SYNTHESIS AND STRUCTURE-BASED STUDIES OF FMN RIBOSWITCH LIGANDS: EXPLORING FMN RIBOSWITCH TARGET TO FIND NEW ANTIBIOTICS

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Antibiotic resistance is rising worldwide to dangerously high levels causing 25000 deaths, each year in Europe alone. We are standing amid the antimicrobial resistance crisis and the deficit of effective antibiotics urges us to look for new modes and targets to combat antibiotic-resistant bacteria.(1) Riboswitches are noncoding RNAs that regulate gene expression as a response to metabolite binding.(2) They have emerged as new targets for antimicrobial drugs. Recently some FMN ligands have been reported in the literature such as Ribocil C, which has shown high selectivity towards bacterial cell growth of *E. coli* MB5746 and in a mouse *E. coli* septicaemia infection model.(3) The discovery of Ribocil as small-molecule drug, have paved the way for researchers worldwide into the nascent and exploding field of riboswitch based drug discovery. In this context, there is an urgent need to explore and expand the chemical space of ligands targeting riboswitches.

In this work, we have prepared Ribocil C, and its analogue in addition to several fragments of Ribocil C. We aim to probe the chemical space of FMN riboswitch ligands with the help of the synthesized fragments and the analogue.

The information regarding the structure-activity relationship will be collected through biophysical methods (such as isothermal titration calorimetry (ITC) and surface plasmon resonance (SPR) experiments).

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