PREFACE

The drug is a substance that is used for the purpose of diagnosis, prevention, relief or cure of disease in human beings or animals. The action of a drug may be determined by its chemical structure alone or by its physico-chemical properties. Pharmaceutical chemistry is a specialized science and occupies an important place among the related sciences. It has registered a phenomenal growth during the last few decades and drug therapy has a vital role in the fighting against diseases and in maintaining better quality of human health. Safety and efficacy of bioactive compounds (drugs) are two fundamental issues of importance in drug therapy. A majority of the drugs used are of generally synthetic origin. These are biologically active chemical substances generally formulated into convenient dosage forms such as tablets, suspensions, capsules, injections and ointments.

With ever growing demand on drug specificity to fight against new illness, the newer drugs arrive into market at such a great pace that it has become difficult to keep abreast of their merits and demerits. Nevertheless a strict control on the quality of the drugs and their therapeutic action is essential. Hence, the pharmaceutical analysis occupies a pivotal role to statutory certification of drugs and their formulations either by the industry or by the regulatory authorities. It is expected that such analysis should be precise, accurate, selective and sensitive. At the same time it should be rapid and economical.
Among several analytical techniques available for the assay of drugs, the chromatographic and spectrophotometric techniques are simple and reliable. The selectivity and sensitivity of spectrophotometric methods depend only on the nature of chemical reactions involved in color development or formation of chromophores but not on the sophistication of the instrument. HPLC is a versatile tool for both qualitative and quantitative analysis of drugs.

In the present study, the investigator has selected different class of drugs such as antidepressant, antiepileptic, anticonvulsant, gastrointestinal agent, β-lactum antibiotic, anticholesteremic agent and peripheral vasodilator, and developed simple, cost effective, rapid, sensitive, reasonably precise and accurate analytical methods for their assay in bulk and formulations.

The contents of the thesis are divided into nine chapters. Each chapter deals with general profile of the drug(s), literature survey, experimental, results and discussion including statistical data analysis and conclusions (except for chapters I and IX).

Chapter I opens with an introduction to analytical chemistry in general and pharmaceutical analysis in particular. Besides this, theory of spectrophotometry and chromatography and statistical parameters employed in the present study have been included. The list of drugs selected is also given. The scope of the present study is also outlined at the end of the chapter.

Chapter II incorporates the results of two simple, rapid and sensitive spectrophotometric methods of assay of trazodone hydrochloride (TRZH) in pure and pharmaceutical formulations. These methods are based on the
formation of chloroform soluble ion-association complexes of TRZH with bromocresol purple (BCP) in NaOAc-AcOH buffer of pH 3.6 [Method I] and with methyl orange (MO) in NaOAc-HCl buffer of pH 3.29 [Method II] with absorption maxima at 408 and at 422 nm for Methods I and II respectively. The systems obeyed Beer's law in the ranges of 0.2-14.1 μg/ml and 1-20 μg/ml with molar absorptivity values of 2.92 x 10^4 and 1.37 x 10^4 l/mol/cm of TRZH for BCP and MO, respectively. Recovery studies yielded satisfactory results. Various analytical parameters have been evaluated and the results have been validated by statistical data. Effects of common excipients have been investigated. The utility of the proposed methods was examined by analyzing TRZH in various pharmaceutical formulations.

Chapter III gives the details of three precise and accurate spectrophotometric methods of determination of oxcarbazepine (OXC) in pure and pharmaceutical preparations. The methods are based on the measurement of absorbances of tris (1,10-phenanthroline) iron (II) [Method A] and tris (2,2'-bipyridyl) iron (II) [Method B] and oxidative coupling of OXC with 3-methylbenzothiazolin-2-one hydrazone in presence of iron (III) chloride in 1M hydrochloric acid [Method C] at 510 nm, 522 nm and 620 nm, respectively. The spectral characteristics, optimum reaction conditions and effects of excipients have been discussed. The results of analysis were found to be in good conformity within ±2.1% error. The absorbances were found to increase linearly with increase in concentrations of OXC, which were corroborated by correlation coefficient values (0.9992, 0.9994 and 0.9977 for Methods A, B and
C, resp.). Low values of limits of detection and limits of quantification indicated the high sensitivity of the proposed methods.

**Chapter IV** incorporates the spectrophotometric assay of \( \beta \)-lactum antibiotic, cefadroxil (CFX) based on the coupling of diazotized sulphanillic acid (DSA)[Method I] and with p-nitroaniline (DPNA) [Method II] in basic medium. The resultant colored products exhibited absorption maxima at 426 nm and 480 nm for methods I and II, respectively. Beer's law data were found to be \( 2.96 \times 10^4 \) and \( 2.56 \times 10^4 \) l/mol/cm while Sandell's sensitivity values were observed to be 12.27 and 14.19 ng/cm\(^2\) for methods I and II, respectively. Regression analysis, optical characteristics, precision and accuracy data have been given. Common excipients and additives generally present in various pharmaceutical preparations did not interfere in the proposed methods. Results of analysis of formulations by the proposed methods compare favorably with those of Official method.

**Chapter V** describes the investigations of two simple, rapid and sensitive spectrophotometric methods of assay of nortryptilline hydrochloride (NTPH) in pure and pharmaceutical formulations. These methods are based on the formation of yellow colored ion-association complexes of NTPH with bromophenolblue (BPB) in NaOAc-HCl buffer of pH 3.29 [Method I] and with methyl orange (MO) in KCl-HCl buffer of pH 2.0 [Method II] with absorption maxima at 410 and at 422 nm for Methods I and II respectively. The systems obeyed Beer's law in the ranges of 0.1-7.2 \( \mu \)g/ml and 0.3-9.8 \( \mu \)g/ml with molar absorptivity values of \( 3.44 \times 10^4 \) and \( 2.29 \times 10^4 \) l/mol/cm of NTPH for BCP
and MO, respectively. Recovery studies yielded satisfactory results. Effects of common excipients have been investigated. The utility of the proposed methods was examined by analyzing NTPH in various pharmaceutical formulations.

Chapter VI gives the details of three precise and accurate spectrophotometric methods of determination of tegaserod maleate (TGM) in pure and pharmaceutical preparations. The methods are based on the measurement of absorbances of tris (o-phenanthroline) iron (II) [Method A] and tris (bipyridyl) iron (II) [Method B] and oxidative coupling of TGM with 3-methylbenzothiazolin-2-one hydrazone in presence of iron (III) chloride in 1M hydrochloric acid [Method C] at 510 nm, 522 nm and 556 nm, respectively. The spectral characteristics, optimum reaction conditions and effects of excipients have been discussed. The results of analysis were found to be in good conformity within ± 2.1% error. The complexes obeyed Beer's law over the concentration range of 0.3-2.6, 0.5-4.0 and 0.5-6.0 µg/ml with molar absorptivity values of 11.16 x 10^4, 6.61 x 10^4 and 4.89 x 10^4 l/mol/cm in methods A, B and C, respectively. Optical characteristics, accuracy and precision and recovery results have been included.

Chapter VII comprises high performance liquid chromatographic (HPLC) method for the determination of ezetimibe (EZT) in pharmaceutical formulations and human plasma samples. The analysis of EZT was carried out on a CLC C_{18} (5µ, 25 cm x 4.6 mm i.d) column using UV detector at 200 nm with the mobile phase consisting of acetonitrile-water (90:10 v/v) by
maintaining the flow rate of 1 ml/min. Piroxicam (PRX) was used as an internal standard. System performance parameters have been evaluated and these were found to be ideal for chromatographic assay of EZT.

Chapter VIII describes RP-HPLC method for the assay of pentoxifylline (PTF). The method is successfully applied to the assay of PTF in human plasma and pharmaceutical preparations. Throughout the study, the suitability of the chromatographic system was monitored by calculating the capacity factor ($k^1$), the resolution (R), the selectivity ($\alpha$), height equivalent to theoretical plates and the peak asymmetry (T). The results of analysis have been well supported by statistical data and suitable conclusions were drawn.

Chapter IX outlines the concluding remarks of the investigator.