ABSTRACT

In this thesis, we examined the concepts of molecular similarity / dissimilarity and the growth of Diversity Oriented Synthesis (DOS) as an alternative to combinatorial chemistry. A brief description of the procedures for the synthesis of hybrid compounds using DOS via “Platform technology” is followed by detailed experimental analysis for synthesizing natural product inspired hybrids using the pyrroloisoquinoline scaffold as a platform. The hybrids were screened against several phenotypes for cytotoxicity, antiplasmodial activity and anti-malarial activity. A cheminformatics study was undertaken for comparing the physico-chemical properties of the synthesized hybrids against similar commercial drugs.

We also studied the dissimilarity / similarity features of the chemical libraries through an analysis of the topological properties of threshold Chemical Space Networks (CSNs). During the process, we developed QuaLDI (Quantitative Library Diversity Index), a simple measure for quantifying diversity in DOS, Focussed and PubChem Libraries. The effectiveness of QuaLDI was evaluated by comparing the results from QuaLDI with other diversity measures. We used correlation matrix guided approach combined with QuaLDI measure as an effective approach for selecting minimally correlated descriptors for QSAR modelling.