaf extract of C. papaya and the cocktail were the most efficacious as pathological lesions were not observed in the kidney sections of the rats stained with Haematoxylin and Eosin. However, aqueous leaf extracts of M. indica was observed to be the least potent. Photomicrographs of the uninfected control group (Group I) appeared normal as endemic inflammation was not observed, the renal cortex showed normal glomeruli with normal mesangial cells and capsular spaces, while the renal tubules including the distal and proximal convoluted tubules appeared normal (Figure 1). Kidney sections of the

infected-untreated group (Group II) showed moderately normal architecture (Figure 2), the renal cortex showed normal glomeruli with normal mesangial cells and capsular spaces, however, some of the renal tubules contained eosinophilic cast while the interstitial spaces appeared normal (Figure 2). Histology of the kidneys of rats administered with the cocktail (Group III) showed moderately normal architecture of the renal cortex and tubules as seen in lower magnification of X100 (Figure 3), the interstitial spaces also appeared normal as no pathological lesion was observed (Figure 3). Kidney sections of rats administered with aqueous leaf extract of A. indica (Group IV) showed a moderate architecture with the renal cortex showing normal glomeruli with normal mesangial cells and capsular spaces, however a focal area of moderately accumulated fluid was observed adjacent to the glomerulus (Figure 4), most of the renal tubules appear normal, however, some tubules show tubular necrosis (Figure 4). Comparison between the uninfected group administered with distilled water only and the groups treated with the aqueous leaf extract of M. indica (Group V) showed the presence of mild to moderate aggregate of inflammatory cells within the interstitial spaces (Figure 5) however, the renal cortex showed normal glomeruli with normal mesangial cells and capsular spaces (Figure 5). Kidney histology of the group administered with aqueous leaf extract of C. papaya (Group VI) was observed to be normal on comparison with the uninfected untreated group administered with distilled water only (Figure 6), the renal cortex showed normal glomeruli with normal mesangial cells and pathological lesion was not seen (Figure 6). Photomicrographs of the kidney sections of the group administered with the aqueous juice extract of C. limon (Group VII) appeared normal; however, there was presence of eosinophilic cast within the renal tubules (Figure 7).

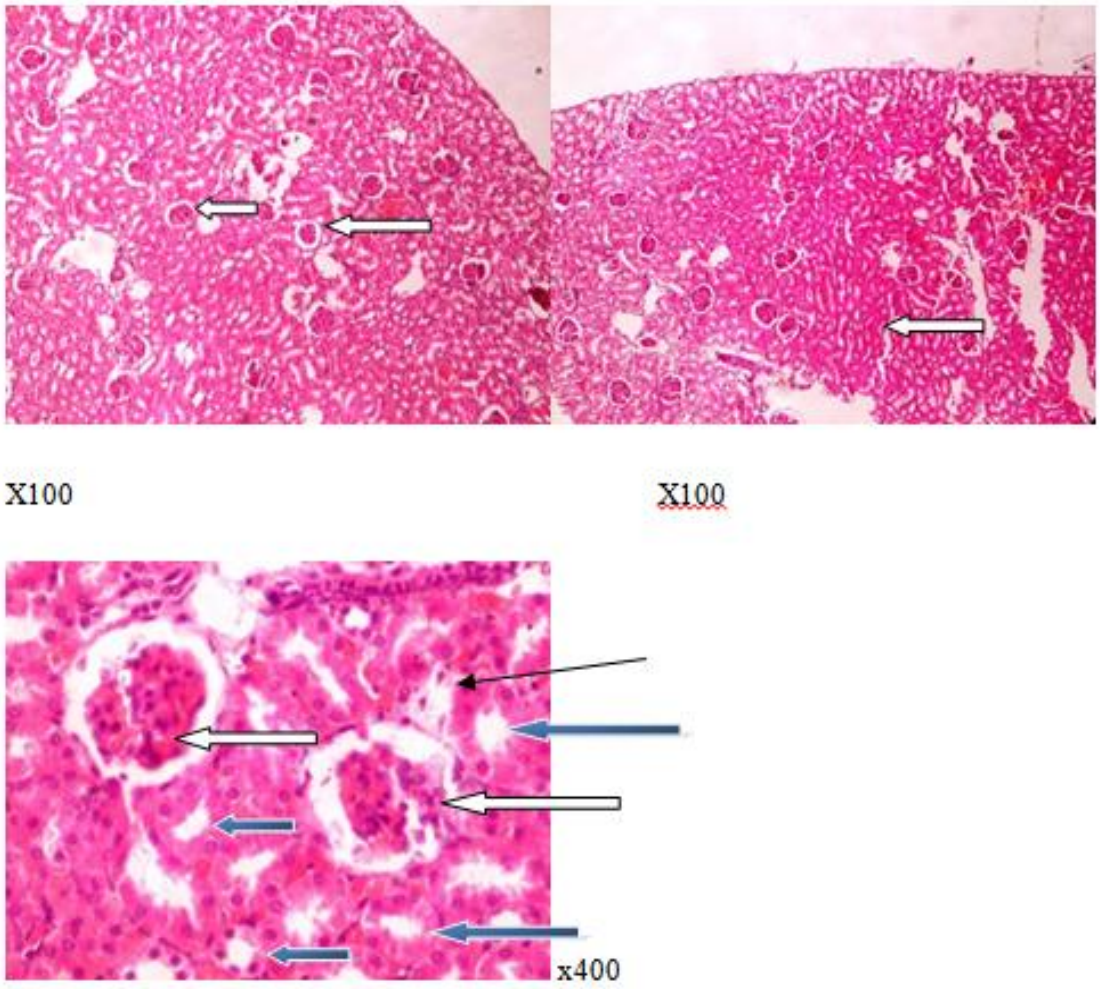

Figure 1. *Photomicrographs of kidney sections showing normal architecture as seen in lower magnification x100, the renal cortex show normal glomeruli with normal mesangial cells and capsular spaces (white arrow), the renal tubules including Distal convoluted tubules and Proximal convoluted tubules appear normal, (blue arrow), the interstitial spaces appear normal (slender arrow). Pathological lesion was not detected.*

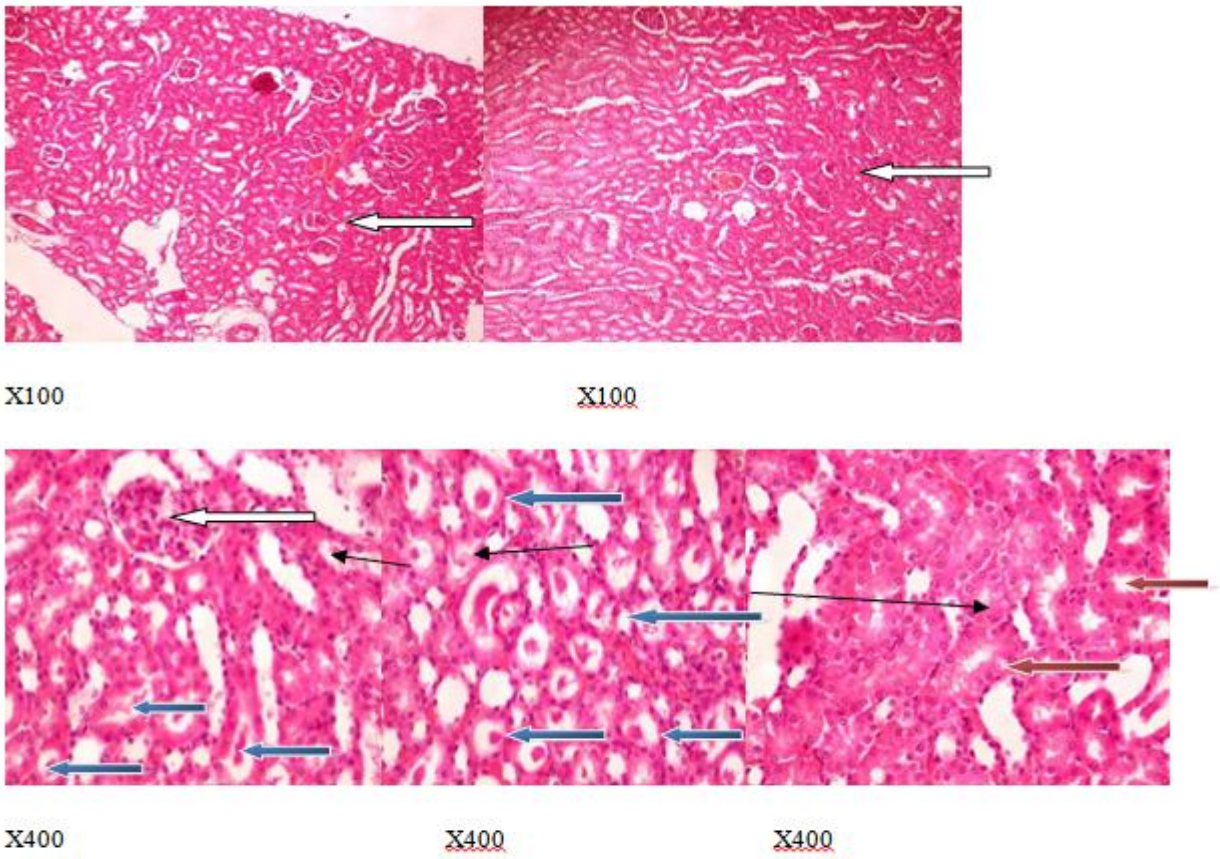

Figure 2 *Kidney sections of the infected-untreated rats administered with distilled water only showing moderately normal architecture as seen in lower magnification x100, the renal cortex show normal glomeruli with normal mesangial cells and capsular spaces (white arrow), the renal tubules show eosinophilic cast within the tubules (blue arrow), some other tubules are normal (red arrow), the interstitial spaces appear normal (slender arrow).*

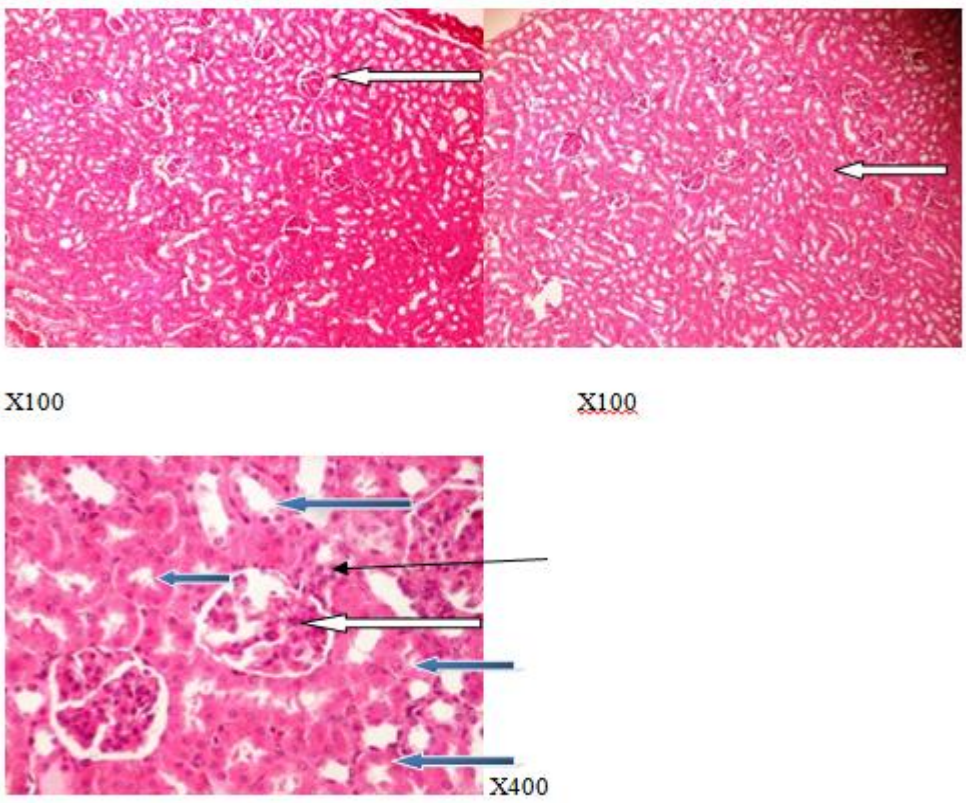

Figure 3. *Kidney sections of infected rat administered with the cocktail showing normal architecture as seen in lower magnification x100, the renal cortex show normal glomeruli with normal mesangial cells and capsular spaces (white arrow), the renal tubules including Distal convoluted tubules and Proximal convoluted tubules appear normal, (blue arrow), the interstitial spaces appear normal (slender arrow). There is absence of pathological lesion.*

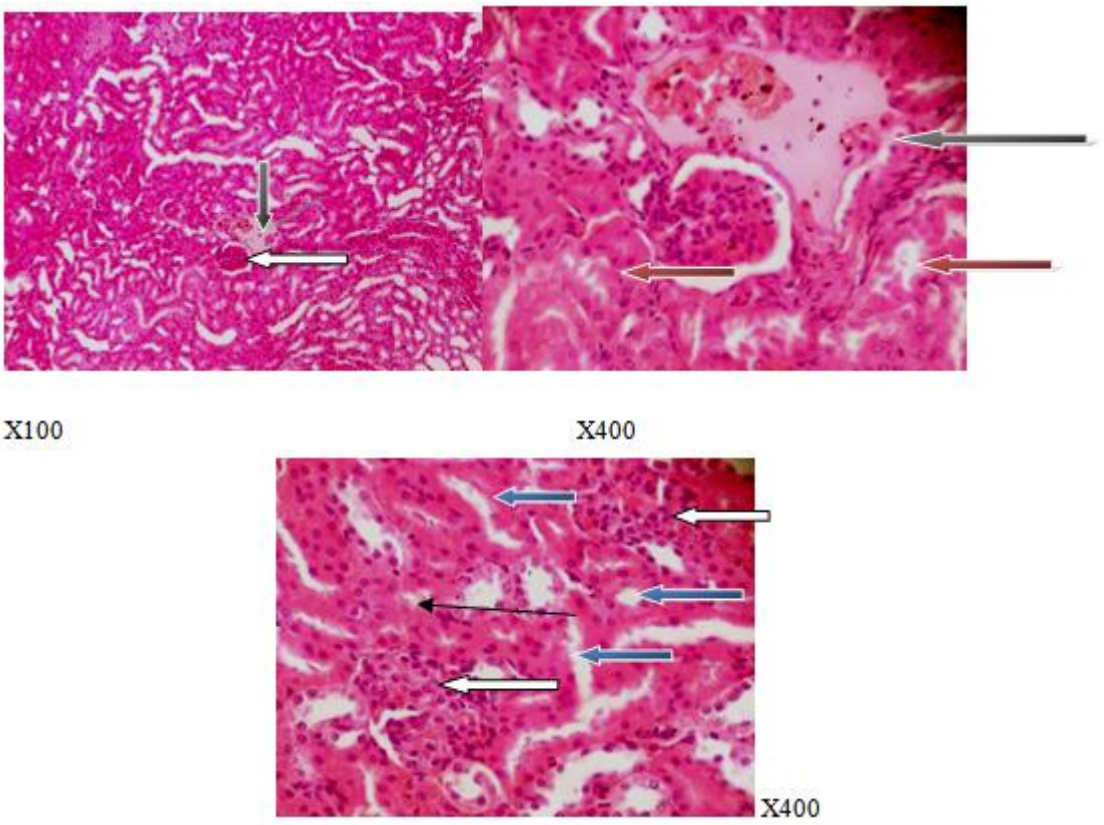

Figure 4 *Photomicrographs of kidney sections of rat treated with aqueous extract of A. indica showing moderately architecture, the renal cortex showed normal glomeruli with normal mesangial cells and capsular spaces (white arrow), there is focal area of moderately accumulated fluid seen adjacent to the glomerulus (black arrow), the renal tubules appear normal, (blue arrow), however, some tubules show tubular necrosis (red arrow), the interstitial spaces appear normal (slender arrow).*

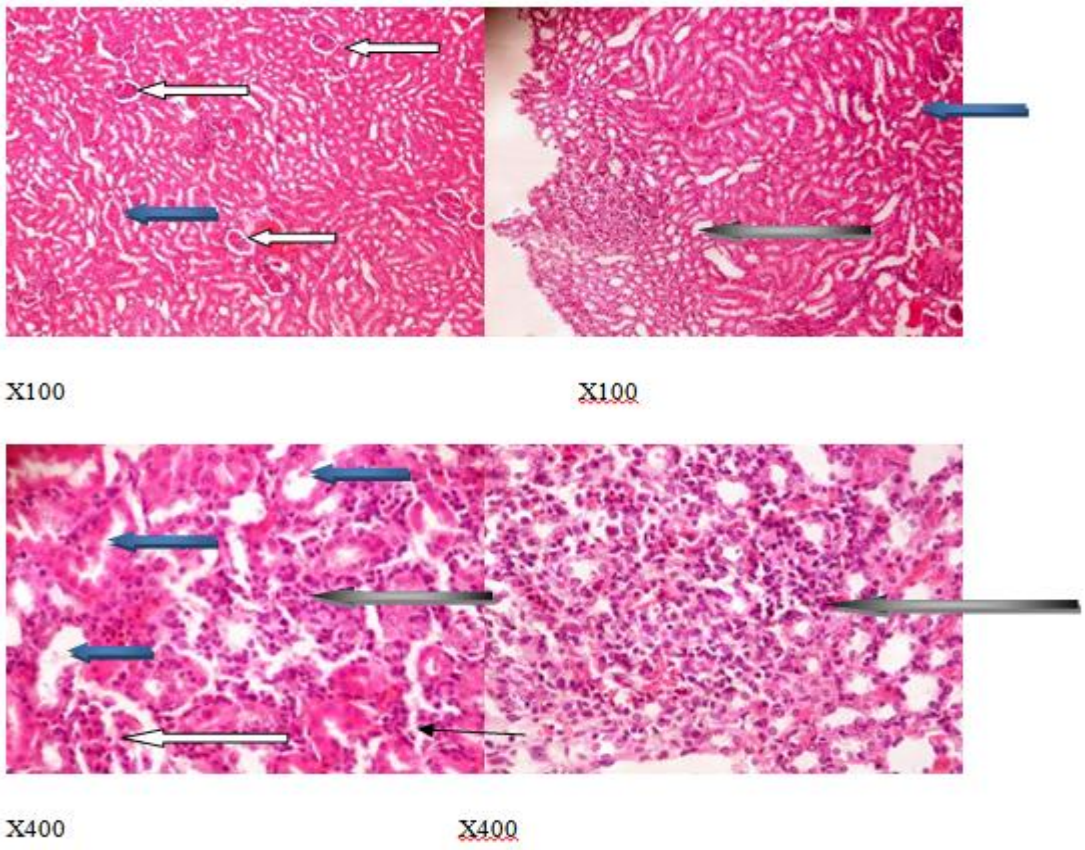

Figure 5. *Photomicrographs of kidney sections of rats administered with aqueous leaf extractof M. indicashowing normal architecture as seen in lower magnification x100, the renal cortex show normal glomeruli with normal mesangial cells and capsular spaces (white arrow), the renal tubules appear normal, (blue arrow), the interstitial spaces show focal area of mild to moderate aggregate of inflammatory cells (slender arrow).*

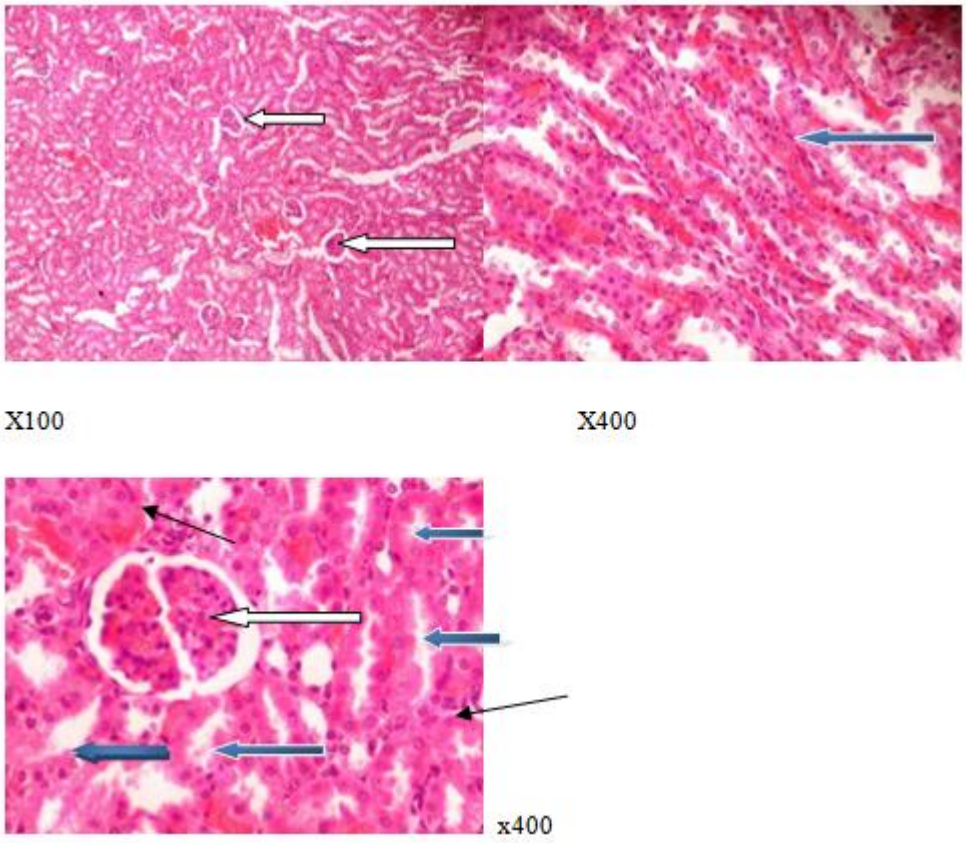

Figure 6. *Photomicrographs of kidney sections of rats treated with aqueous leaf extract of C. papaya showing normal architecture as seen in lower magnification x100, the renal cortex showed normal glomeruli with normal mesangial cells and capsular spaces (white arrow), the renal tubules including Distal convoluted tubules and Proximal convoluted tubules appear normal, (blue arrow), the interstitial spaces appear normal (slender arrow), There is also absence of pathological lesion.*

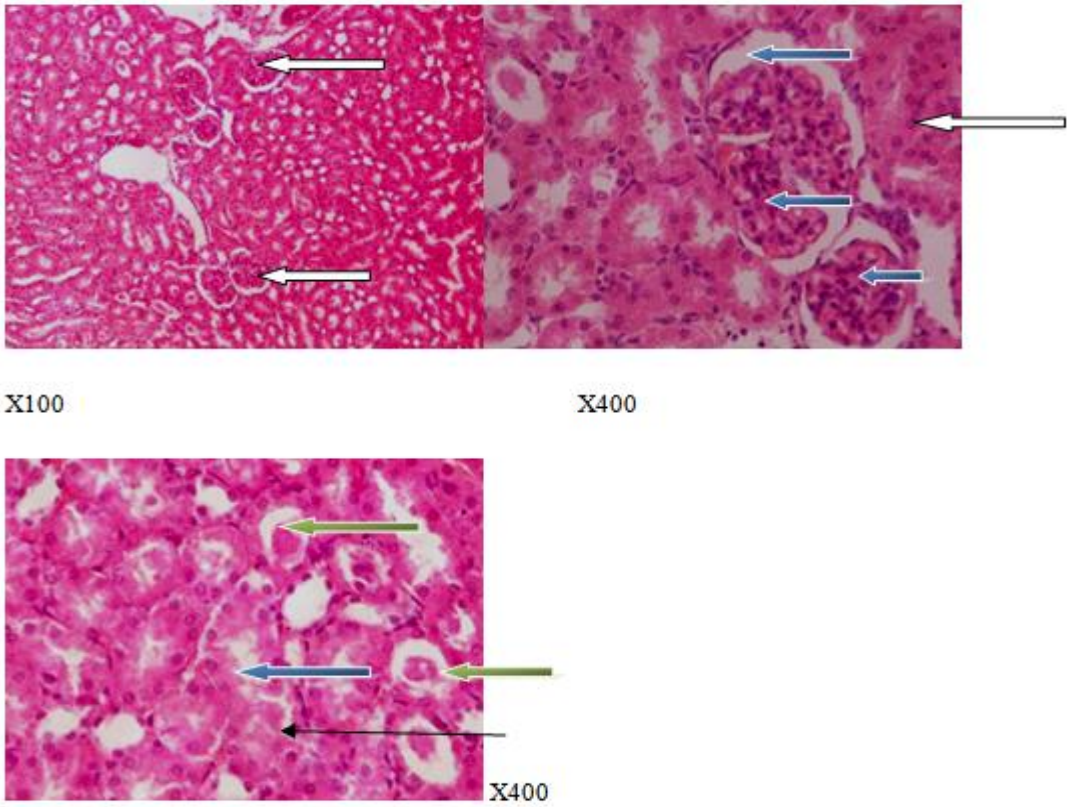

Figure 7. *Photomicrographs of kidney sections of rats administered with C. limon showing normal architecture as seen in lower magnification x100, the renal cortex showed normal glomeruli with normal mesangial cells and capsular spaces (white arrow), most of the renal tubules appear normal (blue arrow), some shows presence of eosinophilic cast within their lumen (green arrow), the interstitial spaces appear normal (slender arrow).*

BIOCHEMICAL STUDIES

Table 1.0 shows the mean and standard deviation of the electrolyte values obtained in all groups. Table 2.0 shows the comparative analysis of the electrolyte values obtained in all group administered with the cocktail or either extract contained therein. Statistical variations were observed in the Sodium (Na^+) values of rats administered with the extracts of *M. indica, C. papaya, C. limon* when compared with the uninfected control group administered with distilled water only ($p<0.03$). Table 2.0a. Comparison of the (Na^+) values in the group administered with the cocktail or either of the extract with the infected untreated group administered with distilled water only showed a statistically significant difference in rats administered with *M. indica* and *C. limon* ($p<0.04$) while those administered with *A. indica* and *C. papaya* was not statistically significant ($p> 0.05$). Table 2.0a. Groups administered with aqueous extract of *M. indica* and *C. limon* showed a significant statistical difference in (Na^+) values on comparison with the group administered with the cocktail $p<0.04$ while the groups administered with *A. indica* and *C. papaya* was not statistically significant $p> 0.05$ Table 2.0b. showed absence of significant variations among individual extract upon comparison with each other ($p>0.05$) table 2.0b. Potassium (K^+) values were observed to be stable in the infected untreated group and group administered with aqueous leaf extract of *M. indica* when compared with the uninfected control group ($p>0.05$) Table 2.0a However, showed statistical significant difference in the K^+ values among the group treated with the cocktail, aqueous extract of *A.indica, C. papaya* and *C. limon* ($p<0.01$) Table 2.0a. Comparison of different groups administered with the cocktail or either extract was not significant upon comparison with the infected control group ($p>0.05$) Table 2.0a. Comparison of the K^+ values among various extracts and the groups administered with the cocktail was not statistically different ($p> 0.05$) Table 2.0b. Chloride (Cl^-) values were observed to be normal across board and there was also absence of statistical variation observed in all groups with the exception of the group administered with the cocktail upon comparison with the infected untreated group ($p<0.04$) Table 2.0a. There was no statistically significant variation in the Bicarbonate (HCO_3^-) values in the various groups upon comparison ($p>0.05$). Table 2.0 Table 3.0 shows the mean and standard deviation of Urea and Creatinine values obtained in all groups. Table 4.0 shows the comparative analysis of urea and creatinine values obtained in all groups administered with the cocktail or various individual extracts. Urea value were observed to be normal among all groups with the exception of the group administered with aqueous leaf extract of *C. papaya* on comparison with the uninfected control group administered with distilled water only ($p<0.03$). Table 4a. Creatinine values were observed to be within the normal range among the various test groups on comparison with the uninfected control group ($p>0.05$) Table 4a, however, statistically significant variations were observed among the groups administered with the aqueous extract of *M. indica, C. papaya* and *C. limon* on comparison with the group administered with the cocktail ($p<0.04$). Table 4b.

BIOCHEMICAL STUDIES

TABLE 1.0 *Mean and standard deviation of electrolytes obtained in all groups.*

Parameter	Negative	Infected-untreated group	Cocktail	*Azadirachta indica*	*Mangifera indica*	*Carica papaya*	*Citrus limon*
Na+	141±2	142±1	142±1	144±1	149±2	148±2	150±2
K+	3.6±1	4.8±0.5	4.7±0.3	5.1±0.1	4.5±0.5	4.8±0.2	4.6±0.2
Cl-	92±1	93±7	96±1	92±3	96±2	88±8	96±2
HCO_3^-	27±1	27±1	26±1	29±2	29±2	31±2	29±3

TABLE 2.0a *Comparative analysis of electrolytes obtained in all groups administered with the cocktail or various individual extracts.*

Parameter		Negative control vs Infected untreated group	Negative control Vs Cocktail	Negative control Vs *Azadirachta indica*	Negative control Vs *Mangifera indica*	Negative control Vs *Carica papaya*	Negative control Vs *Citrus limon*	Infected untreated group Vs Cocktail	Infected untreated group Vs *Azadirachta indica*	Infected untreated group Vs *Mangifera indica*	Infected untreated group Vs *Carica papaya*	Infected untreated group Vs *Citrus limon*
Na+	"t"	0.00	0.00	-0.90	-2.47	-2.12	-2.82	0.00	-1.41	-3.13	-2.68	-3.58
	"p"	0.50	0.50	0.23	0.04*	0.03*	0.03*	0.03*	0.15	0.04*	0.06	0.04*
K+	"t"	-2.20	3.67	-1.50	-1.8	-6.0	-5.0	0.17	-0.60	0.42	0.00	0.37
	"p"	0.08	0.03*	0.02*	0.11	0.01*	0.02*	0.43	0.31	0.35	0.50	0.37
Cl-	"t"	0.14	-2.82	0.57	-1.79	0.50	1.79	-0.42	0.13	-0.41	0.47	-0.41
	"p"	0.45	0.05	0.31	0.10	0.33	0.11	0.04*	0.45	0.36	0.34	0.36
HCO_3^-	"t"	0.00	1.34	-0.89	-0.89	0.87	0.78	0.71	-0.89	-0.89	-1.79	-0.63
	"p"	0.50	0.16	0.23	0.23	0.33	0.21	0.28	0.23	0.23	0.11	0.30

TABLE 2.0 b *Comparative analysis of electrolytes obtained in all groups administered with the cocktail or various individual extracts.*

Parameter		Cocktail Vs *Azadirachta indica*	Cocktail Vs *Mangifera indica*	Cocktail Vs *Carica papaya*	Cocktail Vs *Citrus limon*	*Azadirachta indica vs Mangifera indica*	*Azadirachta indica vs Carica papaya*	*Azadirachta indica vs Citrus limon*	*Mangifera indica vs Carica papaya*	*Mangifera indica vs Citrus limon*	*Carica papaya Vs Citrus limon*
Na+	"t"	-1.41	-3.13	-2.68	-3.57	-2.24	-1.79	-2.68	0.35	-0.35	-0.70
	"p"	0.15	0.04*	0.06	0.04*	0.07	0.11	0.06	0.39	0.39	0.28
K+	"t"	-1.15	0.34	-0.27	0.27	1.18	1-34	2.24	-0.56	-0.19	0.71
	"p"	0.18	0.38	0.40	0.40	0.18	0.16	0.08	0.32	0.43	0.28
Cl-	"t"	1.26	0.00	0.99	0.00	-1.11	0.00	-1.11	0.77	0.00	0.97
	"p"	0.17	0.5	0.21	0.50	0.19	0.50	0.19	0.22	0.50	0.22
HCO_3^-	"t"	-1.34	-1.34	-2.23	-0.95	0.00	-1.34	-0.32	-0.71	0.00	0.55
	"p"	0.16	0.16	0.08	0.22	0.50	0.16	0.39	0.27	0.50	0.32

Table 3 *Mean and standard deviation of Urea and Creatinine obtained in all groups.*

Parameter	Negative control	Infected untreated group	Cocktail	*Azadirachta indica*	*Mangifera indica*	*Carica papaya*	*Citrus limon*
Urea	38±1	46±8	37±3	37±5	40±2	33±2	37±3
Creatinine	0.6±0.1	0.6±0.1	0.8±0.1	0.6±`0.1	0.5±0.1	0.5±0.1	0.5±0.1

Table 4a: *Comparative analysis of urea and creatinine values obtained in all groups administered with the cocktail or various individual extracts.*

Parameter		Negative control vs Infected untreated group	Negative control Vs Cocktail	Negative control Vs *Azadirachta indica*	Negative control Vs *Mangifera indica*	Negative control Vs *Carica papaya*	Negative control Vs *Citrus limon*	Infected untreated group Vs Cocktail	Infected untreated group Vs *Azadirachta indica*	Infected untreated group Vs *Mangifera indica*	Infected untreated group Vs *Carica papaya*	Infected untreated group Vs *Citrus limon*
Urea	"t"	-0.99	0.31	0.19	-0.89	2.23	0.32	1.05	0.95	0.72	1.58	1.05
	"p"	0.21	0.39	0.43	0.23	0.03*	0.39	0.20	0.22	0.27	0.13	0.21
Creatinine	"t"	0.00	-1.41	0.00	1.94	1.94	1.94	-1.41	0.00	1.94	1.94	1.94
	"p"	0.50	0.15	0.50	0.09	0.09	0.09	0.15	0.50	0.09	0.09	0.09

Table 4b. *Comparative analysis of urea and creatinine values obtained in all groups administered with the cocktail or various individual extracts.*

Parameter		Cocktail Vs *Azadirachta indica*	Cocktail Vs *Mangifera indica*	Cocktail Vs *Carica papaya*	Cocktail Vs *Citrus limon*	*Azadirachta indica vs Mangifera indica*	*Azadirachta indica vs Carica papaya*	*Azadirachta indica vs Citrus limon*	*Mangifera indica vs Carica papaya*	*Mangifera indica vs Citrus limon*	*Carica papaya Vs Citrus limon*
Urea	"t"	0.00	-8.30	1.11	0.00	-0.50	0.74	0.00	2.47	0.83	-1.11
	"p"	0.50	0.25	0.19	0.50	0.32	0.27	0.50	0.07	0.25	0.12
Creatinine	"t"	1.41	3.04	3.04	3.04	1.94	1.94	1.94	0.00	0.00	0.00
	"p"	0.15	0.04*	0.04*	0.04*	0.09	0.09	0.09	0.50	0.50	0.50

DISCUSSION

Phytomedicine could be an alternative source for prevention and treatment of malaria. Malaria remains a major public health problem in Nigeria with increase in Plasmodial resistance and high cost of effective antimalarial drugs. We have been able to provide evidence that the plants used in this study possess antiplasmodial potentials which could be harnessed in the production of antimalarial drugs. Furthermore, findings in this study is corroborated by that of Akinpelu et al., (2018) who reported that A. indica, M. indica, C. papaya and fruit extract of C. limon possess antiplasmodial properties. Histopathological findings in this study revealed that the kidney sections of infected rats administered with the cocktail or aqueous leaf extract of C. papaya showed absence of malaria associated pathology when compared with the uninfected group administered with distilled water only. However, comparison of other extracts with the infected untreated group showed presence of malaria induced pathology on the kidney sections indicating that the antiplamodial content present in them may not be as potent as that of C. papaya at the dosage administered. Rats treated with aqueous leaf extracts of A. indica showed the presence of tubular necrosis and accumulation of fluids in some regions of the kidney. In addition, the findings of Adebayo and Krettli, (2011) who reported the antiplamodial properties of leaf extracts of A. indica, M. indica and C. papaya further corroborates this study. Akin-Osanaiye, (2013) also reported the antiplamodial properties of A. indica in P. berghei infected mice. Extract of M. indica were observed to be the least potent as histological sections of the rats treated with the aqueous leaf extract showed the presence of inflammatory cell within the interstitial spaces, however the renal cortex and the tubular spaces appeared normal; this observation is in line with that of Akinpelu et al.,(2018) who reported a weak antiplamodial potency of M. indica in rats infected with P. berghei. Kidney sections of the rats treated with the fruit extract of C. limon revealed the presence of eosinophilic cast within the renal tubules. Biochemical studies showed altered activity in the electrolyte values in the various test group on comparison with the uninfected group administered with distilled water only. Sodium (Na+) levels in the rats administered with the extracts of M. indica, C. papaya and C. limon were observed to be statistically significant ($p<0.03$) while the rats treated with the cocktail or A. indica showed absence of significant alterations in their Na+ levels ($p>0.05$). Rats treated with the cocktail and extracts of M. indica and C. limon showed statistical variations in Na+ values ($p<0.03$) while the rats administered with the A. indica and C. papaya were statistically insignificant ($p>0.05$). Statistically significant variations were observed in the groups administered with extracts of M. indica and C. limon on comparison with the groups administered with the cocktail ($p< 0.04$) while other groups were statistically insignificant ($p>0.05$). Statistically significant variations were observed in the Potassium (K+) levels of the group administered with the cocktail, aqueous extracts of A. indica, C. papaya and C. limon ($p<0.01$) while the rats administered with extract of M. indica and the infected untreated group administered with distilled water showed absence of significant variation in their potassium values ($p>0.05$). K+ values was observed to be stable in other groups upon comparison with each other ($p>0.05$). The chloride (Cl-) values remain stable in all the test group on comparison with the uninfected group ($p>0.05$). However, the group administered with the cocktail showed a statistical variation in the Cl- levels ($p<0.04$) on comparison with the infected untreated group. The bicarbonate ($HCO3-$) values was observed to be normal across all groups ($p>0.05$). The urea values were normal with absence of variations with the exception of the group administered with C. papaya upon comparison with the uninfected control group administered with distilled water only ($p<0.03$). Comparative analysis of the creatinine levels between the various test group and the uninfected groups showed absence of statistical variations ($p>0.05$). However, the groups administered with extracts of M. indica, C. papaya and C. limon showed a statistically significant variation ($p<0.04$) on comparison with the rats administered with the cocktail.

CONCLUSION

There are medicinal plants in Nigeria with antiplasmodial capabilities that could be harnessed in producing antimalarial drugs to tackle the menace of malaria. It is hereby recommended that the active constituent that confers the anti-plasmodial activities on the above-mentioned plants be further studied.

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