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Effects of Aqueous Stem Bark Extract of *Jatropha curcas* on Some Biochemical Indices of Mice Infected with *Plasmodium berghei*

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Abstract The aim of this research work was to investigate the effect of *Jatropha curcas* plant in Mice infected with *Plasmodium berghei* in order to ascertain the efficacy of the plant stem bark extract in the treatment of malaria as claimed by traditional practitioners in Nigeria. The LD_{50} of the plant extract was determined. Six groups of fifteen mice each were used for the research. Group 1 was uninfected and untreated, group 2 was infected, but untreated, Groups 3, 4 and 5 were infected and treated with 250mg/kg, 500mg/kg, and 750mg/kg of aqueous stem bark extract of *Jatropha curcas* respectively. While Group 6 was infected and treated with Arthemether (20mg/kg). Treatment commenced on the third day and lasted for a period of 12 days. Then, the animals were sacrificed, blood was collected and used for biochemical investigations. Our findings shows that infection caused a significant ($p< 0.05$) increase in the activities of AST, ALT, ALP and the concentration of total bilirubin and urea when compared to control. However, treatment with the plant extract and arthemether significantly decreased ($p<0.05$) the activities of liver enzymes and the concentration of total bilirubin and urea compared untreated control. The total protein in infected extract-treated and Arthemether treated animals were found to increase ($p<0.05$) significantly when compared with the infected untreated mice. Our findings revealed that the decrease in values for AST, ALT, and ALP activity by the plant extract may suggest that the extract has some inhibitory effect on malaria parasite, since the there were no physiological disturbances in the biochemical parameters investigated. Our research had revealed the LD_{50} was greater than 5000mg/kg, suggesting that the plant extract was relatively safe for oral medication. The percentage parasitemia has decreased from 9.25 to 7.80 for the treated group, where as the infected and untreated has the parasitemia increased from 9.30% to 18.70%. Suggesting that the plant extract possess some anti-malarial properties. Our findings support the possibility of using *Jatropha curcas* plant leaf as anti bacterial agent.

Keywords *Plasmodium berghei*, *Jatropha curcas*, Biochemical indices, Parasitemia Malaria parasite

1. Introduction

Malaria remains one of the major killers of humans worldwide, threatening the lives of more than one-third of the world's population. It thrives in the tropical areas of Asia, Africa, and Central and South America, where it affects millions of people. Each year 350 to 500 million cases of malaria occur worldwide. Sadly, more than 1 million of its victims, mostly young children, die yearly [1]. Although malaria has been virtually eradicated in the United States and other regions with temperate climates, it continues to affect hundreds of people in Nigeria every year. The Centers for Disease Control and Prevention (CDC) estimated 1,200 cases of malaria are diagnosed each year in the United States.

Plants have been recognized for their several life saving and therapeutic properties. Several herbs are parts of socio-cultural and socio-economic heritage. Even in the present times rural populations turn to herbal medicine as the most preferred therapeutic source. *Jatropha curcas* is a drought resistant large shrub or small tree, belonging to the genus *Euphorbiaceae*, producing oil containing seeds [2]. *Jatropha curcas* is the commonest specie found in Nigeria, but many species exist in different parts of the world. Traditionally, *Jatropha curcas* is used for the treatment of fever, mouth infections, jaundice, guinea worm, sores and joint rheumatism [3, 4]. Previous studies also reveals the presence of antibacterial agents in different parts of *Jatropha curcas* [5]. For developing herbal treatment for malaria from various parts of *Jatropha curcas* which part will be more effective against *Plasmodium berghei*. The present study aims to investigate the antiplasmodial potential of the stem bark of *Jatropha curcas* using the aqueous extract on *Plasmodium berghei*. The people of Jada local government area and its inhabitants widely use *Jatropha curcas* stem bark for the treatment of many ailments including malaria.

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However, there are no scientific bases for this treatment. Therefore, this research is designed to provide the scientific evidence for the use of the aqueous stem bark extract of *Jatropha curcas* in the treatment of malaria and its safety in the medication.

2. Materials and Methods

Collection of Plant Material

Fresh *Jatropha curcas* Linn plantwas collected from the Staff quarters of Government Secondary School, Jada Local Government Area of Adamawa State, Nigeria and was taxonomically identified and authenticated in the Plant Science Department of Modibbo Adama University of Technology, Yola.

Chemicals and Reagents

Assay kits for enzymes (ALT, AST and ALP) and liver function indices (Albumin, Total and direct Bilirubin and total protein) were obtained from Randox Laboratories Ltd, UK while those of creatinine and urea were obtained from Agappe Diagnostics, Switzerland. All other reagents and solvents used were of analytical grade.

Experimental Animals

Ninety mice weighing between18-22g were obtained from Animal Facility Centre, National Veterinary Research Institute Vom, Jos, Nigeria. The mice were housed in polypropylene cages, and given standard laboratory diet and water and maintained under standard laboratory conditions.

Malaria Parasite

The malaria parasite (*Plasmodium berghei* NK-65) was obtained from National Institute for Medical Research (NIMR), Lagos, Nigeria.

Extract Preparation

The stem bark was carefully removed from the *Jatropha curcas* plant and washed thoroughly with tap water then rinsed twice with distilled water and allowed to sun dry. The dried stem bark was crushed to powder with pestle and mortar and two hundred grams of the powder was cold macerated in 1000ml of distilled water for 24 hours with constant shaking and filtered using Whitman's filter paper No. 1. It was then concentrated to dryness on water bath at 40°C and the crude extract was kept in desiccator and dried.

Acute Toxicity Test

The LD_{50} of the aqueous extract of the stem bark was tested using [6] method in order to determine its safety. The aqueous extract of the stem bark of *Jatropha curcas* was administered in doses of 1000, 3000 and 5000 mg/kg body weight to four groups of mice (n = 3). The mice were kept under same conditions and observed for toxic signs and mortality for 24hs.

Parasite Inoculation

The inoculation of the parasite was carried out by determining both the percentage parasitemia and erythrocytes count of the donor mouse using a haemocytometer and appropriate dilutions of the infected blood with isotonic saline were made. Each mouse was inoculated intraperitoneally with 0.2 ml of infected blood containing about 1 x 10^7 *Plasmodium berghei* parasitized red blood cells. After 72 hours the mice were treated for malaria conditions for twelve days.

Experimental Design

Ninety Swiss albino mice were divided into six groups of fifteen [15] mice each. Groups 2-6 were inoculated with the rodent malaria parasite *Plasmodium berghei* from the same donor mouse. Groups 3, 4 and 5 were treated with 250, 500 and 750 mg/Kg body weight of the aqueous leaf stem bark extract of *Jatrophacurcas* respectively. Group 6 was treated with 20 mg/Kg body weight of arthemether. Groups 1 and 2 served as normal and untreated controls respectively.

Determination of Biochemical Parameters

Test for liver function indices

Bilirubin was determined by the method of Walter and Gerard [7]. Total protein was determined by the Method of Tietz [8] while albumin was determined as described by Doumas et al [9].

Test for kidney function indices

Serum urea concentration was determined according to the method described by Fawcett and Scott [10] while Creatinine was determined as described by Bartels et al [11].

Enzyme assays

Alkaline phosphatase activity of serum was determined as described by Wright et al [12]. Alanine and aspartate aminotransferase activities were assayed by the method of Reitman and Frankel [13].

Statistical Analysis

Results were expressed as mean ± SEM. Student t-test was used to analyse the data between groups at p values($p<0.05$) was considered significant in all cases (SPSS version 21 was used).

3. Results and Discussion

Acute Toxicity Tests

Our findings had shown that there was no mortality recorded in the mice at a dose of 5000 mg/kgbody weight of the aqueous extract of the stem bark of *Jatropha curcas*, suggesting that the plant extract was not toxic and relatively safe for oral consumption.

The antimalarial properties observed in this study could be attributed to bioactive constituents in the extract. Guido et al [14] reported that antimalarial activity could be attributed to alkaloids in plants extract. Our findings in table 1 had shown that the aqueous stem bark extract of *Jatropha curcas* produced some antiplasmodial effects on the parasitemic levels when compared to the standard anti malarial drug. in a related development Abiodun et al [15] reported that ethyl

acetate extract of leaves of *Ocimum gratissimum Linn*. (Labiatae) and hexane extract of stem bark of *Trema orientalis (L.) Blume (Ulmaceae*) showed the highest antiplasmodial activity against P. falciparum K1 strain but elicited low cytotoxicity. Thus the percentage of parastitemia has decreased from 9.25 to 7.80 for the treated group, where as the infected and untreated has the parisetemia increased from 9.30 to 18.70. However, it was observed that at higher dose of the extract was able to exhibit a considerable effect comparable to the standard drug. Hence use of standard drug has percentage parastitemia decreased from 9.30 to 2.10, suggesting that aqueous extract of the stem bark of *Jatropha curcas* posessess some anti malaria activities. A review conducted by Sabandar et al [16] had shown that, the genus *Jatropha (Euphorbiaceae)* comprises of about 170 species of woody trees, shrubs, sub shrubs or herbs are used in medicinal folklore to cure various diseases of 80% of the human population in Africa, Asia and Latin America. Species from this genus have been popular to cure stomachache, toothache, swelling and inflammation.

Biochemical tests related to the hepatocyte integrity can be observed to follow hepatocellular integrity and liver injury. Serum activities of AST and ALT were employed to access liver status. Within an hour after being bitten by aninfected anopheles mosquito, the sporozoites enter the liver and multiply into exo-erythrocytic merozoites. The changes in the activity of the hepatocyte due to the infection of *plasmodium* may change the activities of the liver enzymes. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), Alkaline phosphatase (ALP) are considered indices for hepatocellular health [17, 18]. Infection caused asignificant ($p<0.05$) increase in the activities of AST, ALT, and ALP in the blood ofparasitized mice compared to the normal control group. The increased activities of the enzymes may be as a result of liver injury and altered hepatocyte integrity caused by the *Plasmodium* infection and consequent release of the enzymes into the blood stream. However, the administration of the plant extract improved the situation. This finding is in agreement with previous reports by Cotran et al [19]. Although the liver enzymes normalization were effective at higher doses of 500mg and 750mg/kg body weight of the extract. It could be suggesting that plant extract possess some anti-malarial activities. Treatment with the plant extract had some protective effects the hepatocyte integrity of the parasitized mice.

Table 1. Percentage (%) Parasitemia

Groups / Days	Group 2	Group 3	Group 4	Group 5	Group 6
0	-	-	-	-	-
7	9.30	9.25	6.70	3.47	2.40
14	18.70	7.80	5.80	3.01	2.10

Table 2. Effects of Aqueous Stem Bark Extract of *Jatropha curcas* on some Biochemical indices in Mice

Parameters/days	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5	GROUP 6
AST(IU/L)						
DAYS						
0	16.00±2.73	25.50±2.50^{c}	17.40±0.90^{d}	16.79±0.39^{d}	12.20±0.91^{ad}	11.40±0.88^{ad}
7	18.40±4.00	27.33±1.98^{c}	13.0±0.58^{ad}	15.67±3.33^{ad}	10.3±0.33^{ad}	10.67±0.43^{ad}
14	15.00±1.54	35.33±2.20^{c}	12.00±0.58^{ad}	12.33±2.19^{ad}	13.00±3.60^{ad}	10.00±0.50^{ad}
ALT(IU/L)						
0	12.33±0.33	19.30±0.35^{c}	14.20±0.50^{ad}	10.22±0.70^{ad}	10.00±0.90^{ad}	9.90±0.88^{ad}
7	13.40±0.50	21.50±0.50^{c}	13.50±0.50^{d}	9.70±0.50^{ad}	9.20±1.50^{ad}	9.01±0.31^{ad}
14	11.33±0.14	28.60±0.70^{c}	12.51±0.50^{ad}	9.40±0.01^{ad}	9.10±0.20^{ad}	8.50±0.17^{ad}
ALP(IU/L)						
DAYS						
0	11.67±4.88	20.45±2.00^{c}	14.25±1.45^{cd}	12.30±0.40^{d}	11.35±0.25^{d}	11.00±1.30^{d}
7	12.20±0.50	21.02±3.00^{c}	12.90±2.50^{d}	10.50±0.50^{d}	11.00±0.90^{d}	10.86±2.70^{d}
14	11.57±2.88	25.65±0.25^{c}	10.54±0.54^{d}	10.20±0.50^{d}	9.96±1.04^{d}	9.89±0.60^{d}

All values are the mean ± SEM, (n=5) at ($p<0.05$); a-Significantly lower than group 1,
b=Significantly higher than group 2, c=Significantly higher than group 1, d=Significantly lower than group 2, Bio. Par. represents Biochemical Parameters, AST represents Aspartate aminotransferase, ALT represents Alanine aminotransferase, ALP represents Alkaline phosphatase.

Table 3. Effects of Aqueous Stem Bark Extract of *Jatropha curcas* on TP, ALB, Urea and Creatinine in Mice

Bio. Par.	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5	GROUP 6
TP(g/l)						
DAYS						
0	7.49±0.43	5.04±0.45^{a}	6.00±0.50	6.20±0.70	6.30±1.00^{b}	7.20±1.12^{b}
7	8.01±0.50	4.75±0.12^{a}	6.60±0.40^{b}	6.67±0.50^{b}	6.85±0.33^{b}	7.67±0.43^{b}
14	7.48±0.69	3.89±0.08^{a}	6.70±0.50^{bc}	6.83±0.20^{bc}	6.90±0.60^{bc}	7.00±0.50^{bc}
ALB(g/l)						
0	3.96±0.05	2.28±0.50^{a}	1.90±0.45^{ad}	2.00±0.55^{a}	3.20±0.45^{b}	3.90±0.80^{b}
7	3.98±0.50	2.20±0.50^{a}	1.20±0.50^{ad}	2.80±0.50^{a}	3.50±0.20^{b}	4.01±0.31^{b}
14	3.89±0.56	0.60±0.20^{a}	2.51±0.50^{b}	3.50± 0.01^{b}	3.71± 0.20^{b}	4.50± 1.47^{b}
UREA(mmol/L)						
DAYS						
0	21.44±0.15	25.80±0.40^{c}	24.20±0.50	23.50±1.00^{d}	21.22±0.56^{d}	19.50±0.45^{d}
7	22.20±0.60	27.33±1.98^{c}	23.00±0.58^{d}	23.67±2.33^{d}	24.33±2.33^{d}	21.28±2.43^{d}
14	21.29±0.12	42.63±1.31^{c}	24.28±0.58^{cd}	22.33±2.19^{d}	23.00±3.60^{d}	22.00±3.50^{d}
TB(mmol/L)						
DAYS						
0	8.15 ± 0.45	30.45±0.50^{c}	22.25±0.50^{cd}	19.20±0.57^{cd}	15.25±0.25^{cd}	13.10±1.50^{cd}
7	9.25±0.56	33.20±0.50^{c}	19.15±0.33^{cd}	16.45±0.70^{cd}	13.66±1.00^{cd}	12.60±2.00^{cd}
14	9.00±0.80	38.25±0.65^{c}	14.00±0.84^{cd}	14.25±0.55^{cd}	12.00±1.50^{cd}	9.00±0.40^{d}

All values are the mean ± SEM, (n=5) at ($p<0.05$) a=Significantly lower than group 1,
b=Significantly higher than group 2, c= Significantly higher than group 1, d= Significantly lower than group 2, Bio. Par. represents Biochemical Parameters: TP represents Total Protein, ALB represents Albumin, Urea and TB represents Total bilirubin.

Our findings also show an increase in serum total bilirubin concentration in the infected untreated mice. Bilirubin is the major bile pigment produced in heme catabolism. The increase in the concentration of serum bilirubin in severe malaria are due to numerous factors which include intravascular haemolysis of parasitized red blood cells, hepatic dysfunction and possibly an element of microangiopathic haemolysis associated with disseminated intravascular coagulation [20]. Consequently, jaundice in malaria has been reported to range from 20-31.7% and it is predominantly haemolytic rather than hepatic, as shown by pre-eminence of unconjugated bilirubinemia [21]. Therefore, the increased serum bilirubin observed in the infected untreated mice in this study signifies the impairment of hepatic bilirubin excretion or haemolysis which is in agreement with the report by Kochar et al [22]. But, the administration of the extract to the infected mice was able to ameliorate these anomalies to a considerable extent, suggesting that the extract may be hepatoprotective [23, 24].

Furthermore, this study showed significant ($p<0.05$) decrease in the concentration of total protein of infected-animal groups as shown in table 3. This agrees with many other studies that reported significant decrease of plasma total proteins in malaria infections compared with normal control [24]. The total protein in infected extract-treated and Arthemether treated animals was found to increase ($p<0.05$) significantly when compared with the infected untreated mice. This study agreed to the report by Balaji, et al [25] that the values of total protein can be influenced by the degree of infection. Amah et al (26) reported significant reduction in serum levels of albumin in malaria patients in endemic regions of Calabar, Nigeria. Many researchers have proposed the use of serum albumin levels as a reliable biochemical marker for establishing severe pathologic conditions such as malnutrition and infectiousdiseases [27, 28]. Malaria infections are accompanied with significant decrease in plasma albumin concentrations as well as in malnutrition and pregnancy [28]. However, the prevailing plasma albumin concentration in malaria infection is dependent on the nutritional status of the affected individual and hepatic functionality [29, 30]. Possibly, based on the nutritional and hepatic status of the infected animals in this study groups, showed significant ($p<0.05$) reduction in serum albumin levels in the infected animals compared to normal control. However, in another studies, Oguche et al [31] reported that there was initially significant ($p<0.05$) increase in serum levels of albumin in low and moderate malaria infections, but decreased as the malaria density increased. This study agrees with that the previous report by Oguche et al [31] observed a significant ($p<0.05$) decrease in the levels of albumin on day 14. But the administration of the extract appeared to increase the levels of albumin with increase in concentration of the dose of the extract in all the treated mice.

The observed increased serum urea levels in the infected untreated from days 7 to 14 is supported by a study reported by [32] in malaria patients in Minna. Studies also reported that increased Urea: Creatinine ratio in malaria patients also indicate that the causes of Ureamia in these patients are largely prerenal and may be due to reduced renal blood flow,

rather than organic renal involvement [32]. The reduced blood flow to the glomeruli due to malaria-associated hypotension may be responsible for the reduced glomerular filtration rate and hence decreased renal excretion of the analytes [32]. However, the extract reduced the levels of urea in the treated groups showed an improvement malaria attenuation or parasite clearance. Increased urea levels in children with typhoid fever and also in malaria in children, adults and also in sickle celled patients [32].

The result presented in this study indicated that serum creatinine was significantly higher ($p<0.05$) in the infected untreated mice. In a study reported by Idonije et al [32] showed that increase in serum creatinine level is mostly likely as a result of impaired glomerular filtration of urea and creatinine; and that is also an indicator for malaria severity. Creatinine level can also increase temporarily as a result of muscle injury and are generally slightly lower during pregnancy. High levels of creatinine in children and adults with malaria infection, and also in disease and infections such as hepatitis, typhoid, urinary infections, kidney infections, diabetes which indicates acute renal failure [32]. However, the administration of the extract and the Artemether significantly ($p<0.05$) reduced the values of the creatinine at the various doses on days 7 to 14. This suggests that the plant extract has not affected the excretory function of the kidney in the infected treated mice as revealed in table 3.

4. Conclusions

The aqueous stem bark extract of *Jatropha curcas* possess some antimalarial properties. The extract showed protective effect on liver tissues and kidney indices. This suggest the possibility of using *Jatropha curcas* extract in the treatment of malaria and perhaps a promising future for this new class of anti bacterial agent could be actualized.

5. Recommendations

Further studies should be carried out other parts of *Jatropha curcas* as a source of antimalarial remedy and isolation and characterization of the active components responsible for the antimalarial property should be investigated.

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