ABSTRACT

Our aim is to Design and synthesize a new lead molecule for MDR – TB compound. A New series of 3-(substituted benzylideneamino) - 7-chloro2-phenyl quinazoline-4(3H)-one/7-chloro2-phenyl-3-(1-phenylethylideneamino) quinazoline-4(3H)-one & 3-(substituted benzylideneamino)-7-chloro2-(4-chlorophenyl) quinazoline-4(3H)-one/7-chloro2-(4-chlorophenyl)-3-(1-phenylethylideneamino) quinazoline-4(3H)-one Schiff based molecules were synthesized condensing with various substituted aromatic aldehyde/ketones based on the preliminary Docking studies. The mode of action of these active compounds was carried out by docking of receptor Mycobacterium tuberculosis Mycolic acid cyclopropane synthetase (cmA2) with newly synthesized ligands. These compounds exhibited well established bonds with one or more amino acids CYS26, LEU180 and TRP83 in the receptor active site. The synthesized compounds assign all the parameters of the Lipinski’s rule of – Five. From the Docking studies, compound CQ-4 was considered to be the best inhibitor. All the New molecules were characterized by spectral Analysis. The absorption peaks around 1600cm⁻¹ indicates that the formation of C=N imines of quinazoline. Amide C=O stretching vibrations were observed near 1640-1690cm⁻¹. Aromatic C=C linkage was confirmed with 1467-1445cm⁻¹ and all other relevant groups absorption were observed for all the synthesized compounds.¹H nuclear magnetic spectra were taken for synthesized compounds. Aromatic protons were observed 6.5-8.3δ ppm, imine and CH singlet proton was observed in 9.3-9.5δ-ppm and all other protons also appeared.
The newly synthesized compounds were screened for their anti-bacterial studies, and it is clear that (series-2) electronegative groups have more active (DCQ4, DCQ7 and DCQ9) than unsubstituted compounds. The most active derivatives in this series were DCQ4 and CQ7 compounds. However, none of the synthesized compounds were found superior than the standard ciprofloxacin. The MIC value of the compound CQ-7 & DCQ - 4 (where no bacterial growth was observed) was found to be 64 μg/ml (test tube no.3 & 7).

The newly synthesized compounds were screened for their anti-mycobacterial studies based on the promising preliminary anti bacterial result. Among the tested compounds CQ-4 (series-1) found to be more active at 3.125 μg/ml concentration and DCQ-10 (series-2) at 6.25μg/ml were active at against MDR- Mycobacterium tuberculosis H37RV strain by Microplate Alamar Blue Assay (MABA) using Isoniazid 0.8 μg/ml as standard.