CHAPTER 2

Analysis of Drugs
The methods of analysis of various drugs are discussed in the following paragraphs.

Pharmacology is the study of understanding of the preparation of various drugs and their application in diagnosis, prevention and cure of diseases. It not only deals with the scientific aspects but its relation to the alleviation of a disease. The chemical structure of a drug decides its characteristic action and this relationship has helped in the synthesis of many valuable drugs. The adverse effect is called toxicity. The toxic effect of pharmacological agents employed in the therapy draws our attention to the general principles applicable to the prevention, recognition and treatment of drug poisoning of any kind. The adverse effect is balanced as far as possible by developing drug formulations. The drug formulations are effective as antacids, fever reducers, antithyroids, antibiotics, central nervous system stimulators etc.

The drug formulation not only contains the drug, but also the binding material associated with it. Since newly developed drugs are often more physiologically active, they can be administered in smaller amounts and hence more sensitive analytical methods are needed for the monitoring of these drugs.

A simple and rapid method for the analysis is important, it is because large number of samples are to be analysed, particularly at the production stage. Number of techniques are reported for the analysis of drugs in recent years. They include Gas Liquid Chromatography (GLC), Thin Layer Chromatography (TLC), High Performance Liquid Chromatography (HPLC). However, colorimetry,
Spectrofluorimetry and Spectrophotometry proved extremely useful in the field of pharmaceutical analysis.

General TLC procedures were reported for a number of common pharmaceuticals including benzodiazepines and local anaesthetics, amino-acrinehydrochloride, clotiazepam and oxyphenbutazone. High performance thin layer chromatography was used to assay cisplatin and related derivatives, methylnicotinic, lanetoside, aspirin, phenacetin, mebeverine hydrochloride, caffeine. Reversed phase conditions were employed in two of these procedures (loc. cit.) Phenacetin and caffeine have been determined in combination with phenazine using HPLC. Thin layer plates with a bonded chemical phase have been used to determine the optical purity of DOPA. Several barbiturates were separated on silica gel plates impregnated with various copper salts and alkyl amines. HPLC has been employed in the analysis of salicylic acid and tetracyclines.

The spectral methods can provide significant information in many areas. For example, this method of evaluation is useful in the study of pharmaceuticals and their metabolites, their degradation products, their chemical analogs etc. Chloropromazine and its sulphoxide impurity in dosage forms are characterised by UV spectroscopy. Vakulskya et al. employed EPR and polarography for the determination of intrazoles and introimidazoles. Gamot et al. used Raman spectroscopy in the toxicological investigations of crystalline and aqueous solutions of cocaine. Turezan et al. used NMR spectroscopy for the determination of bisulphan in tablets. Hoffman et al. employed mass and IR spectral methods associated with chromatographic techniques for the determination of
benzimidazoles. Hydrazone products were identified by IR and mass spectra. Roy has reviewed the use of mass fragmentometry. Using PMR spectroscopy Ashmaur et al. determined ascorbic acid.

A number of determinations of colorimetric methods have been employed for the antibiotics, analgesics and anti-inflammatory. Abdel Khalek employed spectrophotometry for the determination of penicillin using ammonium vanadate. Mayanna suggested a spectrophotometric method for the determination of penicillin employing ninhydrin as the reagent. For the specific determination of phenoxy-methyl penicillin, Christopher et al. used spectrophotometry. Anant et al. determined microgram amounts of penicillin employing azure-b. Sastry developed an indirect spectrophotometric method for the determination of antibiotics. Murillo et al. determined amoxycillin and cephalaxin in a mixture by using derivative spectrophotometry. For the colorimetric determination of benzyl penicillin Utpal Saha employed Cu(II) acetate as a complexing agent. Khalek suggested a method for the determination of cephalosporins using ninhydrin. Wu et al. proposed an improved hydroxylamine method for the assay of penicillin. Dessouky studied the spectrophotometric and gamma radiation effect on ampicillin. The biological activity of carbapenam and cephalosporins was studied by Matsuda et al. Oliyai et al. proposed isothermal heat conduction colorimetry for the study of ampicillin in aqueous solutions. Spectrophotometric methods for the determination of cephalosporins were proposed by Fogg et al. and Morel.

Various workers employed spectrophotometric method for the determination of tetracyclines. In the determination of salicyclic acid, Utpal Saha
used Cu(II) acetate as colour developer. Gupta\textsuperscript{61} and Aktual \textit{et al.}\textsuperscript{62} carried out colorimetric assay of salicylic acid. Spectrophotometric determination of acetaminophen and salicylamide was carried out by Abdine \textit{et al.}\textsuperscript{63}

The spectrophotometric assay of paracetamol and phenacetin was studied by different workers.\textsuperscript{64-70} Fogg\textsuperscript{71} has developed a selective colorimetric method using indophenol reaction for the determination of paracetamol. A colorimetric method was developed by Singhai\textsuperscript{72} for determining ibuprofen in presence of paracetamol. Huang \textit{et al.}\textsuperscript{73} employed a simultaneous spectrophotometric method for the determination of paracetamol and diclofenac sodium.

Several methods are available for the spectrophotometric determination of ascorbic acid\textsuperscript{74-85}. Extraction procedures for determining ascorbic acid in pharmaceutical preparations are also reported.\textsuperscript{86} Catalytic kinetic spectrophotometry for the determination of ascorbic acid was employed by Zhang Zhiqui \textit{et al.}\textsuperscript{87} A method for the qualitative determination of ascorbic acid based on the reaction of ascorbic acid with ninhydrin was developed by Biryuk \textit{et al.}\textsuperscript{88} Ferroin was used by Zhao \textit{et al.}\textsuperscript{89} for the colorimetric estimation of ascorbic acid.

To determine sulphamatrol and trimethoprim mixture in tablets, Abounassif \textit{et al.}\textsuperscript{90} used derivative spectrophotometry. Subramanyam \textit{et al.}\textsuperscript{91} proposed a method for the simultaneous determination of trimethoprim and sulphadizine in combined dosage forms. Sulphonamide was determined employing colorimetry by Bosch \textit{et al.}\textsuperscript{92} The physico-chemical behaviour of sulpha drugs was studied by Benedetti \textit{et al.}\textsuperscript{93}
The spectrophotometric methods reported in literature suffer from many disadvantages like high temperature requirement, high acid concentration and time consumption etc. In many cases sulphuric acid of very high concentration is employed to effect the hydrolysis of the drugs being studied. In order to develop the colour the reaction mixture is required to be heated to a high temperature in certain other cases. Besides certain reactions require about 2-3 hrs for going to completion or for the establishment of equilibrium. A routine laboratory engaged in the analysis of various drugs particularly antibiotics finds it inconvenient and cumbersome to adopt such lengthy and laborious procedures. Hence it is felt by the author that there is an urgent need to develop simple, rapid and sensitive analytical procedures for the determination of drugs, in particular tetracyclines and other drugs.