PREFACE

In industry, the quality assurance and quality control departments play major role in bringing out a safe and effective drug or dosage form. The pharmaceutical industry is to deliver market safe, efficacious product that fulfill medical needs of public.

Development of new analytical methods for the determination of drugs quantitatively and qualitatively in pharmaceutical dosage forms is more important in pharmacokinetic, toxicological and biological studies. The current good manufacturing practices (CGMP) and the Food Drug Administration (FDA) guidelines insist for adoption of sound methods of analysis with greater sensitivity and reproducibility. Pharmaceutical analysis occupies a pivotal role in statutory certification of drugs and their formulations either by the industry or by the regulatory authorities. Therefore, the complexity of problems encountered in pharmaceutical analysis with the importance of achieving the selectivity, speed, low cost, simplicity, sensitivity, specificity, precision and accuracy in estimation of drugs.

Analytical testing is one of the more interesting ways for scientists to take part in quality process by providing actual data on the identity, content and purity of the drug products. Pharmaceutical analyst plays a major role in all quantity and quality controlling divisions of industry. Chemistry involves separating, identifying, and determining the relative amounts of components in a sample matrix. The commonly used tests of pharmaceutical analysis generally entail compendia testing method development, setting specifications, and method validation. Today pharmaceutical analysis entails much more than the analysis of active pharmaceutical ingredients or the formulated products.

The pharmaceutical analyst plays a major role in assuring identity, safety, efficacy, purity, and quality of a drug product. The need for pharmaceutical analysis is driven largely by regulatory requirements. New methods are now being developed with a great deal of consideration to worldwide harmonization. As a result, new products can be assured to have comparable quality and can be brought to international markets faster.
Analysis comprises procedures necessary to determine “identity, strength, quality and purity of the drug substances and drug products.

Qualitative analysis reveals the chemical identity of the sample. Qualitative analysis is required before a quantitative analysis can be undertaken. A separation step is usually a necessary part of both a qualitative and quantitative analysis. The primary responsibility of quality control division was making the decisions on release or reject of production batches, for all these pharmaceutical analysis is prerequisite.

Quantitative analysis establishes the relative amount of one or more of these species or analytes in numerical terms.

The present investigation deals with the Development of new analytical methods for the quantitative determination of selected drugs in bulk and its Pharmaceutical Dosage forms. The drugs studied are Zopiclone, Pizotifen, Sirolimus, Stanozolal, Stavudine, Buspirone, Quetiapine, Telmesartan, Darunavir, Diacerin, Carvidiol and Levetiracetam.

The number of drugs invented and implemented is constantly increasing to cater the needs of public. This requires new methods for controlling their quality. Most of the modern drugs are potential and hence sensitive methods are needed for their estimation in pharmaceutical formulations or in bulk drugs.

HPLC technique has been regarded as the best among various instrumental ones in spite of its heavy cost and maintenance problems. HPLC is a versatile tool for the qualitative and quantitative analysis of drugs and pharmaceuticals, chemical and biological materials and has become indispensable in pharmacokinetics studies. The development of highly efficient micro particulate bonded phase has increased the versatility of the technique and has greatly improved the analysis of multi-component mixtures. The system used are often described a belonging to one or more among four mechanistic types, adsorption, partition, ion exchange, and size exclusion. Adsorption and partition system can be normal phase (stationary phase more polar than eluent) or reversed phase (stationary phase less polar than eluent).

We have examined the present state of development of such analytical methods for some widely used drugs belong to categories such as Zopiclone, Pizotifen, Sirolimus,
Stanozolal, Stavudine, Buspirone, Quetiapine, Telmesartan, Darunavir, Diacerin, Carvidilol and Levetiracetam.

In HPLC, the choice of stationary and mobile phases, internal standard, column conditions and detecting devices are important. Retention in HPLC is manifestation of multi types of interaction between the analytes with both mobile phases and stationary phase. The interactions can be hydrophobic (dispersive), polar, ionic or combination depending on the analyte. For given pair of analytes to be separated the stationary phase must be able to recognize the difference between them. Traditional alkyl stationary phases, such as C8 or C18 can differentiate analytes of different hydrophobicity. In the present investigation HPLC has been utilized for the determination of Zopiclone, Pizotifen, Sirolimus, Stanozolal, Stavudine, Buspirone, Quetiapine, Telmisartan, Darunavir, Diacerin, Carvidilol and Levetiracetam.

HPLC procedures were carried out on Chromosil C18 column 250 ×4.6 mm ID with 5 µ particle size. For these drugs studied in this thesis there are a few analytical methods reported and hence there is wide scope for the development of new analytical methods for their quantitative analysis.

This dissertation describes the proposed methods can be used as alternative methods to reported ones and provides a wide choice for routine determination of the above mentioned drugs. The data and information concerning drugs, reagents and techniques given in results reveal that the proposed methods are simple, specific and accurate with reasonable precision. Results of analysis reveal that the proposed methods are suitable for their analysis and these methods can be adopted for routine determination of these drugs in bulk and pharmaceutical preparations.

CHAPTER 1 describes brief information on general analytical methodology, selection of drugs and also gives information on systemic procedure to be followed for development of new chromatographic methods for the selected drugs.

CHAPTERS 2 to 13 give a brief literature survey and determination of pharmaceutical formulations by different chromatographic and serum analysis methods. This has been developed using suitable mobile phases.
Chapter 2: ZOPICLONE (Acetonitrile: Methanol: THF: 0.1% OPA in the ratio of 45:20:5:30 v/v), Chromosil C<sub>18</sub> column.

Chapter 3: PIZOTIFEN (Methanol: Acetonitrile in the ratio of 10:90 v/v), Chromosil C<sub>18</sub> column.

Chapter 4: SIROLIMUS (Methanol: Acetonitrile in the ratio of 80:20 v/v) Chromosil C<sub>18</sub> column.

Chapter 5: STANZOLAL (Methanol: water in the ratio of 90:10 v/v), Chromosil C<sub>18</sub> column.

Chapter 6: STAVUDINE (Methanol: 0.1% orthophosphoric acid: Acetonitrile in the ratio of 40: 50:10 v/v/v), Chromosil C<sub>18</sub> column.

Chapter 7: BUSPIRONE : (Methanol: Water: Acetonitrile in the ratio of 20:45:35 v/v). Chromosil C<sub>18</sub> column

Chapter 8: QUETIAPINE (Methanol: water: 1% OP in the ratio of 90:9:1 v/v), Chromosil C<sub>18</sub> column.

Chapter 9: TELMESARTAN : (Methanol: 0.1% orthophosphoric Acid: Acetonitrile in the ratio of 40: 50:10 v/v/v), Chromosil C<sub>18</sub> column.

Chapter 10: DARUNAVIR (Acetonitrile: Methanol in the ratio of 90:10 v/v) Chromosil C<sub>18</sub> column.

Chapter 11: DIACEREIN (Methanol: Water in the ratio of 80:20 v/v), Chromosil C<sub>18</sub> column.

Chapter 12: CARVIDILOL (Acetonitrile: Methanol in the ratio of 90:10 v/v), Chromosil C<sub>18</sub> column.

Chapter 13: LEVETIRACETAM (Methanol: Acetonitrile in the ratio of 80:20 v/v) Chromosil C<sub>18</sub> column.
In addition, selectivity to each selected drug in its formulation was achieved by selecting the appropriate combination of solvent system, acids or bases in sample solution preparation present in drug but not in the excipient, additives or other active ingredients present in the formulations and serum sample solution to the extent possible. The proposed methods can be used as alternative methods to the reported ones and provide a wide choice for routine determination of above mentioned drugs depending upon the availability of chemicals and situation arising due to the presence of concomitants.

This thesis is framed with an Introduction followed by Drug profile, Review of Literature, Objective and plan of work, RP-HPLC Method development and validation, Formulation analysis, analysis of drug in serum, Results and discussion, and appropriate references.