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CERTIFICATE

This is to certify that the thesis entitled “**Design, Synthesis and Biological Evaluation of Novel PPAR Agonists as Antihyperglycemic and Antihyperlipidemic Agents**” is being submitted to The Maharaja Sayajirao University of Baroda, Vadodara for the award of the degree of **DOCTOR OF PHILOSOPHY IN CHEMISTRY** is a result of original research work completed by **Mr. Pandurang Zaware** under our supervision and guidance at Zydus Research Centre, Ahmedabad and work embodied in this thesis has not formed earlier basis for award of any degree or similar title of this or any other university or examining body.

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DECLARATION

The thesis entitled “**Design, Synthesis and Biological Evaluation of Novel PPAR Agonists as Antihyperglycemic and Antihyperlipidemic Agents**” submitted herewith to The Maharaja Sayajirao University of Baroda, Vadodara of the fulfillment for the award of the degree of **DOCTOR OF PHILOSOPHY IN CHEMISTRY** is the result of the work carried out by me in Chemistry Department at Zydus Research Centre. The results of this work have not been previously submitted for any degree/fellowship to any university or institution.

Date:

Place: Ahmedabad

Pandurang Zaware

PREFACE

This thesis is the outcome of my research work carried out at Zydus Research Centre and the Department of Chemistry, The Maharaja Sayajirao University of Baroda, Vadodara, India. This research work has been also part of my job as scientist at Zydus Research Centre, Ahmadabad, India to which I have been affiliated since July 2002.

The thesis consists of four major sections which covers various aspects of Type 2 diabetes and development of PPAR agonists for the treatment of type 2 diabetes and associated dyslipdemia.

In the '**Introduction**' section, general information about Type 2 diabetes, wherein detailed pathophysiology of the disease and available current treatment options are discussed. In this section, history of PPAR discovery, detailed of the receptor structure, structural homology, tissue distribution and therapeutic significance of PPAR subtypes, in major organs are discussed. Furthermore, natural ligand as well as various class of synthetic ligand, subtype selective, dual, pan and partial agonist with their biological functions for the treatment of metabolic diseases, are described.

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 synthesis, biological activities and molecular modelling studies of the novel compounds. Finally there is **Summary and Conclusion** part of research work.

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 (IR, NMR, ESI-MS and HPLC) of representative compounds from each series (intermediates and final compounds) is enclosed, followed by our publication copy.

Working for this thesis and writing of publication has been great learning experience and satisfaction for me. 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. Hence every endeavor in the direction of developing novel therapies in this area would be a significant contribution towards alleviating human suffering.

PANDURANG ZAWARE

ACKNOWLEDGEMENT

I am grateful to “peers” who have contributed towards shaping this thesis

I wish to express my wholehearted gratitude to my research supervisors **Dr. Shailesh R. Shah** and **Dr. Rajesh Bahekar** for their continuous support, guidance, suggestions and perceptive criticism throughout my research work.

I owe tremendous debt to **Shri. Pankaj R. Patel**, CMD, Zydus Cadila for his constant encouragement and for providing the infrastructure and necessary facilities.

It is my privilege to thank **Prof. Neelima D Kulkarni**, Head, Department of Chemistry, M. S. University of Baroda for her support.

My sincere acknowledgement to **Dr. Ranjit Desai**, **Dr. Mukul Jain** and **Dr. Sanjeev Kumar** for their continuous support and encouragement.

I would like to express my appreciation to **Dr. Harikishore Pingali** for his advice during my doctoral research endeavor. He has constantly enforced me to remain focused on achieving my goal. His observations and comments helped me to establish the overall direction of the research and to move forward with investigation in depth. I thank him for providing me the opportunity to work with a team.

No words can acknowledge **Mr. Pankaj Makadia** for his moral support, encouragement and guidance during my research work and preparation of the thesis which otherwise would have been a difficult task.

I specially thank to Dr. Sanjaykumar to his support during the period of thesis writing.

I would like to thank my lab-friends Pravin Patil, Suresh Pola, Baban Thube and Darshit Patel for their cheerful co-operation and the help in every aspect throughout this work.

My sincere thanks to analytical group for recording the NMR, IR, MASS and HPLC spectra quick enough to do my work faster.

I am extremely thankful to Dr. Ashish Goel, Megha Patel, Dinesh Suthar, Maanan Shah and Dr. Priyanka Priyadarshini for *in vitro* biological evaluation of the compounds.

I am also thankful to Dr. Suresh Giri and his team for conducting animal experiments and to Mr. Harilal Patel and his team for conducting pharmacokinetic studies.

I am extremely thankful to Dr. Sairam Kalapatapu and Jeevankumar Jamili for their help in molecular modelling studies.

I would like to extend my thanks to Kaushik Banerjee for his whole hearted support and encouragement throughout this work.

I take this opportunity to thank my friends and colleagues, Dr. Saurin Raval, Dr. Preeti Raval, Dr. Jigar Desai, Dr. Vrajesh Pandya, Dr. Anil Argade, Dr. Gautam Patel, Sanjay Gite, Archana Gite, Amitgiri Goswami and Prashant Deshmukh for their help and encouragement during this work.

I am extremely thankful to Mrs. Clarine Pathak for her support.

I would like to extend my thanks to Darshan Mahashya for his help during this work.

My heartfelt thanks to H.R. Department of ZRC for timely help and support.

Finally, no words can express the feelings towards my parents and family members, who have contributed and sacrificed a lot to reach me at this stage and will always remain a sole source of inspiration in my life.

PANDURANG ZAWARE