CHAPTER - III

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

The drug formulations not only contain the drug, but also the binding material associated with it. Because of the fact that 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 rapid analysis is important, as a large number of samples are to be analysed particularly at the production stage. The use of the electroanalytical methods in the broad field of pharmacy has to be estimated with respect to the morbidity and mortality rate of the world population. The electrochemical methods are almost similar to
Biological reactions taking place inside the body. Therefore an approximate understanding of the physiological reactions can be achieved through electrochemical reactions.

The similarities are:

1. In electrochemical reactions, the electron transfer takes place at the electrode-solution interface. In biological reactions, it occurs at the enzyme-solution interface.
2. Both types of reactions take place at similar pH and, in presence of similar inert electrolytes.
3. Both types of reactions can occur effectively under nonaqueous conditions and at similar temperatures.
4. In both the processes, the substrate molecule has to be oriented in a specific fashion before the electron transfer takes place.

In addition to the electro-analytical methods, thin layer chromatography (TLC), gas-liquid chromatography (GLC), high performance liquid chromatography (HPLC), colorimetry, spectro fluorimetry and spectrophotometry proved extremely useful in the field of pharmaceutical analysis.

A variety of colorimetric methods have been reported for the analysis of antibiotics antinflammatories and analgesics. Abdel khalek\textsuperscript{13} employed spectrophotometry for the determination of pencillin.
using ammonium vanadate. Employing ninhydrin as the reagent, Mayall suggested a spectrophotometric method for the determination of penicillin. Christopher et al used spectrophotometry for the specific determination of phenoxy methyl penicillin. Anant et al determined microgram amounts of penicillin employing azure-B. Sastry developed an indirect spectrophotometric method for the determination of antibiotics. Murillo determined amoxycillin and cephalaxin in a mixture by using derivative spectrophotometry. Utpal Saha employed copper (II) acetate as a complexing agent for the colorimetric determination of benzyl penicillin. By employing ninhydrin, Khalek proposed a method for the determination of cephalosporins. Derivative spectrophotometry was employed by Barary, Magda et al for the determination of cephalosporins from their alkali induced degradation products. Dessouky studied the spectrophotometric and gamma radiation effect on ampicillin. Derivative spectrophotometry was employed by various workers for the determination of penicillin derivatives. Matsuda et al studied the biological activity of carbapenam and cephalosporins. Fogg et al and Morelli proposed spectrophotometric methods for the determination of cephalosporins.

Spectrophotometric determination of tetracyclines was carried out by various workers. Derivative spectrophotometry is also employed for the determination of tetracycline derivatives in dosage forms. Spectrophotometric determination of acetaminophen and salicylamide was carried out by Abdino et al.
Different workers\textsuperscript{40-46} have studied the spectrophotometric assay of paracetamol and phenacetin. Fogg\textsuperscript{47} has developed a selective colorimetric method using indophenol reaction for the determination of paracetamol. Third derivative\textsuperscript{48} spectrophotometry is employed for the simultaneous determination of paracetamol and mephenoxalon. Singhal\textsuperscript{49} developed a colorimetric method for determining ibuprofen in presence of paracetamol. Spectrophotometric method for the simultaneous determination of paracetamol and diclofenac sodium is also reported.\textsuperscript{50}

Various methods for the spectrophotometric determination of ascorbic acid are reported in the literature.\textsuperscript{61-62} Extraction spectrophotometric method\textsuperscript{63} for determining ascorbic acid in pharmaceutical preparations is also reported. Zhiqui et al.\textsuperscript{64} employed catalytic kinetic spectrophotometry for the determination of ascorbic acid. Based on the reaction of ascorbic acid with ninhydrin, Biryuk et al.\textsuperscript{65} developed a method for the quantitative determination of ascorbic acid. Zhao et al.\textsuperscript{66} used Ferroin for the colorimetric estimation of ascorbic acid. Abounassif et al.\textsuperscript{67} used derivative spectrophotometry to determine sulphamethoxazole and trimethoprim mixture in tablets. Subramanyam et al.\textsuperscript{68} proposed simultaneous determination of trimethoprim and sulphadiazine in combined dosage forms. Bosch et al.\textsuperscript{69} determined sulphonamide employing colorimetry. Benedetti et al.\textsuperscript{70} studied the physico chemical behaviour of sulpha drugs.
The spectrophotometric methods suffer from certain disadvantages like high temperature requirement, high acid concentration and time consumption and so on. An attempt is made to develop simple, rapid and selective methods for the determination of drugs based on spectrophotometry. Electro analytical techniques have proved effective in the investigation of numerous types of drugs. From the very beginning, since early thirties, dc polarography has been applied as an important method in the analysis of physiologically and pharmacologically active compounds and drugs. Owing to such an orientation towards these important organic compounds, fundamental knowledge of reduction and oxidation mechanisms at mercury electrodes has been collected using classical polarography, which even now forms the main treasure of information.

D6 Polarography assay of tetracyclines was proposed by Chatten et al.71 Squella72 used dc polarography for the analysis of cephalexin Doan and Riedel73 proposed a method for polarographic estimation of penicillin. Fatma Incl, Foggg et al74 developed electrochemical methods for the assay of a group of cephalosporins. Various workers78-83 studied the electrochemical behaviour of diazepines. Electrochemical behaviour of paracetamol was studied by different workers.84,85

Square wave polarographic and voltammetric analysis of antibiotics was studied by Yarnitzky at al.86 Agarwal et al87 studied the electrochemical behaviour of some surface active agents on
Cobalt (II) - asparinate system at dme. Calusaru\textsuperscript{88} studied the catalytic polarographic behaviour of 2-mercapto benzothiazole. Dityanseva et al\textsuperscript{89} used polarographic method for the determination of streptomycin. Pulse polarography of cysteine and its derivatives was developed by Malressa.\textsuperscript{90} Selgerman Howard\textsuperscript{91} studied the polarographic behaviour of antibiotics and antibacterial agents. Different electrochemical methods were employed for the analysis of certain cephalosporins.\textsuperscript{92,93} Kazandzhieva\textsuperscript{94} et al., used polarography for the determination of chloramphenicol. Simultaneous differential pulse voltammetric determination of ascorbic acid, caffeine and paracetamol was studied by different workers.\textsuperscript{95}

Differential pulse polarographic determination of degradation products of cephalosporins was proposed by Fogg et al\textsuperscript{96}. Enzyme loaded glass electrode is employed for the determination of penicillins in complex media.\textsuperscript{97} Sengun et al\textsuperscript{98} used cathode ray polarography for the analytical investigation of penicillins. Ying sing et al\textsuperscript{99} developed a method for salicylic acid determination by employing differential pulse voltammetry. Helena et al\textsuperscript{100} developed chronoamperometric determination of paracetamol. Orata et al\textsuperscript{101} studied the electrochemical behaviour of ascorbic acid on a polyaniline coated electrode. Korell et al\textsuperscript{102} proposed an amperometric method for the determination of ascorbic acid based on its reaction with zinc chloride salt of diazotized l-amino anthraquinone. Voltammetric determination of some heterocyclic mercaptans was carried out by Lynch et al\textsuperscript{103}. Bersier et al\textsuperscript{104} studied the polarographic and
voltammetric behaviour of soframycin. Differential pulse polarographic analysis of ascorbic acid\textsuperscript{105,106} and salicylic acid\textsuperscript{107} were proposed by various workers.

In general, polarographic methods make themselves useful in assays of pharmaceuticals in tablets, injections, and various other solutions. A climax in the application of dc polarographic methods in drug analysis was seemingly attained by introducing these methods in pharmacopoeias of some countries.\textsuperscript{108,109} DC Polarography served for determining pure substances such as ascorbic acid, nicotinamide, chloramphenicol and also the contents of drugs in some preparations viz., tablets or injections. The method can be conveniently employed to determine concentrations of substances which are not very low.