ABSTRACT

Determination of impurity profile for pharmaceutical compounds has a great importance while evaluating safety and efficacy of the drug product. In order to determine the impurity profiles, analytical testing of pharmaceutical compounds by means of suitable analytical techniques is required. The thesis discusses the role of chromatographic techniques and need for the development of stability indicating analytical methods. The thesis also describes the current challenges in the chromatographic method development and re-emphasizes the advantages of systematic method development approaches. Specific separation problems are illustrated by selecting typical molecules that possess a variety of separation issues. The methodology further describes the way forward to resolve such separation problems. The method development activity mainly focuses on the selection of suitable stationary phases and systematic optimization of chromatographic conditions. The specificity of the developed analytical methods is demonstrated by analyzing forced degradation samples and evaluating the spectral homogeneity of the compounds. In addition, possible degradation pathways are established based on LCMS analysis of the degradation impurities.

The whole thesis has been organized into five chapters, wherein the first chapter describes the introduction to the impurity profile, sources of impurities, the importance of chromatographic method development and the various steps involved in the systematic method development. The
rest of each chapter reflects the specific separation problems and development of simple, fast LC methods that utilize the recent advancements of the chromatography. Additionally, the thesis throws light on Computer Simulated Software (Dry lab) for the optimization of chromatographic method parameters as discussed in chapter-4 and Design of Experiments (Design expert) concept for the optimization of the method parameters as presented in chapter-5. The initial sections of these chapters (chapter-2 to 5) discuss the biological activities of the selected drugs and the existing literature information pertaining to the analytical methods for assay and impurity determinations. The later sections include the proposed analytical method development strategies, experimental, results and conclusions. These sections mainly deal with the details of chemicals, reagents and equipments utilized, the preparation of standard and sample solutions, the method conditions, a wholesome description of the steps that are adopted during the method development, analytical validation protocols and their results. Typical chromatograms, tables, figures, and equations are depicted appropriately. The developed method is applied for the analysis of real time samples and stability samples to determine the impurity profiles of the selected drugs and intermediates.