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.

The first chapter, general information about solid state is provided and the importance of crystal polymorphism and salt formation in drug development is discussed. General techniques for preparation of polymorphs, solvates and hydrates, salts and co-crystals are described as well as the various agents including solvents, salt formers and co-formers has been detailed. History of the development of this branch of study is also described. Methods of characterization of these alternate solid forms are discussed. The importance and significance of such work in drug development are described with various examples.

The second chapter describes the work done in improving the pharmaceutical properties of a cannabinoid receptor antagonist, which was identified at the R&D Centre but whose development was stopped due to unfavourable physic-chemical properties.

The third chapter describes the work done to improve the physico-chemical and biological properties on a p38 MAP kinase inhibitor developed in-house, which was also shelved because of developmental challenges.

The fourth chapter describes the preparation of novel salt of a commercially available drug Plavix, having certain beneficial properties.

The fifth chapter describes the use of certain crystal modifiers, which have not been used earlier for organic compounds, to change the morphology of the crystalline form of compounds. Biological studies have been carried out for each of the modified compounds and results are provided.

Copies of spectra (IR, NMR, ESI-MS, XRD, DSC) of representative compounds (intermediates and final compounds) are enclosed after each chapter, and at the

end, copies of the publications which resulted from the research work are enclosed.

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 since there is a significant need to pursue such strategies for improving the quality of several existing drugs in order to meet the unmet medical needs. Such strategies can provide significant opportunities for developing better drugs quickly and with much lesser expenses that developing completely new drugs.

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