PREFACE

The number of new drugs being designed and introduced for therapy is constantly increasing. Consequently, the dosage forms that include these drugs are introduced into the market in huge numbers. So, there is always a necessity for developing newer and efficient methods for determining these drugs in bulk samples and formulations. The introduction of large number of newer drugs and their formulations may also lead to widespread distribution of substandard or even counterfeit drugs and their formulations in the market. Quality control and quality assurance of pharmaceutical chemicals and their formulations are essential for ensuring the availability of safe and effective drug formulations to the consumers and safeguarding the general public against the hazards of substandard drugs. Pharmaceutical analysis is indispensable in the process of quality control for statutory certification of drugs and their formulations either by the industry or by the regulatory authorities. Thus, constant development of new and improved analytical methods for accurate determination of drugs in raw materials and in pharmaceutical dosage forms is essential for quality control, pharmacokinetic, bioequivalence and toxicological studies.

Pharmaceutical analysis deals with the analysis of not only the drugs but also their formulations. It is also necessary to check the quality of the raw materials including the bulk drugs that go into the formulation of the dosage forms. There are several valid reasons for developing new analytical methods. The existing methods may be erratic or unreliable i.e. having poor accuracy and precision. The existing method may be time consuming or may be too expensive. The advent of new techniques and improved instrumentation in the field of analysis may give way to more sensitive, precise and accurate methods.
In order to develop a newer or improved analytical method, the analyst has to set some goals. It is necessary to determine the analyte at trace levels accurately. The method should be precise to the drug under study. The method should be simple consuming minimum analysis time and using cheaper chemicals and materials. The method should yield reproducible results, when carried out by different analysts and in different laboratories. It should also be robust giving accurate results even there are slight variations in the conditions of the method. It is not sufficient to develop and optimize analytical methods using the pure standard drugs but, it is necessary that these methods should be validated appropriately and the methods should be applicable for estimation of these drugs in their dosage forms.

High Performance Liquid Chromatography is the fastest growing analytical technique for the analysis of drugs. Its simplicity and wide range of sensitivity and short analysis time makes it ideal for analysis of many drugs in both dosage forms and biological fluids. With the development of more sophisticated instrumentation, efficient column materials and moderate pricing, the HPLC technique has now become more reliable and indispensable. In view of this the author has chosen to develop HPLC methods for determination of some of the recent drugs.

The present study incorporated in the thesis was taken up by the author with an aim to develop more efficient and validated new high performance liquid chromatographic methods for estimation of some important drugs namely Levetiracetam, Lornoxicame, Tenofovir, Emtricitabine, Candesartan, Hydrochlorothiazide, Olmesartan, Amitriptyline and Chlordiazepoxide in their bulk as well as in dosage forms. The study design involves the development of new reverse phase HPLC methods for estimation of the selected drugs both individually or in combination with other drugs, validation of the methods thus developed and testing their
suitability for estimation of the drugs in their pharmaceutical dosage forms. All the methods were carried out by adopting reverse phase HPLC technique. The methods were validated as per ICH guidelines.

A literature survey on the analytical methods of Levetiracetam, Lornoxicam, Tenofovir, Emtricitabine, Candesartan, Hydrochlorothiazide, Olmesartan, Amitriptyline and Chlordiazepoxide revealed that a few HPLC methods are available for their estimation in dosage forms in addition to other techniques. Some of these methods have certain drawbacks like gradient elution technique, long run time, less resolution and lack of sufficient sensitivity, precision and accuracy. Furthermore, some methods lacked proper validation and documentation. Hence, the author had attempted to develop simple, fast, accurate and precise HPLC methods for determination of these drugs. The methods proposed by the author are economical, quick and the solvents used in them are of moderate cost and are thus easily affordable by the laboratories equipped with standard HPLC systems. The proposed methods can be used as alternative methods to those reported by the earlier workers and provide good choice for the routine determination of the chosen drugs in their formulations and also in their clinical, pharmacokinetic and biological studies.

The thesis incorporates the results of experimentation carried out by the author for determination of the drugs listed above in pure form, validation of the method so developed and applicability of the method for the estimation of the drugs in their dosage forms by HPLC.

The thesis has been presented in seven chapters. Chapter 1 incorporates introductory information about HPLC and its technique. This is followed by the general guidelines and methodology to be followed for developing a new method for estimation
of drugs by HPLC. Later, the procedures adopted to determine various parameters for validation of the developed method have been given.

Chapter 2 to chapter 7 of the thesis deals with the details of the author’s experimentation and results obtained in the HPLC method development for the assay of the selected drugs namely **Levetiracetam, Lornoxicam, Tenofovir, Emtricitabine, Candesartan, Hydrochlorothiazide, Olmesartan, Amitriptyline and Chlordiazepoxide**. The data in chapter 2 to chapter 8 have been divided into six parts, each part being devoted to one drug or combination of two drugs. The contents in each part have been presented under the following heads.

a) Drug profile(s)

b) Review of the past work on the analytical methods

c) Experimental and results

   i. *Material and methods*

   ii. *Method development and Optimization of chromatographic conditions*

   iii. *Validation of the proposed method*

   iv. *Estimation of the drug from the dosage forms*

d) Summary of the results and Conclusion

e) References

The results obtained in these experiments have been thoroughly discussed. The references cited in the text of the thesis have been given at the end of each part.