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Effect of Artesunate on Haematological and Plasma Biochemical Parameters in Female Wistar Rats

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This study was designed to investigate effect of artesunate on blood parameters in female rats. Ten female Wistar rats (130 – 150 g) were grouped into control and artesunate (1.43 mg/kg) – treated groups for blood assay. The artesunate was administered orally for 50 days. Hematological assay was carried out using hemocytometer, while biochemical assay was carried out using spectrophotometry. Mean +/- SEM and student's t-test at $p<0.05$ were determined. Artesunate (1.43 mg/kg) significantly reduced RBC, platelet and lymphocyte counts when compared to their controls. It also significantly decreased total protein, ALT and ALP values relative to their controls. However, it induced no significant changes in the PCV, Hb, TWBC, neutrophil, monocyte, eosinophil, MCV, MCHC, MCH, albumin, globulin, AST, BUN and creatinine values relative to their controls. Conclusively, it can be suggested that artesunate had both harmful and advantageous effects on blood parameters in female rats.

Keywords: Artesunate, Red blood cell, Lymphocyte, Total protein, Rats.

Artesunate is a drug used to cure malaria [1]. It belongs to the artemisinin class of drugs. It is frequently administered in the form of combination therapy, for example artesunate combine with mefloquine. It is not used as a prophylaxis. Artesunate can be administered through intravenous injection, muscular injection as well as through oral and rectal administrations [2].

The drug is well tolerated when taken [3]. It is preferred during the gestation period because of its high safety index, however contrary results were suggested by animal studies [4]. It is also allowed to be taken by lactating mothers. Liu Xu invented this drug in 1977 [5] and the World Health Organization has listed it as an essential medicine [6]. Although artesunate is used mainly to treat malaria, evidence abounds that it could also has advantageous effects on infection due *Schistosoma haematobium* [7], but this has not been proven convincingly.

Its efficacy is similar to that of arthemeter when used to treat adults' malaria induced by *P. falciparum* [8], however artesunate in combination with other drugs has superior advantages relative to artemether-based drugs, vis-à-vis, through uptake and through the routes of administration and probably could be more efficacious when treating serious malaria in children[9]. Drugs that inactivate

hepatic enzyme CYP2A6 should not be taking alongside with artesunate, examples of such drugs are amiodarone, letrozole isoniazid e.t.c.

The effect of artesunate on: rats' kidneys toxicity [10], hemolysis and hypoglycemia induction in rats [11], developmental toxicities in rats and rabbits [12], hepatic histopathological changes in rats [13], embryotoxicity and toxicokinetics in rats [14], bone development toxicity in rats [15], reproductive function in female rats [16], stroke and other central nervous system therapeutic effects [17] as well as on sub-chronic hemato-biochemical effects in rats [18] have been reported.

But, as a result of limited information obtained concerning the activities of artesunate on blood parameters in female rats, hence, this research intends to bridge this gap.

MATERIALS AND METHODS

Experimental Animals

Ten female rodents of weight range 130 – 150 g raised in the Animal Holding of ABUAD were used in the current study. These rodents were accommodated in a conducive laboratory atmosphere with unlimited supply of feed and water; the acclimatization period was for two weeks. All animal experiments were carried out in accordance with ABUAD Ethical Committee (16/MHS01/015) on care and use of laboratory animals.

Drug

Artesunate (Green Energy, China) was purchased from Danax Pharmacy, Ibadan, Nigeria. Among these, artesunate (50 mg) was liquefied in 10 ml of distilled water to produce a concentration of 5.0 mg/ml. The dosage of the artesunate considered in this research was as recommended by the manufacturer.

Dosage: According to the manufacturer, for adult 2 tablets (each tablet weighed 50 mg) were to be given orally per day for a 70 kg adult.

Hence, 50 mg (x2) per day in a 70 kg adult.

Therefore, dose to be used = 100/70 mg/kg

=1.43 mg/kg

Experimental Design

Ten matured female rats (five per group) used for this study received the following oral doses of artesunate and distilled water (control) for 50 days as follows:

Group A rodents (control group) were given 0.5 ml/100 g of distilled water.

Group B rodents were given 1.43 mg/kg of artesunate.

Blood sample collection

On day 51, blood samples were collected from the rodents and prepared as previously described [19].

Haematological Parameters Determination

The red blood cells (RBC) count, white blood cells (WBC) count, hemoglobin (Hb) concentration, packed cell volume (PCV), mean

Table 1. Effect of treating rats with artesunate for 50 days on haematological parameters

Parameters	Control	Artesunate (1.43 mg/kg)
PCV (%)	51.50 ± 0.66	49.00 ± 0.15
Hb (g/dL)	16.75 ± 0.34	15.90 ± 0.61
RBC ($\times 10^6/\mu L$)	8.66 ± 0.04	7.98 ± 0.11*
TWBC ($\times 10^3/\mu L$)	10.76 ± 0.36	4.24 ± 0.83
Platelet ($\times 10^5/\mu L$)	1.34 ± 0.08	0.68 ± 0.07*
Lymphocyte (%)	74.25 ± 0.85	71.75 ± 0.83*
Neutrophil (%)	23.50 ± 0.89	25.25 ± 0.75
Monocyte (%)	1.75 ±0.31	1.50 ± 0.28
Eosinophil (%)	0.50 ±0.14	1.50 ± 0.36
MCV (FL)	59.46 ± 0.15	61.33 ± 0.12
MCHC (g/dL)	32.53 ± 0.24	32.47 ± 0.21
MCH (pg)	19.34 ± 0.14	19.91 ± 0.20

(n=5, *$p<0.05$)

corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were determined as previously reported [19].

Biochemical Parameters Determination

The total protein concentration, albumin concentration, globulin concentration, activities of plasma alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP), levels of creatinine and urea (BUN) were determined as previously reported [20].

Statistcal analysis

Mean +/- SEM and student's t-test at $p<0.05$ were determined.

RESULTS

From table 1, treatment of rodents with artesunate (1.43 mg/kg) induced significant ($p<0.05$) reductions in RBC, platelet and lymphocyte values relative to their controls. However, the table also revealed that treatment of rodents with artesunate (1.43 mg/kg) caused non-significant ($p>0.05$) changes in the other parameters as shown in the table.

From table 2, it was revealed that treatment of rodents with artesunate (1.43 mg/kg) caused significant ($p<0.05$) reductions in total protein, ALT and ALP values when compared to their controls. However, the table also revealed that treatment of rodents with artesunate (1.43 mg/kg) produced non-significant ($p>0.05$) changes in the other parameters as shown in the table.

DISCUSSION

The results have revealed that artesunate induced significant reduction in RBC value which suggests that the drug prevented erythropoietin secretion by the kidneys and caused decrease in oxygen binding capacity of blood with ultimate reduction in the quantity of oxygen transported to the tissues. Similar account was given by [21] in rodents treated with extract of *Plectranthus amboinicus*. This result was corroborated by the assertions of [22, 23].

Also, artesunate induced significant decrease in the platelet count which suggests that it prevented the haemostatic function of the body. Opposite result was given by [24] in rats treated with extract of *Fadogia agrestis*.

The drug caused insignificant change in TWBC value which suggests that it had no effect on resistance of the body to foreign pathogens. Opposite result was given by [25] in rodents treated with extract of *Viscum album*. This result was supported by the assertions of [26].

Artesunate produced significant decrease in lymphocyte count which could signify the body acquired immune suppression. Opposite result was given by [27] in rodents treated with isolated ergosterol.

Further, the drug produced non-significant change in eosinophil value which suggests the absence of anti-allergic and anti-parasitic infectious responses by the drug. Opposite result was given by [28] in rats and mice treated with extract of *Arctotis actotoides*.

Table 2. Effect of treating rats with artesunate for 50 days on plasma biochemical parameters

Parameters	Control	Artesunate (1.43 mg/kg)
Total Protein (g %)	8.70 ± 0.07	8.33 ± 0.12*
Albumin (gm %)	3.40 ± 0.08	3.40 ± 0.14
Globulin (gm %)	5.30 ±0.04	4.93 ± 0.12
AST (µ/L)	45.00 ± 0.92	42.25 ± 1.03
ALT (µ/L)	33.25 ± 0.63	31.50 ± 0.74*
ALP (IU/L)	113.00 ± 1.93	110.50 ± 2.23*
BUN (mg/dL)	17.53 ± 0.17	17.30 ± 0.13
Creatinine (µmol/L)	0.78 ± 0.02	0.73 ± 0.03

(n=5, *$p<0.05$)

Artesunate caused non-significant change in the neutrophil value which suggests the drug had no effect on the body response to pathogenic bacteria, viruses and other harmful agents. Opposite result was given by [29] in rodents treated with extract of *Dennettia tripetala*.

The drug induced non-significant change in the monocyte value which suggests that it lacked phagocytic function [30]. Opposite result was given by [31] in hens fed with *Saccharomyces cerevisiae*.

Artesunate produced non-significant changes in MCV and MCH values which suggests the absence of effect on macrocytic anaemia induction. Similar account was given by [32] in rats treated with extract of *Jatropha gossypifolia.*

The drug produced insignificant change in the MCHC value which suggests absence of effect on hereditary spherocytosis induction. Similar account was given by [32] in rats treated with extract of *Jatropha gossypifolia*.

It has been reported that treatment of rats for 45 days with artesunate (2 mg/kg and 4 mg/kg) caused non-significant changes in hemoglobin, RBC, MCH, MCHC, lymphocytes and platelet values; but, the study also revealed that at 8.0 mg/kg, it caused significant ($p< 0.01$) increase in PCV, MCH, TWBC, neutrophil and eosinophil values [18].

The plasma biochemical study results have revealed that artesunate caused significant reduction in total protein level which suggests that the drug inhibited blood buffering capacity and also decrease the colloidal osmotic pressure. Opposite result was given by [33] in rodents treated with extract of *Euphorbia heterophylla*. This result was validated by the assertion of [26]

In addition, artesunate produced significant reduction in ALT activity which could mean that it prevented the induction liver damage. Opposite result was given by [34] in rodents treated with extract of *Moringa oleifera*.

Artesunate caused significant decrease in ALP activity which suggests the inhibition of cholestasis. Opposite result was given by [35] in rats treated with losartan. This result was corroborated by the assertion of [36].

Artesunate induced non-significant change in the level of albumin which suggests that it had no effect on the levels of essential plasma components like amino acids, metals, bilirubin e.t.c. Contrary result was given by [37] in rats treated with extract of *Enicostemma axillare*.

Artesunate caused non-significant change in globulin level which suggests the lack of effect on both the natural and acquired immunity of the body. Similar account was given by [38] in rats treated with extracts of *Portulaca oleracea*.

The drug caused insignificant change in AST activity which could mean the lack of effect on induction of tissue necrosis. Opposite result was given by [39] in rodents treated with extract of *Sida rhombifolia*.

Artesunate caused non-significant change in BUN level which suggests the absence of nephrotoxicism. Opposite result was given by [40] in rats treated with extract of *Passiflora edulis*. This result was corroborated by the assertion of [41].

Artesunate produced non-significant change in creatinine level which suggests the absence of renal dysfunction. Opposite result was given by [42] *Mucuna pruriens* extract treated rats.

It has also been reported that treatment of rats for 45 days with artesunate (4 mg/kg and 8 mg/kg) caused significant ($p< 0.05–0.001$) increase in SGOT, SGPT, ALP, TC, TG values; at 8.0 mg/kg, it also caused significant ($p< 0.05$) increase in bilirubin level. However, at 2.0 mg/kg, 4.0 mg/kg and 8.0 mg/kg, it caused non-significant changes in total protein, albumin, creatinine and urea levels [18].

CONCLUSION

Conclusively, it can be suggested that artesunate had both harmful and advantageous effects on blood parameters in female Wistar rats.

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Limitations of the sudy

Scantiness of prior research studies on the topic: There were limited information obtained from literature concerning the activities of artesunate on blood parameters in female rats prior to the commencement of this study.

Competing interest

There is absence of conflicting interests in this study.

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