Chapter

1

Introduction to Pharmacognosy

The pharmacognosy is the subject which deals with crude drugs, phytopharmaceuticals, excipients, surgical dressings, filtering aids and support media for the production and discovery of drugs from natural sources.

Crude drugs: The word crude drug is used for those natural products (plant or parts of plant, extracts and exudates) which are not processed. Most of crude drugs are obtained from plants. Few are obtained from animals or insects origin (lard, beeswax, honey, etc.) and from the marine origin.

HISTORY

Dioscorides, A Greek physician, who lived in first century A.D. wrote 'De Materia Medica' in 78 A.D. in which he described about 6000 plants having medicinal properties out of which large number of plants are still in use in modern medicine. Aloe, belladonna, colchicum, ergot, hyoscyamus, and opium are few of them which are still in use in the same manner.

Galen (131–200 A.D.) a Greek pharmacist-physician who lived in Rome, described methods of preparing the formula containing plants and animal drugs. As a tribute to his accuracy in recording his observations the term 'galenical' pharmacy originated.

The term materia medica, meaning medicinal materials, was synonymous with the substances and products derived from natural sources and was employed by the physician in that era.

The term pharmacognosy first appears to have its origin in the 18th century by John Adam Schmidt (1759–1809), Professor of General Pathology, Therapeutics, Materia Medica at the Medicosurgical Joseph Academy in Vienna founded in 1785. The term was found in his 'Lehrbuch der Materia Medica' published posthumously in Vienna in 1811. At that time, knowledge of drug was limited and could easily be contained in one subject.

The term pharmacognosy was finally introduced by C.A. Seydler (1815), in Germany. This name was then formed from two Greek words, '*pharmakon*', drug, and '*gnosis*', knowledge.

F.A. Fluckiger (1870), Professor in pharmacy in Strasburg, stated that pharmacognosy is simultaneous application of various disciplines with the object of acquiring knowledge of drugs from every point of view.

In the 18th century, Linnaeus made an important contribution to the development of pharmacognosy through the introduction of his new system of naming and classification of plants.

Though, in 1803 F.W. Serturner isolated morphine from opium and thus the era of drug discovery started in pharmacognosy but till the end of the 18th century crude drugs were still being used as powders, simple extracts or tinctures.

In nineteenth century the name pharmacognosy came into practice and expanded the arena of pharmacognosy beyond botany.

Hence, in broad sense, pharmacognosy is the knowledge of history, distribution, cultivation, collection, preparation, identification evaluation (chemical and biological), preservation and use of drugs and economic substances that affect health of man and animals.

As a part of pharmaceutical curriculum pharmacognosy forms an important link between pharmacognosy and medicinal chemistry on one hand and between pharmacy and clinical pharmacy on the other hand.

SCOPE AND DEVELOPMENT

Seydler in 1815, first time defined pharmacognosy as a pharmaceutical discipline. Alexander Tschirch (1909) gave the following definition to pharmacognosy:

'The name pharmacognosy means the science which has task to learn everything about drugs originating from plants and animals, in all aspects except physiology.'

During 19th century, it was the mother of all present day pharmaceutical disciplines. But in 1899 synthetic chemistry became more important for developing new drugs with the synthesis of aspirin (1990).

In the 19th century, microscopy was introduced for the quality control of pharmaceutical formulations from plants but with the fast decreasing trend in herbal preparations in pharmacy, it became difficult task to maintain the prominent position in pharmaceutical curriculum in sixties and seventies.

Fortunately, in 1967, the development of thin layer chromatography (TLC) by Egon Stahl (1967) again brought the status of pharmacognosist among the pioneers in the analysis of plant materials. Thus, gas chromatography (GC), high performance liquid chromatography (HPLC) and thin layer chromatography (TLC) became the important tools in the study of active compounds. In seventies, spectrophotometric methods such as mass spectrometry (MS) and nuclear magnetic resonance spectrometry (NMR) were also introduced in their search for new biologically active compounds.

In 1999, the international scientist community had shown increasing interest in the field of a pharmacognosy and natural product research which has been illustrated from large number of scientists attending 5 yearly events. In July 1999, at Amsterdom attendance was almost double the number of previous year's meeting, the reason being the increased interest in the field of research in pharmacognosy and natural products which is illustrated from the trend shown in the new drug discovery in the period from 1983 to 1994 from list of the approved drugs, 78% of the new antibiotics and 61% of the new antitumour drugs were natural products or natural product derivatives.

In the beginning of 20th century international scientists had shown the interest in the research in pharmacognosy and natural products, because of the following reasons:

- Search for new leads for drug development.
- Technology for the production of pharmaceuticals.
- Health claims for food (nutraceuticals).
- Validation of traditional medicine.
- Increased interest in phytotherapy.

Currently, the following are the three hot areas of interest of pharmacognosist:

i. Study of new biologically active natural products
ii. Quality control of drugs from natural origin.
iii. Production of drug from natural origin, including new methods such as biotechnology.

Lead finding: Lead finding process has become easy with the introduction of High Throughput Screening (HTS) method. By using molecular targets, large number of samples even up to 100,000 in 24 hours can be screened for single activity. Thus, by the development of HTS large number of plant extracts could be easily fractionated for its biological activity.

Recently, high performance liquid chromatography (HPLC) method has been developed for determining biological activity.

Plant cell culture extract is another intresting option for screening as it can be made from rare plants to ensure the production for the interested activities. Lead finding for drug development using biodiversity or traditional medicine is one of the major area in which pharmacognosy can see a fast growth.

Biotechnology: Biotechnology has opened new perspectives in pharmacognosy. Traditionally, pharmacognosy focuses on plants only and little attention was paid to microorganisms as a source of drug. Plant cells biotechnology emerged as new possibility for the production of secondary metabolites. In mid-seventies, the pharmacognosists eagerly moved into this field. Genetic engineering can be used to increase the production of valuable pharmaceuticals, e.g. proteins in microorganisms (insulin in *E. coli*) or plants (human serum albumin or vaccines).

These new technologies, of course, also require a new type of pharmacists and pharmacognosists. A pharmacognosist need to have not only expertise on the botanical aspects of medicinal plants, but also on phytochemistry, advanced separation techniques, proteins and on molecular biology. In the field of protein, the proteomics is field of interest for pharmacognosist. The molecular biology technique is an important tool in quality control not only for the biotechnological products but also in characterising medicinal plants.

Health claim for food (nutraceuticals): Nutraceuticals are food or part of food that provides medical or health benefits including the prevention and treatment of diseases. Detailed knowledge of the influence of diet on human health has been increased greatly in the global community. The pharmacognosist plays a major role in the biological evaluation of herbs or botanical products and other components used in the formulation of nutraceuticals that claim to be useful in the treatment of diseases without toxicity.

Nutraceuticals on the basis of their natural source and chemical grouping, categorises into **nutrients**, **herbs**, **dietary supplements** and **dietary fibres**. The most rapidly growing segment of industry are dietary supplements (20.5%), dietary fibre and natural/herbal products (about 14.0%). Global nutraceuticals market is about 115 to 120 billion USD.

Phytotherapy: Phytotherapy was introduced in 20th century especially in developed countries like North America, Europe, Australia. Although the traditional medicine was very common in developing countries, but now it is being used worldwide by people/population of many countries especially old age people prefer to use food supplement or others herbal formulations (phytomedicine) to combat the old age problems with the belief that these natural products are safe to use. Hence it becomes challenge for health professional having insufficient knowledge about the natural products. Therefore, it is new era for pharmacognosists to provide information regarding the identification, standardisation/validation of the nutraceuticals for their potency as well as toxicity.

The last decade has seen a greater use of herbal remedies/botanical products among the members of general public through self-selection than ever before. This has greatly increased the relevance of the subject.

SOURCES OF DRUGS

Drugs are derived from minerals, plants, animals and microbes of both terrestrial and marine origin. Now, plant tissue culture (biotechnology) has also been considered to be source of drugs. Plants form an important part of everyday diet of all living being and their nutritional as well as medicinal values have been intensively explored for decades. Henkel et al, 1999 has reported that the origin of 30,000 bioactive natural products are of natural origin, which could be divided among animals (13%), bacteria (33%), fungi (26%), and plants (27%). The potential diversity of bacteria and fungi is quite large with some 5000 out of about 40,000 bacteria and only 70,000 out of about 1.5 million fungi, having been identified. Only a relatively small percentage (5–15%) of higher plants has been

systematically investigated for the presence of biologically active compounds.

About 25% of the prescription drugs are obtained from plants. As per WHO; about 80% of world population depend upon plants for the maintenance and cure of general health and ailments. Plants also serve as building block for the raw material required for the synthesis of drugs and pharmaceutical products. Since ancient times plants remained the source for herbal medicines, used by indigenous systems of medicine by the traditional practitioners. Plants are the source for new chemical entities (NCE) and drugs for the newer discovery.

I. Plants as a Source of Drugs

Plants are used as therapeutic resources in several ways, as herbal teas or other home-made remedies made from medicinal plants. (Medicinal plant is any plant used in order to relieve, prevent, and cure disease or to alter any physiological and pathological process in living being or any plant used as raw material or precursor for the synthesis of medicine). They can be used as crude extracts or therapeutic fractions in pharmaceutical preparation (such as tinctures, fluid extracts, powder or pills and capsules) and they are subjected to isolation of pure compounds as a medicine. About 26% of drugs prescribed world-wide come from plants, as per WHO more than 125 such active compounds being in current use, of the 252 drugs considered as basic and essential, 11% are exclusively of plant origin and number of synthetic drugs are obtained from the precursor of plant origin. Examples of important drugs obtained from plant origin are digoxin from *Digitalis* spp., atropine from *Atropa belladonna*, ajmalicine from *Rauwolfia* spp., artemisinin from *Artemisia* spp., berberine from *Berberis hydrastis*, caffeine from *Camellia sinensis*, codeine from *Papaver somniferum*, digitoxin, digoxin and gitoxin from *Digitalis* spp., podophylotoxin from *Podophyllum peltatum*, hyoscyamine from *Hyoscyamus niger*, morphine from *Papaver somniferum*, peclitaxel from *Taxus* spp., quinine from *Cinchona ledgeriana*, reserpine from *Rauwolfia serpentina*, vincristine and vinblastine from *Catharanthus roseus* and zingiberene from *Zingiber officinalis*. It is estimated that about 60% of antitumour and anti-infectious drugs are already in the market are from the natural origin as most of them yet are not to be synthesised hence are obtained from cultivated or the wild source.

The WHO has included phytotherapy in its health programs in developing countries. Eastern countries, such as China and India have well-developed herbal medicine industries and Latin American countries have been investing in research programs in medicinal plants, standardisation and regulation of phytomedicinal products. In Germany 50% of phytomedicinal products are sold on medical prescription. In North America phytomedicinal products are sold as health foods.

The National Cancer Institute, USA (NCI) has tested more than 50,000 plant samples for anti-HIV activity and about 33,000 samples for antitumour activity.

II. Animals as a Source of Drug

A number of medicines are either contain animal products in the form of tablets, injections, capsules, creams, mixture and vaccines, e.g. **gelatin** (partially hydrolysed collagen usually obtained from bovine (beef) or porcine (pig) in origin. Gelatin is used for making the capsules shell and used as a stabilisers in pharmaceutical products such as vaccines. **Heparin**, an anticoagulant is prepared from a porcine.

Out of 252 essential chemicals selected by WHO, 8.7% are from animals, and out of 150 prescription drugs used in United States of America, 27 are from animals.

Animals used as source of drugs in therapeutics:

Thyroid-modified preparations of thyroid glands of sheep and pigs.

Conjugated oestrogens: These are amorphous preparations containing water soluble conjugated form of mixed oestrogen obtained from urine of pregnant mares, used in the treatment of menopausal systems in female and in dysmenorrhea.

Insulin-prepared from cattles and pigs:

Oxytocin: It is polypeptide hormone secreted by posterior pituitary glands.

Enzymes: Pancreatin, tryptophan, chymotrypsin, fibrinolysin, pepsin and hyallourinidase.

Animal extractive organs: Liver and stomach preparation and bile.

***Natural products from insects*:** Antimicrobial, antifungal, antiviral, anticancer, antioxidant, anti-inflammatory and immunomodulator.

Insects used are ant, bees, wasp, bettels, cockroaches, termites, flies, true bugs and moth.

Entomotherapy (medical use of insects) is an alternative to modern therapy in the many parts of the world including Korea, India, Mexico, China, Spain, Brazil, etc.

Ants and ant by products are used throughout the globe in folk medicine. For example, in Northern India, scabies, wounds and boils are treated through topical applications of paste made from crushed black ants (*Bothroponera rufipes*).

Official Drugs Obtained from Animals

Cantharidin, cochineal, leeches, gelatin, galls, ichthammol, lactose and honey:

Cantharidin: It is obtained from dried beetle (*Lytta vesicatoria*) Latr. Family Meloidae. Major constituent is cantharidin and used for the topical medication.

Cochineal: It is dried female insect *Dactylopius coccus* costa, enclosing the numerous eggs and young larvae, family Coccidae. It contain carminic acid used as colouring agent, therapeutically used in the treatment of urine retention as renal capillary relaxation.

Leeches: *Hirudo medicinalis* Linn (Speckled leech), *Hirudo quinquestriatus* Schmarda (Australian leech), used to revive intraocular pressure in acute glaucoma and in cardiovascular diseases (chemical derived from the saliva of leech).

Gelatin: It is an animal protein obtained from the skin and bones of animals, used in the pharmaceutical preparations and in osteoarthritis and osteoporosis.

Galls (Nut gall, Aleppo galls): It is an excrescent formed on young shoot of *Quercus infectoria* Olivier family Fagaceae used as a source of tannic acid.

Ichthammol: Synonyms ammonium bituminosulfonate, it is the fossil remains of fishes and other marine animals. It is the product of natural origin obtained by dry distillation of sulfur-rich oil shale, followed by sulfonation, and subsequent-neutralisation with ammonia (*Bituminous Schists*). It is used in the treatment of eczema, psoriasis, etc. by local application.

Honey: It is the saccharine secretion deposited in the honeycomb by bee *Apis mellifera* Linn of family Apidae, used as nutrient and sweetener.

Drugs obtained from porcine: There are number of drugs obtained from porcine. For example, anticoagulant (Heparin sodium), Vaccines (rotavirus live and attenuated vaccine, Zoster virus vaccine, etc.) digestive enzymes (amylase, lipase, protease enzymes, etc.)

Bovine: Digestive supplements (*Lactobacillus acidophilus*, *Bovine colostrums*, etc.) plasma volume expander (polygeline), vaccines (hepatitis A vaccine, *Salmonella typhi* live vaccine, etc.) Insulin preparations (insulin, isophane, etc.) and other pharmacological preparation like collagen, haemostatic agents, etc.

Chinese Hamster Ovary (CHO) Cells: Drugs obtained are haemostatic agents, antiplastic, immunomodulator, enzyme replacement therapy, pituitary hormones, etc.

Murine (mouse): Drugs obtained are antineoplastic agents (avastin, herceptin, mabthera, etc.), immunomodifier (remicade, simulect, etc.), anticoagulant (reopro).

Eggs: Number of vaccines are obtained from eggs like influenza virus H1N1, rabies, Coxiella, a Pandemic vaccine, etc.

Equine (Horse): Drugs obtained are antivenom (antithymocyte globulin, black snake antivenom, death adder antivenom), gonadal hormones and haemostatic agents, etc.

Above all, chitin, lanolin, histoplasmin, coccidioidin, immune globulins, etc.

III. Marine Source of Drugs

Sea covers about 70% of the earth, is the promising source of new biological active compounds, because of amazing biological diversity of the sea. The rate of discovery of marine species has been higher than terrestrial since the 1950S, but only 16% of all named species on earth are marine. From the diversity point of view, the ocean is a more diverse as compared to the plant and animal on the land. Marine invertebrates such as sponges, cnidarians and ascidians constitute largest amount of biomass of marine microfauna, which is rich source of both biological and chemical diversity which has been the unique source of biological active compounds for the industrial development as pharmaceuticals, cosmetics and nutritional supplements. During the last few decades numerous novel biologically active compounds have been isolated from the marine organism such as **antibacterial**, **antiviral**, **anticoagulants**, **antimicrobial**, **antibiotics**, **anti-inflammatory**, **antianthelmintic**, **anticancer**, **antitumour** and **cardiovascular active compounds**. Marine compounds reported to act on a variety of molecular targets and thus could potentially contribute to several pharmacologic classes. Hence pharmacological research with marine chemicals continue to contribute towards potentially novel chemical leads to the ongoing global search for therapeutic agents in the treatment of number of diseases. Chemicals are polyketides, peptides, nitrogen containing compounds, terpenes, steroids, polysaccharides, etc.

IIIa. Antibiotics from Microorganisms

Fungi are best source of natural antibacterial and antifungal compounds. It has been reported that 38–59% of test extracts from marine fungi exhibited antibacterial and antifungal activities. The dominant genera in the marine fungi producing antibacterial and antimicrobial compounds are: *Aspergillus* genus (31 strains) and *Penicillium* genus (18 strains).

Examples

Nitrogen Containing Compounds

Peptides: Cyclopeptides, and desmethylisation and few novel peptides isolated from mangrove fungi *Phomopsis* spp. and *Astromyces cruciatus*.

Indole alkaloids example, Asporyzin isolated from *Aspergillus oryzae* active against Gram +ve and Gram –ve bacteria.

Cristatumins A, D and E were isolated from *Eurotium cristatum* and *E. herbariorum* active against both *E. coli* and *S. aureus*.

Pyridines and Pyridone

Isolated from *Trichoderma species* showed activities against Gram+ve *B. subtilis* and *S. epidermidis* and antifungal activity against *Candida albicans* compounds named are trichodin A to D.

Piperazine and Pyrimidine/Pyrimidinone Alkaloids

Aspergicin from *Aspergillus* species derived from mangroves epiphytic fungi.

Steroids and Terpenoids

There are number of steroids and terpenoids compounds isolated from fungi having antifungal activities against *A. niger* and *Alternaria brassicae* and also have antibacterial activities against *E. coli* and *S. aureus*. For example, penicisteroids A. About fifty compounds are reported from *Aspergillus ustus* and *Penicillium chrysogenum*.

Antibacterial sequiterpenoids isolated from *Aspergillus* species and *Leucostoma persoonii*, e.g. Aspergiterpinoids, (–) sydonol and (–) sydonic acid.

***Polyketides*:** Quinones, anthraquinones, xanthones and quinine derivatives. Hence, there is big list of compounds reported from fungi.

More than 5,300 products are reported from sponges and algae, few of them are mentioned below:

Two quinolinols (2n-pentyl-4-quinolinol and 2n-heptyl-4-quinolinol) are isolated from yellow marine *Pseudomonas bromoutilis* of the *Altermonas* species.

A new antibiotic, aplasmomycin, active against Gram +ve bacteria including *Mycobacteria in*

vitro, and plasmodia *in vivo* are reported from ss-20 strain of *Streptomyces griseus* from shallow sea.

The anticancer antibiotics has also been reported from culture broth of marine actinomycete of *Actinomadura* species, e.g. chandrananimycins A, B and C.

Antibiotics from Sponges

Sponges have greatest percentage of antimicrobial activity but are difficult to identify hence many sponges having antimicrobial activity still remained unidentified. However, caribbean sponge of the *Agelas* species reported to have remarkable antimicrobial activity against *S. subtilis*, *E. coli* and *P. atroventum*.

Antibiotics from Algae

Red algae of the genus *Laurencia* contain sesquiterpene phenols as their antibiotic metabolites (Laurinterol and debromolaurinterol).

Antibiotics from Tunicate

Large quantities of geranyl hydroquinone are reported from the genus *Aplidum.*

Hence, the ocean continue to provide novel marine-derived antibiotics.

Anti-inflammatory Drugs from Marine

Sesquiterpene, diterpenes, steroids, polysaccharides, alkaloids, fatty acids, proteins and other chemical compounds are isolated from marine organism having anti-inflammatory activities. Following are few examples:

***From algae*:** Terpenoids (apo-9′ Fucoxanthinone, asta-Xanthin), polyketide (6 6-bieckol).

***From sponges*:** Alkaloids (benzamide A and B), and from fungus alkaloid (Bis-N-norgliovictin).

Antituberculosis Drugs from Marine

Tuberculosis (TB), caused mainly by the *Mycobacterium tuberculosis*, is the second cause of death worldwide due to infectious disease, after human immunodeficiency virus (HIV/AIDS), In 2012 World Health Organisation (WHO, Geneva, Switzerland) reported almost nine million new cases of TB, 1.3 million deaths due to TB and 0.3 million deaths resulting from a co-infection with HIV and TB.

Marine derived natural and semisynthetic compounds examined for *in vitro* activity against *Mycobacterium tuberculosis*. Three new classes of compounds including c-19 hydroxy steroids, scalarin sesquiterpenoids and tetrabromo spiros cyclohexadienyl isoxazolines have been identified as having potential as leads for continued investigations as new tuberculosis agents.

Following is the list of compounds have already been confirmed having antituberculosis activity.

Terpenoids (asperterpenoid A, S. flavaditerpene), terpenoid glycoside (lobophorin G), alkaloid (brevianamide S) and polyketide (urdamycinone).

Antiviral Compounds

Examples of the compounds isolated from sponge, soft coral and fungus used in the treatment by human herpes simplex virus inhibition, HIV protease inhibition, HIV replication inhibition, influenza virus, neuraminidase inhibition and H1N1 influenza virus inhibition are terpenoids (L. arboreum, halistanol sulphate), terpenoid alkaloid (stachyflin), polyketide (massarilactone-H).

Cardiovascular System and Neurophysiological Agents

Lepadiformines A and B (alkaloid) cardiac inward rectifying K^+ current inhibition, zooxanthellamide (polyketide). Vasoconstriction of rat blood.

Immune System Effecting Compounds

Glycosphingolipids (demicoside), obtained from sponge, stimulate the spleen cell proliferation.

Laminarin (polysaccharide) obtained from algae, inhibit the lymphocyte apoptosis.

Cucumariosides (triterpene oligoglycoside), from sea cucumber, stimulates the lymphocytes and neutrophils.

Lobocrassin B (terpenoid), from soft coral, inhibits the dendritic cell activation.

Penicacid (polyketide), isolated from fungus, inhibits the T-lymphocyte proliferation.

Nervous System Affecting Compounds

Asteropsin A (peptide), isolated from sponge, effects the enhancement of neuronal Ca^{2+} influx.

C-consors peptide, isolated from cone snail, causes the muscle relaxation induction.

Convolutamydine A (alkaloid), obtained from Bryozoa (phylum of aquatic invertebrate), has anti-nociceptive activity.

Serinolamide b (alkaloid), obtained from bacterium, effects the CB_1 and CB_2 binding.

FDA Approved Marine Anti-cancer Drugs from Invertebrates

Cytarabine, also known as cytosine arabinoside, obtained from sponges is used in chemotherapy medication for the treatment of acute myeloid leukemia and non-Hodgkins lymphoma. It acts as DNA polymerase inhibitor.

Ziconotide (peptide), isolated from cone snail, is used as a modulator of neuronal calcium channels (kill pain).

Trabectedin (alkaloid), isolated from tunicate, is anti-cancer agent. It inhibit the cancer cell growth and also affect the tumor micro-environments.

Eribulin mesylata (Macrolide) isolated from sponge, is an anti-breast cancer compound.

Bren tuximab (antibody drug conjugate), obtained from Mollusk, effective in lymphoma.

IV. Plants Tissue Culture

Proved to be important source of drugs either through organogenesis or by genetic transformation. Plant tissue culture has great potential as a source of valuable secondary metabolites, used as pharmaceuticals, nutraceuticals and additives. Moreover, the production by plant tissue culture is independent of environmental conditions and quality fluctuations unlike the conventional agriculture production of secondary metabolites: alkaloids, flavonoids, terpenoids, carotenoids, saponins, steroidal alkaloids, sterols, tannins and several others components.

Since the last decade considerable success has been achieved in increasing the yield of secondary plant metabolites because of recent advances in the field of plant biotechnology by controlling the factors affecting its synthesis and/or accumulation. Examples of plant derived products of importance; ajmaline (*Rauwolfia serpentina*), camptothecin (*Camptotheca acuminate*), codeine (*Papaver somniferum*), colchicine (*Colchicum autumnale*), elipticine (*Ochorosia elliptica*), shikonin (*Lithospermum erythrorhizon*), taxol (*Taxus brevifolia*), vinblastine (*Catharanthus roseus*).

Examples of food additives from plant cell culture: Anthocyanins, crocin, carotenoids, anthraquinones and napthaquinones. Flavours (vanillin, garlic, coffee and cocoa, etc.). Pungent (capsaicin), sweetner (stevioside, glycyrrhizin).

It is also possible to increase the yield of secondary metabolites by the selection of high-yielding cell lines, e.g. Shikonin (*Lithospermum erythrorhizon*), Serpentine (*Catharanthus roseus*), Sanguinarine (*Papaver somniferum*), Anthraquinone (*Morinda citrifolia*).

To overcome the hurdles of harvesting and extraction processing, the tissue culture is the alternative method of assured regular uniform supply of the material for the whole years. Moreover most of the secondary metabolites accumulate after certain age or maturity of the plant, examples cinchona, rauwolfia, camptotheca, taxus, Ochrosia spp., etc. attain maturity in few years to accumulate the active compounds in high amounts, as well as it is difficult to increase the area of cultivation for particular species and growth of plants takes its own course of time. To meet the ever increasing demand the natural source is not sufficient, the plant cell/tissue culture is the only alternative source.

ORGANISED AND UNORGANISED DRUGS

Crude drugs are classified into two main classes:

I. Organised Drugs

As the name indicates, these drugs are cellular in nature, having definite shape and size.

These are obtained from plants/animals, as entire or parts of the plants/animals; aerial part or herbs; leaf, flowers, fruits, seeds, stem, roots, rhizomes and bulb. They can be characterised by morphological, microscopical and chemical tests.

Drugs from aerial part

These are herbaceous in nature and generally short-lived and outgrowth is rapid. They are small in size (< 2 feet), soft and short, e.g. chirayata (*Swertia chirata* Wall), brahmi (*Bacopa monnieri* Linn), pudina (*Mentha arvensis* Linn), tulsi (*Ocimum sanctum* Linn), kalmegh (*Andrographis paniculata* Burm), lajwanti (*Mimosa pudica* Linn), etc.

Leaves

Leaves arise out of the stem. They prepare food for the plant through photosynthesis and they also store some secondary metabolites. Hence they are used as drug, e.g. Deadly nightshade (*Atropa belladonna* L), Digitalis common name tilpushpi (Hindi) foxglove (English) (*Digilalis purpura* Linn), Paan patta (Betal) (*Piper betle* Linn), Chai (Tea plant) (*Camellia sinensis* Kuntze), Sanai patti (Hindi), Senna leaflet (English) *Cassia acutifolia* Delite (Botanical source).

Flowers

Flowers are the essential reproductive organ of a plant, generally coloured to attract the insects for pollination. Flowers are of great botanical importance but few of them are used as drug in pharmacy, e.g. Jasmine (*Jasminum grandiflorum* L), Chamomile (*Matricaria recutita* L), Calendula (*Calendula officinalis*), Primrose (*Primula veris* L, *P. officinalis* Linn), Rose (*Rosa damascena*, *R. gallica*, *R. alba*), hops (*Humulus lupulus* L).

Fruits and Seeds

Fruit is a matured ovary of the plant. It is the organ of plant (angiosperm) which disseminates seeds. Seeds are matured ovule.

Fruits and seeds have yielded important therapeutical drugs, e.g. Caraway (*Carum carvi* L), Fennel (*Foeniculum vulgare* Miller), Nutmeg (*Myristica fragrans* Houtt), Linseed (*Linum usitatissimum* Linn), Coriander (*Coriandrum sativum* Linn), Colchicum seed (*Colchicum luteum* Baker), Fenugreek (*Trigonella foenum-graecum* Linn), Nux vomica (*Strychnos nux-vomica* Linn), Ispaghula (*Plantago ovate* Forssk), Mustard (rai) (*Brassica juncea* Czern & Coss), white mustard (*Sinapis alba* L).

Stem

It transports water and minerals from the soil to the other part of the plant. Moreover, it supports the plant. Woody species has clear distinction between bark (outer) and wood (inner), e.g. drugs being used in medicine as stem: Ephedra (*Ephedra sinica* Stapf), liquorice (*Glycyrrhiza glabra* Linn).

Bark

Bark consists of all tissue outside the cambium. In botany, all the tissue lying outside periderm. The pharmacognostical bark consists of epidermis, primary cortex, endodermis, pericyle and phloem.

Following are medicinally important barks:

Cinchona: *Cinchona succirubra* pavon

Cascara: *Rhamnus purshiana* DC

Quillaia: *Quillaja saponaria*

Wild cherry bark: *Prunus serotina*

Cinnamon: *Cinnamomum zeylanicum*

Kurchi: *Holarrhena antidysenterica.*

Wood

Inner of the stem consisting of xylem tissue, e.g. Quassia: *Picrasma excelsa* also known as *Jamaica quassia*.

Sandal wood: *Santalum album*.

Root

It develops from the radicle (tap root) or its branches or adventitious. It is main organ of the plant for the uptake of water and inorganic nutrients. It generally stores secondary metabolites and surplus energy in the form of starch and roots inulin (polysaccharide).

Following are medicinally important roots:

Jalap: *Ipomoea purga*

Aconite: Dried roots of *Aconitum napellus*

Belladonna: Roots of *Atropa belladonna*
Rauwolfia: *Rauwolfia serpentina*
Senega: *Polygala senega* L
Velerian root: *Valeriana officinalis*, *Valeriana wallichii*
Liquorice: *Glycyrrhiza glabra* Kuth.
Rhizomes: Zinger: *Zingber officinalis*
Rhubarb: *Rheum palmatum* L
Podophyllum: *Podophyllum hexandrum*
Ipecac: *Ciphaelis ipecacuanha* (Brotero)
Sarsaparilla: *Smilax regelii* Kilip
Bulb: Scilla (Squill) *Urginea maritina*
Diascorea: *Dioscorea deltoidea* Wall
Garlic: *Allium sativum* Linn
Onion: *Allium cepa* Linn.

II. Unorganised Drugs

Unorganised drugs are solid, semisolid or liquid in nature. They do not have specific shape, size and structure and are without cellular structure.

They are obtained from plants or animals by extraction such as decoction, e.g. agar; expression, e.g. olive oil; distillation, e.g. volatile oils; incision, e.g. opium and natural secretion like resin, oleo resin; exudates, gums; dried juices, e.g. aloe.

These drugs can be identified and characterised by their colour, odour, fracture, solubilities in organic solvents (ether chloroform or alcohol) and by specific chemical tests.

Classification

1. **Dried juice,** e.g. Aloe
2. **Latex,** e.g. opium
3. **Extracts,** e.g. Catechu, agar
4. **Oil and fats,** e.g. Olive oil, cod liver oil, almond oil, lard wool fat.
5. **Gums,** e.g. Tragacanth, acacia gum.
6. **Resins,** e.g. Colophony, myrrh.
7. **Waxes:** Spermaceti, beeswax.
8. **Volatile oils:** Clove oil, cinnamon oil.
9. **Balsams:** Storax, tolu, benzoin.

- **Aloe:** It is dried form of juice. The residue obtained by evaporating the liquid to dryness, obtained by draining from the leaves cut from various species of Aloe.
  Aloe ferox Mill yield Cape aloe.
  Aloe vera Linn var. officinalis, family Liliaceae.

  Aloe contain aloin and other water-soluble components. It is an anthraquinone containing drug used as laxative, and in skin diseases and as inflammatory.

- **Latices (Latex):** Latex is the milky aqueous liquid formed in certain plants in tube-like structures which are either known as vessels or special cells called coenocytes (laticiferous cells) formed by breakdown of the dividing cell walls formed by nuclear division. Plants belonging to family Euphorbiaceae.

  Opium is the only official latex, occurs in laticiferous vessels in the walls of unripe capsules of *Papaver somniferum*, family Papaveraceae.

  Gutta-percha is the dried purified latex occurs in laticiferous vessels in the trunk of species of *Palaquium* and *Payena* tree indigenous to Sumatra, Ceylon and Peninsula.

- **Juices:** Juices are aqueous liquid containing dissolved substances occurring in specialised tissue other than laticiferous cells or vessels. Juices are obtained by incisions, e.g. dried form of juice of aloe.

- **Extracts:** Extracts are the water soluble components leftover after the evaporation. For the extraction usually decoction is employed to isolate the constituents drug, e.g. catechu and agar.

  Catechu

  Synonyms: Pale catechu, Gambier

  Botanical source: A dried aqueous extract prepared from the leaves and young shoots of *Uncaria gambir* (Hunter) Roxb, family Rubiaceae. It contains catechin, an astringent substance.

  It is available as reddish brown coloured or pale brown coloured cubes about 2–5 cm along edges. Readily broken and reduced to powder. Taste is astringent and gives positive test for tannins.

Agar

Agar is the dried, hydrophilic, colloidal substance extracted from: (i) *Gelidium cartilagineum* (Linn) Gaillon, family Gellidiaceae. (ii) *Gracilaria confervoides* (Linn) Greville, family Gracilariaceae. (iii) Red alge (class Rhodophyceae).

Agar may be light yellowish orange, yellowish grey to pale yellow to colourless, brittle, odourless with mucilaginous taste.

Chemically, it is the calcium salt of strongly ionised, acidic polysaccharides. It contains two major compounds—agarose and agropectin. Used as laxative and as suspending agent.

Exudates

- **Gums:** Gums are formed by degenerative changes in cell walls by enzyme action, the process is called **gummosis**. Gums are insoluble in alcohol and organic solvents but they swell and form mucilaginous mixture with water.

  The gums exude from tree and shrubs in tears like striated nodules or amorphous lumps. On drying they become hard, glassy, in different colours. For example:

  Gum acacia: White to pale amber.

  Karaya gum: Pale grey to dark brown.

  Tragacanth: White to dark brown.

  Gum exudes from plant by making incision, injury or stripping the bark of the tree or shrub. Excretion of exudation is affected by temperature and humidity.

  Use: They are used as thickening, emulsifying and stabilising agents, e.g. Gum acacia, Gum tragacanth.

  Gum acacia: *Synonyms:* Gum acacia; Gum arabica.

  Source: Dried gummy exudation from the stem and branches of *Acacia senegal* wild and other species of Acacia.

  Family Leguminosae: Gum acacia tears are rounded or ovoid 0.5–6.0 cm in diameter or even sometimes are angular fragments. They are colourless or pale yellow in colour but freshly broken pieces are opaque and glassy in appearance. However, the Indian acacia tears are too dark in colour, because of tannins. Official gum acacia is native to Africa, i.e. kordofan or sudan gum, which is completely soluble in water to give mucilaginous suspension, whereas Indian gum has insoluble material in the suspension.

  Used as emulsifying, suspending and binding agents.

  Indian (ghatti) gum is exuded from the stem of *Anogeissus latifolia* Wallich family Combretaceae.

Tragacanth

Synonym: Gum Dragon

Source: Dried gummy exudation obtained by incision from *Astragalus gummifer* Labill and some other species of *Astragalus* (Persian tragacanth), family Leguminosae.

Indian tragacanth is obtained from *Sterculia urens* Roxb and other species of *Sterculia*. This is obtained by incision given on trees grown wild in India. It is of inferior quality.

Tragacanth appears as ribbon-like flakes about 23 × 12 mm in size usually curved and twisted.

They are white or pale yellow; more or less translucent; **Fracture** is short and horny and have no odour.

Tragacanth is partially soluble in water. The soluble portion is called **tragacanthin** and insoluble portion termed **bassorin.** Tragacanthin is a complex carbohydrate whereas the bassorin contains along with complex carbohydrate the sugars; tragacanthose and xylose.

Uses: Emulsifying, suspending and thickening agent in pharmaceutical formulation.

- **Resin, Gum resin and Oleo resin:**
  Resins used in pharmacy are obtained from living natural sources. Most of them are plant product except shellac an insect.

  Resins are solid amorphous substance obtained from plants, produced in special tubes (Resin ducts).

  Resins are insoluble in water and petroleum ether but-dissolve all most

completely in alcohol, chloroform and ether. On heating they soften and finally melt. **Chemically,** they are made-up of complex mixture of resin acids, alcohols (resinols) phenols (resinotannols), esters (consisting mostly of resinols and cinnamic, benzoic and ferulic acids) and also contain neutral substance known as resenes.

A solution of resin in volatile oil, when painted on a smooth surface, they immediately evaporate leaving behind hard transparent film.

Classification of resinous exudates: The resinous exudates may contain **resin only**, e.g. benzoin.

Resin and volatile oil together, i.e. oleo resin, e.g. turpentine and copaiba, may be associated with gum and volatile oil together known as **oleo gum resin**, e.g. myrrh.

When gum resin or oleo-gum resin contains benzoin or cinnamic acid alone or combined form the resin are known as **balsams,** e.g. balsam tolu, balsam peru and storax.

Resin

Benzoin

Sumatra and Siam benzoin

Sumatra benzoin: It is obtained from incised stem of *Styrax benzoin* and *S. paralleloneurus* Perkins. In commerce known as Sumatra benzoin.

Note: Styrax is the Greek name of storax.

Family: Styraceae

Sumatra benzoin occurs as blocks or irregular masses composed of different size tears embedded in translucent or opaque matrix.

Tears are milky white and become soft on warming. The matrix is reddish or greyish brown.

Chemical composition: It contains balsamic acids (6%), triterpene acids and traces of vanillin and esters (phenylpropyl cinnamate, etc.).

Siam benzoin: It is made from hard, brittle, flattened tears, from 1 to 5 cm long, pale yellowish-brown, the fractured surface is milky white in appearance.

Chemically contain mainly coniferyl benzoate (60–70%) along with small amount of free benzoic acid (10%), triterpenes (siaresinol 6%) and traces of vanillin.

Solubility: Sumatra benzoin yields alcohol soluble extractive not <75%, whereas the Siam benzoin yields not <90% extractive.

Uses: Antiseptic, stimulant, expectorant and diuretic.

Oleo-resin

Turpentine

Turpentine (volatile oil) is collected from the long pine leaves of *Pinus palustris* Miller and from other species of *Pinus* family Pinaceae.

The oleo resin is secreted in ducts located directly beneath the cambium in the sapwood. The collected oleo resin on steam distillation yields volatile oil (turpentine oil). The product of the first year cutting is of superior quality and is known as "Virgin" turpentine. The residue left over after filtration while hot is known as rosin or colophony.

The United States of America is major producer of turpentine oil. Important constituents of turpentine oil are α-pinene (64%) and β-pinene (33%).

Uses: Used as counterirritant in the OTC drugs.

Colophony or Rosin: It is the residue left over after distilling the volatile oil from the oleo-resin collected from various species of Pinus family Pinaceae.

Major supplier south-east USA and south-west France.

Colophony usually occurs as shiny, sharp, angular fragments, translucent often covered with yellowish dust.

It is hard, brittle and easily pulverisable and soluble in alcohol, ether, benzene, carbon disulfide, acetic acid, fixed oils,

volatile oil and in solution of sodium or potassium hydroxide (alkali).

Odour: Like turpentine. On heating, a sticky mass is formed.

Colophony consists of 80 to 90% anhydride of abietic acid; sylvic acid (decomposition product of abietic acid); saponic acid, pimaric acid and resene (hydrocarbon).

Uses: Used as stiffening agent in plasters and ointments. Commercially, it is used in the manufacture of varnishes and paint dryer.

Copaiba (oleo-resin)

Botanical source: It is an oleo-resin obtained from South American species of *Copaifera* Linn family Leguminosae.

The oleo-resin is formed in schizolysigenous cavities in the wood. The trees are tapped or boxed in the centre. The colour of the resin is yellow to yellowish brown depending on the varieties mixed together. *C. reticulata* (yellowish brown), *C. guianensis* (yellowish brown), *C. multijuga* (brown) and *C. officinalis* (yellowish brown).

Odour: Aromatic because of volatile content.

Taste: Bitter, acrid and persistent.

Uses: Used as genitourinary disinfectant.

Gum resins

As the name indicates it contains gum and resin but in some cases small proportion of volatile oils.

Composition of gum is also like gum acacia. Gum resins form emulsion with water, they are present in plant cells as such (emulsion) hence they exude from the plant on giving incision and dries at the surface, e.g. Asafoetida.

Oleo-gum resin

Asafoetida

Botanical source: Obtained by incision from the living roots and rhizome of *Ferula foetida* Regel and *F. rubricaulis* Boiss and other species of Ferula, family Umbelliferae.

Geographical source: Afghanistan (Distt. Karan and Chagai) and eastern Persia.

Asafoetida occurs as agglutinated tears or as separate ovoid tears (1–4 cm in diameter). Their colour is yellowish-white, when fresh but turns pinkish, violet-streaked and finally reddish brown. They are soft when fresh but become hard and brittle on drying. **Odour** is alliaceous, and **taste** is bitter or acrid.

Composition: The drug contains about 5–20% of volatile oils, 40–65% of resin and 25% of gum and small quantities of terpenes. Resin consists of asaresinotannol free or in combination with ferulic acid.

The oil contain sulphur compounds, responsible for the evil smell of asafoetida.

Contains at least 24 sesquiterpene hydrocarbons and number of diterpenes.

Uses: Used as carminative, expectorant, antispasmodic and laxative.

Myrrh

The name myrrh is derived from the Arabic 'murr', meaning bitter; 'commiphora' is Greek means gum bearing, "molmol" is the native Somali.

Botanical source: The oleo-gum resin obtained from the stem of *Commiphora molmol* Eng and other species of *Commiphora*.

Family: Burseraceae

Geographical source: Somaliland (central and western).

The myrrh exudes naturally or after the incision given in the bark of the plant. When freshly exuded it is yellowish in colour but soon becomes harder and darker in colour and then it is collected. Two varieties of myrrh are available– **Somali** (African) and **Yemen** myrrh (Arabian) but the Somali myrrh considered to be of better quality. Commercially Somali myrrh is the main supply.

Composition: Myrrh contains volatile oils responsible for the characteristic odour of myrrh, which contains eugenol, m-cresol and cuminaldehyde. On exposure to air, gets resinified.

Resin contents are about 25 to 40%; containing resin acid (α-β-commiphoric acid) resene and phenolic compounds.

Gum is about 60% consisting of soluble and insoluble portion forming mucilage with water that does not ferment readily.

Uses: Stomachic, stimulant, and as mouth wash; being astringent.

Balsams

Balsams are aromatic, oily and resinous mixtures that contain large proportions of benzoic, cinnamic or both the acids or esters of these acids.

Storax

It is the balsam obtained from the wounded trunk of *Liquidambar orientalis* Miller (Levant storx); *L. styraciflua* Linn (American storax).

Family: Hamamelidaceae.

The balsam storax is pathological product which exudes into natural pockets (new wood formed) between the bark and wood, formed by injury, in large quantity even up to 4 kg. It is scraped with a knife having small curved blade and collected into the containers. It is exported in tin cans.

The **Levant storax** is greyish to greyish-brown in colour, viscid, more or less opaque and semisolid mass. It is deposited as dark brown oleo-resin layers on standing.

The **American storax** is nearly clear yellowish brown semisolid that becomes hard, opaque and darker coloured on standing **odour:** Balsamic.

Solubility: Insoluble in water. Completely soluble is warm alcohol.

Chemistry

Storax contains cinnamic acid and their esters. Made from alcohol storesinol, partly in free state and partly in combined form. It also contains vanillin responsible for the odour.

Pharmacopoeial requirement is that storax should contain balsamic acid up to 30% with reference to the substance dried on water bath for one hour.

Uses: It is component of compound benzoin tincture and used as stimulant and expectorant.

Balsam of Tolu

Name tolu is on the name of place tolu near Cortagena.

Botanical source: Solid or semisolid resin obtained by incision from the trunk of *Myroxylon balsamum* Linn and *Myroxylon toluifera* H.B. and K.

Family: Leguminosae

Geographical source: Columbia, San Salvador (United States) gets balsam and tolu from Great Britain.

This balsam is a pathological product secreted in oleo-resin duct in the new wood, formed as a result of injury. It is obtained from trees by making V-shaped incision in the wood through bark.

Balsam tolu occurs as plastic solid that gradually hardens, becoming yellowish brown to brown. Thin layers are translucent, dried one is brittle and shows numerous crystals of cinnamic acid. **Odour** resembles vanilla; **taste** is slightly pungent.

Composition

It contain cinnamic acid 10–15%, benzoic acid 6.8%, balsamic esters 7.5% made-up of chiefly benzyl benzoate with small amount of benzyl cinnamate and resin esters (75–80%), consisting of toluresinotannol along with cinnamic acid.

Uses: Used as flavouring in medicinal syrups, confectionary and chewing gums.

Balsam of peru

Botanical source: It is obtained from the trunk of *Myroxylon pereirae* (Royl) Klostzsch, after beating and scorching the bark.

Family: Leguminosae.

Peru refers to the early importation of the balsam into Spain via Lima, Peru.

The balsam is a pathological product, produced by injury to tree. The bark of the tree is removed by beating and scorching with torch. The intermediate strips are left uninjured to save the tree from dying. After the removal of bark, trunk is wrapped in rags, the saturated rags with balsams are changed with new one. The rags are boiled with water, on cooling the balsam settles out, recovered, strained and packed.

Peruvian balsam occurs as dark brown viscid liquid. In thin layer it appears reddish brown and translucent. Its **odour** is like vanilla and taste bitter, acrid and persistent.

Balsam peru contain 60–70% balsamic ester consisting of benzyl cinnamate and benzyl benzoate); resin esters (peru resinotannol, cinnamic and benzoic acid), vanillin, and free cinnamic acid.

Uses: Local protectant, rubifacient, antiseptic in alcohol solution or in the form of an ointment.

FURTHER READING

1. Alejandro M, Mayer S, et al. Marine pharmacology in 2012–2013.
2. Bruneton J. 1999. Pharmacognosy, Phytochemistry Medicinal Plants. 2nd ed. Lavoisier Publication.
3. Chemotaxonomy and Serotaxonomy—Google Books *https://books.google.com›Science›Life Sciences› Biochemistry*
4. Cronquist A. (1981). An integrated system of classification of flowering plants. Columbia University Press, New York.
5. Divya A. Pharmacognosy: Facts and Future. Research & Reviews: Journal of Pharmacognosy and Phytochemistry. 2015;3(2):1–8.
6. Doshi, et. al. Novel Antibiotics from Marine Sources. www.reseachgate.net (pdf) Antibiotics from Marine Organism.
7. Evans WC. 2009. Trease and Evans Pharmacognosy, 16th ed., Elsevier; New York.
8. Global Tuberculosis Report 2013. http://www.who.int/tb/publication/global_report/en/
9. Kalia AN. Textbook of Industrial Pharmacogonsy. (2005). CBS Publishers and Distributors, New Delhi.
10. Kirikar KR, Basu BD. Indian Medicinal Plants Vol. 1–4. Allahabad, India 1933.
11. Namraj Dhami. Trends in Pharmacognosy: A modern science of natural medicines. Journal of Herbal Medicine. 2013;3(4):123–31.
12. Quality control methods for herbal material—WHO, updated edition of quality control methods for medicinal plant materials, 1998. Through www.who.int
13. Rotblatt M, Ziment I, eds. 2002. Evidence-Based Herbal Medicine. Philadelphia: Hanley & BelfusInc.
14. Satyajit D Sarker. Pharmacog may in modern pharmacy curricula. Pharmacogn Mag. 2012; 8(30): 91–2.
15. Serotaxonomy/Encyclopedia.com https://www.encyclopedia.com›science›serotaxonomy
16. Serotaxonomy: Definition, History and Roles/ Plant Taxonomy www.biologydiscussion.com› plant-taxonomy›serotaxonomy-definition
17. SMK. Rates Plants as source of Drugs Review. Toxicon. 2001;39:603–13.
18. Stuessy T. (1990). Plant Taxonomy. Columbia, NY.
19. Takhtazan AL. Outline of the classification of flowering plants (Magnoliophya). Bot Rev. 1980;46(3):225–359.
20. Thorne RF. Phytochemistry and angiosperm phylogeny: a summary statement. In: Young DA, Seigler DS (eds) Phytochemistry and angiosperm phylogeny. Praeger, New York, 1981;233–95.
21. Tyler VE, Brady LR, Robbers JE. 1988. Pharmacognosy, 9th Edition-Leo and Fabiger. Philadelphia.
22. Wallis TE. Textbook of pharmacognosy. CBS Publishers and Distributors, New Delhi, 2005; 68–101.
23. Wilson JE, Metzger KL. Trends in Taxonomy revealed by the published literature. Bio Science. 1998;48:121–8.