DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL BIO-ACTIVE MOLECULES

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The work embodied in this thesis is based on the opportunities offered by antibiotics for the design and synthesis of novel bio-active compounds. Oxazolidinones are the newest class of antibiotics introduced and approved for use in humans against nosocomial infections. Linezolid, is the only drug from this class of antibacterial agents, and has a novel mechanism of action and lacks cross resistance against the existing antibacterial drugs.

This thesis describes the design and synthesis of novel oxazolidinones based on Eperezolid (Pharmacia) as the lead compound. The following three cores were synthesized

- (S)-N-[[3-[3-[Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl acetamide (**piperazinyl core**),
- (S)-N-[[3-[3-[Fluoro-4-(N-1-homopiperazinyl)phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide (**homopiperazinyl core**),
- (S)-N-[[3-[3-Fluoro-4-{N-1-(2-methyl)-piperazinyl}-phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (**2-methyl-piperazinyl core**),

and attached to various five membered mono-heterocycles. Optimization of - the substituent on the heterocycle, the heteroatom of the heterocycle, and the linkers attaching the heterocycle with the cores, were carried out. The **homopiperazinyl core** and the **2-methyl-piperazinyl core** synthesized were bio-isosteres of the **piperazinyl core**. These compounds were evaluated for their biological activity against resistant and susceptible strains of *Staphylococcus aureus* and enterococci.

This work explores some newer dimensions of oxazolidinone- antibiotics for the design and synthesis of new chemical entities against novel targets in the new drug discovery programme.