PREFACE

The discovery of efficacious new human therapeutic agents is one of humanity's most crucial responsibilities. In an ideal world, no education would be complete without some exposure to the ways in which new medicines are discovered and developed.

One of the prominent disease tuberculosis (TB), claiming nearly 1.8 million deaths in 2008 including 500,000 people with HIV. After AIDS, tuberculosis is the leading cause of death among infectious diseases in the world. The regimens were optimized along with the working of the directly observed therapy short course (DOTS) and much work done insights into the mechanisms of action of the antitubercular drugs currently used. The serious challenges to overcome includes lack of qualified human resources, poor infection control, unavailability of new drugs, insufficient laboratory capacity and weak surveillance systems. The limitations of available treatment options- including non-prequalified drugs, high drug costs, and barriers to registering and procuring quality-assured drugs - hamper universal access to health services for the prevention, management and control of MDR-TB. The emergence of extensively drug-resistant TB (XDR-TB) is another significant challenge to the already complex field of drug-resistant TB.

It is therefore vital that TB control is managed properly and new tools developed to prevent, treat and diagnose the disease. The greater effort is required to find better drugs in order to meet the desired goals of killing persistent tubercle bacilli (latent TB) and reducing TB treatment duration from 6 to less than 3 months. Therefore, attempts are being made to develop new antituberculosis drugs with a novel and new mode of action.

The work embodied in this thesis has been carried out in the Medicinal and Process Chemistry Division, Central Drug Research Institute, Lucknow-226001, CSIR, India during the period 2005 to 2010. The thesis is divided into five chapters.

Chapter 1. illustrate an overview on tuberculosis which mainly deals the drugs currently used in tuberculosis treatments with their mode of action, antitubercular drug targets, present day problems, the compounds undergoing clinical trials followed by antitubercular agents developed within last 10 years is being given.
Chapter 2. describes the synthesis of cyclopropyl[(benzyloxy)phenyl]methanone, methanoles and other derivatives with their biological evaluation against *M. tuberculosis* H37Rv and H37Rv.

Chapter 3. elaborates the synthesis of a preliminary series of 4-(butenolid-5-methyldienyl)-1,4-dihydropyridines and their antitubercular evaluation.

Chapter 4. has been divided into two sections:

Chapter 4A. describes the hybridization of two antitubercular pharmacophore (pyrrolidine and chroman) to get novel molecules and their bio-evaluations against *M. tuberculosis* H37Rv.

Chapter 4B. deals with the application of 3+2 dipolar cycloaddition reaction in the synthesis of 5-benzyl-3-phenyl dihydroisoazoles as antitubercular agents.

Chapter 5. comprises of two sections:

Chapter 5A. describes the stereoselective synthesis of butenoyl C-glycosides, polyfunctional alkanonyl glycosides and their enzyme inhibitory, antituberculer activities.

Chapter 5B. describes the synthesis of pyranosyl homo-C-nucleoside and evaluated for their antidiabetic potential using α-glucosidase, glycogen phosphorylase and glucose-6-phosphatase.

Relevant references are given at the end of each chapter. Parts of this thesis have already been published and the list of publication is given at the end of thesis.