ABSTRACT

The thesis entitled with “Design and synthesis of Novel fluoroquinolones as antibacterial agents” comprising of design strategies and synthesis of the designed fluoroquinolone derivatives through multi step reactions. Further, it comprises chemical characterization and biological evaluation of the novel derivatives.

The entire research work is divided into six chapters. Chapter 1 deals with introduction, classification and applications of different classes of fluoroquinolones against various infectious diseases. Chapter 2 describes synthesis of common starting materials (6a & 6b) and thirty novel N-substituted glycinamide derivatives viz. Scaffold 1 (11 a-o) and Scaffold 2 (12 a-o). In addition, comparison studies between compounds derived from scaffold 1 and scaffold 2 for their antibacterial properties.

Chapter 3 deals with concept of bioisostere properties of [1,2,3]-triazoles and amides. Synthesis of twenty new N-substituted aminomethyl-[1,2,3] triazolyl derivatives at C-7 position of fluoroquinolones viz. scaffold 3 (16 a-t). Comparison studies between compounds derived from scaffold 2 and scaffold 3 for their antibacterial properties.

Chapter 4 includes synthesis of six new hydroxamic acid derivatives at C-3 position of fluoroquinolones viz. scaffold 4 (23a-f). Further, it explains the effect on biological properties upon the replacement of 3-carboxylic acid with its bioisostere hydroxamic acid. Chapter 5 deals with synthesis of nine new N-(substituted azetidine-3-carbonyl)-N-methyl-hydrazino derivatives viz. scaffold 5 (28 a-i) at C-7 position of fluoroquinolones. Chapter 6 concludes the overview of the research work.
Overview of the entire research work

Appropriate synthetic methodologies have been developed for the synthesis of new targets and synthesized the new targets as described in schemes 2.1, 2.2, 3.1, 4.1, 4.2 and 5.1. Their purification techniques have been established. All the newly synthesized compounds have been characterized using FTIR, $^1$H NMR, $^{13}$C NMR, mass spectral and elemental analyses.

Further, the target compounds have been evaluated for their in vitro antibacterial activity against *Staphylococcus aureus* (ATCC 6538P), Methicillin-sensitive *Staphylococcus aureus* (ATCC 29213), Methicillin-resistant *Staphylococcus aureus* (ATCC 33591), Vancomycin-resistant *enterococcus faecalis* (ATCC 700802), Linezolid-resistant *Staphylococcus aureus* (Recultured), *Enterococcus faecalis* (ATCC 29212), *Escherichia coli* (ATTC-25922), *Escherichia coli* (ATCC 35218), *Klebsiellapneumoniae* (ATCC 35657) and *Moraxella catarrhalis* (ATCC 25238). Furthermore, fifteen target molecules have been subjected for their anti-proliferative
activity against Lung adenocarcinoma (A549), Cervical adenocarcinoma (HeLa), Colon carcinoma (HCT-116) and Pancreatic carcinoma (PANC1).

From the results of the antimicrobial study, it has been observed that compounds derived from scaffold 2 (amide derivatives) and scaffold 3 (triazole derivatives) exhibited improved antibacterial activity against Gram-positive strains with retention of activity against Gram-negative strains. Moreover, replacement of 3-carboxylic acid of fluoroquinolones with hydroxamic acid group (Scaffold 4) found to have good anticancer activity against A549, HeLa, HCT-116 and PANC1 cell lines.