As per WHO 2013 report, malarial infection kills 1300 young people every day. India account for 52% cases reported in year 2012 from South Asia region (Organization, 2014b). More than one million death was reported under the age of five each year worldwide (Thanh et al., 2010). Amongst four major species, *Plasmodium falciparum* account for 95% cases worldwide. There are several marvelous antimalarial drugs like chloroquine and artemisinin have leads to the emergence of multi-drug resistant strains of *Plasmodium* (Bozdech et al., 2003; S. a Ralph et al., 2004). The polymorphism in multi-drug resistance genes Pfmdr1, Pfcrt and Pfne1, intensify resistance in all antimalarial drug derivatives (Cheruiyot et al., 2014). This situation exhibit extreme requirement to develop new medications towards *Plasmodium falciparum* (Bispo et al., 2013). Molecular biology has uncovered a multitude of biological facts, such as genome sequences and protein properties, but this alone is not sufficient for interpreting biological systems. The deep system-level understanding to develop the newer path of success achieved by synergistic integration of theory, computational modeling and experiments in laboratories (Kitano, 2002b).

Integrative biology and Systems biology are newly emerging, multi-disciplinary approach that studies the mechanisms underlying complex biological processes. These processes were integrated biological system for many interacting components (Hood, 2003). The integration of all data sets of literature, *in vitro*, genomics, proteomics or metabolomics data for synergistic network model development(Gopalacharyulu et al., 2005). The predictive model can be utilized for Metabolism studies, flux analysis, pharmacokinetics study, interactome analysis as well as drug discovery (Hopkins, 2008; Plata et al., 2010; Vashisht et al., 2012).

In light of this system level understanding our view to study and combat disease has been changed. We realized most of the diseases of humanity today are multifactorial: they are not simply the result of one mutation in one gene, producing one wrong protein that can no longer carry out its job. It depends on many simultaneous genetic and environmental factors. Similarly, in basic biology, processes cannot be optimized by simply changing one component of a complex process. It is the networks of interaction that Systems Biology, the study of how biological networking produces function at the level of the cell, organ and body, focuses on. The idea is that once we know which networks are fired in health, and misfired in disease, we will know how to fix the consequences of misfires by treating networks rather than just component molecules (Ayes et al., 2006; Birkholtz et al., 2006;
The sequencing and annotation of *Plasmodium falciparum* 3D7 provide elementary information to carry out systems biology analysis (Bozdech et al., 2003). The network model creation can be performed by several software tools available free as well as pro versions. The Cell designer, cytoscape and Pathway tools was successor in race for such tool (Funahashi et al., 2008; Paley & Karp, 2006).

*Plasmodium*, a causative agent of malaria has developed resistance to existing drugs of Quinolines, Chloroquine and Artemisine derivatives, which creates an urgent need to find out novel drug target and drug (Spiliotopoulou et al., 2013). Plasmepsin was important to kill *Plasmodium spp.* by blocking hemoglobin degradation in food vacuole (Banerjee et al., 2002). *in silico* drug discovery provide and effective and rapid method to evaluate chemical compounds in computers itself (Crowther et al., 2010). However, several chemical compound libraries were analyzed to find better treatment, but it is important to further evaluate compounds synthesized worldwide. Medicinal plants and Phytochemicals should also provide effective treatment for combinatorial drug discovery approach (Bagavan et al., 2011). *in vitro* analysis provides effective strength to *in silico* drug discovery studies (Ross et al., 2014).

In present study, the virtual screening was performed with Autodock Vina 4.2 software for molecular docking based approach. Whereas, structure-based and ligand-based pharmacophore virtual screening was carried out with Ligandscout Software. The lead molecules screened from virtual screening were analyzed by *in vitro* LDH based activity for *Plasmodium falciparum* and *Plasmodium vivax* (Zofou et al., 2011). Besides that, the obtained results were in depth reanalyzed for investigating polypharmacology properties of lead molecules and selective binding to drug target. The study was also under taken for probing the possible potential for inhibition of Human Immunodeficiency Virus (HIV). The drug like property at *in silico* QSAR study was done for lead molecules.
Integrative biology and systems biology exploration for anti malarial drug discovery was the main aim of present study with following objectives

1. Metadata collection from various resources of *Plasmodium falciparum*.

2. Creation of a comprehensive network model for *Plasmodium falciparum* based on integrated biology and Systems Biology approach.

3. Development of web-based portal for *Plasmodium falciparum* related data deposition, exchange, evaluation and analysis.


5. Creation of *in silico* library of novel compounds for drug discovery.

6. Virtual screening of novel compounds against established and research target.

7. *in vitro* study of potential compounds.