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Biochemical Impacts of Halofantrine Hydrochloride (HALFAN) On Estradiol Levels of Female Wistar Rats

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Abstract: This study evaluated the effect of halofantrine hydrochloride on some biochemical indices of female wistar rats. This drug is used in the therapeutic treatment of malaria. Twenty (20) female wistar rats divided into four (4) groups of five (5) rats each were used. Group A (control) received 0.2ml/kg body weight of normal saline, while groups B,C and D received 0.2ml/kg body weight of halofantrine hydrochloride administered orally three times at six hourly interval for one, two and three weeks duration. Blood sample was collected for the activities of Lipid profile indices (TC, TG, HDL-C, and LDL-C). These parameters were analyzed with standard biochemical techniques. The statistical analysis was carried out using ANOVA by SPSS version 11 package. From the plasma, the hormonal level was determined by radio-immunoassay. The estradiol level following 1 week, 2 weeks and 3 weeks treatment was higher significantly ($P < 0.05$) in all the groups compared with the control. The result therefore appeared to suggest that Halfan may be inducing the steroidogenic enzymes thereby causing high levels of estradiol. These findings could signify the toxicity of the drug and possibly hypercholesterolemia or hyperlipidemia.

Keywords: Halofantrine Hydrochloride, Malaria, Estradiol Levels, Female Wistar Rats, Radioimmunoassay.

1. INTRODUCTION

Malaria has been one of the most ancient diseases which have been studied. It has been one of the greatest burdens to mankind, with a mortality rate that is unmatched by any other modern disease other than tuberculosis. This dreadful disease, caused by four different agents (*Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae and Plasmodium ovale*) of the same genus, is a major health problem in most of the countries in the Tropics (Alaebo *et al*., 2018). Halfan (Pharmacological name Halofantrine) is an anti-malaria drug chemically related to mefloquine and quinine. Halfan emerged from the US Army's huge Post-

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Vietnam anti-malaria drug discovery program. There is no question that safe and effective anti-malaria drugs were needed in the second half of the twentieth century, once it became apparent that the *Plasmodium* had developed resistance to the mainstay of anti-malaria therapy, namely chloroquine (Halfan Product Data, 1988). Halofantrine is schizonticidal and exerts its action at the erythrocytic stage of the life cycle (trophozoite and schizont). It is not effective against exo-erythrocytic (hepatic) schizonts or against the sporozoite, merozoite or gametozoite stages of the life cycle of Plasmodium species investigated (Ugochukwu *et al.*, 2008). In the treatment of acute uncomplicated malaria due to Plasmodium falciparum and Plasmodium vivax, including those strains resistant to chloroquine. Administration of halofantrine in the treatment of malaria caused by P. vivax should be followed up by treatment with an 8-aminoquinoline derivative to eliminate hepatic forms (Adjene and Agoreyo, 2013). Estradiol is the steroid hormone that is produced by the cells lining the ovarian follicles in response to FSH, and the very high levels of estradiol within the leading follicle nourish and mature the egg (Wiselogle, 1986). Some estradiol reaches the blood to cause the lining of the uterus to grow, the secretion of ovulatory cervical mucus, and to provide feedback to the brain and pituitary that another cohort of follicles has been recruited and is growing (Agoreyo and Adjene, 2002). Estradiol, or more precisely, 17β-estradiol, is a human sex hormone and steroid, and the primary female sex hormone. Estradiol is essential for the development and maintenance of female reproductive tissues but it also has important effects in many other tissues including bone (Ugochukwu *et al.*, 2008).

II. MATERIALS AND METHODOLOGY

A. Animal Maintenance and Grouping

Twenty (20) female wistar rats were housed and fed until they weighed between 160-215g. They were acclimatized under standard housing conditions of an ambient temperature. The rats were randomly selected and divided into groups 1-4, with each group containing five rats. Group A serves as control while B, C and D serve as treatment groups.

B. Drug Administration

Halofantrine that was used in this research was produced by SmithKline and French Laboratories. The drug suspension was administered to the animals on the basis of their body weight. Usually, 5mls of the drug suspension contain 100mg of halofantrine hydrochloride (Halfan). The therapeutic dose for the experimental animals was thus 0.1ml/kg body weight as against the therapeutic dose of humans, which are 10ml/kg six hourly doses. The suspension of halofantrine was administered orally with the aid of an orogastric tube attached to needle and syringe.

C. Statistical Analysis

The statistical significance between groups was analyzed using one-way analysis of variance (ANOVA) to analyze the experimental groups and was considered as a level of significance followed by Fisher Least Significance Difference (LSD) post hoc test. Statistical tests were performed using SPSS (version 11) package.

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III. RESULTS

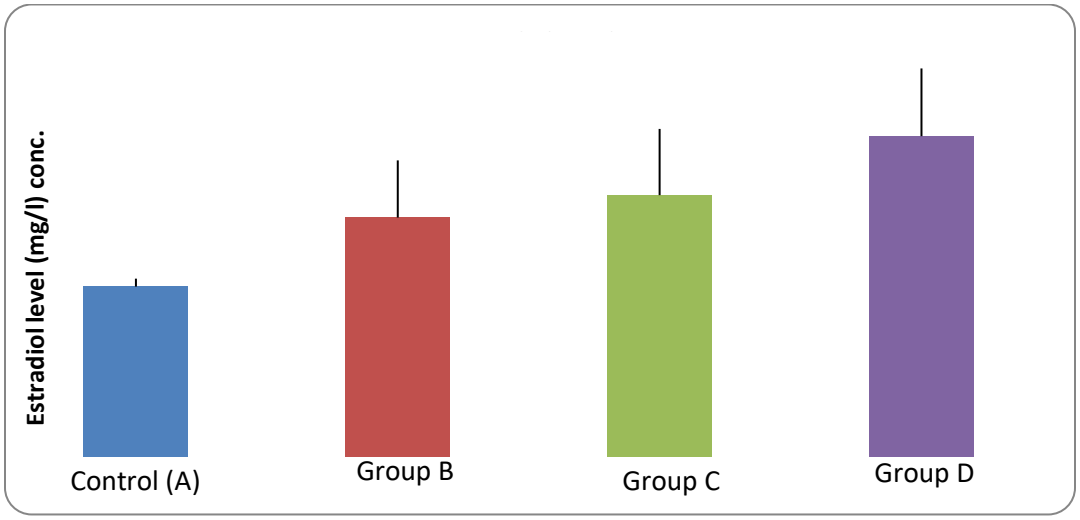

Figure 1: Estradiol levels of female wistar rats administered with Halofantrine hydrochloride

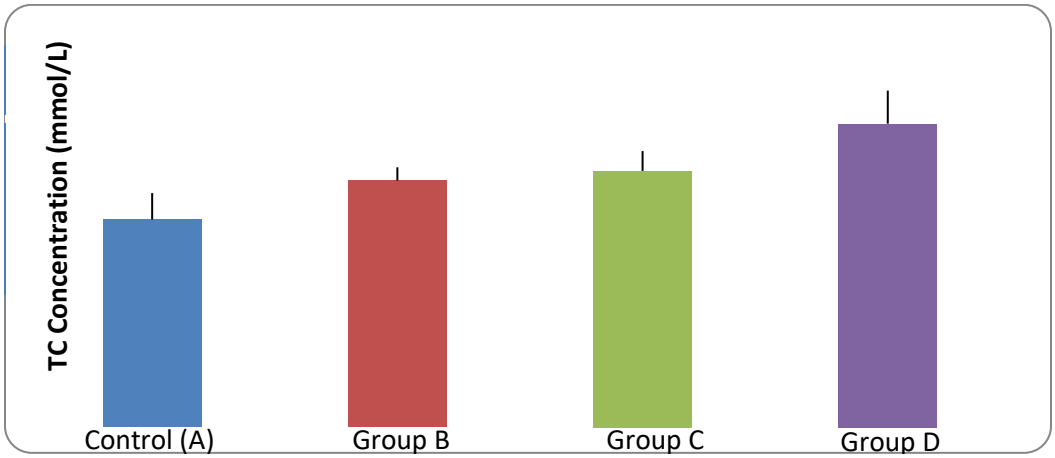

Figure 2: Total cholesterol levels of female wistar rats administered with Halofantrine hydrochloride

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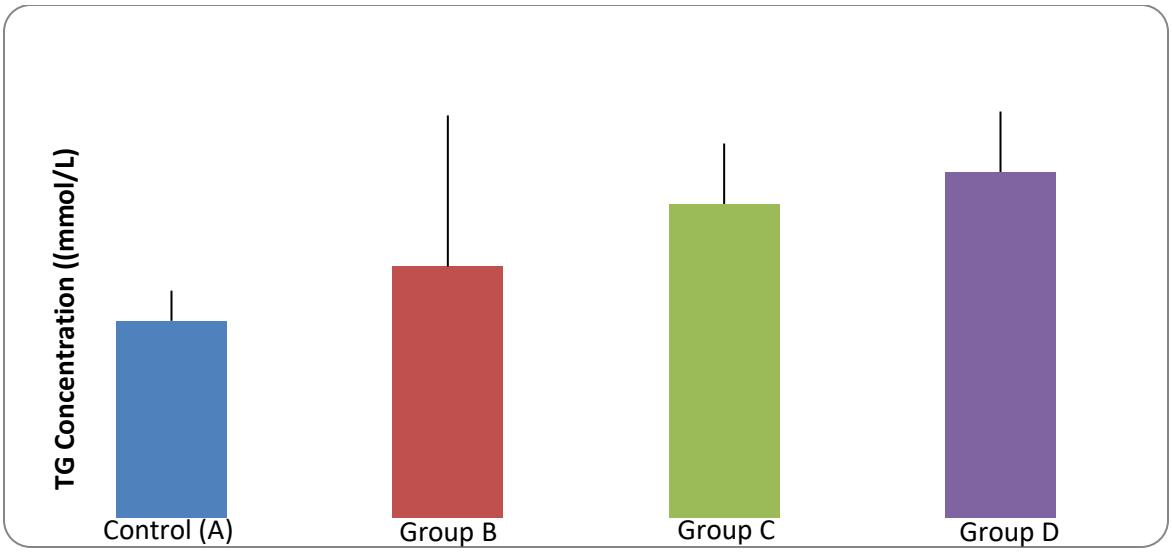

Figure 3: Triglyceride levels of female wistar rats administered with Halofantrine hydrochloride

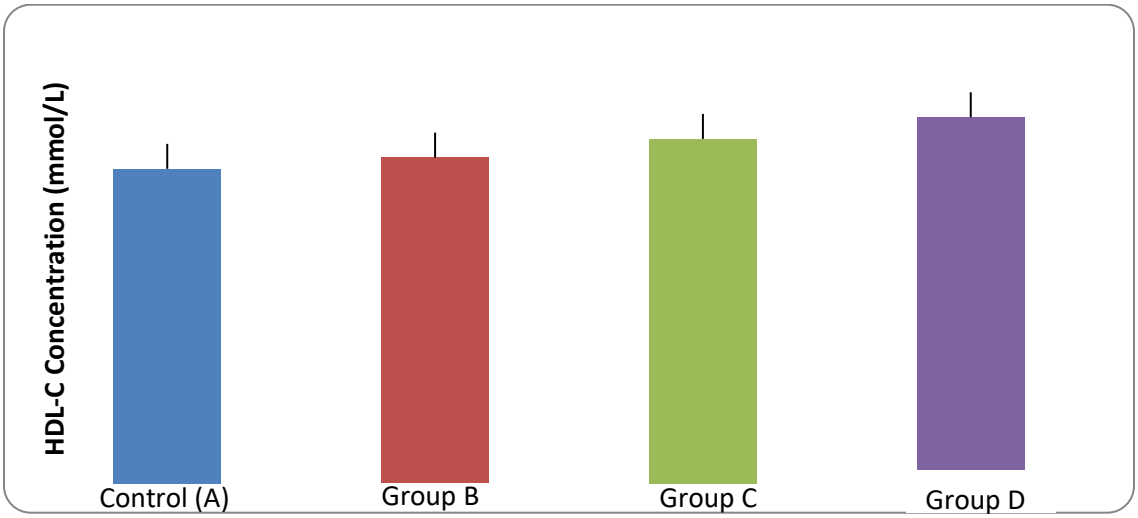

Figure 4: High density lipoprotein-cholesterol levels of female wistar rats administered with Halofantrine hydrochloride.

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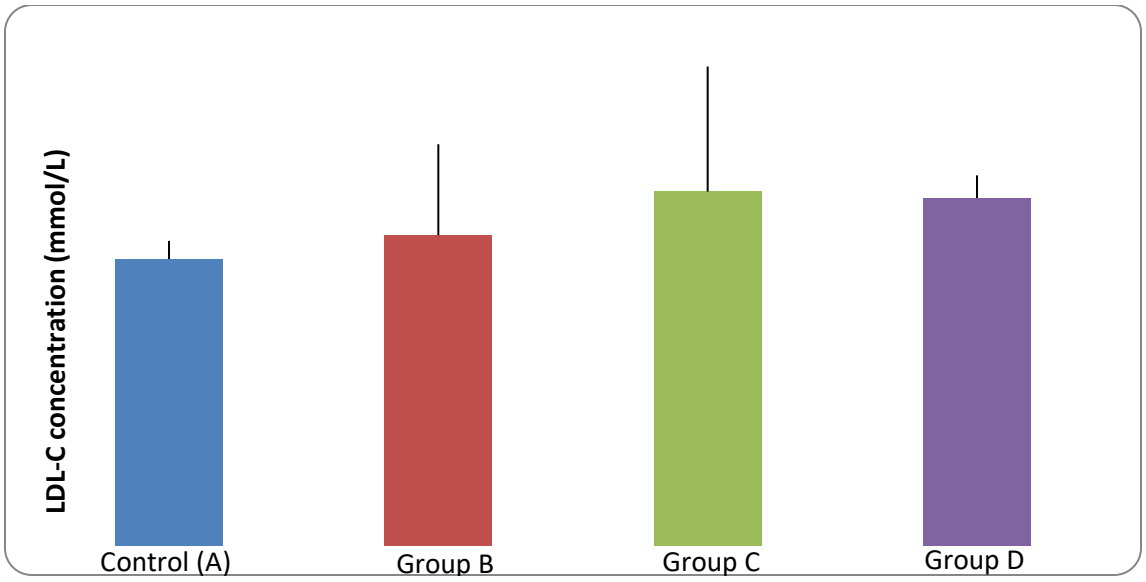

Figure 5: Low density lipoprotein-cholesterol levels of female wistar rats administered with Halofantrine hydrochloride.

IV. DISCUSSION

It was discovered from this study that halofantrine hydrochloride caused a significant increase in the lipid function test of female wistar rats. This could signify the toxicity of the drug in cholesterol levels. High blood cholesterol can increase the chances of getting heart disease, stroke and other problems. Too much blood cholesterol is termed hyperlipidemia. The result therefore appears to suggest that halofantrine hydrochloride may be inducing the steroidogenic enzymes thereby causing high level of estradiol.

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