PRECLINICAL *IN VITRO* STUDY ON AMIDINE-HYDROXAMIC ACID BASED ANTIMALARIAL DRUG CANDIDATE.

BY

OPENIBO, JOHN OLUWAYOMI
B. Sc. Microbiology, Lagos State University, Lagos.
Matriculation number: 14PCQ01212

A DISSERTATION SUBMITTED TO THE DEPARTMENT OF BIOLOGICAL SCIENCES (MICROBIOLOGY UNIT), COLLEGE OF SCIENCE AND TECHNOLOGY, COVENANT UNIVERSITY, OTA, NIGERIA
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Acceptance

This is to attest that this dissertation is accepted in partial fulfilment of the requirements for the award of Master of Science (M.Sc.) degree in Microbiology in the Department of Biological Sciences, College of Sciences, College of Science and Technology, Covenant University, Ota, Ogun.

Mr. J. A. Philip ..…..……..……

(Secretary, School of Postgraduate Studies) Signature and Date

Prof. S. Wara ….……

Dean, School of Postgraduate Studies Signature and Date

Declaration

I hereby declare that this research work titled "**PRECLINICAL *IN VITRO* STUDY ON AMIDINE-HYDROXAMIC ACID BASED ANTIMALARIAL DRUG CANDIDATE**" was undertaken by **OPENIBO, JOHN OLUWAYOMI.** It is based on my original study in the Department of Biological Sciences, College of Science and Technology, Covenant University, Ota, under the supervision of Dr. G. I. Olasehinde and the ideas and the views of other researchers have been duely expressed and acknowledged.

Openibo, John Oluwayomi _____

(Student) **Signature and Date**

Certification

This is to certify that the project titled: **"Preclinical *in vitro* study on amidine-hydroxamic acid based antimalarial drug candidate"** is a record of a project research work carried by out by Mr. **OPENIBO, JOHN OLUWAYOMI** (Matriculation Number: **14PCQ01212**) in the Department of Biological Sciences, School of Natural and Applied Sciences, College of Science and Technology, Covenant University, Ota, under the supervision of **Dr. G.I. Olasehinde**.

Dr. G.I. Olasehinde _____
(Supervisor) **Signature and Date**

Prof. A. A. Ajayi _____

(Head of Department) **Signature and Date**

Prof. A. Sanni _____

(External Examiner) **Signature and Date**

Dedication

This dissertation is dedicated to God Almighty, the giver of wisdom, knowledge and understanding, as well as researchers who are contributing towards the elimination of Malaria disease.

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Openibo John O.

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Abstract

The emergence of drug resistant strains of malaria parasite has led to increased efforts to discover and develop new antimalarial drugs that are structurally distinct from already existing ones.This study was conducted to evaluate the antiplasmodial activity of novel amidine-hydroxamic acid derivatives. Chloroquine-sensitive – Pyrimethamine resistant *Plasmodium falciparum* 3D7 strain was cultured *in vitro* in O^+ human red blood cells in RPMI 1640 medium supplemented with 10% heat inactivated O human serum, 25mM HEPES buffer, 50µg/ml penicillin and 50µg/ml streptomycin under a condition of 90% N_2, 5% O_2 and 5% CO_2. Serially diluted drugs were seeded into 96-well microtitre plates and incubated with aliquots of parasite from 3D7 culture medium containing asynchronized stage of parasite at a parasitemia of 0.2% and an haematocrit of 4% and the asynchronized wild type *P. falciparum* blood sample at a parasitemia of 1% and 4% haematocrit. The results obtained from the inhibitory concentrations (IC_{50}) analyses performed for the novel antimalarial drug candidate compound revealed that the test compound with the code OA2 has IC_{50} values of 15,960nM against *Plasmodium falciparum* 3D7 and 0.3941nM against the wild type *Plasmodium falciparum,* while the standard drugs Artemisinin and Chloroquine were 68.86nM and 68.24nM and 164.5nM and 59.0nM for the wild type and typed strain *Plasmodium falciparum*. From the result obtained, It can be inferred that OA2 is moderately active against the viability of *P. falciparum* in human blood cultures and hence may be promising antimalarial drug candidates.

KEYWORDS: Pre-clinical, *In vitro, Plasmodium* resistance, Novel Drug, Antimalarial.