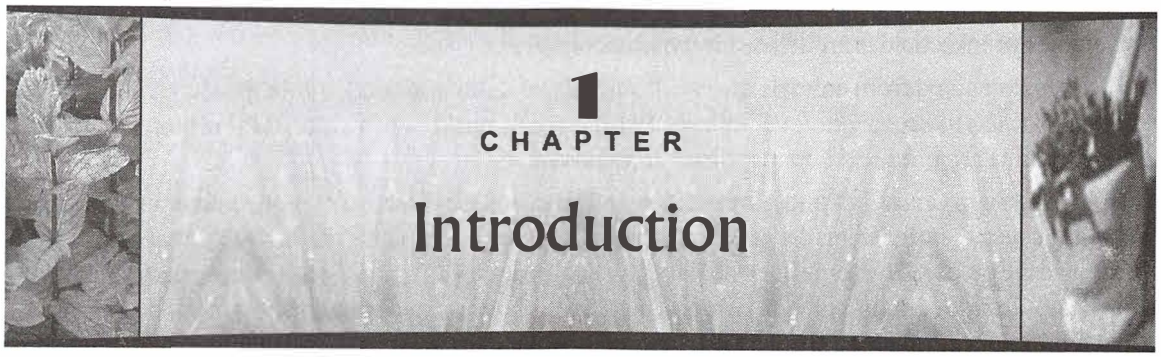

1 CHAPTER
Introduction

Diseases are born with man and drugs came into existence since a very early time to remove the pain of diseases and to cure them. Thus, the story and the history of drugs is as old as the mankind.

Drugs used in medicine today are either obtained from *nature* or are of *synthetic origin.* Natural drugs are obtained from plants, animals or mineral kingdom. Drugs from micro-organisms like antibiotics were not known in the early period. Synthetic drugs or syntheticals like aspirin, sulpha drugs, some vitamins and some antibiotics are synthesized in laboratories from simple chemicals through various chemical reactions.

Natural drugs obtained from plants and animals are called drugs of *biological origin* and the active principles, because of which they have their therapeutic use, are produced in the living cells of plants or animals.

Pharmacognosy is the study of crude drugs obtained from plants, animals and mineral *kingdom* and their constituents. Even though the science of Pharmacognosy is practiced since a very early *period*, the term Pharmacognosy was first used by C. A. Seydler, a German scientist, in 1815 in his book *Analecta Pharmacognostica.* It is derived from two Latin words *Pharmakon,* 'a drug', and *gignosco,* 'to acquire knowledge of'. It means knowledge or science of drugs.

Crude drugs are plants or animals or their parts which after collection are subjected only to drying or making them into transverse or longitudinal slices or peeling them in some cases. Most of the crude drugs used in medicine are obtained form plants and only a small number comes from animal and mineral kingdoms. Drugs obtained from plants consist of entire plants, while senna leaves and pods, nux vomic seeds, ginger rhizome and cinchona bark are parts of the plants. Though in a few cases, as in lemon and orange peels and in colchicum corm, drugs are used in fresh condition, most of the drugs are dried after collections. Crude drugs may also be obtained by simple physical processes like drying or extraction with water. Thus aloe is the dried juice of leaves of *Aloe* species, opium is the dried latex from poppy capsules and black catechu is the dried aqueous extract from the wood of *Acacia catechu.* Plant exudates such as gums, resins and balsams, volatile oils and fixed oils are also considered as crude drugs.

Further drugs used by physicians and surgeons or pharmacists, directly or indirectly, like cotton, silk, jute and nylon in surgical dressing or kaolin, diatomite used in filtration of turbid liquid or gums, wax, gelatin, agar used as pharmaceutical auxiliaries of flavouring or sweetening agents or drugs used as vehicles or insecticides are treated in Pharmacognosy.

Drugs obtained from animals are entire animals, as cantharides, glandular products, like thyroid organ or extracts like liver extract. Similarly, fish liver oils, musk, bees wax, certain hormones, enzymes and antitoxins are products obtained from animal sources.

Drugs are organized or unorganized. Organized drugs are direct parts of the plants and consist of cellular tissues. Unorganized drugs, even though prepared from plants are not the direct parts of the plants and are prepared by some intermediary physical processes like incision, drying, or extraction with water and do not contain cellular tissue. Thus aloe, opium, catechu, gums, resins and other plant exudates are unorganized drugs.

Drugs form mineral sources are kaolin, chalk, diatomite, the well-known *Makardhwaj* and other *bhasmas* of Ayurveda.

A systematic and complete study of crude drugs is done in Pharmacognosy. In the systematic study of crude drugs are described (a) origin, common names, biological source and family; (b) geographical source; (c) history; (d) cultivation, collection, preparation for market and storage; (e) macroscopical, sensory and microscopical character (f) chemical constituents; (g) uses; (h) substitutes and adulterants and (i) evaluation.

Each drug is always obtained from the same plant or animal. The Latin name of the plant or animal is called its botanical or zoological source. The family to which this plant or animal belongs is also mentioned, e.g. Vasaka leaves are obtained from *Adhatoda vasica* plant family Acanthaceae. Vasaka leaves are included in the Indian Pharmacopoeia and are, therefore called official leaves. The botanical source is thus called official source. Geographical source or habitat gives the information about the country or place where the drug is produced. Ginger is produced in Jamaica and nux vomica and ispaghula in India. In some cases the original native place of a drug is not the same as the present geographical source, e.g. cinchona is a native of South America and is at present cultivated in Indonesia, India and Congo. History of the drugs gives the useful information about how the drug was known, where it was growing originally and how it was introduced into the modern medicine. History of some drugs like cinchona bark, coca leaves, rauwolfia root and opium is very interesting. Politics plays its part in the drugs also. Thus there was restriction on the import of buchu leaves into India from South Africa because of poor political relations with that country earlier.

One of the requirements of the drugs is that they should possess maximum activity and thus should contain maximum percentage of active chemical constituents. For this reason many of the drugs like digitalis leaves, belladonna herb and roots, Ceylon cinnamon bark, linseed, fennel and other umbelliferous fruits are obtained from cultivated plants only. In cultivation attention is paid to the selection of proper strains of seeds, type of soil, optimum climatic factors, like light, temperature, elevation, rainfall, fertilizer, plant growth factors etc. so that strong and sturdy plants rich in active chemical constituents would grow. The crude drugs obtained in this way are usually more active.

Drugs are collected during definite season, at particular time of the day and in some special conditions at a definite stage of development. Thus ephedra, wild cherry bark and most of the

subterranean drugs consisting of roots and rhizomes are collected in autumn. Leaf drugs are collected during the flowering season. Solanaceous herbs like hyoscyamus, belladonna etc. are collected in the morning and during dry weather. Clove is collected in bud condition, santonica, when flower heads are closed, chamomile flowers when fully expanded and coriander fruits when completely ripe. However, some of the drugs, mostly because of economic considerations are obtained from wild plants. Thus gentian roots in Europe, nux vomica seeds in India and strophanthus seeds in Africa are obtained from wild pants.

Crude drugs consist of definite parts of the plants, e.g. leaf, flower, fruit, seed, wood, bark and root etc. Systematic morphological or macrcscopically description of these parts is undertaken with naked eye or with magnifying lens. In this description general condition of the drug, size, shape, markings on outer surface, inner surface, fracture etc. are described. Thus each part of the plant is described according to a definite system characteristic of each group. Drugs can be identified as above only if they are in entire condition. Sensory or organoleptic characters describe colour, odour, taste, consistency etc. By the sensory characters often useful information is obtained. If leaf drugs are not thoroughly dried they are tough or flexible, but if over dried they become brittle. If leaves, flowers and some herbs like lobelia are dried directly in the sunlight they become pale, bleached and yellow but retain green colour, if dried in shade. Different species of *Mentha* can be determined by an experienced worker by smell only. The quality of some volatile oil containing drugs like clove and cardamom can be determined by smell only. In ergot rancid and ammoniacal odour indicates inferior drug; taste tells us about bitter drugs like gentian and pungent drugs like ginger and capsicum. If the drugs are in broken or even in powdered condition their microscopic characters are studied by use of microscope. In case of leaves, surface preparation and transverse section, preferably through mid-rib are made and nature of epidermis, trichomes, stomata, arrangement of tissues like palisade cells, vascular bundles and nature of cell contents are studied. Similarly in case of barks, roots, rhizomes and wood, transverse and longitudinal sections are made and from characteristic arrangement of tissues of each drug and from diagnostic elements like stone cells, fibers, vessels etc. the drugs are identified. The diagnostic elements persist even when the drugs are in fine powdered condition and help further in identification of the drugs. Linear measurements and other methods of quantitative microscopy help further in the identification of drugs. The sections or the powdered drug samples are cleared by clearing agents, mostly by chloral hydrate solution, before mounting on the slide.

The basic chemical nature of the cell wall of almost all plants is cellulose. However, lignin, suberin, cutin or mucilage are deposited on to the cellulose. Cellulose gives blue colour with chlorzinc iodine solution and dissolves in cuoxam (copper-oxide-ammonia) reagent. Lignin is present in the middle lamella and secondary cell walls of many vessels, tracheids, fibers and sclereids and gives red colour with phloroglucinol and concentrated hydrochloric acid. Suberin is present in cork and endodermis cells, while cutin in the cuticle of the leaf. Both of these material are fatty in nature and when heated with Sudan red III give red colour. Mucilage gives red colour with ruthenium red. The chemical constituents present in the drugs can be identified by chemical or microchemical tests. Cascara bark and rhubarb rhizome give with 5% potassium hydroxide red colour because of anthraquinone derivatives. Strychnine present in nux vomica gives purplish-red colour with ammonium vanadate and concentrated sulphuric acid.

Recently, paper chromatography, thin layer chromatography, gas chromatography and high-pressure liquid chromatography are utilized in identification of drugs, their adulterants and their chemical constituents. Methods have been developed for quantitative estimation of the chemical constituents by paper and thin layer chromatography, gas chromatography and high preesure liquid chromatography.

Drugs contain chemical constituents in different proportions which give us information about active and other constituents. Thus quinine is an alkaloid present in cinchona bark; eugenol is a constituent of clove oil, wild cherry bark contains cyanogenetic glycosides, jalap and podophyllum contain resins and mucilage is the chemical constituent of ispaghula and linseed. The study of Pharmacognosy also includes the use of drugs and the pharmacological action of their chemical constituents. Thus cinchona bark is used in malaria; rauwolfia root in high blood pressure and insanity, digitalis in cardiac diseases, some drugs or their products have pharmaceutical applications, e.g. starch as a disintegrating agent in tablets, gums as binding and suspending agents, agar as an emulsifier and diatomite for filtration.

Sometimes crude drugs are adulterated. An adulterant is the drug resembling the original or authentic drug but it is usually quite different or inferior, less effective, containing less percentage of active constituents and sometimes containing more extraneous matter than permitted. Nature of adulteration can be determined by the study of pharmacognostic evaluation.

Evaluation of the drugs means determining their identity, purity and quality or activity. It may be expressed as (a) organoleptic evaluation (b) microscopical evaluation, (c) biological evaluation (d) physical evaluation and (e) chemical evaluation and is described later.

HISTORY OF PHARMACOGNOSY

In the early period, primitive man went in search of food and ate at random plants or parts like tubers, fruits, leaves etc. If he found that no harmful effects were observed, he considered them as edible materials and used them as food. If he found that by their eating other actions were found they were considered inedible and according to the actions he used them in treating symptoms or diseases. If it caused diarrhoea, it was used as a purgative, if vomiting, it was used as an emetic and if it was found poisonous and death was caused, he used it as an arrow poison. The knowledge was empirical and was obtained by trial and error. He used drugs as such or as their infusions and decoctions. The results were passed from one generation to another generation and new knowledge was added in the same way.

In India knowledge of medicinal plants is very old and medicinal properties of plants are described in Rigveda and in Atharvaveda (3500-1500 B.C.) from which Ayurveda has developed. In Ayurveda, the ancient well-known treatises are Charak Samhita dealing mostly with plants and Sushrut Samhita in which surgery is also mentioned. In Egypt, people were familiar with medicinal properties of plants and animals. They were familiar with human anatomy and knew of enbalming the dead and preserving their bodies as described in Papyrus Ebers (1550 B.C.), an ancient book found in one of the mummies.

Greek scientists contributed much to the knowledge of natural history. Hippocrates (460-370 B.C.) is referred to as father of medicine and is remembered for his famous oath which is even now administered to doctors. Aristotle (384-322 B.C), a student of Plato was a philosopher and is known for his writing on animal kingdom which is considered authoritative even in twentieth century. Theophrastus (370-287 B.C.) a student of Aristotle, wrote about plant kingdom. Dioscorides, a

physician who lived in the first century A. D., described medicinal plants, some of which like belladonna, ergot, opium, colchicum are used even today. Pliny wrote 37 volumes of natural history and Galen (131-200 A.D.) devised methods of preparations of plant and animal drugs, known as 'galenicals' in his honour.

Pharmacy separated from medicine and material medica, the science of material medicines, describing collection, preparation and compounding, emerged. As mentioned earlier in 1815 Seydler introduced the name pharmacognosy.

Even upto the beginning of 20^{th} century Pharmacognosy was more a descriptive subject akin mainly to botanical science and it consisted of identification of drugs both in entire and powdered conditions and concerned with their history, commerce, collection, preparation and storage.

Period 1934-1960 :

The development of modern Pharmacognosy took place later during the period 1934-1960 by simultaneous application of disciplines like organic chemistry, biochemistry, biosynthesis, pharmacology and modern methods and techniques of analytic chemistry, including paper, thin layer and gas chromatography and spectophotometry.

The substances from the plants were isolated, their structures elucidated and pharmacological active constituents studied. The development was mainly due to the following four events :

1. Isolation of penicillin in 1928 by William Fleming and large scale production in 1941 by Florey and Chain.
2. Isolation of resperpine form Rauwolfia roots and confirming its hypotensive and tranquilizing properties.
3. Isolation of vinca alkaloids, especially vincristine and vinblastine. Vincristine was found useful in the treatment of leukemia. These alkaloids also have anticancer properties.
4. Steroid hormones like progesterone were isolated by partial synthesis from diosgenin and other steroid saponins by Marker's method. Form progesterone by chemical and microbial reaction cortisone and hydrocortisone are obtained.

Antibiotic Age :

This period is also antibiotic age, as besides pencillin, active antibiotics like streptomycin, chloramphenicol, tetracycline and several hundred antibiotics have been isolated and studied extensively.

Some of the important aspects of the natural products which led to the modern development of drugs and pharmaceuticals are as follows :

Isolation of phytochemicals **:** Strong acting substances such as glycosides of digitalis and scilla, alkaloids of hyoscyamus and belladonna, ergot, rauwolfia, morphine and other alkaloids of opium were isolated and their clinical uses studied.

Structure activity relationship : Tubocurarine and toxiferine from curare have muscle relaxant properties because of quaternary ammonium groups. The hypotensive and tranquillising actions of reserpine are attributed to the trimethoxy benzoic acid moiety which is considered essential. Mescaline and psilocybine have psychocative properties. Presence of a lactone ring is essential for the action of cardiac glycosides. Likewise anthraquinone glycosides cannot have their action without satisfying the positions at C_3, C_1, C_8, C_9 and C_{10}.

Drugs obtained by partial synthesis of natural products : Oxytocic activity of methyl ergometrine is more than that of ergometrine. In ergotamine, by 9:10 hydrogenation, oxytocic activity is suppressed and spasmolytic activity increases. We have already referred to the preparation of steroid hormones from diosgenin by acetolysis and oxidation and further preparation of cortisone by microbial reactions .

Steroid hormones and their semisynthetic analogues represent a multimillion dollar industry in U.S.A

Natural products as models for synthesis of new drugs : Morphine is the model of a large group of potent analgesics, cocaine for local anaesthetics, atropine for certain spasmolytics, dicoumarol for anticoagulants and salicin for salicylic acid derivatives. Without model substances from plants a large number of synthetics would have been missed.

Drugs of direct therapeutic uses : Among the natural constituents, which even now cannot be replaced, are important groups of antibiotics, steroids, ergot alkaloids and certain antitumour substances. Further, drugs as digitoxin, strophanthus glycosides, morphine, atropine and several others are known since long and have survived their later day synthetic analogues.

Biosynthetic pathways : Biosynthetic pathways are of primary and secondary metabolites. Some of the important pathway are Calvin's cycle of photosynthesis, shikimic acid pathway of aromatic compounds, acetate hypothesis for anthracene glycosides and isoprenoid hypothesis for terpenes and steroids via acetatemevalonic acid-isopentyl pyrophosphate and squalene.

Progress from 1960 onwards : During this period only a few active constituents mainly antibiotics, hormones and antitumour drugs were isolated or new possibilities for their production were found. From 6-amino penicillanic acid, which has very little antibiotic action of its own, important broad spectrum semi-synthetic penicillins like ampicillin and amoxicillin were developed.

From ergocryptine, an alkaloid of ergot, bromocryptine has been synthesised. Bromocryptine is a prolactin inhibitor and also has activity in Parkinson's disease and in cancer. By applications of several disciplines, pharmacognosy from a descriptive subject has again developed into an integral and important disciplines of pharmaceutical sciences.

Technical Products :

Natural products besides being used as drugs and as therapeutic aids are used in a number of other industries as beverages, condiments, spices, in confectioneries and as technical products.

The coffee beans and tea leaves besides being the source of caffein are used as popular beverages. Ginger and wintergreen oil are used less pharmaceutically but are more used in preparation of soft drinks. Mustard seed and clove are used in spice and in condiment industry. Cinnamon oil and Peppermint oil besides being used as carminatives are used as flavouring agents in candies and chewing gum. Colophony resin, turpentine oil, linseed oil, acacia, pectin and numerous other natural products are used widely in other industries and are called technical products.

Pharmaceuticals Aids :

Some of the natural products obtained from plants and animals are used as pharmaceutical aids. Thus gums like acacia and tragacanth are used as binding, suspending and emulsifying agents. Guar gum is used as a thickening agent and as a binder and a disintegrating agent in the manufacture of tablets.

Sterculia and tragacanth because of thier swelling property are used as bulk laxative drugs. Mucilage containing drugs like isabgul and linseed are used as demulcents or as soothing agents and as bulk laxatives. Starch is used as a disintegrating agent in the manufacture of tablets and because of its demulcent and absorbent properties used in dusting powders. Sodium alginate is used as a establishing, thickening, emulsifying defloculating, gelling and filming agent. Carbohydrate containing drugs like glucose, sucrose and honey are used as sweetening agents and as laxative by osmosis.

Agar is used as a laxatives by osmosis. Agar is also used as an emulsifying agent and in culture media in microbiology. Saponins and saponin containing drugs are used as detergents, emulsifying and frothing agents and as fire extinguishers. Tincture quillaia is used in preparation of coaltar emulsions. Saponins are toxic and their internal use requires great care and in some countries internal use as frothing agents is restricted. Glycyrrhiza is used as sweetening agent for masking the taste of bitter and salty preparations.

Fixed oils and fats are used as emollients and as ointment bases and vehicles for other drugs. Volatile oils are used as flavouring agents.

Gelatin is used in coating of pills and tablets and in preparation of suppositories, as culture media in microbiology and in preparation of artificial blood plasma. Animal fats like lard and suet are used as ointment bases. Beeswax is used as ointment base and thickening agent in ointments. Wool fat and wool alcohols are used as absorbable ointment bases.

Thus from the above description it can be seen that many of the natural products have applications as pharmaceutical aids.

Phytochemistry :

Phytochemicals are non-nutritive plant chemicals that contain protective and disease-preventing compounds. They are often lumped together under the term "phytochemicals" - *phyto* from the Greek word for plant, denoting their plant origins. More than 900 different phytochemicals have been identified as components of food, and many more phytochemicals continue to be discovered today. It is estimated that there may be more than 100 different phytochemicals in just one serving of vegetables. As early as 1980, the National Cancer Institute Chemoprevention Program of the Division of Cancer Prevention and Control began evaluating phytochemicals for safety, efficacy and applicability for preventing and treating diseases. Researchers have long known that there are phytochemicals present for protection in plants, but it has only been recently that they are being recommended for protection against human disease.

Phytochemicals are not yet classified as nutrients or substances necessary for sustaining life. They have been identified as containing properties for aiding in disease prevention. They are associated with the prevention and /or treatment of amongst others at least four of the leading causes of deaths in the United States and elsewhere - cancer, diabetes, cardiovascular disease and hypertension. They are involved in many processes including ones that help prevent cell damage, prevent cancer cell replication, and decrease cholesterol levels. Some phytochemicals work as antioxidants, while others are enzyme inhibitors. One compound might have an impact via several different mechanisms.

The Importance of Phytochemicals :

Scientists have long known the importance of plants and the chemicals they produce in overcoming disease. Over 25% of all prescription drugs still use plants as their principal ingredient. Research is now starting to reveal that these compelling compounds protect humans, just like they do plants, by keeping degenerative diseases at lower levels or preventing them completely when used on a regular basis.

Discovery of New Medicines form Plants - Nutraceutical use versus Drug Development :

Little work was carried out by the pharmaceutical industry during 1950-1980's; however, during the 1980-1990's massive growth has occurred. This has resulted in new developments in the area of combinatorial chemistry, new advances in the analysis and assaying of plant materials and a heightened awareness of the potential plant materials as drug leads by conservationists. New plant drug development programs are traditionally undertaken by either random screening or an ethnobotanical approach, a method based on the historical medicinal/ food use of the plant. One reason why there has been resurgence in this area is that conservationists especially in U.S.A. have argued that by finding new drug leads form the rainforest, the value of the rainforests to society is proven and that this would prevent these areas being cut down for unsustainable timber use. However, Tropical forests have produced only 47 major pharmaceutical drugs of world-wide importance. It is estimated that a lot more, say about 300 potential drugs of major importance may need to be discovered. These new drugs would be worth $147 billion. It is thought that 1,25,000 flowering plant species are of pharmacological relevance in the tropical forests. It takes 50,000 to one million screening tests to discover ONE profitable drug. Even in developed countries there is a huge potential for the development of nutraceuticals and pharmaceuticals from herbal materials. For example the UK herbal materia medica contains around 300 species, whereas the Chinese herbal materia medica contains around 7000 species. One can imagine what lies in store in the flora-rich India !