UNIT
1

Sources, Classification and Quality Control of Crude Drugs

INTRODUCTION OF PHARMACOGNOSY

INTRODUCTION

Crude drugs are drugs, which are obtained from natural sources like plants, animals, minerals and they are used as either they occur in nature without any processing except, drying and size reduction or processed form (decoction, infusion, extract, etc). The term pharmacognosy is derived from two words, pharmakon means medicine (drug) and gignosco means to acquire knowledge of something. The word pharmacognosy can be defined in various ways as given below:

- Pharmacognosy is the systematic study of crude drugs obtained from natural origins like a plant, animals, and minerals.
- Pharmacognosy may be defined as a branch of pharmaceutical science that involves detailed study of drugs obtained from natural origin including name, habitat, collection, cultivation, macroscopy, microscopy, physical properties, chemical constituents, therapeutic actions, uses, and adulterants."
- Pharmacognosy is "the study of the physical, chemical, biochemical and biological properties of crude drugs or potential drugs or drug substances of natural origin as well as the search for new drugs from natural sources".
- Pharmacognosy is the study of medicinal uses of various naturally occurring drugs and their history, sources, distributions, method of cultivation, active constituents, medicinal uses, identification test, preservation methods, substituent, and adulterants.

HISTORICAL DEVELOPMENT OF PHARMACOGNOSY

In the early period, the primitive man went in search of food and ate at random, plants or their parts like tubers, fruits, leaves, etc. As no harmful effects were observed he considered them as edible materials and used them as food. If he observed other effects by their eating they were considered inedible, and according to the actions he used

them in treating symptoms or diseases. If it caused diarrhea it was used as purgative, if vomiting it was used as 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 on from one generation to the other, and new knowledge was added in the same way.

Pharmacognosy in Ancient Times (Before the Nineteenth Century)

- The medicines originated in Egypt and India.
- Medicines were recorded both in *Papyrus Ebers* of Egypt about 1,500 BC and later in Ayurveda of India. In papyrus, crocus, dried ox-bile juice, castor oil, and so on were mentioned.
- In about 77 AD, Dioscorides, a Greek doctor, kept a record of about 600 kinds of crude drugs in his compiled book *De Materia Medica*, a book that had played an important role in pharmacology and botany by the fifteenth century.
- Charaka made 50 groups of 10 herbs each of which, according to him, would suffice an ordinary physician's need.
- Similarly, Sushrutha arranged 760 herbs in 7 distinct sets based on some of their common properties.
- A large portion of the Indian population even today depends on the Indian System of Medicine–Ayurveda, 'An ancient science of life'. The well-known treatises in Ayurveda are Charaka Samhita and Sushrutha Samhita.
- Ancient Rome also promoted its development.
- The *Historia*, written by Pliny (23–79 AD), gave a brief account of nearly 1,000 species of plants, most of which could be used for medicines. From ancient times to the middle of the nineteenth century, pharmacology had been in its traditional stage for all countries in the world. At that time, knowledge about medicines came mainly from senses and practical experiences.

Pharmacognosy in Early Modern Times (1815–1930)

- It was at the beginning of the nineteenth century that pharmacognosy came into its real being. In 1815, CA Seydler, a German who used the word "pharmakognosie" in his book named *Analecta Pharmacognostica*.
- In 1806, Sertürner, a German, clarified the cell to be the basic unit of plant structure, and then microscopes were used to research the internal structure of crude drugs.
- In 1803, the French pharmacist, Derosne isolated narcotine from opium.
- In 1803, Friedrich Sertürner isolated morphine from opium, and its role in alleviating pain was recognized. Meanwhile, the qualitative and quantitative methods of chemistry were used in crude drug identification. Fluorescence analysis and chromatography were used in sequence in the latter half of the nineteenth century.
- All in all, the reason why pharmacognosy has become an independent subject is closely related to the development of international traffic and trade at that time.
- In the first half of the nineteenth century, the rapid progress in international trade gave rise to an increase in the variety of medicines and resulted in enlarging the scope of raw materials and medium products.

Pharmacognosy in Modern Times (1930 to the Late 1990s)

- Since the 1930s, the development of biology and chemistry enriched methods and ways of studying goods pharmacognosy.
- The development of the bioassay of the intensity of drug action (biological potency) advanced the study of active ingredients of crude drugs and strengthened the quality evaluation of them.
- Chemical and physical methods, such as colorimetry, spectrophotometry, and fluorescence analysis, were all applied to the identification of crude drugs gradually.

DEVELOPMENTAL EVENTS

1. Isolation of Penicillin in 1928 by William Fleming and large-scale production in 1941.
2. Isolation of reserpine from rauwolfia root 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.

Period of Natural Pharmacognosy (At the End of the Nineteenth Century to the Early Twenty-First Century)

- Going through the first three stages of development, pharmacognosy became an established applied discipline with advanced technology and theory.
- In the 1970s and 1980s, many universities canceled the "pharmacognosy" course from their curriculum. However, at the end of this century, with humans "returning to nature" and the uprising of modern life science, pharmacognosy has presented a strong vitality and broad prospects.
- Progresses in the separation of the chemical composition, structure determination, and quantitative technology made ^{1}H NMR, ^{13}C NMR, DNA fingerprint identification, etc. possible to be used in the identification of crude drugs thus promoting its standardization and normalization.

Modern Concept

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

- **Isolation of phytochemical:** Strong acting substances such as glycosides of digitalis, alkaloids of hyoscyamus and belladonna, ergot, rauwolfia, morphine, and other alkaloids of opium were isolated and their clinical uses studied.
- **Structure-activity relationship:** The 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 C1, C3, C8, C9, and C10. 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. The preparation of steroid hormones from diosgenin by acetolysis and oxidation, and further preparation of cortisone by microbial reactions. Steroid hormones and their semisynthetic analogs represent a multimillion-dollar industry in the United States.

Natural Products as Models for the Synthesis of New Drugs

Morphine is the model of a large group of potent analgesics, cocaine for local anesthetics, 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 antitumor substances. Further, drugs such as digitoxin, strophanthus glycosides, morphine, atropine, and several others are known for long and have survived their later day synthetic analogs.

Biosynthetic Pathways

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

Progress from 1960 onwards

During this period only a few active constituents mainly antibiotics, hormones, and antitumor 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 semisynthetic penicillins, like ampicillin and amoxicillin were developed. From ergocryptine, an alkaloid of ergot, bromocryptine has been synthesized. Bromocryptine is a prolactin inhibitor and also has activity in Parkinson's disease and cancer. By applications of several disciplines, pharmacognosy from a descriptive subject has again developed into an integral and important discipline of pharmaceutical sciences.

SCOPE OF PHARMACOGNOSY

- Pharmacognosy gives a sound knowledge of the vegetable drugs under botany and animal drugs under zoology.
- It also includes plant taxonomy, plant breeding, plant pathology, plant genetics, and by this knowledge one can improve the cultivation methods for both medicinal and aromatic plants.
- Nowadays, phytochemistry (plant chemistry) has undergone significant improvement.
- This includes a variety of substances that are accumulated by plants and synthesized by plants.

A vital contribution to the advancement of natural science:

- This has been done by the advanced technologies of cultivation, purification, identification (characterization) of pharmaceuticals from nature.
- Concepts of biochemistry and chemical engineering help in the improvement of the collection, processing, and storage technologies of pharmaceuticals.
- It also gives knowledge of chemotaxonomy, biogenic pathways for the formation of acute ingredients.
- It is concerned with the enormous variety of substances that are synthesized and accumulated by plants and the structural elucidation of these substances. Extraction, isolation, purification, and characterization of phytochemicals from natural sources are important for the advancement of the medical system.
- Pharmacognosy is an important branch of pharmacy which is playing a key role in new drug discovery and development by using natural products. Pharmacognosy has given many leads for new drug discovery and development.
- It is an important link between modern medicine systems (allopathy) and the traditional system of medicine. It is a part medicinal system that is affordable as well as accessible to the common man. As part of an integrative system of medicine, pharmacognosy can help to increase the effectiveness of the modern medicine system.
- It is acting as a bridge between pharmacology, medicinal chemistry and pharmacotherapeutics, and also pharmaceutics. It also bridges pharmaceutics with other pharmacy subjects.
- More than 60 percent of the world's population is still using a natural product for their primary healthcare needs. Pharmacognosy can provide safe and effective drugs in combination with the modern medicine system.
- Pharmacognosy includes knowledge about the safe use of herbal drugs including toxicity, side effects, drug interaction thereby increasing the effectiveness of modern medicine.

A vital link between pharmacology and medicinal chemistry

- Newly detected plant drugs are converted into medicine as purified phytochemicals.
- Pharmacognosy is essential for the evolution of new medicines because crude drugs are used for the preparation of galenical or as sources of therapeutically active metabolites.
- In short, pharmacognosy is an important link between pharmaceuticals and basic science as well as an ayurvedic and allopathic system of medicines.
- In another way, the complete knowledge of pharmacognosy will help in the recent trend that is in industries,
- As research tools and in new drug delivery systems, all the departments of pharmaceuticals can improve the healthcare facilities across the world.
- Pharmacognosy is a science of active principles of crude drugs which can help dispense, formulate, and manufacture dosage forms.
- The development of pharmacognosy also leads to the development of botany, taxonomy, plant biotechnology, plant genetics, plant pathology, pharmaceutics, pharmacology, phytochemistry, and other branches of science.

SOURCES OF DRUGS

INTRODUCTION

The crude drug can be obtained from plants, animals, micro-organisms (marine) and minerals, etc. The plant tissue culture technique is also a good source of the drug nowaday. It is an *in vitro* cultivation and production of the drug under the aseptic condition in a laboratory. Therefore, drugs are obtained from five major sources:

- Plants
- Animals
- Minerals
- Marines
- Plant tissue culture

Plants Source

Plant source is the oldest source of drugs. Most of the drugs in ancient times were derived from plants. Almost all parts of the plants are used, i.e. leaves, stem, bark, fruits, roots, etc.

Leaves: The leaves of *digitalis purpurea* are the source of digitoxin and digoxin, which are cardiac glycosides. Leaves of eucalyptus give oil, which is an important component of cough syrup. Tobacco leaves give nicotine. *Atropa belladonna* gives atropine.

Flowers: Clove gives eugenol. *Vinca rosea* gives vincristine and vinblastine. Rose gives rose water used as a tonic.

Fruits: Senna pod gives anthracene, which is a purgative (used in constipation). Calabar beans give physostigmine, which is a cholinomimetic agent.

Seeds: Seeds of nux vomica give strychnine, which is a CNS stimulant. Castor seeds give castor oil. Calabar beans give physostigmine, which is a cholinomimetic drug.

Roots: Ipecacuanha root gives emetine, used to induce vomiting as in accidental poisoning. It also has amoebicidal properties. *Rauwolfia serpentina* gives reserpine, a hypotensive agent. Reserpine was used for hypertension treatment.

Bark: Cinchona bark gives quinine and quinidine, which are antimalarial drugs. Quinidine also has antiarrhythmic properties.

Stem: Kalmegh has hepatoprotective activity

Animal Sources

- The pancreas is a source of insulin, used in the treatment of diabetes.
- Sheep thyroid is a source of thyroxin, used in hypertension.
- Cod liver is used as a source of vitamin A and D.
- The blood of animals is used in the preparation of vaccines.
- Cochineal (dried full-grown female insects) consists of carminic acid used as a coloring agent for foods, drugs, and cosmetic products.
- The urine of pregnant women gives human chorionic gonadotropin (hCG) used for the treatment of infertility.

- Sheep thyroid is a source of thyroxin, used in hypertension.
- The anterior pituitary is a source of pituitary gonadotropins, used in the treatment of infertility.

Mineral Sources

Metallic and non-metallic sources: Iron is used in the treatment of iron deficiency anemia. Mercurial salts are used in syphilis. Zinc is used as a zinc supplement. Zinc oxide paste is used in wounds and eczema. Iodine is antiseptic. Iodine supplements are also used. Gold salts are used in the treatment of rheumatoid arthritis.

Miscellaneous sources: Fluorine has antiseptic properties. Borax has antiseptic properties as well. Selenium as selenium sulfide is used in anti-dandruff shampoos. Petroleum is used in the preparation of liquid paraffin.

Marines Sources

The greater part of the earth's surface is covered by seas and ocean, which contains about 5, 00,000 species of marine organisms. Many of these compounds have shown pronounced biological activity. In western medicine agar, alginic acid, carrageenan, protamine sulfate, spermaceti and cod, and halibut liver oils are the established marine medicinal products. Macroalgae or seaweeds have been used as crude drugs in the treatment of iodine deficiency states such as goiter, etc. Some seaweed has also been utilized as a source of additional vitamins and in the treatment of anemia during pregnancy. During the last 30–40 years, numerous novel compounds have been isolated from marine organisms having biological activities such as antibacterial, antiviral, antitumor, antiparasitic, anticoagulants, antimicrobial, antiinflammatory, and cardiovascular active products.

Importance of Marine Drugs

- Marine organisms are a potential source for drug discovery.
- Life has originated from the oceans that cover over 70% of the surface of the earth and contain highly ecological, chemical, and biological diversity starting from micro-organisms to vertebrates.
- This diversity has been the source of unique chemical compounds, which hold tremendous pharmaceutical potential.
- Because of the high chemical and physical harsh conditions in the marine environment, the organisms produce a variety of molecules with unique structural features and exhibit various types of biological activities.
- The majority of the marine natural products have been isolated from sponges, coelenterates (sea whips, sea fans, and soft corals), tunicates, echinoderms (starfish, sea cucumbers, etc.) and bryozoans, and a wide variety of marine micro-organisms in their tissues.

Classification of Drugs from Marine Organisms

The enormous quantum of newer and potent drug molecules derived from the wide spectrum of marine organisms across the world has been classified based on their specific pharmacologic actions as stated below:

- Antimicrobial drugs
- Cytotoxic/antineoplastic agents

- Cardiovascular active drugs
- Marine toxins
- Antibiotic substances
- Anti-inflammatory and antispasmodic agents
- Miscellaneous pharmacologically active substances.

Antimicrobial

1. **Zonarol and isozoranol**
   - *Biosource:* Zonarol and isozonarol are both obtained from *Dictyopteris zonaroides* (brown algae).
   - *Chemistry:* Flavonoid
   - *Use:* Antimicrobial
2. **Tetrabromo-2-heptanone**
   - *Biosource:* It is obtained from another species of *Bonnemaisonia hemifera* (red algae).
   - *Chemistry:* Bromophenol compound
   - *Use:* Antimicrobial
3. **2-cyano-4, 5-dibromopyrrole:** It is perhaps one of the rarest examples of a chemical entity isolated from a marine organism that contains a cyano (-CN) function group.
   - *Biosource:* It is obtained from *Agelas oroides*, a specific type of sponge found in marine sources.
   - *Use:* Antimicrobial
4. **Eunicin**
   - *Biosource:* It is obtained from *Gorgonian corals, Eunicea mammosa.*
   - *Chemistry:* Diterpene
   - *Use:* Antimicrobial

Anticancer

1. **Sinularin**
   - *Source:* Soft coral *Sinularia flexibilis*
   - *Chemistry:* Cembranoids (14 C cyclic diterpenoid with eocyclic lactone)
   - *Use:* Anticancer
2. **Asperdiol**
   - *Source:* From gorgonian coral *Eunicea knighti*
   - *Chemistry:* Non-lactone cembranoid
   - *Use:* Leukemia
3. **Geranyl hydro-quinone**
   - *Source:* Aplidium species
   - *Chemistry:* Quinone
   - *Use:* Anticancer

Antibiotics

1. **Cycloeudesmol**
   - *Biosource:* Red algae *Chondria oppositiclada*
   - *Chemistry:* Eudesmol (sesquiterpenoid)
   - *Use:* Antibiotic

2. **Variabilin**
   - *Biosource:* Sponge, *Ircinia oros*
   - *Chemistry:* Furanose ester terpene
   - *Use:* Antibiotic

Anticoagulant

1. **Chemical compound: Galaxtan sulphuric acid**
   - *Biosource: Iridae laminarioides*
   - *Use:* Anticoagulant
2. **Chemical compound associated with an unknown plasma factor**
   - *Biosource: Codium fragile* ssp
   - *Use:* Antithrombin activity
3. **Chemical compound: High molecular wt. proteoglycans**
   - *Biosource: C. fragile ssp atlanticum*
   - *Use:* Anticoagulant activity.

Antiparasitic

1. **Organism:** *Digenia simplex* (red algae)
   - *Chemical compound*: Alpha-kainic acid
   - *Use*: Broad-spectrum anthelmintic. Effective against parasitic roundworms, whipworm, and tapeworm.
2. **Organism:** ***Laminaria angustata***
   - *Chemical compound*: Laminine
   - *Use*: Anthelmintic as well as a smooth muscle relaxant and hypotensive;
3. **Organism:** Sea cucumber
   - *Chemical compound*: Cucumechinoside F.
   - *Use:* Antiprotozoal.

Cardiovascular Agents

1. **Eptatretin**
   - *Biosource:* It is found in the bronchial hearts of pacific hogfish, i.e. *Eptatretus stoutii*
   - *Use:* It is a potent cardiac stimulant with direct stimulant action on the mammalian myocardium.
2. **Laminine**
   - *Biosource:* It is obtained from marine algae, *Laminaria angustata*
   - *Use:* Hypotensive agent
3. **Anthopleurins**
   - *Biosource:* It is obtained from coelenterates—*Anthropleura xanthogrammica*
   - *Use:* Cardiotonic (35 times more potent as compared to digitoxin)

Marine Toxins

1. **Ciguatoxin**
   - *Biosource:* It is found in red tide dinoflagellate; i.e. *Gambierdiscus toxicus*
   - *Toxic symptoms:* Neurological, cardiovascular, GIT disorders
2. **Palytoxin**
   - *Biosource:* It presents in *Palythoa* species
   - *Toxic symptoms:* On coronary arteries

Antispasmodic Agents

- Agelasidine A
- *Biosource:* It is obtained from Okinawa sea sponge *Agelas* spp
- *Chemical compound:* Agelasidine A is the first marine natural product containing Guanine and sulfone units.
- *Use:* Antispasmodic agent

Anti-inflammatory

- **Bio-indol**
  - *Biosource:* It is obtained from marine *Cyanobacterium, rivularia firma*
  - *Chemical compound:* Bio-indol derivative
  - *Use:* Anti-inflammatory agent
- **Butanolide**
  - *Biosource:* It is obtained from marine *Euplexaura flava*
  - *Chemical compound:* Butanolide derivative
  - *Use:* Anti-inflammatory agent

Marketed product from marine source

- Ara-A: Semisynthetic antiviral agent
- Bryostatin: Anticancer agents
- Octopamine: Cardiovascular agent
- Bio-indol derivatives: Anti-inflammatory

Plant Tissue Culture

Tissue culture is *in vitro* cultivation of plant cells or tissue under aseptic and controlled environmental conditions, in liquid or on semisolid well-defined nutrient medium for the production of primary and secondary metabolites or to regenerate plant. This technique affords an alternative solution to problems arising due to the current rate of extinction and decimation of flora and ecosystem. The whole process requires a well-equipped culture laboratory and nutrient medium. This process involves various steps, viz. preparation of nutrient medium containing inorganic and organic salts, supplemented with vitamins, plant growth hormone(s), and amino acids as well as sterilization of explant (source of plant tissue), glassware, and other accessories inoculation and incubation.

Applications

- Production of phytopharmaceuticals
- Biochemical conversions
- Clonal propagation (micro-propagation)
- Production of immobilized plant cell

There are various secondary metabolites are obtained from different tissue cultures methods. Soure of drug from plant tissue culture is given in Table 1.1.

Table 1.1: Source of drug from plant tissue culture

Compound	***Plant species***	***Culture type***
Anthraquinones	*Cassia angustifolia*	Callus
Caffeine	*Coffee arabica*	Callus
Cardenolides	*Digitalis purpurea*	Suspension and callus
Codeine	*Papaver somniferum*	Suspension
Diosgenin	*Dioscorea composita*	Callus
Glycyrrhizin	*Glycyrrhiza glabra*	Suspension
Papain	*Carica papaya*	Callus
Reserpine	*Rauwolfia serpentina*	Suspension
Rosmarinic acid	*Coleus blumei*	Callus and suspension
Trigonelline	*Trigonella foenum-graecum*	Suspension
Vinblastine	*Catharanthus roseus*	Callus
Visnagin	*Ammi visnaga*	Suspension
Xanthotoxin	*Ruta graveolens*	Suspension

Synthetic/Semi-synthetic Sources

- *Synthetic sources:* When the nucleus of the drug from a natural source as well as its chemical structure is altered, we call it synthetic. Examples include emetine bismuth iodide
- *Semi-synthetic sources:* When the nucleus of a drug obtained from a natural source is retained but the chemical structure is altered, we call it semi-synthetic. Examples include apomorphine, diacetyl morphine, ethinyl estradiol, homatropine, ampicillin, and methyl testosterone. Most of the drugs used nowadays (such as antianxiety drugs, anti-convulsants) are semisynthetic forms.

Microbiological Sources

Penicillium notatum is a fungus that gives penicillin. *Actinobacteria* gives streptomycin. Aminoglycosides such as gentamicin and tobramycin are obtained from Streptomyces and Micromonosporas.

Recombinant DNA Technology

Recombinant DNA technology involves the cleavage of DNA by enzyme restriction endonucleases. The desired gene is coupled to rapidly replicating DNA (viral, bacterial, or plasmid). The new genetic combination is inserted into the bacterial cultures which allow the production of a vast amount of genetic material.

Advantages

- Huge amounts of drugs can be produced.
- Drugs can be obtained in pure form.
- It is less antigenic.

Disadvantages

- A well-equipped lab is required.
- Highly trained staff is required.
- It is a complex and complicated technique.

Organized Drugs

The morphological plant parts or the entire plant itself can be called organized drugs. Organized drugs consist of the organized cellular structure in the form of anatomical features. Organized drugs comprise those crude drug materials which represent a part of the plant and are, therefore, made up of cells.

- **Leaves:** Senna, adulsa, datura
- **Flowering part:** Clove
- **Bark:** Cinchona
- **Wood:** Sandalwood, quassia
- **Seed:** Nux-vomica
- **Root:** Rauwolfia.

Unorganized Drugs

Unorganized drugs do not have the morphological or anatomical organization as such. These include products like plant exudates such as gums, oleogums, oleogum resins, plant lattices like that of opium, aloetic juices like aloes, or dried extracts of black and pale catechu, agar, alginic acid, etc., are products coming under this group. Other products like essential oils, fixed oils, fats, and waxes are obtained from vegetables or animals. These products may be solid, semisolid, or liquid, and the physical, chemical, and analytical standards may be applied for testing their quality and purity. The differences between organized and unorganized drugs are given in Table 1.2.

Table 1.2: Differences between organized drug and unorganized drug

Organized drug	***Unorganized drug***
Cellular structure present	The cellular structure is absent
Organized drugs are part of the plant, animal-like, fruits, seeds, roots, etc.	Unorganized drugs are obtained from parts of plants and animals by extraction, distillation incision, expression or exudates, secretion, etc.
For the study of organized drugs properly T S or L S is taken and study under a microscope	For the study of unorganized drugs, physical constituents like density, viscosity, refractive index, optical rotation and chemical test are important criteria
They are solid	They are solid, semi-solid, or liquid
Example: Clove, fennel, dill, digitalis	Lemon oil, starch, catechu.

- **Latex:** Latex is a product presents in special tissue of plant; it is white, aqueous, suspension, the suspended particles are protein, sugar, minerals, alkaloid, resin, or starch, e.g. opium, papain
- **Dried juices:** The juices are obtained from fleshy leaves (aloes) or the stems of the trees (kino).

- **Dried extracts:** Pharmacognostic origin drugs are obtained by treating the part of the plant with water or distillation followed by concentration. Pharmaceutical origin drugs are obtained by alcoholic or hydroalcoholic solutions and adjusting the product to standard strength, e.g. agar, black catechu, gelatin
- **Gums:** Amorphous substances are pathological products produced when the plant is under unfavorable conditions or injured.
- **Mucilage:** A thick, gluey substance produced by most plants and some microorganisms. The differences between gums and mucilage are given in Table 1.3.

Table 1.3: Differences between gums and mucilage

Gums	*Mucilage*
Gums are produced by the plant when it injured, diseased, or by a process " Gummosis"	Mucilage is the normal product of plant growth
Gum is produced outside the plant cell.	Mucilage is produced inside the cell
Gums are soluble in water to form an adhesive solution	Mucilage is not soluble in water, it forms a slimy solution with water
Gums are made up of sugar, salts of uronic acid, e.g. gum acacia, gum tragacanth	Mucilage is made up of ester and sulphuric acid, e.g. mucilage is present in agar, senna, isapgol

Oleoresins and Oleo-gum Resins

- **Oleoresins:** Homogenous mixture of volatile oil and resin is called oleoresin, e.g. oleoresin of ginger.
- **Oleo-gum resins:** Homogenous mixture of volatile oil, gum and resin, e.g. myrrh, asafoetida.

Official Drugs: Any substance or drug (crude or prepared), which is included in the issue of the pharmacopeia of a country and is officially used for therapeutic purposes, is called an official drug. Whole plant catharanthus and its active constituents (vincristine and vinblastin) are used in treating cancer diseases. Latex of fruits of poppy plants (*Papaver* sp.) and its active constituents (morphine) as used as narcotic. Caffeine from the seeds of coffee plants and thiamine from leaves of tea plants is used as stimulants.

Unofficial Drug: A drug, which has once been recognized as a drug in the pharmacopeia, but not included in the issue of the pharmacopeia or any official drug literature, is designated as an unofficial drug.

CLASSIFICATION OF CRUDE DRUGS

INTRODUCTION

The most important natural sources of drugs are higher plants, microbes and animals, and marine organisms. Some useful products are obtained from minerals that are both organic and inorganic. To pursue (or to follow) the study of the individual drugs, one must adopt some particular sequence of arrangement, and this is referred to as a system of classification of drugs.

A method of classification should be:

- Simple,
- Easy to use,
- Free from confusion and ambiguities.

Because of their wide distribution, each arrangement of classification has its own merits and demerits, but for study, the drugs are classified in the following different ways:

- Alphabetical classification
- Morphological classification
- Pharmacological classification
- Chemical classification
- Taxonomical classification
- Chemotaxonomical classification
- Serotaxonomical classification

Alphabetical Classification

Alphabetical classification is the simplest way of classification of any disconnected items. Crude drugs are arranged in alphabetical order of their Latin and English names (common names) or sometimes local language names (vernacular names). Some of the pharmacopoeias, dictionaries, and reference books that classify crude drugs according to this system are as follows:

- Indian Pharmacopoeia
- British Pharmacopoeia
- British Herbal Pharmacopoeia
- European Pharmacopoeia
- United States Pharmacopoeia and National Formulary

Merits

- It is easy and quick to use.
- There is no repetition of entries and is devoid of confusion.
- In this system location, tracing and addition of drug entries are easy.

Demerits

- There is no relationship between previous and successive drug entries.
- This system also does not correlate between the chemical constituents and pharmacological activity of the drugs.
- This system also does not give any idea of taxonomy characters

Examples: Acacia, benzoin, cinchona, dill, ergot, fennel, gentian, hyoscyamus, ipecacuanha, jalap, kurchi, liquorice, mints, nux vomica, opium, podophyllum, quassia, rauwolfia, senna, vasaka, wool fat, yellow beeswax, zeodary.

Morphological Classification

In this system, the drugs are arranged according to the morphological or external characters of the plant parts or animal parts, i.e. which part of the plant is used as a drug, e.g. leaves, roots, stem, etc. Organized drugs, e.g. rhizomes, barks, leaves, fruits,

entire plants, hairs and fibers. Unorganized drugs, e.g. aloe juice, opium latex, agar, gambir, honey, beeswax, lemongrass oil, etc.

Organized Drugs

- **Woods:** Quassia, sandalwood and red sandalwood.
- **Leaves:** Digitalis, eucalyptus, senna, tulsi, vasaka, tea.
- **Barks:** Arjuna, ashoka, cinchona, cinnamon, kurchi, wild cherry.
- **Flowering parts:** Clove, pyrethrum, saffron, santonica, chamomile.
- **Fruits:** Amla, bael, capsicum, caraway, cardamom, hirda, senna pod.
- **Seeds:** Black mustard, cardamom, ispaghula, linseed, nux vomica
- **Roots and rhizomes:** Aconite, ashwagandha, ginger, ginseng, rauwolfia, turmeric, valerian, squill.
- **Plants and herbs:** Bacopa, andrographis, kalmegh, vinca, centella.
- **Hair and fibres:** Cotton, hemp, jute, silk, flax.

Unorganized Drugs

- **Dried latex:** Opium, papain
- **Dried juice:** Aloe, kino dried extracts: Agar, alginate, black catechu, pale catechu, pectin
- **Waxes:** Beeswax, spermaceti, carnauba wax
- **Gums:** Acacia, guar gum, Indian gum, sterculia, tragacenth
- **Resins:** Asafoetida, benzoin, colophony, guggul, tolu balsam, storax
- **Volatile oil:** Peppermint, sandalwood, lemon, dill, clove, eucalyptus
- **Fixed oils and fats:** Arachis, castor, coconut, linseed, olive, sesame, almond, spermaceti wax, wool fat, musk, lactose.
- **Fossil organism and minerals:** Bentonite, kaolin, kieselguhr, talc.

Merits

- Morphological classification is more helpful to identify and detect adulteration.
- This system of classification is more convenient for practical study especially when the chemical nature of the drug is not clearly understood.

Demerits

- The main drawback of morphological classification is that there is no correlation of chemical constituents with therapeutic actions.

Pharmacological Classification

Grouping of drugs according to their pharmacological action or their therapeutic use is termed as pharmacological or therapeutic classification of drug. This classification is more relevant and is mostly a followed method. Drugs like digitalis, squill, and strophanthus having cardiotonic action are grouped irrespective of their parts used or phylogenetic relationship or the nature of phytoconstituents they contain.

- *Drug acting on GIT:* Bitter cinchona, quassia, gentian
- *Carminative:* Fennel, cardamom, mentha, emetic ipecac
- *Laxative:* Agar, isabgol, banana

- *Purgative:* Senna, castor oil
- *Expectorant:* Vasaka, liquorice, ipecac
- *Antitussive:* Opium (codeine)

Merits: This system of classification can be used for suggesting substitutes for drugs, if they are not available at a particular place or point in time.

Demerits: Drugs having different actions on the body get classified separately in more than one group causes ambiguity and confusion. Cinchona is an antimalarial drug because of the presence of quinine but can be put under the group of the drug affecting the heart because of antiarrhythmic action of quinidine.

Chemical Classification

Depending upon the active constituents, the crude drugs are classified. The plants contain various constituents in them like alkaloids, glycosides, tannins, carbohydrates, saponins, etc. Irrespective of the morphological or taxonomical characters, the drugs with similar chemical constituents are grouped into the same group.

1. **Carbohydrates:** Carbohydrates are polyhydroxy aldehydes or ketones containing an unbroken chain of carbon atoms.
   - *Gums:* Acacia, tragacanth, guargum
   - *Mucilages:* Plantago seed
   - *Others:* Starch, honey, agar, pectin, cotton
2. **Glycosides:** Glycosides are compounds that upon hydrolysis give rise to one or more sugars (glycone) and non-sugar (aglycone).
   - *Anthraquinone glycosides:* Aloe, cascara, rhubarb, senna
   - *Saponins glycosides:* Quillaia, Arjuna, glycyrrhiza
   - *Cyanophore glycosides:* Wild cherry bark
   - *Isothiocyanate glycosides:* Mustard
   - *Cardiac glycosides:* Digitalis, strophanthus
   - *Bitter glycosides:* Gentian, calumba, quassia, chirata, kalmegh
3. **Tannins:** Tannins are complex organic, non-nitrogenous derivatives of polyhydroxy benzoic acids, e.g. pale catechu, black catechu, ashoka bark, galls, myrobalan, bahera, amla
4. **Volatile oils:** Monoterpenes and sesquiterpenes obtained from plants, e.g. cinnamon, fennel, dill, caraway, coriander, cardamom, orange peel, mint, clove, valerian
5. **Lipids**
   - *Fixed oils*: Castor, olive, almond, shark liver oil
   - *Fats*: Theobroma, lanolin
   - *Waxes*: Beeswax, spermaceti
6. **Resins:** Complex mixture of compounds like resinols, resin acids, resinotannols, resenes. Examples: Colophony, podophyllum, cannabis, jalap, capsicum, turmeric, balsam of tolu and peru, asafoetida, myrrh, ginger
7. **Alkaloids:** Nitrogenous substance of plant origin
   - *Pyridine and piperidine:* Lobelia, nicotiana
   - *Tropane:* Coca, belladonna, datura, stramonium, hyoscyamus, henbane
   - *Quinoline:* Cinchona

- *Isoquinoline:* Opium, ipecac, calumba
- *Indole:* Ergot, rauwolfia
- *Amines:* Ephedra
- *Purine:* Tea, coffee

8. **Protein:** Gelatin, ficin, papain
9. **Vitamins:** Yeast
10. **Triterpenes:** Rasna, colocynth

Merits: It is a popular approach for phytochemical studies

Demerits: Ambiguities arise when particular drugs possess several compounds belonging to different groups of compounds.

Taxonomical Classification

Taxonomical classification is purely a botanical classification and is based on principles of natural relationships and evolutionary developments. All the plants possess different characteristics of morphological, microscopical, chemical, embryological, serological, and genetics. In this classification, the crude drugs are classified according to kingdom, subkingdom, division, class, order, family, genus, and species as follows.

Merits: Taxonomical classification helps study evolutionary developments.

Demerits: This system does not correlate between the chemical constituents and pharmacological activity of the drugs.

Chemotaxonomical Classification

This system of classification relies on the chemical similarity of a taxon, i.e. it is based on the existence of a relationship between constituents in various plants. Certain types of chemical constituents characterize certain classes of plants. This gives birth to an entirely new concept of chemotaxonomy that utilizes chemical facts/characters for understanding the taxonomical status, relationships, and evolution of the plants. For example, tropane alkaloids generally occur among the members of Solanaceae, thereby, serving as a chemotaxonomic marker. Similarly, other secondary plant metabolites can serve as the basis of the classification of crude drugs. The berberine alkaloid in berberis and argemone, rutin in Rutaceae members, Ranunculaceae alkaloids among its members, etc., are other examples.

It is the latest system of classification that gives more scope for understanding the relationship between chemical constituents, their biosynthesis, and their possible action.

Serotaxonomical Classification

Serology is defined as that portion of biology, which is concerned with the nature and interactions of antigenic material and antibodies. Smith (1976) defined it as "the study of the origins and properties of antisera." When foreign cells or particles (antigens) are introduced into an organism, antibodies are produced in the blood (antiserum). The substance capable of stimulating the formation of an antibody is called antigen and the highly specific protein molecule produced by plasma cells in the immune system in response to the antigen is called an antibody. Phytoserology, which deals

with immunochemical reactions, between serum antibodies and antigens, has also established itself as a valid method in systematics because it helps to detect homologous proteins. It uses the specific properties of antisera produced by animals against plant proteins as characters to assess plant relationships.

Serotaxonomy developed and became popular in Germany, which has been an active center since the beginning of this century. The classification of very similar plants uses differences in the proteins they contain. The technique is based on the highly specific relationship between antigens and the antibodies produced in response to them. Protein extracted from a plant is injected into the blood of an animal, where it behaves as an antigen. After an interval for the production of antibodies, a blood sample is taken. This can be used to compare the first plant protein (antigen) with extracts taken from other plants.

The study of antigen-antibody reaction is called serology. The substance capable of stimulating the formation of an antibody is an antigen. A specific protein molecule produced by plasma cells in the immune system is an antibody. The antibodies combine chemically with specific antigens and this combination elevates an immune response. The application of serology in solving taxonomic problems is called serotaxonomy.

Process of Serotaxonomy

The process of serotaxonomy involves the following steps

- The protein extract of the plant origin, i.e. the antigen is extracted.
- The antigen is injected into the bloodstream of an experimental animal to form antibodies.
- The experimental animal produces a specific antibody in response to the antigen.
- The serum with antibodies is called antiserum. Antiserum is made to react *in vitro* with antigenic protein as well as proteins of other taxa, whose affinities are to be determined.
- The amount of precipitation shows the degree of homology.

For example, to know the closeness of the taxon A with B, C, D, E. The proteins from A are extracted and are injected into the experimental animal rabbit or mice. The experimental animal in return produces antibodies. These antibodies are extracted from the blood of the experimental animal in the form of antiserum. When this antiserum is allowed to react with the original protein extract from A, complete coagulation takes place. When this antiserum is allowed to react with the protein extracts from other taxa B, C, D, E the degree of coagulation varies. The degrees of coagulation are compared to know the closeness of the taxa. Greater the degree of coagulation, greater is the closeness.

Importance of Serotaxonomy

- Based on the serotaxonomic studies Fairbrothers and Jhonson showed that genera Magnolia and Michelia show the closest affinity within Magnoliaceae
- Simon in 1971 demonstrated a close relationship between Nymphaeaceae and Nelumbonaceae based on serological data.
- Klos applied serotaxonomic data in the classification of Leguminosae.

QUALITY CONTROL OF CRUDE DRUGS

INTRODUCTION

Quality control (QC) is a procedure or set of procedures intended to ensure that a manufactured product or performed service adheres to a defined set of quality criteria or meets the requirements of the client or customer. QC is similar to, but not identical with, quality assurance (QA). Quality control techniques are needed to be done to ensure about adulterated drugs convert into purified drugs.

Quality control of crude drugs or evaluation of crude drug means:-

- Authentication of identity.
- Determination of quality and clarity.
- Detection of nature of corruption (adulteration).
- Determination of purity
- Toxicity, metabolism, absorption, elimination are also determined
- Evaluation of crude drug is necessary because-
- Biochemical variation in crude drug.
- Deterioration due to treatment and storage.
- Replacement and adulteration (results of carelessness, ignorance, or fraud).
- Also to take care of medicines.
- To avoid the risks for the medicines

Drug Adulteration

Adulteration may be defined as mixing or substituting the original drug material with other spurious, inferior, defective, spoiled, useless other parts of the same or different plant or harmful substances or drugs which do not conform with the official standards.

Adulteration may take place in two ways:

1. Direct or intentional adulteration
2. Indirect or unintentional adulteration

1. Direct or Intentional Adulteration

Direct or intentional adulteration is done intentionally which usually includes practices in which an herbal drug is substituted partially or fully with other inferior products. Due to morphological resemblance to the authentic herb, many different inferior commercial varieties are used as adulterants. These may or may not have any chemical or therapeutic potential. Substitution by "exhausted" drugs entails adulteration of the plant material with the same plant material devoid of the active constituents. This practice is most common in the case of volatile oil-containing materials, where the dried exhausted material resembles the original drug but is free of essential oils.

1. **With artificially manufactured materials:** Substances artificially manufactured being resembled the original drug are used as substitutes. This practice is generally followed for much costlier drugs, e.g. nutmeg is adulterated with basswood prepared to the required shape and size; the colored paraffin wax is used in place of beeswax.
2. **With inferior quality materials:** Inferior quality material may or may not have the same chemical or therapeutic value as that of the original natural drug due

to their morphological resemblance to authentic drugs; they are marketed as adulterants, e.g. *Belladonna* leaves are substituted with *Ailanthus* leaves, papaya seeds to adulterate *Piper nigrum*, mother cloves, and clove stalks are mixed with clove, beeswax is substituted by Japan wax.

3. **With exhausted material:** Many drugs extracted on large scale for isolation of active principle, volatile oils, etc. the exhausted material may be used entirely or in part as a substituent for the genuine drugs, e.g. umbelliferous fruits and cloves (without volatile oils) are adulterated with exhausted (without volatile oils) original drugs, exhausted jalap and Indian hemp (without resins) are used as an adulterant.
4. **With the foreign matter:** Sometimes synthetic chemicals are used to enhance the natural character, e.g. addition of benzyl benzoate to balsam of Peru, citral to citrus oils like oil of lemon and orange oil, etc.
5. **With harmful/fictitious substances:** Sometimes the wastes from the market are collected and admixed with authentic drugs, particularly for liquids or unorganized drugs, e.g. pieces of amber-colored glass in colophony, limestone in asafetida, lead shot in opium, white oil in coconut oil, cocoa butter with stearin or paraffin.
6. **Adulteration of powders:** Besides entire drug powder form is frequently found to be adulterated, e.g. powder liquorice or gentian admixed with powder olive stones, under the name of cinchona, *C. calisaya* wedd., *C. officinalis* Linn.f., *C. ledgeriana* and *C. succirubra* are available as mixtures.

2. Indirect or Unintentional Adulteration

Unintentional or undeliberately adulteration sometimes occurs without the bad intention of the manufacturer or supplier. Sometimes in the absence of proper means of evaluation, an authentic drug partially or fully devoid of the active ingredients may enter the market. Factors such as geographical sources, growing conditions, processing, and storage are all factors that influence the quality of the drug.

1. **Faulty collection:** Some of the herbal adulterations are due to the carelessness of herbal collectors and suppliers. The correct part of the genuine plant should be collected. Another less valuable part of the genuine plant should not be collected. Moreover, the collection should be carried out at a proper season and time when the active constituents reach maximum. *Datura strumarium* leaves should be collected during the flowering stage and wild cherry bark in autumn, etc. collection from another plant by ignorance, due to similarity in the appearance, color, lack of knowledge may lead to adulteration. For example, in place of *Aconitum napellus*, the other *Aconitum deinorrhizum* may be collected or in place of *Rhamnus purshiana* (cascara bark), *Rhamnus colifornica* is generally collected. The confusion existing in the common vernacular name of the different plants in various states of India may lead to this type of adulteration. Often in different states, the same plant is known by different vernacular names, while quite different drugs are known by the same name. This creates confusion which is best illustrated by punarnava and brahmi. The Indian pharmacopoeia drugs *Trianthema portulacastrum* L. and *Boerhaavia diffusa* L. are both known by the same vernacular name "Punarnava".
2. **Imperfect preparation:** Non-removal of associated structures, e.g. stems are collected with leaves, flowers, fruits. Non-removal of undesirable parts or structures, e.g. cork should be removed from the ginger rhizome. Proper drying conditions should adhere. Improper drying may lead to unintentional adulteration, e.g. if

digitalis leaves are dried above 65°C decomposition of glycosides by enzymatic hydrolysis. Use of excessive heat in separating the cod liver oil from livers, where the proportions of vitamins, odor, color, etc. are adversely affected.

3. **Incorrect storage:** Deterioration especially during storage leads to the loss of the active ingredients, production of metabolites with no activity, and, in extreme cases, the production of toxic metabolites. Physical factors such as air (oxygen), humidity, light, and temperature can bring about deterioration directly or indirectly. These factors, alone or in combination, can lead to the development of organisms such as molds, mites, and bacteria. Oxidation of the constituents of a drug can be brought about by oxygen in the air, causing some products, such as essential oils, to resinify or to become rancid. Moisture or humidity and elevated temperatures can accelerate enzymatic activities, leading to changes in the physical appearance and decomposition of the herb. For example, volatile oils should be protected from light and stored in well-closed containers in a cool place. Belladonna leaf should be stored in moisture-free containers, which may cause enzymatic action leading to decomposition of medicinally active constituents. Mites, nematode worms, insects/moths, and beetles can also destroy herbal drugs during storage.
4. **Gross substitution with plant material:** Due to morphological resemblance, i.e similarity in appearance, colors, etc. the genuine crude drugs are substituted with others are very often sold in the market, e.g. *Podophyllum peltatum* L. is used as a substitute for *P. hexandrum*, *Belladona* leaves are substituted with Ailanthus leaves, saffron is admixed with dried flowers of *Carthamus tinctorius*, mother cloves and clove stalks are mixed with clove.
5. **Substitution with exhausted drugs:** In this type, the same drug is admixed but devoid of any medicinally active constituents as they are already extracted out. This practice is more common in the case of volatile oil-containing drugs like fennel, clove, coriander, caraway, etc. sometimes, natural characteristics of exhausted drugs like color and taste are manipulated by adding other additives, and then it is substituted, e.g. exhausted gentian made bitter with aloes.

DRUG EVALUATION

Evaluation means confirmation of its identity and determination of the quality and purity of the herbal drug. Drug evaluation may be defined as the determination of the identity, purity, and quality of a drug.

- Identity: Identification of the biological source of the drug.
- Quality: The quantity of the active constituents present.
- Purity: The extent of foreign organic material present in a crude drug.

Evaluation of crude drug is necessary because of three main reasons: Biochemical variations in the drug, deterioration due to treatment and storage, substitution and adulteration as a result of carelessness, ignorance or fraud, or variability caused by differences in growth, geographical location, and time of harvesting. For the quality control of traditional medicine, the traditional methods are procured and studied, and documents and the traditional information about the identity and quality assessment are interpreted in terms of modern assessment or monograph in herbal.

The crude drug can be evaluated or identified by five methods.

Organoleptic Evaluation or Morphological Evaluation

It means evaluation of drugs by the organs of sense (skin, eye, tongue, nose, and ear) or macroscopic evaluation and it includes evaluation of drugs by color, odor, taste, size, shape, and special feature, like touch, texture, etc. It is the technique of qualitative evaluation based on the study of the morphological and sensory profile of whole drugs. For examples:

- The fractured surfaces in cinchona, quillia and cascara barks, and quassia wood are important characteristics.
- The aromatic odor of umbelliferous fruits and the sweet taste of liquorice are examples of this type of evaluation where the odor of the drug depends upon the type and quality of odorous principles (volatile oils) present.
- The shape of the drug may be cylindrical (sarsapilla), subcylindrical (podophyllum), conical (aconite), fusiform (jalap), etc, size represents the length, breadth, thickness, diameter, etc.
- Color means external color which varies from white to brownish-black is an important diagnostic character.
- The general appearance (external marking) of the weight of a crude drug often indicates whether it is likely to comply with a prescribed standard like furrows (alternate depression or valleys), wrinkles (fine delicate furrows), annulations (transverse rings), fissures (splits), nodules (rounded outgrowth), scars (spot left after falling of leaves, stems or roots).
- Taste is a specific type of sensation felt by the epithelial layer of the tongue. It may be acidic (sour), saline (salt-like), saccharic (sweetish), bitter or tasteless (possessing no taste).

Microscopic Evaluations

It involves a detailed examination of the drug and it can be used to identify the organized drugs by their known histological characters. It is mostly used for qualitative evaluation of organized crude drugs in entire and powder forms with help of a microscope. Using a microscope detecting various cellular tissues, trichomes, stomata, starch granules, calcium oxalate crystals, and aleurone grains are some of the important parameters which play important role in the identification of the certain crude drug. The crude drug can also be identified microscopically by cutting the thin TS (transverse section), LS (longitudinal section) especially in the case of wood, and by staining them with proper staining reagents, e.g. starch and hemicelluloses are identified by blue color with iodine solution, all lignified tissues give pink stain with phloroglucinol and HCl, etc. mucilage is stained pink with ruthenium red can be used to distinguish cellular structure. The microscopic evaluation also includes the study of constituents in the powdered drug by the use of chemical reagents. Quantitative aspects of microscopy include the study of stomatal number and index, palisade ratio, vein-islet number, size of starch grains, length of fibers, etc. which play important role in the identification of the drug.

Leaf Constant Parameters

- **Palisade ratio:** It is defined as the average number of palisade cells below the epidermal cell. It is determined from powdered drugs with the help of camera-lucida. Examples:
  - *Atropa belladonna*: 05–70

- *Adhatoda vasica:* 5.5–6.5
- *Cassia angustifolia*: 5.5–10.0 upper, 4.0–7.4 lower (senna)
- *Digitalis lanata*: 2.5–6.5 1

- **Vein-islet number:** It is defined as the number of vein-islet per sq mm on leaf surface between midrib and margin.
  - *Andrographis paniculata*: 9–12
  - *Bacopa monnieri*: 6–13
  - *Cannabis sativa* : 18–24
  - *Cannabis sativa*: 18–24
  - *Digitalis purpurea:* 2.5–3
  - *Eucalpytus globulus:* 8–13.
- **Vein-termination:** It is defined as the number of vein-terminations per sq mm of the leaf surface between midrib and margin.
- **Stomatal number:** It is defined as the average number of stomata per sq mm of the epidermis of the leaf. Examples:
  a. *Atropa belladonna:* Upper epidermis—07–10, lower epidermis—77–115
  b. *Datura metel*: Upper epidermis—147–160, lower epidermis—200–209
  c. *Ocimum sanctum:* Upper epidermis—64–72, lower epidermis—175–250
- **Stomatal index:** It is the percentage which the number of stomata forms to the total number of epidermal cells; each stoma being counted as one cell.
  SI = S/E + S × 100
  SI = stomatal index
  S = number of stomata per unit area
  E = number of epidermal cells in the same unit area
  Example: *Atropa belladonna*—upper epidermis—nil, lower epidermis—20.2–23.0 3.
- **Trichomes**
  - They are usually called plant hairs.
  - Consist of two parts; root (in the epidermis) and body (outside the epidermis).
  - They are tubular elongated or glandular outgrowths of the epidermal cell.
  - They are functionless but sometimes, perform secretary functions.
  - They excrete water and at times, volatile oil as in the case of peppermint.
  - They present mostly in the aerial part and are absent in roots.
  - Depending upon the structure and the number of cells presents in trichomes, they are classified as given below:
    I. *Covering trichome* or *non-glandular* or *clothing trichome*.
       a. Unicellular (nux-vomica)
       b. Ulticellular (datura)
    II. *Glandular trichome:* Characterized by the presence of glandular (spherical) cells all the top of the trichome.
       - *Unicellular glandular trichome:* The stalk is absent, e.g. piper, betel, vasaka, etc.
       - Multicellular glandular trichome
         - They have a unicellular head and stalk (*Digitalis purpurea*).
         - Unicellular head and uniseriate multicellular stalk (belladonna).

- Short stalk with secreting head formed of rosette or cloud-shaped of secretory cells (cannabis sativa).
- Multicellular

III. *Hydathode:* These are the organs of absorption or secretion of water developed in certain plants (Indian hemp and tobacco)

Stomata

- A stoma is a minute epidermal opening.
- Having a central pore and two kidney-shaped similar cells containing chloroplasts known as guard cells.
- It is for gas exchange and transpiration.
- They are present in the green parts of the plant and absent in roots.
- The distribution of stomata between the upper and lower epidermis in dicot leaves shows great variation.
- It can be classified into 4 types based on the arrangement of a subsidiary and epidermal cells (Table 1.4)

Table 1.4: Types of stomata

Anomocytic	***Anisocytic***	***Diacytic***	***Paracytic***
In this type, the stoma is surrounded by varying numbers of subsidiary cells resembling other epidermal cells, e.g. digitalis.	In this type, the stoma is surrounded by three subsidiary cells of which one is markedly smaller than the other two, e.g. datura, belladonna.	In this type, the stoma is surrounded by two subsidiary cells which are at a right angle to that stoma, e.g. peppermint, vasaka.	In this type, the stoma is surrounded by two subsidiary cells which are parallel to the longitudinal axis of the pore and guard cell, e.g. coca

Calcium Oxalate Crystals

Several cell contents are present in vegetable drugs. The inorganic crystalline compounds by their specific shapes can be utilized for the identification of herbal drugs. Due to this reason, they are called diagnostic characters of the plant.

1. Cubical (cube shape) e.g., senna, glycyrrhiza.
2. Rhombic (diamond shape)
3. Tetragonal, e.g., onion.
4. Monoclinic (all three axes are unequal), e.g. gall.
5. Acicular (long slender, pointed, bundles), e.g. squill, cinnamon.
6. Rosettes–clusters (aggregation of crystals), e.g. clove, arjuna.
7. Microsphenoidal (minute in structures), e.g. henbane.
8. Calcium oxalate crystals.

Quantitative Microscopy

Lycopodium Spore Method

It is used when especially chemical and other methods of evaluation of drugs fail to determine quality. Lycopodium spores are much characterized in shape and appearance

and uniform in size (25 μm) on average, 94000 spores present in 1 mg of lycopodium powder. It consists of:

- Well-defined particles may be counted.
- Single layered cells or tissues the area of which may be traced under suitable magnification and actual area calculated
- The objects of uniform thickness, the length of which can be measured, and the actual area calculated.

The percentage purity of an authentic ginger powder is calculated as follows:

$$\frac{N \times W \times 94,000 \times 100}{S \times M \times P}$$

where, N = number of characteristic structures (starch grains) in 26 fields
W = weight in mg of lycopodium taken
S = number of lycopodium spores in the same 25 fields
M = weight in mg of sample calculated on basis of the dried sample at 105°C
P = 2, 86,000 in case of ginger starch grain powder

Chemical Evaluations

Most drugs have definite chemical constituents to which their biological or pharmacological activity is attributed. Qualitative chemical tests are used to identify certain drugs or to test their purity. The isolation, purification, identification of active constituents is based on chemical methods of evaluation. Qualitative chemical tests such as acid value, saponification value, etc. Some of these are useful in the evaluation of resins (acid value, sulfated ash), balsams (acid value, saponification value, and ester values), volatile oils (acetyl and ester values), and gums (methoxy determination and volatile acidity). Preliminary phytochemical screening is a part of the chemical evaluation. These qualitative chemical tests are useful in the identification of chemical constituents and detection of adulteration.

The following are various methods of chemical evaluation

1. Instrumental methods
2. Chemical tests
3. Individual constituent chemical tests
4. Microchemical tests

1. **Instrumental methods**: They make use of various instruments for evaluation like colorimetry, fluorimetry, spectrophotometry, chromatography, etc.
2. **Chemical constants tests**: These are like acid value, iodine value and ester value, etc. are used for the identification of fixed oils and fats.
3. **Individual chemical tests:** These are the tests that are used for identifying particular drugs.
4. **Microchemical tests**: These are the tests that are carried on slides. Example: eugenol in clove oil is precipitated as potassium alginate crystals.
   - Murexide test—caffeine
   - Thalleoquine test—quinine
   - Vitali-Morin's test—tropane alkaloids

Method for Chemical Evaluation

- The extract obtained using petroleum ether, chloroform, ethanol, and water is prepared using the respective solvent.
- These extracts along with positive and negative controls are tested for the presence of active phytochemicals, viz: Tannins, alkaloids, phytosterols, triterpenoids, flavonoids, cardiac glycosides, anthraquinone glycosides, saponins, carbohydrates, proteins, amino acids, and fixed oils and fats following standard methods

Tannins

1. **Ferric chloride test:** Added a few drops of 5% ferric chloride solution to 2 ml of the test solution. The formation of blue color indicated the presence of hydrolyzable tannins.
2. **Gelatin test:** Added five drops of 1% gelatin containing 10% sodium chloride to 1 ml of the test solution. The formation of white precipitates confirms the test.

Alkaloids

Approximately 50 mg of the extract is dissolved in 5 ml of distilled water. Further 2 M hydrochloric acid is added until an acid reaction occurred and is filtered. The filtrate is tested for the presence of alkaloids as detailed below.

1. **Dragendorff's test:** To 2 ml of the filtrate is added 1 ml of Dragendorff's reagent. The formation of an orange or reddish-brown precipitate indicates the test as positive.
2. **Mayer's test:** To 1 ml of test solution or filtrate is added a drop or two of Mayer's reagent, white or a creamy precipitate confirms the test as positive.
3. **Hager's test:** To 1 ml of test solution or filtrate, a drop or two of Hager's reagent formation of yellow precipitate indicated the test as positive.
4. **Wagner test:** Two drops of Wagner's reagent are added to 1ml of the test solution. The formation of yellow or brown precipitate confirms the test as positive for alkaloids.

Phytosterols

Liebermann-Burchard's test: The extract (2 mg) is dissolved in 2 ml of acetic anhydride, heated to boiling, cooled and then 1 ml of concentrated sulfuric acid is added. A brown ring formation at the junction and the turning of the upper layer to dark green color confirm the test for the presence of phytosterols.

Triterpenoids

Salkowski test: Approximately 2 mg of dry extract is shaken with 1 ml of chloroform and a few drops of concentrated sulfuric acid are added. A red-brown color formed at the interface indicated the test as positive for triterpenoids.

Flavonoids

1. **Shinoda test:** A few magnesium turnings and 5 drops of concentrated hydrochloric acid are added dropwise to 1 ml of test solution. A pink, scarlet, crimson red, or occasionally green to blue color appeared after a few minutes confirming the test.

2. **Alkaline reagent test:** The addition of 5 drops of 5% sodium hydroxide to 1 ml of the test solution increase the intensity of the yellow color which became colorless on the addition of a few drops of 2 M hydrochloric acid which indicate the presence of flavonoids.
3. **Lead acetate test:** A few drops of 10% lead acetate add to 1 ml of the test solution result in the formation of yellow precipitate confirming the presence of flavonoids.

Saponins

1. **Foam test:** 5 ml of the test solution taken in a test tube is shaken well for five minutes. The formation of stable foam confirms the test.
2. **Olive oil test**: Added a few drops of olive oil to 2 ml of the test solution and shaken well. The formation of a soluble emulsion confirmed the test.

Cardiac Glycosides

1. **Keller -Kiliani test:** Added 0.4 ml of glacial acetic acid and a few drops of 5% ferric chloride solution to a little dry extract. Further 0.5 ml of concentrated sulfuric acid is added. The formation of blue color in the acetic acid layer confirms the test.

Physical Evaluations

Physical constants are sometimes taken into consideration to evaluate certain drugs. These include moisture content, specific gravity, optical *rotation*, refractive, melting point, viscosity, and solubility in different solvents. All these physical properties are useful in the identification and detection of constituents present in the plant.

A few of them are:

- Moisture content
- Viscosity
- Melting point
- Optical rotation
- Refractive index
- Ash content
- Extractive values
- Volatile oil content
- Solubility
- Foreign organic matter
- Swelling index
- Foaming index
- Bitterness value

Moisture Content

- The presence of moisture in a crude drug can lead to its deterioration due to either activation of certain enzymes or growth of microbes.
- Moisture content can be determined by heating the drug at 150°C in an oven to a constant weight and calculating the loss of weight.
  - *Aloes:* Not more than 10.2%w/w.
  - *Digitalis:* Not more than 5.3%w/w.
  - *Starch:* Not more than 15%w/w

Viscosity

- The viscosity of a liquid is constant at a given temperature and is an index of its composition.
- Hence, it is used as a means of standardizing liquid drugs. Example: Liquid paraffin– less than 64 centistokes.

Melting Point

- It is one of the parameters to judge the purity of crude drugs containing lipids as constituents.
- They may be of animal or plant origin and contain fixed oils, fats, and waxes.
- The purity of the following crude drugs can be ascertained by determining their melting points in the range shown against each of them
  Example: Coca butter (30°–33°C)

Optical Rotation

- Many substances of biological origin, having a chiral center, can rotate the plane of polarised light either to right or to the left.
- The extent of rotation is expressed in degrees, plus (+) indicating rotation to the right and minus (–) indication rotation in the left.
- Such compound is optically active and hence called optical rotation.
  - Caraway oil: + 75° to +80°
  - Clove oil: 0° to +6.0°
  - Honey: +3° to –15°

Refractive Index

- When a ray of light passes from one medium to another medium of different densities, it is bent from its original path.
- Thus, the ratio of the velocity of light in a vacuum to its velocity in the substance is said to be the refractive index of the second medium.
- It is measured employing a refractometer.
- Example: Arachis oil 1.4678–1.4698

Ash Content

- The residue remaining after incineration of a known quantity of the air-dried crude drug is known as the ash content of the drug.
- Ash simply represents the inorganic salts naturally occurring in the drug or adhering to it or deliberately added to it as a form of adulteration. Example: Total ash
  - *Ashoka:* 11.00 % w/w
  - *Ginger:* 6.00 % w/w

Extractive Values

- In crude drugs, sometimes the active chemical constitutes cannot be determined by normal procedures.
- In such cases, water, alcohol, or ether soluble extractive values are determined for the evaluation of such drugs. Example:
  - *Water soluble extractive (% W/W)*
  - *Aloe vera:* NLT 25.0
  - *Linseed:* NLT 20.0
  - *Senna leaves:* NLT 30.0
  - *Ginger:* NLT 10.0
  - *Glycyrrhiza:* NLT 20.0

NLT—not less than

Volatile Oil Content

- The efficiency of several drugs is due to their odorous principle (volatile oils).
- Such crude drugs are standardized based on their volatile oil contents.
- Weighed quantity of the drug is boiled with water in a round-bottomed flask fitted with clevenger apparatus. The distillate collected is graduated into volatile oil.
- The amount thus obtained is recorded from the tube.
- Volatile oil content is measured as % w/w
  Example:
  - *Caraway NLT 2.5*
  - *Clove NLT 15.0*
  - *Fennel NLT 1.4*

Solubility

The presence of adulterants in a drug could be indicated by solubility studies. Example
- Castor oil soluble in 3 volumes of alcohol
- Balsam of Peru soluble in chloral hydrate solution
- Asafoetida soluble in carbon disulfide
- Alkaloid bases soluble in chloroform
- Colophony soluble in light petroleum

Foreign Organic Matter

The parts of the organ or organs other than those named in the definition and description of the drug are defined as foreign organic matter.
- The maximum limit for the foreign organic matter is defined in the monograph of the crude drug. If it exceeds the limits, deterioration in the quality of the drug takes place.
- The physical or physicochemical parameters useful in the quality profile of a crude drug evaluation

Swelling Factor

Significances
- Useful in the evaluation of crude drugs containing mucilage
- Useful for the detection of identity, quality, and purity of the crude drug

Determination

1. Transfer 1 gm of the seeds to a 25 ml stoppered cylinder
2. Fill up to the 20 ml mark on the cylinder with water. Agitate gently and occasionally during 24 hours and allowed to stand
3. Measure the volume occupied by the swollen seeds

Determination of Foaming Index

Many medicinal plant materials contain saponins that can cause persistent foam when an aqueous decoction is shaken. The foaming ability of an aqueous decoction of plant materials and their extracts is measured in terms of a foaming index.

Bitterness Value

Medicinal plant materials that have a strong bitter taste ("bitters") are employed therapeutically, mostly as appetizing agents. Their bitterness stimulates secretions in the gastrointestinal tract, especially gastric juice. Bitter substances can be determined chemically. However, since they are mostly composed of two or more constituents with various degrees of bitterness, it is first necessary to measure total bitterness by taste. The bitter properties of plant material are determined by comparing the threshold bitter concentration of an extract of the materials with that of a dilute solution of quinine hydrochloride R. The bitterness value is expressed in units equivalent to the bitterness of a solution containing 1 g of quinine hydrochloride R in 2000 ml.

Biological Evaluations

Some drugs have a specific biological and pharmacological activity that is utilized for their evaluation. This activity is due to a specific type of constituents present in the plant extract. For evaluation, the experiments were carried out on both intact and isolated organs of living animals. With the help of bioassays (testing the drugs on living animals), the strength of the drug in its preparation can also be evaluated.

Indication of Biological Evaluation

- When the chemical nature of the drug is not known but it has a biological action.
- When chemical methods are not available.
- When the quantity of the drug is small and so it cannot be evaluated chemically.
- Drugs that have different chemical compositions but the same biological activity.
- Example: Cardiac glycosides are evaluated by this method on cats, frogs, or pigeons.

Significance

- The method is generally used when standardization is not done satisfactorily by chemical or physical methods
- When the quantity of the drug/sample is very less than the drugs are evaluated by biological methods.
- These methods are performed on living animals, isolating living organs and tissue, animal preparation, and microorganism (bioassay)

CAMERA LUCIDA

A camera lucida (CL) is an optical device used for drawing diagrams of microscopic structures with the help of a compound microscope. It was invented in 1806 by WH. Wollaston and Christian Gobrecht. The term"camera lucida" means "lit room" in Latin. The CL performs an optical superimposition of the subject being viewed and the surface on which the observer is drawing. The person sees both the image of the specimen and the drawing surface simultaneously, as in a photographic double exposure, This allows the person to trace the outlines of the image using a pencil. If white paper is used, the superimposition of the paper with the scene tends to wash out the scene, making it

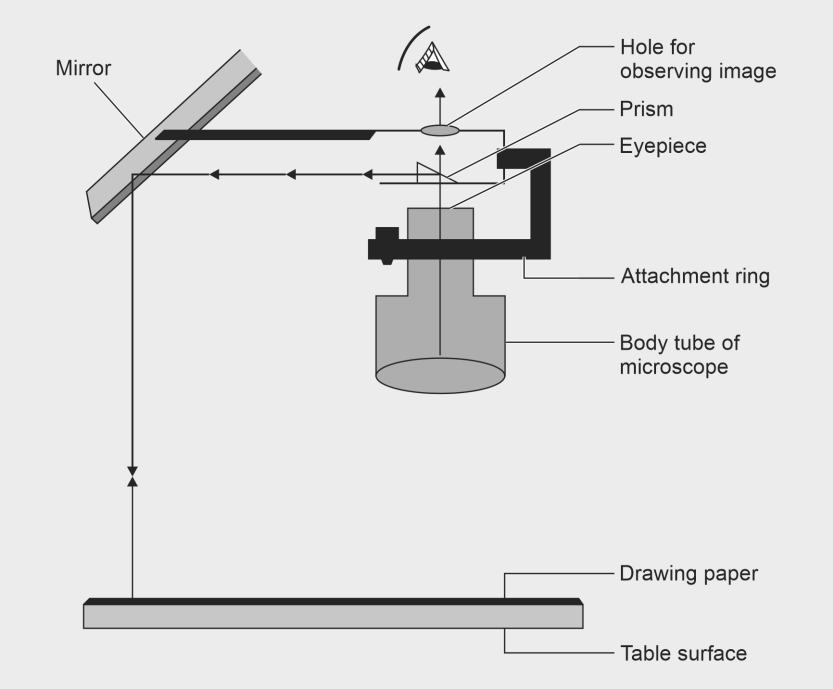

Fig. 1.1: Diagrammatic represents of camera lucida

difficult to view. CL works on a simple optical principle reflecting the beam of light through a prism and a plane mirror. CL (Fig. 1.1), when attached with a compound microscope, helps draw microscope images of objects on paper.

The microscopic image of the object is reflected by the prism onto the plane mirror and there from the image is reflected onto the plane white paper. The person who observes moves the pencil on the lines of the image and draws a correct and faithful figure of the object on the paper. There are three main parts of a CL the attachment ring, the prism, and the mirror. The attachment ring attaches the CL with the body tube of the microscope. The prism rests just above the eyepiece when the instrument is attached to the microscope. The observer now views the image of the object under the microscope through the prism which reflects the image horizontally onto the plane mirror. The plane mirror, attached at the tip of an arm rotates and is set at an angle of 45° about the prism and the plane paper.

Working Principle

CL works on a simple optical principle reflecting a beam of light through a prism and a plane mirror. The microscopic image of the object is reflected by the prism onto the plane mirror and there from the image is reflected onto the plane paper. When working with a CL it is beneficial to use black paper and to draw with a white pencil. CL sketches are often used to supplement photomicrographs to make clear illustrations of a structure. In many cases, drawings on camera lucida may provide more clarity and comprehension than photomicrographs. Thus, histological and microanatomical illustrations are often camera lucida drawings rather than photomicrographs.

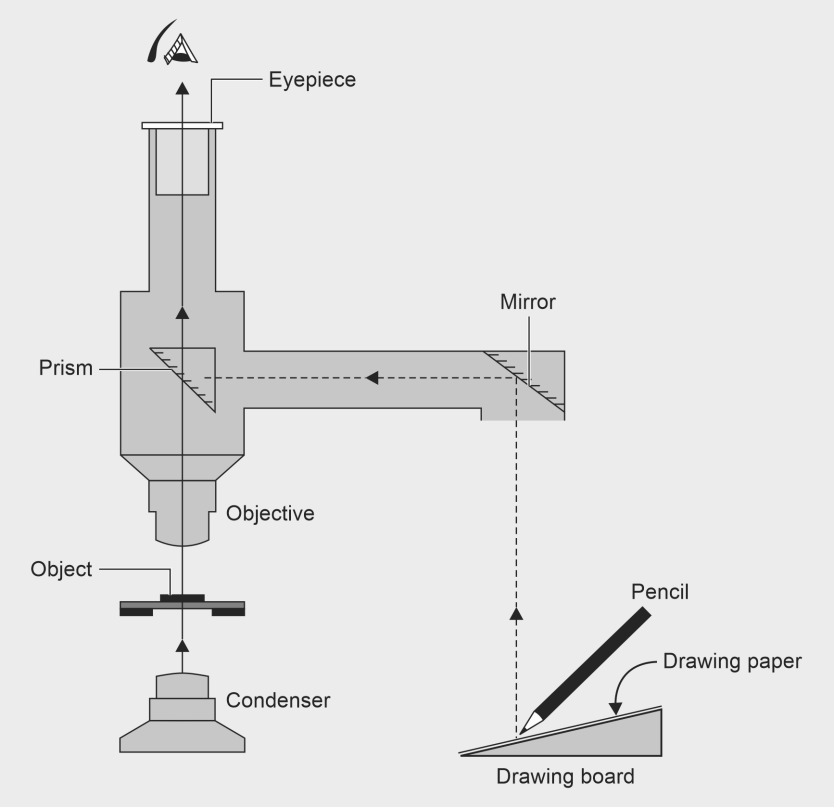

Fig. 1.2: Diagrammatic represents working principle of camera lucida

Application of Camera Lucida in Pharmacognosy

- It can be used for the determination of stomatal numbers in a leaf
- It can be used for the determination of vein termination numbers in a leaf
- It can be used for the determination of vein islet number in a leaf
- It can be used for the determination of palisade ration in a leaf
- It can be used for the determination of the stomatal index in a leaf
- It can be used for the determination of stomatal numbers in a leaf
- It can be used for the determination of crystals in a leaf
- It can be used for the determination of starch grain in a leaf

QUESTIONS

Short Questions

1. Define marine pharmacognosy.
2. Write anti-cancer drugs derived from marine sources.
3. Write anti-microbial drugs from marine origin.
4. Classify marine source drugs with examples.

5. Give any three cardiovascular drugs of the marine source.
6. Give any three marine-derived antibiotics.
7. Define crude drug.
8. Name the various methods of drugs evaluation.
9. What do you mean by organized (cellular) and unorganized (acellular) crude drugs, give examples?
10. Define pharmacognosy
11. Compare between organized and unorganized crude drug.

Long Questions

1. Describe the morphological classification of crude drugs with examples.
2. Explain the chemical classification of crude drugs with examples.
3. Explain morphological classification of crude drugs with examples.
4. Explain the pharmacological or therapeutic classification of crude drugs with examples.
5. Write in detail alphabetical and taxonomical or botanical classification of crude drugs.
6. Define chemotaxonomy and serotaxonomy. Give its significance or importance
7. Explain the differences between organized and unorganized crude drugs.
8. Define crude drugs. Explain various methods of classification of crude drugs with examples.
9. Discuss on chemical evaluation of crude drug.
10. Define adulteration. Discuss various methods for adulteration in crude drug.
11. How can you detect adulteration by physical methods?
12. Write scope of pharmacognosy in detail.
13. Discuss the historical development of pharmacognosy.
14. Discuss on medicinal agent from marine source.
15. Enlist the quality control parameters as per WHO guideline.
16. What are the basic working principle and application of camera lucida?