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Abstract - Drug adulteration is commonly reported in Nigeria. Halofantrine purchased in four different locations in Ondo and Ekiti state, Nigeria were tested in mice for their comparative efficacy. The average parasite clearance time (PCT) were 4.4±0.49, 4.2±0.40, 4.4±0.80 and 4.2±0.75 for Halofantrine coded HAL-AK, HAL-IO, HAL-AD and HAL-IK respectively. Also, average parasite clearance rate (PCR) were 8653±2557, 6895±1010, 5426±1850 and 6226±1850 respectively. The result shows that there was no significant difference in the PCR (P>0.05) between the drugs. All the halofantrine drugscompletely cleared the parasites within 4-5 days. The results of this study indicates that adulteration of Halofantrine is not presently in circulation in areas of Ondo and Ekiti states, South Western Nigeria.

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GJMR-B Classification : *NLMC Code: QX 135, WC 405*

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Efficacy of Halofantrine in Mice Infected With Plasmodium berghei

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I. Introduction

Malaria is a vector-borne infectious disease caused by protozoan parasites. It is widespread in tropical and subtropical regions, including parts of the Americas, Asia and Africa. Each year, there are approximately 350-500 million cases of malaria, killing between one and three million people, the majority of whom are young children in Sub-Saharan Africa (Snow *et al,* 2005). Ninety percent of malaria related death occur in Sub-Saharan Africa. Malaria is commonly associated with poverty, but is also a cause of poverty and major hindrance to economic development.

Halofantrine was developed in 1960s by the Walter Reed Army Institute of Research. Halonfantrine is used in the treatment of chloroquine resistant and multi-drug resistant, uncomplicated *P. falciparium* malaria therefore halofantrine is one of the choicest antimalaria drug in Nigeria. However, report from National Agency for Food and Drug Administration and Control (NAFDAC) shows that Nigeria is one of the haven of adulterated drugs in the world (FMH, Nigeria, 2004) but presently, only one brand of halofantrine is circulated and marketed in Nigeria, and no cases of adulteration of this drug has been reported. Although adulteration of another popular antimalaria (artesunate) had been detected in some part of the world (Lon *et al,* 2006), no cases of artesunate has been reported in Nigeria (Ologunde *et al*, 2008).

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This study is aimed at studying the therapeutic efficacy of halofantrine bought from different locations in Ondo and Ekiti states, Nigeria in mice infected with *Plasmodium berghei.*

II. Methodology

Swiss albino mice weighing between 12g and 17g were used in this study. The mice were kept in cages at room temperature where they were fed with standard mouse cubes manufactured by Ladokun Feeds Nigeria Limited, in Lagos state. They were randomly grouped into six groups of five mice each. The environmental conditions for all the mice throughout the period of the investigation were maintained the same.

Plasmodium berghei NK65 strain was obtained from malaria unit of Nigeria Institute of Medical Research Yaba Lagos state (NIMR) maintained by serial passage of blood collected from an infected donor animal to an uninfected mouse (Aina *et al*, 2006). Each mouse was inoculated with 1 x 10^6 paratisized red blood cells suspension blood in phosphate buffer saline (0.1) and were left for 3-7 days for the parasite to manifest. Two halofantrine tablets (250mg each) were dissolved in 10ml of water (which is equivalent to 50mg/ml) and 0.01ml of the prepared drug solution was administered into the mice following 24mg/kg body weight standard of oral halofantrine administration. The groups were coded according to the place of purchase of the drugs. The group that received halofantrine bought in Ikare-Akoko was coded HAL-IK, Akure was coded HAL-AK, Itaogbolu was coded HAL-IO and Ado-Ekiti was coded HAL-AD. However, two groups were not treated with the drug. One was given 0.5ml 0.9% normal saline (negative control) while the other was given chloroquine (positive control).

The blood sample of each mouse in each group was collected by tail snip with a sterile scissors. Thick blood film was made by smearing a drop of blood from tail snip on a microscopic slide and was dried at room temperature. These were viewed under oil immersion lens of light microscopy for the presence of the parasitemia. Responses of the mice to the drug were determined by the method of Ologunde *et al*, 2004, 2007.

III. Results

The results presented in figures 1- 4 show parasite responses to treatment in the four groups

treated with halofantrine, figure 5 show the parasite response to treatment in the negative control and figure 6 show the parasite response to treatment of chloroquine. All the animals in the negative control died after 10 days while those in other groups survived. Paired test was used for statistical significance. Table 1 show average parasite clearance rate (APCR) and average parasite clearance time (APCT). There was no significant difference in the average PCT between the halofantrine drugs ($P>0.05$) and also the average PCR shows no significant difference between the halofantrine drugs ($P>0.05$).

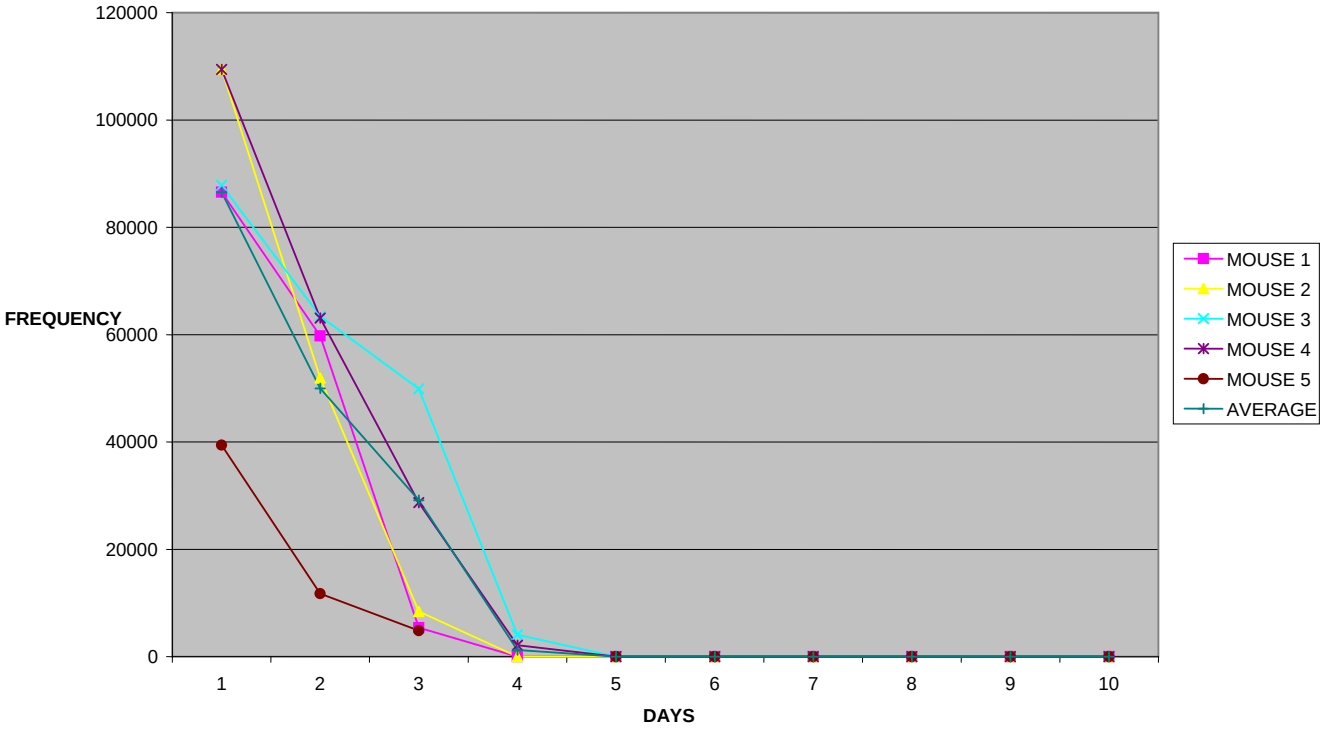

Figure 1 : Shows Parasite Response To Treatment (Hal-Ak).

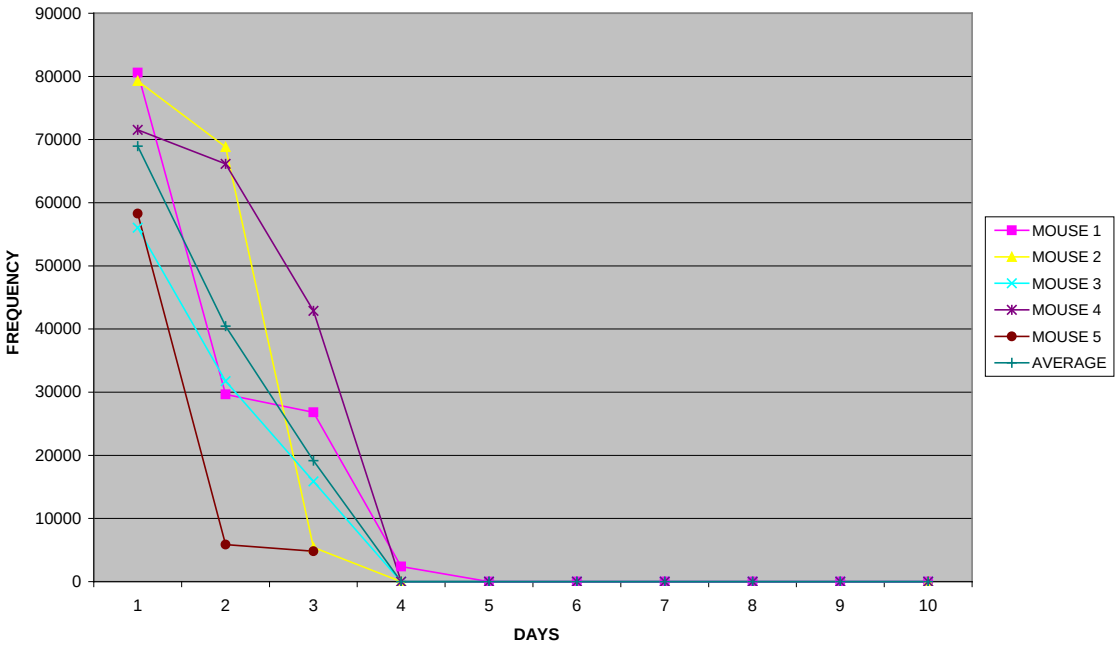

Figure 2 : Shows Parasite Response To Treatment(Hal-Io).

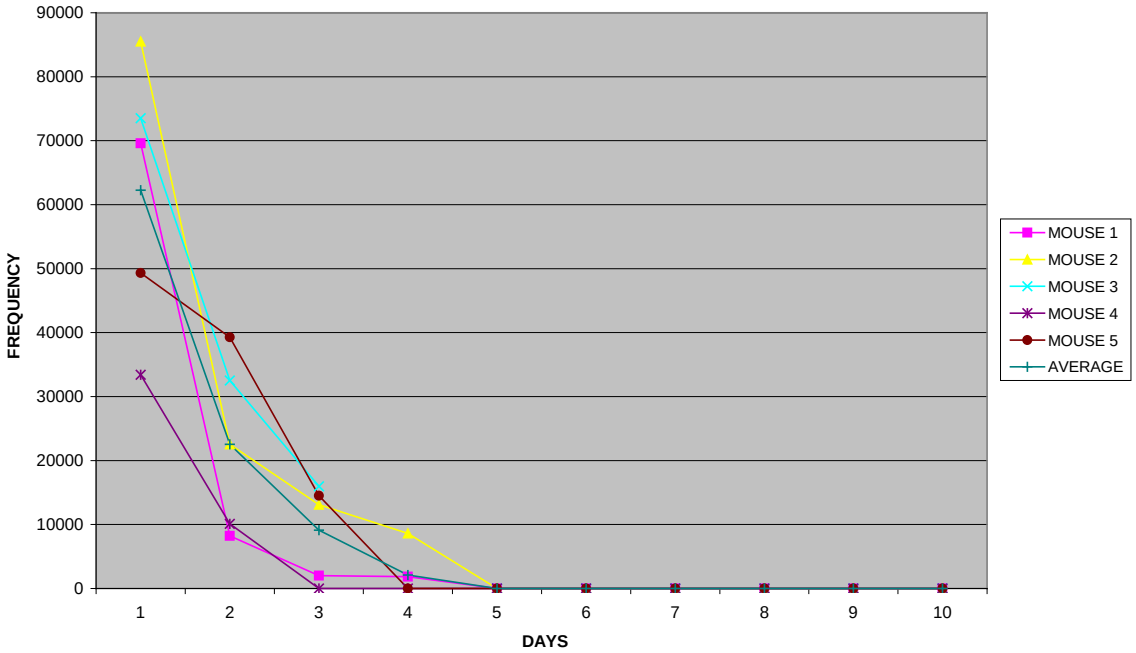

Figure 3 : Shows Parasite Response To Treatment (Hal-Ik).

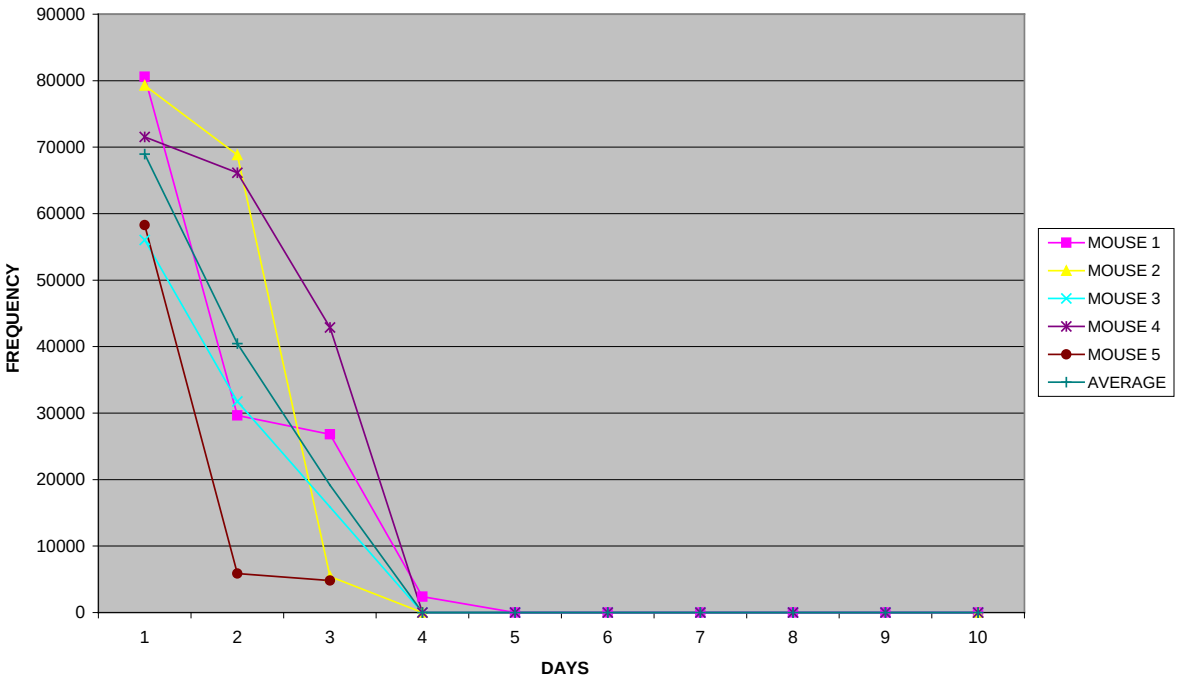

Figure 4 : Shows Parasite Response To Treatment(Hal-Ad).

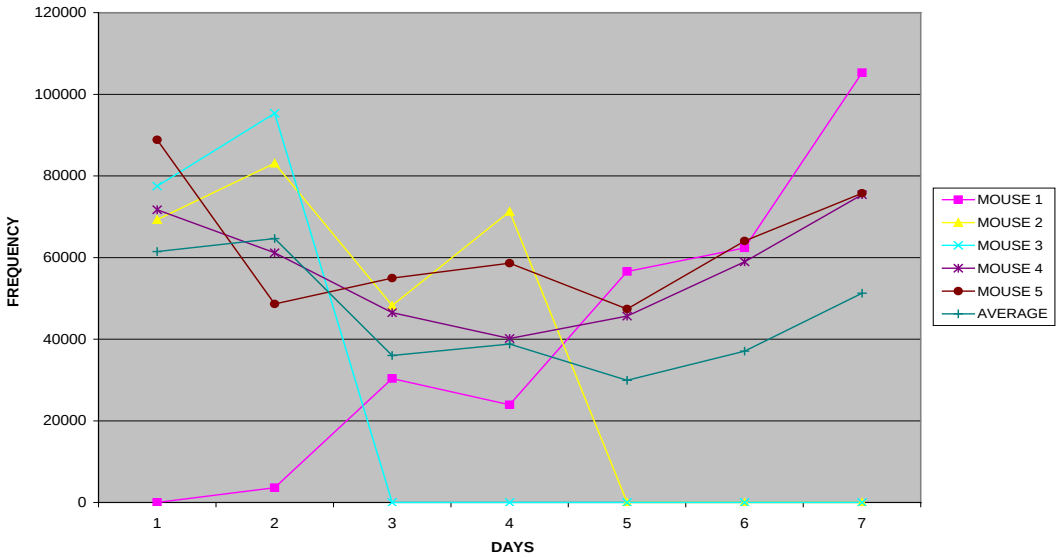

Figure 5 : Shows Parasite Response To Treatment (Negative Control).

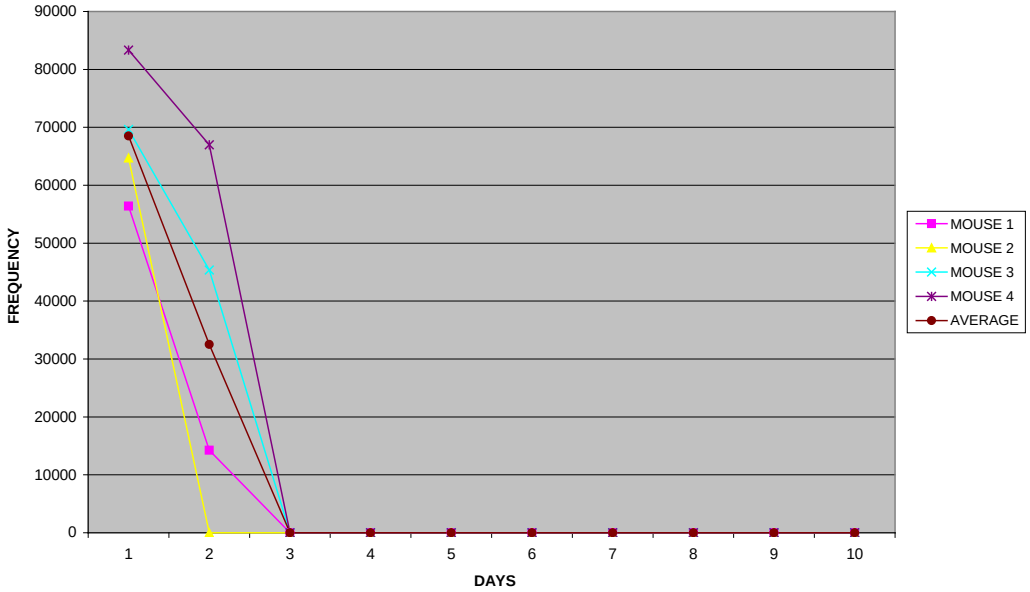

Figure 6 : Shows Parasite Response To Treatment (Chloroquine:Positive Control).

Table 1 : Average Parasite Clearance Rate (APCR) and Average Parasite Clearance Time (APCT).

HALFAN	PCR±SD	PCT±SD
HAL-AK	8653±2557	4.4±0.49
HAL-IO	6895±1010	4-2±0.40
HAL-AD	5426±3312	4.4±0.80
HAL-IK	6226±1850	4.2±0.75

IV. Discussion

The high mortality rate caused by severe malaria can be checked by adequate and effective antimalaria therapy. Malaria causes about 400-900 million cases of fever and approximately one to three million deaths annually (Breman, 20001). Meanwhile the use of chloroquine as the first line of drug in the treatment of malaria in Nigeria and other parts of the world had been stopped due to the presence of chloroquine-resistant strain in the *Plasmodium.* Resistance of *Plasmodium falciparum* has spread recently from Asia to Africa, making the drug ineffective against the most dangerous falciparum strain in many affected regions of the world (White *et al,* 2004). Unfortunately, chloroquine resistance is associated with reduced sensitivity to other drugs such as quinine, and amodiaquinine (Tinto *et al,* 2006).

The halofantrine drugs that were purchased from different locations in Ondo state and Ekiti state showed comparative efficacy in the mice infected with *Plasmodium berghei*. The drugs cleared the parasite to zero level in less than five days in all the mice treated when compared with the control. The parasite clearance clearing time (PCT) and the parasite clearance rate (PCR) showed no significant difference for the drugs ($P>0.05$) which is an indication that the drugs contain the adequate chemical composition and follow adequate stages of production.

The number of days when clearance level occurred in all the drugs differs (3-10days). This might not really show the differences in the efficacy of the drugs but rather factors like physiological state of the mice and parasite density before the administration of the drug. Other factor is depression in parasite response to treatment.

V. Conclusion and Recommendation

The result show that halofantrine drugs bought from different locations showed an effective clearance of the *Plasmodium* without significant difference and therefore it could be concluded that there was no adulterated drugs among the halofantrine drugs that were distributed and used by subjects living in Ekiti and Ondo state, south western Nigeria.

Government should adopt halofantrine drug as the first line of drug in the treatment of malaria in Nigeria and other parts of Africa. Government should also empower the drug enforcement agency in the country in search of adulterated drugs to forestall treatment failure and death from malaria parasite.

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