CHAPTER I

GENERAL INTRODUCTION
INTRODUCTION

Since the dawn of civilization, man has been a victim of destruction by disease, and has tried to find cures. Earliest prescriptions are recorded in a Sumerian tablet of 2100 B. C. describing ointments and medicines containing asafoetida, thyme (source of Thymol), sodium chloride and potassium nitrate. The Ebers Papyrus written in 1550 B. C. contains prescriptions of castor oil, opium, colchicum and other drugs, which are still in use. This historic document was found in a tomb of a mummy in Thebes in Egypt, and is now preserved at the University of Leipzig. Perhaps, Chinese Medicine was about the earliest, dated at about 2500 B. C. Ephedra or Ma Huang was used even in those early days. Ayurveda or Indian Medicine is about equally ancient, and it has given some useful remedies to modern medicine.

Some giants in the history of medicine were Hippocrates, Aristotle, Theophrastus, Pliny, Dioscorides and Galen. Hippocrates (460-370 B. C.) is referred to as the “father of medicine”, and many of his writings dealt with anatomy and physiology. The “Hippocratic Oath” of modern day medicine reflects the high esteem with which this Greek physician is regarded. Hippocrates was the first to recognize disease as an abnormal reaction of the body rather than a visitation from the Gods. Aristotle (384 – 322 B.C.), a student of Plato, is considered to be the most influential Greek Philosopher. He attempted to separate superstition from fact. Theophrastus (370 – 287 B.C.), a student of Aristotle, utilized his teacher’s scientific reasoning, and applied it to the plant kingdoms. Dioscorides, a Greek physician of the first century B. C. described several plants of medicinal value. Later, Pliny (23-70 A. D.) compiled 37 volumes of natural history, which served as reference data for many years. The Hippocratic concept of disease was then lost and did not reappear until the Renaissance (15th Century A. D. marking the transition from the Middle Ages to the modern world). During this dark period the concept of
Galen (131–201 A. D.) and his dogmatic system of polypharmacy prevailed. Galen, a Greek pharmacist physician, who lived in Rome, described many formulae containing plant and animal drugs. He compiled this knowledge in 20 books. Galen’s name is retained in the term “galenical” pharmacy, which includes preparation of crude vegetable drugs.

Paracelsus (1493–1541 A. D.), an outstanding leader of the Renaissance, reintroduced free thought and critical enquiry. He attacked the Galenic system of polypharmacy, and introduced the use of simple chemicals for treating disease. He introduced mercurials in the treatment of syphilis. During his time the first official pharmacopoeia was printed.

Experimental medicine and therapeutics had to wait long for the advances in physiology, which during the decade (1850–1860) become an experimental science. Virchow, the German physiologist in 1855 propounded the concept of “all cells from cells”. Later, with advances in the knowledge of the physiology of circulation, central nervous system, the hormones and enzymes in the body, the study of pharmacology and therapeutics was stabilized. In fact, pharmacology originated as a branch of physiology. The application of scientific method to studies on drugs was generated in France by François Magendie (1783–1855), and was expanded by Claude Bernard (1813–1921) is associated with the development of experimental pharmacology in Germany, and John Jacob Abdel (1857–1938) played a similar role in the United States of America. In India Sir Ram Nath Chopra (1882–1973) was responsible for the development of pharmacology as a well-defined discipline. He was the Founder Director of the Drug Research Laboratory of the Council of Scientific and Industrial Research (CSIR), located at Jammu-Tawi. Sir Chopra has been widely acclaimed as the Father of Indian Pharmacology, because of his investigations on Indian indigenous drugs. The growth of pharmacology was further stimulated by the development of synthetic organic chemistry, which has provided many
new therapeutic agents. Today we live in an era of a "drug explosion" due to the introduction of a large number of drugs, and the knowledge of clinical pharmacology aims at the rational and safe use of drugs in man.

The term "drug" is derived from the French word "Drogue" meaning a dry herb. A drug is defined as a substances used for the diagnosis, prevention, treatment or palliation (relief from symptoms) of disease. A fifth category of drug usage is for prevention of pregnancy i.e., contraception; a non-disease condition. Sixthly, drugs may also be used for maintenance of optimal health.

Sources of Drugs

Drugs are derived from four main sources: (i) plants, examples of which are digitalis, opium and belladonna; (ii) animals, from which drugs like adrenaline, insulin and ACTH are obtained; (iii) minerals or mineral products, such as iron, iodine and magnesium sulphate; and (iv) synthetic chemicals made in the laboratory. Drugs have also been obtained from microorganisms, and their growth products include antibiotics like bacitracin; enzymes like streptokinase; and today genetically modified E. coli produce human insulin, a hormone.

Plant drugs. The roots, leaves and barks of plant were used to treat disease till the beginning of this century. Later, the active principles were extracted and used in modern medicine. Plant products like quinine, morphine, ephedrine and digoxin, continue to be important drugs. Antibiotics produced by living bacteria, yeast and moulds are valuable in the treatment of infectious disease. Penicillin, streptomycin, chloramphenicol and the tetracyclines are some useful antibiotics.
Animal drugs. Animal products used for the treatment of disease are insulin, extracted from pork and beef pancreas, is used for diabetes mellitus; thyroid powder for hypothyroidism; heparin as an anticoagulant; and different hormones for various endocrinial diseases.

Mineral drugs. Minerals as simple elements or their salts provide useful drugs, like ferrous sulphate for anaemia, magnesium trisilicate for hyperacidity and peptic ulcer. Radioactive isotopes of Iodine, Phosphorus and Gold are also used in modern medicine.

Synthetic drugs. Majority of drugs in use today are prepared synthetically from chemical substances. Semisynthetic drugs are naturally occurring substances that have been chemically altered. Some examples are: sulphonamides, thiazide diuretics, oral antidiabetics, synthetic corticosteriods, sympathomimetics and other autonomic agents. Pharmacological activity is a function of the chemical structure and physical properties of drugs. The chemical structure can be modified in search of better, more potent and safer drugs.

The continued and wide spread use of synthetic organic compounds in therapy has given rise to a new area in chemical analysis-pharmaceutical analysis.

1.2. Scope of the present work

Pharmaceutical analysis, in general terms, comprises those procedures necessary to determine the “identity, strength, quality and purity” of drugs. However, for practical reasons, it is proper to broaden the scope of this definition to include the analysis of raw materials and intermediates in the manufacture of drugs. Analytical chemists in the pharmaceutical industry as well as in those chemical industries that produce pharmaceutical raw materials must perform such analyses.

Pharmaceutical analysis plays a key role not only for the quality assurance of drugs and their formulations, but also to guarantee to the consumer a safe and reliable product. Devising
accurate procedures for each ingredient of complex dosage formulations containing several therapeutically and chemically compatible drugs with very similar chemical nature is a tough task. The presence of additives, excipients and decomposition products further complicates the development of analytical procedures. The increasing complexities of pharmaceutical preparations and the marked emphasis on quality control by the ethical manufacturers have placed a greater load on the ingenuity of the quality control chemist.

An analytical chemist who is in need of an analytical method may be obliged to survey tremendous amount of literature in order to select one procedure which may appear to suit his need and facilities available, but when he subjects the selected procedure to actual test, he may find that he cannot reproduce the method. It is, therefore essential that that practicing analytical chemist should have access to analytical procedures, which are simple, reliable and responsible under routine laboratory conditions.

Analytical techniques currently used in pharmaceutical analysis rely increasingly on complex techniques of analysis such as HPLC, GC-MS, FIA-spectrofluorimetry, FIA-spectrophotometry, stripping voltammetry and capillary electrophoresis that require expensive equipments and highly specialized personnel. Such techniques are not of much help in countries lacking these resources. For most part, modern analytical techniques merely permit analysis to be carried out more rapidly than the conventional method of analysis. Even if a manufacturer is ready to procure and install modern instruments/equipments, their maintenance in the fittest condition is an Herculian task. Non-availability of trained analytical personnel and simple, accurate precise and cost-effective methods of analysis is a major handicap for pharmaceutical manufacturers in developing countries.
Taking into consideration the technical and economical constraints, it is necessary that the recommended methods should permit their use by pharmaceutical industries located in the developing countries. It is significant to stress that even simple techniques like titrimetry and spectrophotometry result in sensitive and accurate measurements with clear advantages of speed, simplicity, cost-effectiveness and zero/or easy maintenance. The large volume of literature devoted to their application in almost every field of scientific research constitute irrefutable evidence of their utility. It is, therefore, reasonable to assume that the analytical procedures involving the use of such simple techniques will find wider applications.

Furthermore, majority of the methods currently in use in pharmaceutical analysis, like HPLC, TLC, HPTLC, GC, GC-MS, Capillary-electrophoresis, etc., are purely physical methods. Hence, there is a widespread sense that “the chemistry was going out of analytical chemistry”. More recently, it has been recognized that a combination of physical and chemical approaches to the analysis can often accomplish more than either of them alone.

Keeping the above trends in view, the author has carried out detailed investigation and developed new analytical methods based on chemical reactions for the assay of six synthetic drugs. All the methods (except one) are based on a variety of chemical reactions, the finish to the determination being made with techniques such as titrimetry, spectrophotometry and reaction rate measurements. To add variety to the techniques employed, one purely physical method, HPLC has also been used in the study.
Drugs used in the present investigation.

<table>
<thead>
<tr>
<th>Name</th>
<th>Abbreviation</th>
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<tbody>
<tr>
<td>Salbutamol Sulphate</td>
<td>SBS</td>
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<tr>
<td>Pefloxacin mesylate dihydrate</td>
<td>PFM</td>
</tr>
<tr>
<td>Captopril</td>
<td>CPT</td>
</tr>
<tr>
<td>Famotidine</td>
<td>FMT</td>
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<tr>
<td>Albendazole</td>
<td>ALB</td>
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<tr>
<td>Acyclovir</td>
<td>ACL</td>
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**Pharmaceutical preparations used**

The following pharmaceutical preparations were used in the study:

1. **SBS**
   - Tablets (mg/tablet)
     - 1. Salbetol tablets (F. D. C.) 2.0, 4.0
     - 2. Salmoplaten tablets (Khandelwala), 2.0, 8.0
     - 3. Ventrolin CR Capsules (Glaxo Allendrugs) 8.0

2. **PFM**
   - Tablets (mg / tablet)
     - 1. Peflox tablet (Woekhardt Pvt. Ltd) 200, 400
   - Injections (mg / ml)
     - 3. Pebid tablet (Indehemie Pvt. Ltd) 400
     - 4. Qucin tablet (Aristo pharmaceuticals Ltd) 400
     - 5. Peflobid injection (2 mg/ ml)

3. **CPT**
   - Tablets (mg/tablet)
     - 1. Acetin (Wockhdart Ltd ) 25
     - 2. Angiopril (Torrent pharmaceuticals) 25, 50
     - 3. Captopril (Lupin lab Ltd, India) 12.5, 25

4. **FMT**
   - Tablets (mg / tablet)
     - 1. Acredin (Sarabhai Chemicals), 20
     - 2. Facid (Intas Pvt. Ltd) 20
   - Injection (mg/ml)
     - 3. Famocid (Sun-Pharma), 20, 40
     - 4. Facid injection (Intas Pvt. Ltd), 2 mg/ ml

5. **ALB**
   - Tablets (mg/tablet)
     - 1. Alminth (Torrent Pharmaceuticals), 200
     - 2. Albental (Micro Labs), 400
     - 3. Zoleban (Combat Drugs), 500
     - 4. Zentel (SmithKline Beecham), 400
     - 5. Albazole (Geno Pharm Ltd) 200, 400
6. Dispel (Indian Drugs and Pharmaceuticals), 400

6. ACL

1. Acyvir DT (Cipla India Ltd), 200, 400, 800
2. Ocuvir (FDC, India), 200, 400, 800

Reagents used in the study

1. Bromate-bromide mixture
2. Chloramine-T
3. Sodium metavanadate
4. Potassium iodate
5. Sodium periodate
6. Iron (III) chloride-ferricyanide
7. Metol
8. Sulphanilic acid
9. 2,7-dichlorofluoroscien
10. Methyl orange
11. Indigo carmine
12. Ferrous ammonium sulphate
13. Folin-Ciocalteu reagent
14. Hydrogen peroxide
REFERENCES


