Chapter 5

Conclusions

The malarial infection causes consistent loss of million people every year, imposes sincere responsibility to research scientists and healthcare professionals to safeguard the life by eliminating the infection at the earliest. This responsibility shall be fulfilled only by the design and development of novel, potent and safe anti-malarial compounds especially against *P. falciparum*, the causative agent of severe malaria, which has gained resistance to most of the anti-malarial compounds, including artemisinin derivatives.

Considering the above facts, molecular modeling studies are carried out. In this present study, the molecular docking and 3D-QSAR CoMFA analyses have been successfully carried out with novel quinolinyl chalcone derivatives and heterocyclic substituted chalcone derivatives.

These studies are executed to examine the critical structural requirements for the design and development of more active inhibitors against P*f* lactate dehydrogenase and *Pf* cysteine proteases. The binding mode of the novel inhibitors is assessed by Surflex-docking program. The output of the docking study recommends that the hydrogen bond interactions are the major interaction which could be considered as critical in the alteration of inhibitory activities of novel quinolinyl chalcone derivatives and heterocyclic substituted chalcone derivatives.

Based on the finest docked poses, best predictive CoMFA models are developed. The model provides statistically significant results in terms of cross-validated coefficient q^2 of 0.850, conventional coefficient r^2 of 0.912, $r^2_{(pred)}$ of 0.855, correlation graph and small *SEE* of 0.280 for novel quinolinyl chalcone derivatives. Cross-validated coefficient q^2 of 0.912, conventional coefficient r^2 of 0.901, $r^2_{(pred)}$ of 0.924, correlation graph and small *SEE* of 0.210 for novel heterocyclic substituted chalcone derivatives indicating the presence of better statistical relationship between the descriptors and inhibitory activity.

Both the docking studies and 3D-QSAR CoMFA models have presented the harmonized details. The 3D contour plots derived from the CoMFA models deliver the relationship between the structure and activity and provides the suggestions for the alteration in the substitutions which will result in enhanced activity.

The results from the current study could be utilized for design and development of lead and potent *P. falciparum* lactate dehydrogenase and cysteine protease inhibitors to combat malaria.