PREFACE

A wide variety of heterocycles that have been explored for developing pharmaceutically important molecules which played an important role in medicinal chemistry. The increasing clinical importance of drug-resistant microbial pathogens has lent additional urgency in microbiological research. It is an object of one aspect of this synthesis and biological evaluation to provide novel biologically active compounds which can be used for the preparation of medicaments. The search for new antimicrobial agents will consequently always remain as an important and challenging task for medicinal chemists. Thus the aim of this work is to develop newer synthetic methodology for heterocyclic ring system and to synthesize newer heterocycles for further testing and if successful to apply this methodology to the synthesis of other related heterocycles which may show similar or improved bioactivity.

A large number of drugs and biologically relevant molecules contain heterocyclic systems. Often the presence of hetero atoms or groupings imparts preferential specificities in their biological responses. Amongst the heterocyclic systems, compounds containing hetero atoms such as nitrogen and sulfur e.g., triazole, imidazole, benzothiazole, thiazolinedione etc. have great importance due to their diverse biological activity. Hence, our present work deals with the synthesis and antimicrobial studies of such nitrogen and sulfur containing heterocycles.

Recently in M. Phil. studies, I have synthesized 40 new triazoles bearing benzothiazoles with 10 substituted hydrazino benzothiazoles and four oxadiazoles and tested their antibacterial, antifungal and antitubercular activity; some of them displayed very good activities. From these work, I have published few articles given below:

➢ “Pharmacological evaluation and characterizations of newly synthesized 1,2,4-triazoles”; *European Journal of Medicinal Chemistry*, 45, 4293-4299, 2010.
“Antimycobacterial and antimicrobial study of new 1,2,4-triazoles with benzothiazoles”; *Archiv Der Pharmazie*, 343, 692-699, 2010.

“Synthesis of 1,2,4-triazole derivatives containing benzothiazoles as pharmacologically active molecule”; *Journal of Enzyme Inhibition and Medicinal Chemistry*, 26 (4), 527-534, 2011.

“Anti-HIV, antimycobacterial and antimicrobial studies of newly synthesized 1,2,4-triazole clubbed benzothiazoles”; *Medicinal Chemistry Research*, 22, 1320-1329, 2013.

The azole drugs may be regarded as a new class providing truly effective drugs which are reported to inhibit the bacteria by blocking the biosynthesis of certain bacterial lipids and/or by additional mechanism, we have tried to incorporate biologically active azole scaffold i.e. 1,2,4-triazole clubbed with imidazole, imidazolone bearing thiazolidinedione, benzothiazolyl imidazole and thiazolidine dione clubbed heterocycles to check their biological activity.

We report herein the synthesis of more potent new heterocycles of triazole clubbed imidazole, imidazolone clubbed thiazolidinedione, benzothiazolyl imidazole and thiazolidinediones as possible antimicrobial and antitubercular agent.

Present thesis consists of five Chapters in which, Chapter I contains three Sections. Section I contains introduction & literature review of 1,2,4-Triazole, Section II contains introduction & literature review of Imidazole and Section III contains introduction & literature review of 1,3-Thaizolidine-2,4-dione.

Chapter II contains four sections including experimental, spectral, biological (antibacterial, antifungal and antitubercular activities) studies and result and discussion of *N*-[3-(penta/tetrafluorophenyl)-5-substituted heterocycles-4H-1,2,4-triazol-4yl]-1H-benimidazole-2-amine.

Chapter III contains four sections including experimental, spectral, biological (antibacterial, antifungal and antitubercular activities) studies and result and discussion of 5-{3-[(substituted-benzylidine)-5-oxo-2-phenyl-4,5-dihydro-imidazol-1-yl]-benzylidene}-thiazolelidine-2,4-dione.

Chapter IV contains four sections including experimental, spectral, biological (antibacterial, antifungal and antitubercular activities) studies and result and discussion of substituted -1-hetercycle-4a, 10a-dihydro-9-thia-2,4,4b.10-tetraaza-indeno[1,2-a]indene-3-thiol.
Chapter V contains four sections including experimental, spectral, biological (antibacterial, antifungal and antitubercular activities) studies and result and discussion of 2-(5-{4-[2-(5-ethyl-pyridin-2-yl)-ethoxy]-benzylidine}-2,4-dioxothiazolidin-3-yl)-N-heterocycle-acetamide.

All the new synthesized compounds have been proved by elemental, spectral studies like IR, $^1$H NMR and $^{13}$C NMR spectra and few compounds were analyzed for Mass spectra. Antibacterial activity (MIC) against Gram positive bacteria (S. aureus and S. pyogenes) and Gram negative (P. aeruginosa and E. coli) bacteria by broth dilution method were compared with standard drugs ampicillin, chloramphenicol, ciprofloxacin, norfloxacin and gentamycin. Antifungal activity (MIC) against C. albicans, A. niger and A. clavatus by broth dilution method was compared with standard drugs greseofulvin and nystain. Antitubercular activity (MIC) against M. tuberculosis H$_{37}$Rv by Lowenstein-Jensen method was compared with standard drug rifampicin.

2-Thiobenzylpyridine, quinolonic acid and ciprofloxacin based oxadiazole 9b, 8d and 8e showed good activity towards Gram negative bacteria E. coli. Norfloxacin based 1,3,4-oxadiazole 8f and 1,2,4-triazole 11f showed very good activity against M. tuberculosis. 4-Methoxy phenyl substituted thiazolidinedione based imidazolone 3g showed good activity towards Gram negative bacteria E. coli. Nitro and flouro substituted phenyl derivatives of imidazolyl benzthiazole showed good activity towards Gram negative bacteria E. coli. Nitro and chloro substituted benzthizolyl imidazolone and thiopyrimidine are active against E. coli and M. tuberculosis. Methyl substituted benzothiazole clubbed with thiazolidinedione 6g is active against M. tuberculosis.