DECLARATION

I hereby declare that the thesis entitled "*IN-SILICO* APPROACHES TO LOCATE POTENTIAL ANTI-MALARIAL COMPOUNDS: A STUDY ON QUINOLINYL CHALCONE DERIVATIVES AND HETEROCYCLIC SUBSTITUTED CHALCONE DERIVATIVES" submitted by me, for the award of the degree of *Doctor of Philosophy* to VIT University is a record of bonafide work carried out by me under the supervision of Dr. Sudha Ramaiah.

I further declare that the work reported in this thesis has not been submitted and will not be submitted, either in part or in full, for the award of any degree or diploma in this institute or any other institute or university.

Place: Vellore
Date: 25/11/2016

T. Mahalakshmi
Signature of the Candidate

CERTIFICATE

This is to certify that the thesis entitled "*IN-SILICO* APPROACHES TO LOCATE POTENTIAL ANTI-MALARIAL COMPOUNDS: A STUDY ON QUINOLINYL CHALCONE DERIVATIVES AND HETEROCYCLIC SUBSTITUTED CHALCONE DERIVATIVES" submitted by MAHALAKSHMI.T. (School of Bio Sciences and Technology) VIT University, for the award of the degree of *Doctor of Philosophy*, is a record of bonafide work carried out by her under my supervision, as per the VIT code of academic and research ethics.

The contents of this report have not been submitted and will not be submitted either in part or in full, for the award of any other degree or diploma in this institute or any other institute or university. The thesis fulfills the requirements and regulations of the University and in my opinion meets the necessary standards for submission.

Place: Vellore
Date: 25.11.16

Signature of the Guide
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ABSTRACT

The computational studies namely Molecular Docking Simulations and Comparative Molecular Field Analysis (CoMFA) are executed on series of quinolinyl chalcone derivatives and heterocyclic substituted chalcone derivatives using *Plasmodium falciparum* lactate dehydrogenase and cysteine proteases (falcipain-2) as vital targets. In the present study, the correlation between different molecular field effects namely steric and electrostatic interactions and chemical structures to the inhibitory activities of novel quinolinyl chalcones analogs and heterocyclic substituted chalcone derivatives are inferred to perceive the major structural prerequisites for the rational design and development of potent and novel lead anti-malarial compound. The apparent binding conformations of quinolinyl chalcone derivatives at the active site of lactate dehydrogenase and heterocyclic substituted chalcone derivatives at falcipain-2; the hydrogen-bond interactions which could be used to modify the inhibitory activities are identified by using Surflex-dock study. Statistically significant CoMFA models have been developed with the cross-validated correlation coefficient (q^2) of 0.850 & 0.912, the non-cross-validated correlation coefficient (r^2) of 0.912 & 0.901. Standard error of estimation (*SEE*) of 0.280 & 0.210, with the optimum number of components five & ten for quinolinyl chalcone derivatives and heterocyclic substituted chalcone derivatives respectively. The predictability of the derived models are examined with a test set consists of thirteen and sixteen compounds and the predicted r^2 values are found to be 0.885 and 0.924 for quinolinyl chalcone derivatives and heterocyclic substituted chalcone derivatives respectively. The docking and QSAR study results confer crucial suggestions for the optimization of novel quinolinyl chalcone derivatives and heterocyclic substituted chalcone analogs for the design and development of effective anti-malarial compounds.