PREFACE

This thesis is the outcome of my Ph.D. study at Zydus Research Centre and the department of Chemistry, The Maharaja Sayajirao University of Baroda, Vadodara, India. This study has been also a part of my job as senior scientist at Zydus Research Centre, Ahmedabad, India to which I have been affiliated since April 2000.

The thesis consists of four major sections which cover various aspects of metabolic syndrome and development of PPAR agonists for the treatment of the syndrome. Five papers have been published in international journals.

The '**Introduction**' section deals with the general information about metabolic syndrome, wherein detailed pathophysiology of the disease and the current treatment options were discussed. This was followed by an introduction to PPARs as targets for the treatment of metabolic disorders.

In the section titled '**Designing PPAR agonists**', the strategies and rationale for designing novel and sub-type selective PPAR agonists are discussed.

The '**Results & Discussion**' section describes the synthesis, biological activities and molecular modeling studies of the novel compounds.

The '**Experimental**' is the section where the detailed procedures for the synthesis of the compounds as well as the characterization data are presented. The details of biological experiments were also described in this section.

Copy of spectra of most of the compounds and copy of publications are incorporated at the end of the thesis.

Working for this thesis has been a great learning experience for me. Understanding the physiological pathways involved in metabolic syndrome and the biological roles of PPARs in this complex disease was very interesting and stimulative. Molecular modeling experiments provided good learning and were instrumental in understanding the ligand receptor interactions and structural requirements of the compounds to be synthesized. Presenting the work in the form of publications was equally a good experience of learning.

Though this work has been carved out of my job as a medicinal chemist, it gives me a feeling of satisfaction, as the design strategies and studies described in this thesis form the basis for the development of novel PPAR agonists, few of which advanced to clinical development for the treatment of metabolic disorders. The satisfaction is not only for the scientific outcome of the present project but also for the social cause, since the medical need for the treatment of metabolic disorders remain highly unmet. Here I would like to state the mission statement of our organization, which says

"ZRC aims to be the most admired pharmaceutical research centre for innovation in life science dedicated to alleviating human suffering"

Hence every endeavor in the direction of developing novel therapies in this area would be a significant contribution towards alleviating human suffering.

Harikishore Pingali