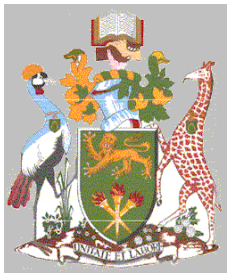

UNIVERSITY OF NAIROBI

MODELING AND SYNTHESIS OF ANTIPLASMODIAL CHROMONES, CHROMANONES AND CHALCONES BASED ON NATURAL PRODUCTS OF KENYA

BY

MANYIM SCOLASTICA

I56/79952/2012

A Thesis Submitted in Partial Fulfillment of the Requirements for the Award of the Degree of Masters of Science (Chemistry) of University of Nairobi.

2016

DECLARATION

I declare that this thesis is my original work and has not been submitted elsewhere for examination, award of a degree or publication. Where other people's work or my own work has been used, this has properly been acknowledged and referenced in accordance with the University of Nairobi's requirements.

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DEDICATION

This work is dedicated to my parents, brothers, sisters, Hillary and Harry.

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ABSTRACT

A significant amount of research has been done on plants of Kenya resulting in the isolation of thousands of natural products, but data on these natural products is not systematically organized in a readily accessible form. This has necessitated the construction of a web-based database of natural products of Kenya. The database is named *mitishamba* and is hosted at http://m*itishamba*.uonbi.ac.ke.

The *mitishamba* database was queried for chromones, chromanones and chalcones that were subjected to structure based drug design using *Fred* (OpenEye) docking utility program with 1TV5 PDB structure of the *Pf*DHODH receptor to identify ligands that bind with the active site. Ligand-based drug design (Shape and electrostatics comparison) was also done on the ligands against query **A77 1726** (**38**) (the ligand that co-crystallized with *Pf*DHODH receptor) using *ROCS* and *EON* programs, respectively, of OpenEye suite. There was an above average similarity among the top performing ligands in the docking studies with shape and electrostatic comparison. This led to the identification of compounds of interest which were targeted for synthesis and antiplasmodial assay.

A chromanone, 7-hydroxy-2-(4-methoxyphenyl) chroman-4-one (**48**) and two intermediate chalcones, 2',4'-dihydroxy-4-methoxychalcone (**45)** and 2',4'-dihydroxy-4-chlorochalcone (**47)**, were synthesized and subjected to antiplasmodial assay. Whereas **45** showed strong activity, **47** and **48** had moderate activity against the chloroquine resistant K1 strain of *P. falciparum* with IC_{50} values of 4.56±1.66, 17.62 ± 5.94 and 18.01 ±1.66 µg/ml, respectively. Since the synthesized compounds showed antiplasmodial potential, there is need for further computational refinement of these compounds to optimize their antiplasmodial activity.

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