ABSTRACT

Tuberculosis is a pandemic disease caused by *Mycobacterium tuberculosis*. It usually infects lungs. Improved public health programs have helped to create a steady decline but problem is far from solved. Many repurposing and repositioning drugs have been focused by many researchers all over the world. First line drugs were more potent so, these are often used with modification for treating tuberculosis infection. Experimental procedures are expensive, time consuming and laborious tasks. Currently *In silico* methods are used to predict the structure. Docking methods are used to predict the complex between ligand and receptor. *In silico* docking methods include shape complimentary and simulation methods known as rigid and flexible docking. In this thesis two first line drugs rifampicin and ethambutol were selected. Total 50 analogues of rifampicin were designed, of which 27 were failed to make complex with its target molecule (RNAP-beta) during *in silico* docking. On the other hand remaining 23 analogues made complexes by docking, of which 22 showed H-bonding with the target, whereas, 1 analogue did not show any interaction with the target in the docked complex. Screening of the 22 analogues on the basis of prediction of their binding affinity, number and strength of the active interactions of analogue with the target in the docked complex and the drug likeness score showed that two of the analogues (as named in this study analogue 3and 4) are the potential candidates for future drug to be tested experimentally. Similarly, 20 analogues of ethambutol were designed. Of these analogues 4 (analogue 2, 3, 17 and 19) were screened as the most potential future drugs to be tested experimentally. We conclude that just some minor derivations of the parent compound produced significant effects through *in silico* studies. Experimental studies will finally lead us for having a stable organic synthesis of these designed compounds followed by its binding studies with the target molecule both *in vitro* and *in vivo* and bioassays for the safety and possible side effects of the drug.