CHAPTER 6

SUMMARY

Modern medicines for human use are required to comply with specific standards and regulations set forth by the concerned authorities. The efficacy and safety of medicinal products can only be assured by analytical monitoring of its quality. Hence, the quality control laboratory forms the heart of drug industry. It is here that various procedures are required for analysis of drug formulations.

Modern scientists have currently available to them, an amazing array of powerful analytical tools for obtaining qualitative and quantitative data about the properties and composition of matter. Pharmaceutical analysis is indispensable for the pharmaceutical industry. It comprises of various methods and techniques dealing with the analysis of drug and other materials used in pharmaceutical preparations. In manufacturing laboratories, pharmacists often have to perform physical, chemical and biological analysis, either in the course of developing dosage forms of new drugs or in the control of quality of products. The pharmaceutical analyst, therefore must be sufficiently well versed in analytical procedures not only to apply known techniques but also to devise new better techniques wherever necessary.

The field of pharmaceutical science is expanding rapidly with the invention of new drugs and novel drug delivery systems. Depending upon requirement of different patient class, different kind of dosage forms such as tablets, capsules, injections, syrups, suspensions, sustained release tablets etc. are designed. Over
the past two decades various regulatory bodies such as USFDA (United States Food and Drug Administration), WHO (World Health Organisation), British Pharmacopoeial Commission have taken very serious view about the quality of bulk drugs and pharmaceuticals which are manufactured. These agencies in consultation and collaboration with various research organizations and industries have been monitoring the efficacy of various drugs and their generic equivalent. Based on these studies some of the parameters, which are introduced, as mandatory requirements for different pharmaceutical products are: type of polymorph, chiral purity of the active molecule and dissolution rate of the dosage form. Considering the importance of pharmacological effect or adverse reactions of these drugs and their metabolites/degradation products/related substances, efforts have been initiated and are on to achieve consistent quality by issuing various guidelines on manufacturing and quality control of these products. Due to these stringent regulatory as well as ethical requirements, it becomes equally important to monitor the quality of these drug substances with respect to their purity and dosage forms at the time of release and at various stages of its shelf life. Quality control and quality assurance functions today have greater significance than ever. There are various analytical techniques, which have been used to monitor the quality of the pharmaceutical products. Looking at various validation criterions an analytical method needs to meet, in today’s stringent quality requirements, chromatographic techniques are the method of choice in most of the cases. High pressure liquid chromatography (HPLC) has been considered as the most versatile technique because of availability of different types of stationary phases, unlimited choice of mobile phases, varieties of detectors to be chosen from a range and as a whole applicability to a wide range of compounds.
which are not possible to analyse using other classical analytical techniques.

It was therefore thought worth to develop new methods of analysis for newly
developed pharmaceutically important formulations using the HPLC technique.
Stability indicating HPLC methods for various categories of drug formulations (which
are required in day to day life) such as Antihypertensive, Anticonvulsant, Antiemetic
and Muscle relaxant have been developed.

Short summary of all these developed methods is given below.

1. Candesartan tablets

   The mobile phase consisted of 6.8 g KH₂PO₄ /1000ml water (buffer )and
   Methanol (40:60).Chromatography was performed on Thermohypersil C18, (250 x
   4.6 mm, 5μm) column at a flow rate of 1.0 ml/min. The drug along with its degraded
   products was detected at 220 nm using PDA detector.

2. Captopril tablets

   A mixture of water : acetonitrile: tetrahydrofuran :methane sulfonic acid in the
   ratio of 80:10:10:0.1 was used as mobile phase. Chromatography was performed on
   Phenomenex, Luna C8, (250 x 4.6 mm, 5μm) column at a flow rate of 1.0 ml/min.
   The drug along with its degraded products was detected at 220 nm using PDA
   detector.

3. Propranolol tablets

   A mixture of 5.0 g Triethylamine /1000ml water pH 4.0 ± 0.1 by HCOOH):
   acetonitrile::70:30. was used as mobile phase. Chromatography was performed on
   Luna C18, (250 x 4.6 mm, 5μm) column at a flow rate of 1.5 ml/min. The drug was
detected at 225 nm along with its degradation products.

Bipin Bihari P.G College,Bundelkhand university,Jhansi ,U.P
4. Terazosin tablets

The mobile phase consisted of Buffer (6.8 g KH₂PO₄ /1000ml) and Methanol. in the ratio of 60:40. Chromatography was performed on Thermohypersil,C18,250 * 4.6 mm,5 μm column at a flow rate of 1.0 ml/min. The detector was set at 245 nm and all the degradants were well separated.

5. Verapamil tablets

A mixture of (1.4 g Na₂HPO₄ /1000ml, pH adjusted to 7.0 ± 0.1 by H₃PO₄) and Acetonitrile in the ratio of 50:50 was used as mobile phase. Chromatography was performed on Thermohypersil C18, (250 x 4.6 mm, 5μm) column at a flow rate of 2.0 ml/min. The drugs along with their degraded products were detected at 232nm using PDA detector.

6. Citalopram Bulk drug

A mixture of buffer (1.3 gm diammonium hydrogen orthophosphate in 1000ml water + 2ml of triethylamine, pH 6.8 ± 0.1 by orthophosphoric acid) and Methanol, Acetonitrile in the ratio of 45: 45:10. .094g of sodium hexane sulphonic acid was added, then filtered and degassed and used as mobile phase. Chromatography was performed on Restek C18, 250*4.6mm, 5μ at a flow rate of 2.0 ml/min. column temperature was kept at 40°C. The drug along with its degraded products was detected at 220 nm.
7. Metaxalone Bulk drug

The mobile phase consisted of aqueous buffer (6.0 gm KH₂PO₄ in 1000 ml water pH 3.0 ± 0.1 by H₃PO₄) and Acetonitrile in the ratio of 50:50. Chromatography was performed at a flow rate of 1.0 ml/min on Hypersil C8, BDS, 250*4.6mm, 5μ column. The detector was set at 225 nm.

8. Ondansetron Bulk drug

The mixture of buffer (2.7 gm KH₂PO₄ in 1000 ml water + 5.0 ml of triethyl amine pH 3.0 ± 0.1 by H₃PO₄) and Acetonitrile in the ratio of 70:30 was used as mobile phase. Chromatography was performed at a flow rate of 1.2 ml/min. on Luna,C8,250*4.6mm, 5μ column The detector was set at 216 nm.

In all, five methods have been developed and validated for five different formulations and three methods for three different bulk drugs. All these methods were found to be simple, rapid, reproducible, stability indicating and capable of assaying the drugs accurately from formulations in presence of excipients and their degradation products, Where as bulk drug method provides method for impurity profiling of the drug. The statistical parameters determined for the estimation of each drug in a formulation and bulk drug were found to be satisfactory. All these methods were found to be robust under variety of test conditions. All these methods can be utilised successfully for the analysis of preformulation studies, in-process analysis, routine quality control analysis, Stability studies of bulk and formulation products.

Bipin Bihari P.G College, Bundelkhand University, Jhansi, U.P