SUMMARY

The growth of pharmaceutical industry, increase in the number and variety of drugs and availability of sophisticated instruments have paved way for rapid progress in providing simple analytical procedures for the analysis of drug in bulk and their pharmaceutical formulations. The availability of new techniques with improved equipments have made the latest techniques attractive. Here, Pharmaceutical analysis plays an important role which generally involves two steps; a) separation of the compound of interest and b) quantitation of the compound and their formulations and also with their precursors. Here the role of an analyst becomes invaluable who carries out both qualitative and quantitative determination of the drug in bulk and their pharmaceutical formulations.

Several methods for the estimation of drugs are classified into physical, chemical, physico-chemical and biological ones. Physical methods involve the study of the physical properties such as solubility, transparency or degree of turbidity, color density, specific gravity etc. The chemical methods include the titrimetry, gravimetric and volumetric procedures which are based on complex formation, redox reactions etc. Physico-chemical methods involve the study of the physical phenomena that occurs as results of chemical reactions. These include optical [spectrophotometric] and chromatographic methods.

Keeping this in view, an attempt was made by the author in the present investigation to develop new analytical methods for some selected drugs in pure and pharmaceutical formulations. All the methods described in the thesis are simple, rapid, reliable and validated. The methods developed by the author could be used not only for quality control but also for process development of bulk drugs. The work carried out in the present investigation was described in five chapters

Chapter-1starts with an introduction giving a brief account of various aspects to be considered for the development of new visible spectrophotometric (**Part-1.1**) and HPLC (**Part-1.2**) methods for the assay of four selected drugs. The introduction includes a brief account on general information and methodology for the development of new analytical methods using visible spectrophotometry and HPLC.

The information given under (**Part-1.1**)includes the general methodology for developing new visible spectrophotometric methods, chemistry and utility of various chromogenic reagents which include **3-methyl-2-benzathiazolinone hydrazone [MBTH]** in presence of **oxidants Ferric chloride Fe[III] & Idoso benzene diacetate [IBDA], Brucine** with **Sodium metaperiodate [$NaIO_4$] oxidant, 2,6-Dichloro Quinone-4-Chlorimide[DCQC], Folin-Ciocaltaeu reagent[FC],** 1,2-Naphthaquinone sulphonic acid sodium salt**[NQS], Sodium Nitro Prusside [SNP]** with **Hydroxyl amine [HA], Ninhydrin** in presence of **ascorbic acid, Anthranilic acid[ATA], 2-Cholorophenyl Hydrazine[2-CPH], 2,4-Dinitrophenyl Hydarzine[2,4-DNPH], P-Dimethyl amino benzaldehyde[PDAB], P-Dimethyl amino cinnamaldehyde[PDAC], Isatin** in the presence of H_2SO_4, **Vanillin** in the presence of H_2SO_4, **Para chloranilic acid[PCA],** 2,3-**Dichloro,5,6-dicyno1,4benzoquinone[DDQ],Bromocresolpurple [BCP],Bromothymol blue(BTB) Alizarin Red S[ARS]** and **Tropelion ooo[TPooo].**

In this part the author had given a brief description on the general criteria to develop and validate new visible spectrophtometric methods which include the **(i)** studies on optimization of various experimental parametrs (effect of pH, reagent concentration and order of addition, keeping time and temperature during each addition, effect of solvent, color development and stability),**(ii)** method validation studies [optical characteristics (Beer's law limits, Sandell's sensitivity, optimum photometric range and molar absorptivity), precision, standard deviation, percent range of error, testing of significance by F-test, accuracy(comparison of the proposed and reference methods of pharmaceutical formulation, testing of significance by t-test and recovery experiments).

The information given under (**Part-1.2**), includes a brief study on HPLC system components (solvent delivery systems, solvent degassing systems, gradient elution devices, sample introduction systems liquid chromatography detectors, column packing materials inclusive of bonded phase, derivatization, gradient elution), performance calculations (relative retention, theoretical plates, plates per meter, height equivalent to theoretical plate, capacity factor, resolution, peak asymmetry), linear fit properties of solvents used in chromatography and validation of analytical methods(recovery, response function, sensitivity, precision and accuracy) in the present investigations.

Chapter-2 gives a brief account of chemical name, structure, mode of action and literature on physicochemical methods reported for granisetron hydrochloride. There are few visible spectrophotometric methods for the assay of Granisetron hydrochloride. The chemical features of analytically useful functional groups in granisetron hydrochloride offers a lot of scope for the development of new methods with better sensitivity precision and accuracy, which prompted the author to carry out investigations in this accord.The author has developed **nine** new visible spectrophotometric methods.

The **tertiary amine** in granisetron was responsible for the development of **oxidative coupling** reaction with **3-methyl-2-benzathiazolinone hydrazone (MBTH)** in presence of **Fe(III)** and **Brucine** in presence **$NaIO_4$(oxidant), redox** reaction with **Folin-Ciocaltaeu reagent[FC]in the presence of Na_2CO_3, complex formation** reaction with **Sodium Nitro Prusside - Hydroxyl amine(SNP – HA)** and **charge-transfer complex** reaction with substituted **p-benzoquinones (PCA & DDQ).** The **basic nitrogen moiety** in granisetron was responsible for the development of **ion-association complex** formation with acid dyes **Bromocresolpurple [BCP], Bromothymol blue(BTB)** and **Alizarin Red-S[ARS]** respectively. The results of the propsed methods are incorporated in **Part-2.1** in the thesis.

The information given under (**Part-2.2**) of this chapter reveals the literature survey of the HPLC methods of granisetron hydrochloride. A very few HPLC methods for the assay of granisetron hydrochloride in pharmaceutical formulations were reported in the literature. Taking all these views of the drug into consideration, the author has developed as simple HPLC method for the quantitative estimation of granisetron hydrochloride. **Gemini NX C_{18} column (25cm x 4.6mm i.d., 5µ) with a mobile phase of sodium dihydrogen phosphate buffer (pH 7.5) and Acetonitrile in the ratio of 80:20 at a flow rate of 1.5ml.min with a detection at 305nm gave sharp and symmetrical peak with retention time of 7.466 for Granisetron HCl.** The results of this investigation are presented in this part.

Chapter-3 focuses on the introduction giving brief account of chemical name, structure, therapeutic importance and analytical survey of carvedilol. There are very few physicochemical methods reported in the literature, hence there is a need for sensitive, accurate and flexible visible spectrophotometric methods for its determination in a wide variety of pharmaceutical formulations. The author has made some attempts in this direction and succeeded in developing **seven** visible spectrophotometric methods based on the analytically useful functional groups present in carvedilol.

The secondary nitrogen group of carvidilol is involved in the **oxidative coupling** reaction with **3-methyl-2-benzathiazolinone hydrazone (MBTH)** in presence of **Fe(III), Brucine** reagent in presence **$NaIO_4$(oxidant)** and with **2,6-Dichloro Quinone-4-Chlorimide[DCQC]; charge-transfer complex** reaction with substituted **p-benzoquinones (PCA & DDQ)** and in **ion-association complex** formation rections with acid dyes [**Alizarin Red S(ARS)** and **Tropacolin-ooo(TPooo)** respectively. The results are provided in **Part-3.1** in the thesis.

Part-3.2 of this chapter gives a brief note on the chemical properties and the literature survey of the HPLC methods of carvedilol. A very few HPLC methods for the assay of

carvedilol in pharmaceutical formulations were reported in the literature. Quantitative estimation of carvedilol was done by the author by using a stainless steel **YMC Pro C_8 RP column (4.6mmx150mm) with with mobile phase (acetonitrile and Potassium dihydrogen phosphate buffer (pH-2.0) in the ratio of 31:69v/v). The detection was carried at 240nm.** The results of this investigation are presented in this part.

Chapter–4 opens with a brief account of chemical name, structure, therapeutic importance, analytically useful functional groups, commercially available formulations and the literature on the physicochemical methods reported so far for memantine hydrochloride.Literature survey reveals that very few visible spectrophotometric methods for the assay of memnatine hydrochloride in pure and pharmaceutical formulations.The author proposed **seven** visible spectrophotimetric methods by exploiting the functional groups present in memantine hydrochloride.

As Memnatine contains primary amino group in its structure involved in **condensation reactions** with **Ninhydrin** in presence of **ascorbic acid, P-Dimethyl amino benzaldehyde[PDAB], P-Dimethyl amino cinnamaldehyde[PDAC], Isatin** in the presence of H_2SO_4 and **Vanillin** in the presence of H_2SO_4 and in **ion-association complex** formation rections with acid dyes [**Alizarin Red S(ARS)** and **Tropacolin-ooo(TPooo).** The results of investigation are incorporated in this part.

Part-4.2 of this chapter reveals the literature survey of the HPLC method of memantine hydrochloride. A very few HPLC methods for the assay of memantine hydrochloride were reported in the literature. The author has developed a simple RP-HPLC method for the quantitative estimation of memantine hydrochloride with a better sensitivity by using, **BDS C_{18}, (4.6 mm i.d x 250 mm, 5µm reversed phase column with 100% methanol as mobile phase at a flow rate of 1.0mL.min^{-1} at ambient temperature (25 ± 2°C) with**

UV detection was performed at 274nm. The results of investigation are incorporated in this part.

Chapter-5 begins with the introduction giving a brief account of chemical name(s), therapeutic importance, structure, analytically useful functional groups, commercially available pharmaceutical formulations and literature on the physicochemical methods reported for donepezil. The author developed **eight** visible spectrophotometric methods for donepezil in pure and pharmaceutical formulations.

Donepezil possesses different functional moieties such as keto and tertiary amine groups of varied reactivity. The **keto group** in **Donepezil** was responsible for **condensation reactions with Anthranilic acid[ATA], 2-Cholorophenyl Hydrazine[2-CPH], 2,4-Dinitrophenyl Hydarzine[2,4-DNPH]. The tertiary amine group** was responsible for **oxidative coupling** reaction with **oxidative coupling** reaction with **3-methyl-2-benzathiazolinone hydrazone (MBTH)** in presence of **IBDA(oxidant), charge-transfer complex** reaction with substituted **p-benzoquinones (PCA & DDQ)** and in **ion-association complex** formation rections with acid dyes [**Alizarin Red S(ARS)** and **Tropacolin-ooo(TPooo)** respectively. The results of the above investigations are incorporated in this part.

Part-5.2 of this chapter reveals the literature survey of the HPLC method of donepezil The author has developed a simple RP-HPLC method for the quantitative estimation of Donepezil HCl with a better sensitivity. The compound was separated **at ambient temperature (25 ± 2°C), on a 250mm × 4.6mm i.d., 5-µm particle, Kromasil 100 C_8 Reverse column with 60:40 (*v/v*) Potassium dihydrogen phosphate buffer (pH 2.2) - Methanol as mobile phase at a flow rate of 1.2mL min^{-1}** with **UV detection at 268nm.** The results of investigation are incorporated in this part.

The work presented in chapters 1-5 of the thesis describes the development and validation of new analytical methods for the assay of some selected drugs in pure and

pharmaceutical dosage forms. The methods are simple, rapid, sensitive, reliable and validated. The methods are useful for quality assurance of the drugs investigated in the present work. The probable mechanisams for various colored reactions with different chromogenic reagents for all the selected drugs were given at the end of each chapter.

Two papers were published and two papers were communicated and two supporting papers were published.