Original Research Article

THE EFFECT OF *Arthrospira platensis* (PHORMIDIACEAE) ON THE ACUTE TOXICITY OF ARTEMETER LUMEFANTRINE IN MALARIA PATIENTS

ABSTRACT

Malaria has remained one of the leading causes of morbidity and mortality in most developing countries. This pathology is caused by the *Plasmodium spp*. Current World Health Organization (WHO) guidelines for the treatment of uncomplicated *falciparum* malaria recommends the use of artemisinin-based combination therapy (ACT). *Arthrospira platensis* is a microscopic filamentous alga that is rich in proteins, vitamins, essential amino acids, minerals and essential fatty acids like γ-linolenic acid (GLA). The current study was carried out to evaluate the effect of *Arthrospira platensis* on the liver and kidney toxicity induced by ACT. Malaria patients were randomized into two groups to receive therapeutic dose of either artemether-lumefantrine 20/120 mg (group 1) or artemether-lumefantrine 20/120 mg + *Arthrospira platensis* 8 g daily (group 2) as an adjunct therapy and follow-up for 7 days (D). After treatment, the activity levels/concentrations of liver and kidney biochemical markers (ALT, AST, ALB, UREA, CREAT) were analyzed. Both pre- and post-treatment samples were analyzed, and the results gotten compared with control group made up of malaria negative patients. Serum activity of selected biomarkers (ALT, AST, ALB, UREA) of malaria patients were statistically significant ($P<0.05$) on D0 when compared to that of malaria negative patients. The serum activity of CREAT though not statistically significant ($P>0.05$), increased compared to malaria negative patients. The serum level of ALT, AST, UREA and CREAT increased from D0 to D3 and decreased on D7 after treatment while ALB decreased from D0 to D3 and increased on D7 in both groups when compared with the negative control group. The concentration of these biochemical markers varied across the groups from D0 to D7. The results obtained from this study indicate that *Arthrospira platensis* has a positive effect on the liver and kidney toxicity induced by ACT and hence could be administered together with ACT in malaria treatment.

Keywords: Malaria, ACT, Toxicity, *Arthrospira platensis*, oxidative damage.

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1. Background

Malaria is one of the life-threatening diseases in Cameroon and in other parts of sub-Saharan Africa. It is caused by a parasite called *Plasmodium* sp. There are 5 types of this parasite that can infect human: *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, *Plasmodium knowlesi,* and *Plasmodium falciparum* which is responsible for about 95% of all malaria cases [1]. It was estimated in 2020, that malaria still causes about 241 million cases and 627,000 deaths globally with children below 5 years and pregnant women being the most vulnerable group to the disease [2].

Malaria control strategies such as the use of insecticide treated bed nets (ITNs), indoor residual spraying (IRS), larval source management, have led to major changes in malaria epidemiology and vector biology [3], though most have faced challenges due to resistance. Artemisinin-based combination therapies (ACTs) has been recommended as the first line treatment for patients infected with uncomplicated *Plasmodium falciparum* [4] due to the increase resistance of parasites to older drugs such as chloroquine and mefloquine [5] and artemether/Lumefantrine (AL) has been one of the approved and most successful fixed dose ACT used in the treatment of uncomplicated malaria by *P. falciparum.* In a recent study, Metoh *et al.* (2021) showed the efficacy and safety of Artemether-lumefantrine, Artesunate-mefloquine and Dihydroartemisinin-piperaquine in the treatment of *P. falciparum* malaria in children [6]. Despite these, recent partial artemisinin resistance has been reported which is seen to be characterized by slow parasitological response (delayed parasite clearance to treatment during the 3 days treatment with AL). Also, AL causes malaria parasite death through the generation of free radicals such as reactive oxygen species (ROS) [7]. These excessive generation of free radicals may deplete the antioxidant defense system causing detrimental effects on target cellular components such as DNA, proteins, and lipids.

Hepatotoxicity associated with ACT has also been described in animal models [8] and several series in humans have shown elevation of liver enzymes of undetermined clinical significance [9]. Treatment of uncomplicated falciparum malaria with AL has proven to have a potential cause in liver enzyme abnormalities in the first days of treatment [10].

Arthrospira platensis, a cyanobacteria has nutraceutical value and also therapeutic value in many cases like Human Immunodeficiency Virus (HIV) infections, cancer, diabetes, hypertension, obesity, cardiovascular disease [11]. It has also proven to be effective in the medical domain as an adjunct therapy to AL to curb oxidative stress caused by AL used in the management of malaria [22]. Thus, with these numerous therapeutic potentials, this study

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aimed to investigate the alleviating effect of *Arthrospira platensis* on the acute toxicity of artemether-lumefantrine on kidneys and liver of malaria patients.

2. Materials and methods

2.1. Study Area

The study was carried out in the Bamenda Regional Hospital, situated in the North West Region of Cameroon, where it functions as the regional administrative headquarter. Bamenda is found in Mezam division, and located between latitudes 5056‟ to 5058‟ North of Equator and between longitude 100 08‟ and 10010‟ East of Greenwich Meridian [12]; and occupies a total surface area of 3,125 hectares [13]. . The major malaria vectors in the area are *An. gambiae*, *An. coluzzii* and *An. funestus*. Bamenda is the capital city of the Nord-West Region, malaria transmission is hypoendemic with parasite inoculation rates varying from 4.9 to 11 infective bites/person/year in the highland areas of the North-West region [1].

2.2. Study design

This study is a randomized open label clinical trial (longitudinal study) conducted from July to October 2021. Volunteer malaria patients (3-15 years) diagnosed at The Regional Hospital, Bamenda, were recruited. The participants were randomly assigned to two groups, both administered ACT, and in addition, *Arthrospira platensis* was administered to group two. Samples were collected 4-7 days post administration and analyzed for biochemical markers.

2.3. Inclusion/Exclusion criteria

Patients excluded from the study include non-willful patients, patients with parasitic load less than 2000 trophozoites per micro liter of blood as stated by WHO, patients with severe malaria needing immediate medical attention, and patients with other diseases aside from malaria. Only out-patients were recruited.

2.4. Drug regimen

Artemether/lumefantrine was administered as per body weight for 3 days as seen inTable 1 [14].

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Table 1: Dose of Artemether/lumefantrine per body weight

	20/120 mg tablet		80/480 mg tablet			
Weight	**D1**	**D2**	**D3**	**D1**	**D2**	**D3**
5 to <15 kg	1 cp x 2	1 cp x 2	1 cp x 2	-	-	-
15 to <25 kg	2 cp x 2	2 cp x 2	2 cp x 2	-	-	-
25 to <35 kg	3 tab x 2	3 tab x 2	3 tab x 2	-	-	-
≥ 35 kg	4 cp x 2	4 cp x 2	4 cp x 2	1 tab x 2	1 tab x 2	1 tab x 2

cp: capsules, tab: tablets, kg: kilogram

The recommended dose of *Arthrospira platensis* (8 to 10 g daily) was also administered to patients in the test group. That is, 16 to 20 caps of 500 mg *Arthrospira platensis*. Patients recruited for this study were administered 8 g maximum of *Arthrospira platensis* daily. These 8 g were encapsulated in 16 capsules of 500 mg each.

2.5. Malaria Parasite Density

Blood samples were collected from patients on D0 upon recruitment by finger pricking using lancets and the slides properly labelled. The blood was then made to drop on a clean sterilized microscopic slide (approximately 10 ul) and a thick smear made in a circular motion. The slides were allowed to air dry before staining with Giemsa. Air dried slides were fixed with methanol by dipping into methanol container for 2–3 minutes. The slides were then placed back-to-back in a staining trough containing 10% Giemsa solution making sure all fixed sample faced to one direction and allowed for 20 minutes. After which the slides were rinsed with clean water, allowed to air dry for 5 minutes then viewed under the microscope. The slides were examined under the x100 oil immersion objective lens of a light microscope. The asexual parasites density was counted against WBCs counted in microscopic field examination. A patient was considered positive if *P. falciparum* was seen during the microscopic examination.

2.6. Biochemical analysis

Four (4) milliliters of intravenous blood was collected and dispensed into serum separating tube (SST). It was allowed to clot after which it was centrifuged at the speed of 2200 rpm for

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about 15 mins. Serum was separated from the clotted sample into serum tube and stored (frozen) until ready for analysis. Biochemical analysis was done within 72 hours of sample collection. They were all measured in the serum samples using kits from Chronolab Systems, S.L.—Barcelona, Spain.

Serum albumin test

One milliliter of bromocresol was placed in three test tubes (blank, standard and sample) 5 µl of aqueous albumin and 5 µl of blood serum were then added to standard and sample test tubes respectively. The mixtures were then incubated for 5 minutes at 37 ^{o}C and their optical densities (ODs) read at 630 nm. The concentrations were calculated in g/L and the values obtained recorded.

Serum creatinine test

A mixture of 100 µL of serum sample and 1 ml of alkaline solution containing picrate was prepared in a 1 cm cuvette. Under these conditions, picrate reacted with creatinine to from an orange complex, whose formation rate between 30 seconds and 90 seconds (ΔAbSample = Sample30s − Sample30s) is determined spectrophotometrically at 492 nm. A standard solution of creatinine (2 mg/dl) was also analyzed under the same conditions, and the corresponding change in absorbance (ΔAbStd = Std90s − Std30s) was used to calculate the creatinine concentration in the serum sample as follows:

$$\mathbf{Creatinine(\mu M)} = \frac{\mathbf{\Delta AbSample}}{\mathbf{\Delta AbStd}} \mathbf{\times 2 \times 88.4.}$$

Urea test

Determination of serum uric acid was done using a colorimetric kit from Chronolab Systems, with slight modifications of the protocol. The Working reagent (WR) was prepared as described by the kit manufacturer, and the original assay protocol modified to suit a microplate adaptation. Briefly, 200 µL of the working reagent was mixed with either 5 µL serum samples (test), uric acid standard (Std, 6 mg/dl), or WR (blank), and incubated for 5 min. Upon incubation, the uric acid reacted with the components of the WR to produce a red colour, whose intensity was measured at 520 nm using an ELISA plate reader. The absorbances of sample (ASample), standard (AStd) and blank (Ablank), was used to calculate uric acid concentration as follows:

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$$\textbf{Uric acid (µM)} = \frac{\textbf{ASample} - \textbf{Ablank}}{\textbf{AStd} - \textbf{Ablank}} \times 6 \times 59.5$$

Aminotransferase Enzymes

Each serum sample (100 µL) was mixed with 1 mL working reagent into a 1 cm cuvette to constitute a reaction mixture. In the mixture, aminotransferase enzymes (AST/ALT) from serum sample catalyze the transfer of an amino group from aspartate (for AST) or alanine (for ALT) to α-ketoglutarate forming glutamate (or pyruvate) and oxaloacetate. The oxaloacetate is reduced to malate by malate dehydrogenase and NADH. The rate of decrease in the concentration of NADH (change in absorbance per minute, ΔA/min), which is proportional to the catalytic concentration of AST/ALT in the serum sample analyzed, was measured using a spectrophotometer at 340 nm, and the enzyme activity calculated using the formula: ΔA/min × 1750 = U/AST activity = $\frac{change\ in\ Abs/\min(specimen)}{change\ in\ Abs/\min\ (calibrator)} \times$ calibrator activity

2.7. Data analysis

Results were represented as mean $\pm$ standard deviation in charts and tables. The significant difference in relation to the group treated without *Arthrospira platensis* were calculated with the of SPSS statistics version 21. One-way Anova as well as correlation were used to compare the variance and results were considered statistically significance at $p<0.05$.

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3. Results

3.1. Socio-Demographic Data

The characteristics of the participants enrolled in this study, the number of males, females, and their various ages are displayed in below (Table 2). Of 220 patients aged 3 to 15 years screened for malaria, 70 tested positive, giving a prevalence of 31.8%. Thirty-two malaria positive patients and 15 malaria negative participants were enrolled in the study and follow-up was done for 7 days.

Table 2: Socio-demographic characteristics

Characteristics	Malaria negative Control	Malaria positive Cases	
		AL	AL+S
Sex-ratio (Males/females)	0.87	0.62	0.58
Aged 3 – 9 years	6	5	7
Aged 10 – 15 years	9	11	9

3.2. Effect of malaria on the liver and kidney parameters in malaria patients as compared with control

Results of the various liver and kidney parameters (ALT, AST, ALB, URE and CREAT) analyzed for malaria positive patients (Test group) and malaria negative participants (Control group) shows that, serum level of ALT was seen to increase significantly (p=0.000) in the malaria positive group when compared to that of the malaria negative group. Also, the serum concentration of AST in the malaria positive group was seen to increase and this increase was significant (p=0.000) when compared to that of the malaria negative group. On the other hand, ALB concentration in the malaria positive group was rather seen to decrease and this decrease was also seen to be significant (p=0.000) when compared to that of the malaria negative group. The serum levels of UREA were also seen to increase significantly (p=0.000) as that of ALT and AST when compared with the malaria negative group. Then, for the serum concentration of CREAT, it increased in the malaria positive group, but this increase was not significant statistically (p=0.517) when compared with that of the malaria negative group (Table 3).

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Table 3: Effect of malaria on the liver and kidney parameters in malaria patients as compared with control

GROUP	Mean ± Standard deviation				
	ALT(U/L)	**AST(U/L)**	**ALB(g/L)**	**UREA(mg/dL)**	**CREAT(mg/dL)**
1(Malaria negative)	16.87±3.36	28.75±4.79	40.36±1.19	16.38±1.85	0.63±0.09
2(Malaria positive)	29.04±6.29	41.61±7.30	32.39±3.10	28.00±6.09	0.69±0.18
p-value	0.000	0.000	0.000	0.000	0.517

3.3. Correlation of Parasite Density and individual biochemical parameters

A moderate to high correlation was observed between parasitemia and markers of liver function and kidney function (Fig 1). Figure 1a showed a correlation between parasite density and serum concentration of ALT, and it was a direct correlation with R^2 being 0.6 which signified a moderate correlation. Correlation between AST concentration and parasite density was observed and R^2 for AST concentration vs parasite density was close to 1 (0.71) which signified a moderate correlation between AST conc and parasite density as seen below (Figure 1b). An inverse correlation was observed between ALB concentration and parasite density. There was a moderate correlation between this parameter and parasite density with R^2 = 0.6, (Figure 1c). Also, there was a direct correlation between urea concentration and parasite density. Urea concentration showed a moderate correlation with parasite density as seen in figure 1, R^2= (0.72) (Figure 1d). Finally, a direct correlation was observed between creatinine (CREAT) concentration and parasite density as represented below (Figure 1e). CREAT concentration correlated moderately with parasite density with R^2 =0.77.

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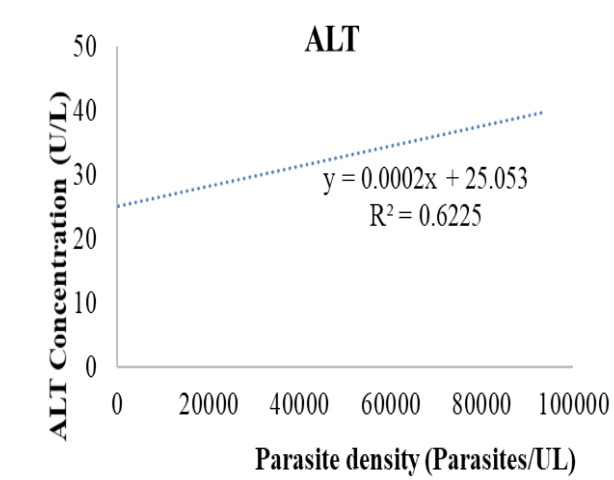

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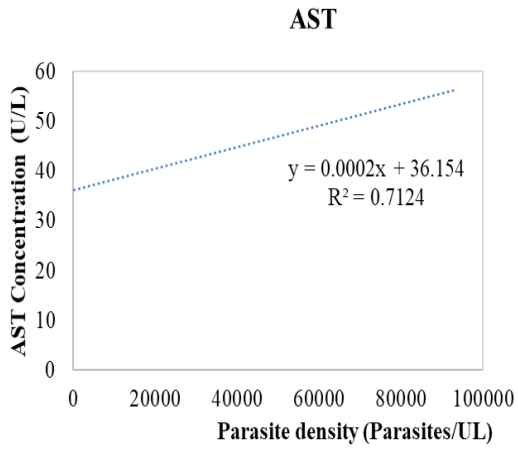

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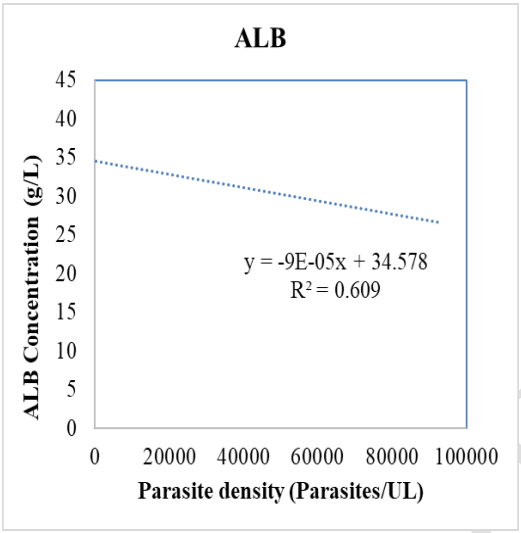

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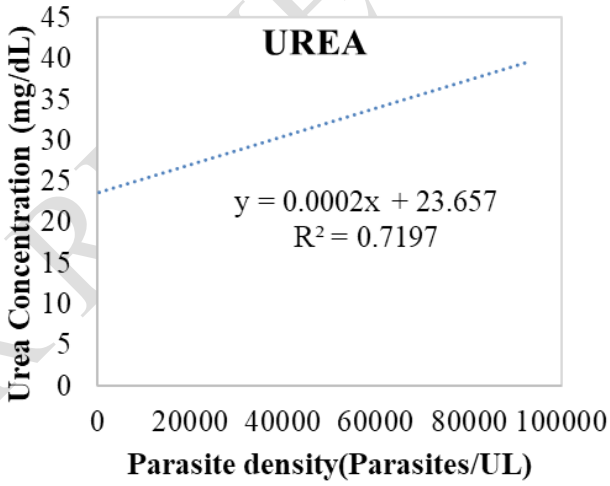

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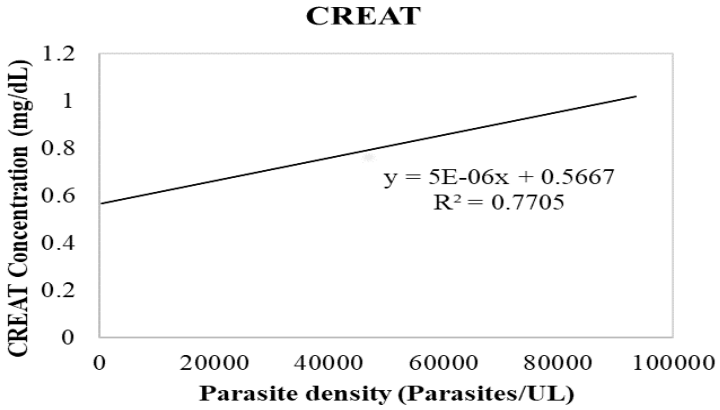

e

Fig 1: Correlation between Parasite density and (a)Alanine transaminase (ALT) concentration (b)Aspartate transaminase (AST) concentration, (c) Serum albumin (ALB) concentration, (d) Urea concentration, and (e) Creatinine (CREAT) concentration

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3.4. Mean concentrations of ALT in different treatment groups

The mean concentrations of ALT in the different groups of treatments are summarized in table 4. From the table it was observed that, the concentration of ALT increased significantly in both groups (group 2 and 3) though with varying levels of significance on the third day when compared to their pre-treatment concentrations (p0.000 and 0.004) respectively. Also, it could be noted that the concentration of this parameter was reduced by the seventh day as compared to that of the third day and this concentration obtained on the seventh day after treatment was seen to be statistically insignificant in both groups when compared with concentration gotten from their pre-treatment (p0.163 and 0.016) for groups 2 and 3 respectively.

Table 4: Mean concentration of ALT (U/L) in different treatment groups

Treatment Days	**GROUPS (Mean ± Standard deviation)**		
	1(Malaria negative)	**2(ACT only)**	**3(ACT + *Arthrospira platensis*)**
D0	16.873±3.3574	29.150±7.0848	28.930±5.4920
D3		44.070±5.7147	39.650±9.3105
D7		34.480±6.1219	19.880±4.4996
	p-value		
Pre-treatment vs post treatment 1		0.000	0.004
Pre-treatment vs post treatment 2		0.163	0.016
Post treatment1 vs post treatment 2		0.006	0.000

3.5. The activity of AST in different treatment groups

The mean concentrations ± standard deviations of AST in the different groups are summarized in table 5. There was an increase in the AST concentration in both group 2 and 3 when compared to the concentration recorded at pre-treatment. This increase in of AST concentration was seen to be statistically significant for groups 2 with p-value of 0.008 and non significant (p=0.463) and 3. Comparing the concentration of AST on day seven with that

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gotten from the pre-treatment showed a non significant (p=0.974) decrease in concentration for group 2 and a significant decrease in concentration (0.012) for group 3.

Table 5: Mean concentrations of AST (U/L) in different treatment groups

Treatment Days	GROUPS (Mean ± Standard deviation)		
	1(Malaria negative)	2(ACT only)	3(ACT + *Arthrospira platensis*)
D0	16.873±3.3574	44.130±4.9737	39.090±9.6184
D3		54.850±10.6300	42.880±6.6258
D7		43.420±4.8387	29.310±3.6290
		p-value	
Pre-treatment vs post treatment 1		0.008	0.463
Pre-treatment vs post treatment 2		0.974	0.012
Post treatment1 vs post treatment 2		0.005	0.001

3.6. Mean concentrations of Serum albumin in the different groups of treatments

The mean concentrations of ALB in the different groups are summarized in table 6. The serum concentration of ALB was seen to decrease in both groups on the third day after treatment with this decrease being statistically non significant when compared to the concentration recorded before treatment with varying p-values for the different groups 0.140 and 0.222 for group 2 and 3 respectively. On the seventh day, the concentration, of ALB was found to increase in both groups when compared with the concentration recorded on the third day. Group 3 for this seventh day had a statistically significant increase when compared with the concentration of D3 (p-value=0.000). This later concentration when compared with that of the pre-treatment for both groups with had p-values 0.916 and 0.016 for groups 2 and 3 respectively.

Table 6: Mean concentrations of ALB (g/L) in different treatment groups

Treatment Days	GROUPS (Mean ± Standard deviation)

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	1(Malaria negative)	2(ACT only)	3(ACT + *Arthrospira platensis*)
D0	40.360±1.1855	30.840±2.7665	33.940±3.4245
D3		26.940±5.2273	30.100±5.5538
D7		30.050±4.8938	40.670±5.7923

	p-value	
Pre-treatment vs post treatment 1	0.140	0.222
Pre-treatment vs post treatment 2	0.916	0.016
Post treatment1 vs post treatment 2	0.276	0.000

3.7. Mean concentrations of Urea in different treatment groups

The concentration of Urea was seen to increase on the third day after treatment in both groups (2 and 3) when compared to the results derived from pre-treatment and the increase in concentration recorded was significant for group 2 (p=0.010) and not significant for group 3 (p=0.533). There was a decrease in concentration of urea on the seventh day when compared to results of day three and this decrease was significant (p=0.020 and p=0.000 for groups 2 and 3 respectively) but it was not significant in group 2 (p=0.949) and significant in group 3 (p=0.001) when compared with results from pre-treatment (Table 7).

Table 7: Mean concentration of Urea (mg/dL) in different treatment groups

Treatment Days	GROUPS (Mean ± Standard deviation)		
	1(Malaria negative)	2(ACT only)	3(ACT + *Arthrospira platensis*)
D0	16.380±1.8459	26.090±6.3387	29.910±5.8404
D3		34.670±6.2208	32.200±4.8431
D7		26.920±5.4705	21.430±3.1127

	p-value	
Pre-treatment vs post treatment 1	0.010	0.533
Pre-treatment vs post treatment 2	0.949	0.001
Post treatment1 vs post treatment 2	0.020	0.000

3.8. Mean concentrations of Creatinine in different treatment groups

There were an increase in the serum concentration of CREAT on day 3 in both groups (group 2 and 3) when compared with results of pre-treatment, and this increase was not

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significant as seen from their p-values (0.137 and 0.969) for groups 2 and 3 respectively. The concentration of CREAT was seen to decrease on approaching day seven and this decrease was not statistically significant when compared to the concentration recorded before treatment p (0.864 and 0.537) for groups 2 and 3 respectively (Table 8).

Table 8: Mean concentrations of CREAT (mg/dL) in different treatment groups

Treatment Days	GROUPS (Mean ± Standard deviation)		
	1(Malaria negative)	**2(ACT only)**	**3(ACT + *Arthrospira platensis*)**
D0	0.627±0.0884	0.700±0.1764	0.680±0.1751
D3		0.930±0.3683	0.700±0.2108
D7		0.760±0.1897	0.590±0.1729
	p-value		
Pre-treatment vs post treatment 1		0.137	0.969
Pre-treatment vs posttreatment 2		0.864	0.537
Post treatment1 vs post treatment 2		0.325	0.399

4.DISCUSSION

Malaria is a major parasitic disease that is responsible for a high death rate in children in the world, especially in the tropical region where it is endemic. Almost all the complications and death that occur as a result of malaria infection in children are caused by *P. falciparum*. Among complications that are associated with *falciparum* malaria, renal and hepatic dysfunctions are common in both children and adults living in malaria endemic regions [15]. Hepatic dysfunction is a well-known feature of severe malaria, contributing to clinically significant complications such as hypoglycaemia, metabolic acidosis, impaired drug metabolism, and finally organ failure. Malaria-associated liver damage in uncomplicated malaria, however, has rarely been investigated so far. Malaria can damage the kidneys or liver or cause the spleen to rupture. Any of these conditions can be life-threatening and it may also result in not having enough red blood cells for an adequate supply of oxygen to your body's tissues (anemia) [16].

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From our study which was aimed at evaluating the effect of *Arthrospira platensis* on the liver and kidney toxicity of artermether lumefantrine used in the treatment of uncomplicated malaria in children, the malaria positive group either increased or decreased in their mean concentration of ALT, AST, ALB, UREA and CREAT when compared with that of the malaria negative group. This could be as a result of the effect of this pathology on the Liver and Kidney. The results showed an increase in the serum levels of ALT, AST, UREA, CREAT and a decrease in serum ALB levels. Alanine aminotransferase (ALT) is an enzyme found mainly in kidney and greater concentration in liver cells which metabolizes protein and breakdown food to produce energy. Aspartate aminotransferase is an enzyme found in muscles, kidney and highest concentration in liver and heart which can be released into blood when the liver is damaged [17] since the malaria parasite invades the liver and destroy the liver cells which intend results in an increase in serum levels of these enzymes. An increase in the level of these enzymes suggests organ damage or injury. Increase in serum levels of ALT and AST affirms with the work of Reuling *et al* [16] in which liver injury was reported in patients with uncomplicated *falciparum* malaria shown by an increase in the serum level of ALT, AST and ALP.

Albumin is a protein that is produced in the liver and helps to carry vitamins, enzymes, and other important substances thereby, preventing fluids from leaking out of the bloodstream. Decrease in serum levels of this parameter is similar to the results obtained in previous studies [18] in which malaria infection was the cause of changes in haematological and biochemical parameters of affected individuals to varying degrees resulting in changes in body. This was seen by an increase in serum levels of AST, ALT and also a reduction in the serum ALB levels in malaria infected patients in Niger state Nigeria. Increase in serum levels of Urea and Creatine could be attributed to the sequestration of the parasite into the renal microvasculature bed which may lead to ischemia. This is in line with the work of Akambi *et al* [15] who reported an increase in the serum levels of UREA and CREAT in malaria positive children sampled in Ondo state, Nigeria.

Comparison made between pretreatment and post treatment within each group showed an increase in toxicity immediately after treatment at Day 3 as compared to Day 7 post treatment in both groups. A significant increase in serum levels of ALT, AST, UREA, CREAT and a decrease in serum ALB was seen immediately after treatment (Day 3). The concentration of these parameters in patients who were administered ACT only showed a significant increase when compared with pre-treatment results for ALT, AST and UREA

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which was different from that obtained from the group which had *Arthrospira platensis* as an adjunct for ALT, AST and UREA. All these changes were non-significant on the 7th day after treatment for the group treated with ACT only for ALT, AST, ALB, UREA and CREAT respectively compared to the group treated with ACT plus *Arthrospira platensis* as an additional therapy with significant changes. Results gotten from groups 2 and 3 when comparing pre and post treatment could be explained by the fact that, two degrees of toxicity were experienced by these organs, first by the pathology and secondly by the therapy. The insignificant results seen on day 7 when compared to the pre-treatment was as a result of recovery from the first degree of toxicity which was that of treatment but the toxicity caused by the pathology still persisted and this is the reason why there was a significant change seen in the group which had *Arthrospira platensis* as an additional therapy. Participants in this group that had *Arthrospira platensis* showed a level of recovery from these two degrees of toxicity. *Arthrospira platensis* accelerated full recovery from this toxicity caused by both the pathology and drug.

These changes could also be as a result of acute toxicity of Artemether lumefanfrine which gradually recovered with time. The results obtained on the 7th day were as a result of self-recovery from the toxicity of Artemether lumefanfrine. The toxicity of this drug (artefan) was seen to be higher in the group taking just ACT than in the group taking ACT in conjunction with *Arthrospira platensis* as the mean values of concentration of these parameters were very different from that in the group taking ACT only in both day 3 and 7. This suggests that *Arthrospira platensis* confers a level of protection to these organs as far as toxicity of ACT is concerned. Though some changes in some of these parameters were not significant, (Creat) they were visible and this result is similar to that of Gilani *et al.*, [19].

Arthrospira platensis is rich in macro and micronutrients, vitamins, flavonoids as well as phycocyanin. Phycocyanin is a pigment-protein complex which exhibits a strong antioxidant activity as it is capable of scavenging hydroxyl, alkoxy, and peroxyl free radicals, involved in the processes of lipoperoxidation and cytotoxicity [20]. This phycocyanin helps to reduce the oxidative stress induced by ACT thereby reducing the toxic effects caused by this drug in accordance with previous studies [21], in which *Phyllanthus amarus* leave and seed extract were used to reduce the acetaminophen-induced nephrotoxicity in rats. Also, a recent study of Metoh *et al.*, showed the efficacy of *Arthrospira platensis* in counteracting artemether/lumefantrine -induced oxidative stress in rats [22]. This explains the higher mean values of concentration of biomarkers observed in

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the group being administered ACT only as compared with *Arthrospira platensis* treatment group

5. CONCLUSION

This present study shows that malaria parasitemia causes liver and kidney damage. Artemether lumefantrine induce changes in liver and kidney biochemical parameters. *Arthrospira platensis* reduces the effect of artemether lumefantrine on liver and kidney parameters. Globally it could be concluded that *Arthrospira platensis* is beneficial in the effective management of malaria and could be used as an adjunct in the treatment of malaria.

Abbreviations

ACT: Artemisinin-Combined Therapy

AL: Artemether-Lumenfantrine

AP: *Arthrospira platensis*

D: Day

LDL: Low Density Lipoprotein.

LLINs: Long lasting insecticidal nets

N: Number

PCR: Polymerase Chain Reaction

RDT: Rapid Diagnostic Test

WHO: World Health Organization

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Ethical Consideration

Ethical approval was obtained from the Regional delegation of public health Bamenda, Northwest Region Cameroon through N/Ref: 110/ATT/NWR/RDPH/BRICAD of 25th May 2021 and the Ethical and Research committee of the University of Bamenda, Cameroon. The health workers and the patients were fully briefed on the objectives of the study. Participation to this study was voluntary. Only participants who gave their consent were enrolled in the study. After explaining the

rational of the study and ensuring their confidentiality, a Proxy-informed consent was obtained from parents/guardians of the children for their willingness to participate in the study

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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