There were an estimated 198 million cases of malaria worldwide (range 124–283 million) in 2013 and an estimated 584 000 deaths (range 367 000–755 000). 90% of all malaria deaths occur in Africa. Emerging parasite resistance to antimalarial medicines and mosquito resistance to insecticides, if left unaddressed, could render some of the current tools ineffective and trigger a rise in global malaria mortality. In recent years, parasite resistance to artemisinin has been detected in five countries of the Greater Mekong sub-region: Cambodia, Laos, Myanmar, Thailand and Viet Nam. In areas along the Cambodia–Thailand border, *P. falciparum* has become resistant to most available antimalarial medicines, and multi-drug resistance is a major concern (Organization, 2014b).

The *P. falciparum*, *Anopheles gambiae* and *Homo sapiens* genome sequences have been completed in the between 2000-2002 and represent new starting points in the centuries-long search for solutions to the malaria problem. For the first time, a wealth of information is available for all three organisms that comprise the life cycle of the malaria parasite, providing abundant opportunities for the study of each species and their complex interactions that result in disease. The work reported on genomics needs to be accompanied by larger efforts to develop new methods of control, including new drugs and vaccines, improved diagnostics and effective vector control techniques. Much remains to be done (Gardner *et al.*, 2002). In the past few years, there have been strong demands to generate and integrate molecular, functional and pharmacological data into a common malaria-related chemogenomic knowledge space (Mestres *et al.*, 2013).

In the present work, we have experimented the integrative approach of using *in silico* study for target finding and molecular docking, pharmacophore based screening in combination with *in vitro* study for screening novel drug candidate against *P. falciparum*.

The Research Database was developed from the genomics, literature and ligand information. Genome data were incorporated into pathologics software and embedded further with current literature information and made available offline and online for researcher. Moreover the user, friendly online docking server for antimalarial drug discovery was also created. These will be a powerful platform for future antimalarial drug discovery by academic and industrial researcher with less IT knowledge. Altogether, the network mode analysis was able to find out the potential less explored the target and find the group of related and potential target for polypharmacological study against *P. falciparum*. 
Search for novel anti *P. falciparum* was done from the Heterobase database library comprising more than 3000 compounds reported from the Ph. D thesis available in Gujarat state University Library. The consecutive *in silico* and *in vitro* screening resulted in 27 lead compounds with potential anti *P. falciparum* activity. The lead compounds can be explored eventually as drug candidate for antimalarial drug discovery.

The consensus matrix analysis for molecular docking, Structure-based pharmacophore and ligand-based pharmacophore based was effective to reduce the shortlisted compounds from individual screening to consensus lead compound with augmented assurance.

The major study was concentrated on the Plasmepsin target from the *P. falciparum* and the top compound recorded from *in silico* screening was 3001. Consequently compound 3001 and similar compounds were explored with *in vitro* study and displayed comparable trend in activity. However, the active lead compounds of *in vitro* study were 3004, 3007 and 3010 against both *P. falciparum* and *P. vivax*. As in either case compound 3007 have the most versatile ability to bind with the multiple targets including multi-drug resistant targets. Substantially, compound 3007 was appeared as the best lead compound of the present study. The *in silico* screening results proposed the need of further study on compound 3007 for anti *P. vivax* and anti-HIV drug discovery.

Polypharmacology *in silico* screening against seven targets for *P. falciparum* extracted 22 compounds with exceptional potential. Furthermore, the compound 518(4-(2-chloro-6,8-dimethylquinolin-3-yl)-6-(3-nitrophenyl)-3,3a,4,5-tetrahydro-2H-indazol-3-one) was obtained as the outstanding compound for dual targeting the HIV and *P. falciparum* in the current study. This can be further explored with *in vitro* testing.

The Integrative biology and Systems biology based methodology applied in the present study with least resources and Open source software was less expensive and more effective for working on a large scale for neglected disease like malaria. Where, Pharmaceutical Company and international researcher from the developed country are less focused. The present study demonstrated that Integrative and interdisciplinary approach can extend the use of data generated from the academic research activity in significant manner.