EXTRACTION OF PLANT MATERIAL:

Introduction

Medicinal plants are the richest bioresource of drugs for traditional systems of medicine, modern medicines, nutraceuticals, food supplements, cosmetic, pharmaceutical intermediates and chemical entities for synthetic drugs.

Hence, plant materials contain numerous active compounds with high nutritional or therapeutic values.

Plants synthesize a vast range of organic compounds that are traditionally classified as primary and secondary metabolites although the precise boundaries between the two groups can in some instances be somewhat blurred. **Primary metabolites** are compounds that have essential roles associated with photosynthesis, respiration, and growth and development. These include phytosterols, lipids, nucleotides, amino acids and organic acids. **Secondary compounds** were once regarded as simple waste products of a plant's metabolism, their function in plants is protecting plants from herbivores, microbial infection, UV radiation,.. etc. Secondary metabolites are also of interest because of their use as dyes, fibres, glues, oils, waxes, flavouring agents, drugs and perfumes, and they are viewed as potential sources of new natural drugs, antibiotics, insecticides and herbicides. Based on their biosynthetic origins, plant secondary metabolites can be divided into three major groups: (i) phenolic and polyphenolic compounds, (ii) terpenoids and (iii) nitrogen-containing alkaloids andsulphur-containing compounds.

(i) Phenolic and polyphenolic compounds

C6–C1 Phenolic acids.

C6–C2 Acetophenones.

C6–C3 Hydroxycinnamic acids.

C6–C4 Naphthoquinones

C6–C1–C6 Xanthones

C6–C2–C6 Stilbenes.

C6–C3–C6 Flavonoids.

Phenolic acids.

They are aromatic alcohols since the hydroxyl group is always attached to a benzene ring.

Addition of a carboxyl group to the basic phenol structure produces a group of C6C1 compounds.

hydroxycinnamic acids.

These are C6C3 compounds, made up of a benzene ring with a threecarbon side chain.

Lignans are compounds with phenylpropane (C6C3) units
Coumarins are lactones of hydroxycinnamic acids, with cyclic C6C3 skeletons.
Flavonoids are polyphenolic compounds comprising fifteen carbons, with two aromatic rings connected by a three-carbon bridge. They are the most numerous of the phenolics and are found throughout the plant kingdom.
Tannins represent the largest group of polyphenols. They are widely distributed in the bark of trees, insect galls, leaves, stems and fruit.
(ii) **Terpenoids, or terpenes**, comprise one of the most important groups of active compounds in plants with over 20 000 known structures. All terpenoid structures may be divided into isoprene (five-carbon) nits containing two unsaturated bonds**.**
(iii) nitrogen-containing alkaloids: alkaloids are alkaline organic compounds containing one or more nitrogen atoms, each connected to at least two carbon atoms within a heterocyclic ring system.
Glycosides are a group of compounds characterised by the fact that chemically they consist of a sugar portion (or moiety) attached by a special bond to one or more non-sugar portions.

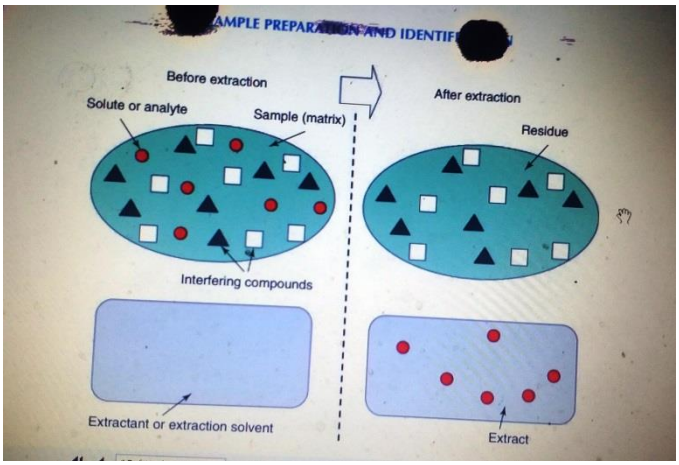
Extraction

The crude drug contains the active constituents, which can be isolated from these drugs by various methods of extraction and separation.
Extraction is defined as the process of isolation of soluble material from an insoluble residue, which may be liquid or solid, by treatment with a solvent on the basis of the chemical and physical nature of crude drug to be extracted, i.e. liquid or solid, the extraction process may be liquid—liquid or solid—liquid extraction.
The products (extract) so obtained from plants are relatively liquids, semisolids or solid of mixture of compounds. These include classes of preparations known as decoctions, infusions, fluid extracts, tinctures, semisolid extracts and solid extracts. Such preparations popularly have been called **galenicals**, named after Galen, the second century Greek physician.

Principle of extraction

The basic principle of extraction refers to the distribution of a compound (active constituent) between two immiscible phases, enabling their further separation and recovery of the extracted compound, and the distribution of a compounds based on the polarity (relative solubility in organic solvents) - like dissolves like.
Commonly, the compounds of interest are called the solutes or analytes; other compounds present with no interest are named interferences or interfering compounds. The initial plant material containing the compound to be extracted is named the sample or sample matrix. The nonmiscible phase is called the extractant

or the extraction solvent, being generally a liquid solvent or a supercritical fluid; however, in some cases, it can be a solid phase (sorbent). Once the extraction step is performed, the sample is discarded from the extraction solvent containing the extracted solute (named the extract); the remaining sample matrix discarded is often referred to as the residue (marc). In some cases, this residue is submitted again to one or more successive extractions (possibly under more stringent conditions), to recover part of the solute not extracted during the first step.

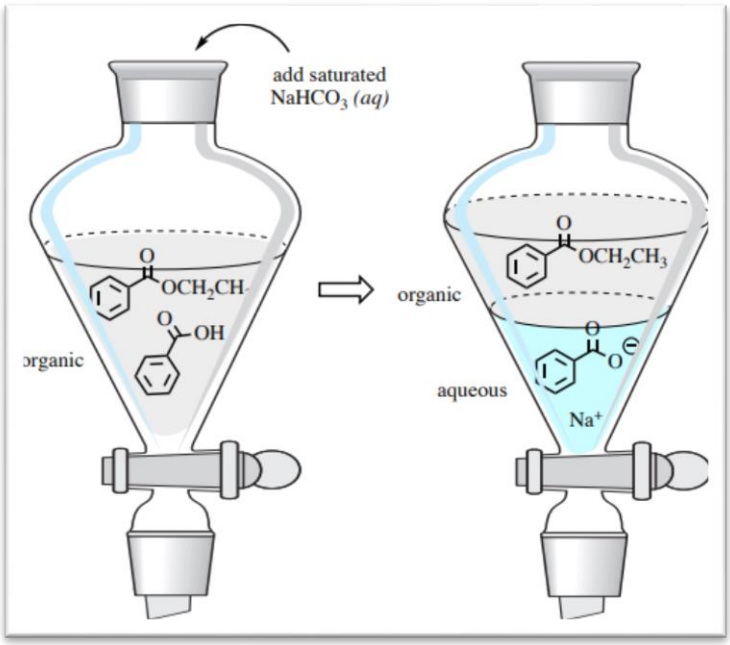


The main challenge of the extraction step is to selectively (i.e., without those interfering compounds) and possibly quantitatively (i.e., all the analyte molecules initially in the sample) extract the analytes. To achieve this goal, efficient contact between the sample and the extractant is required; as discussed later, this can be achieved by mixing, but other ways are also used.

Extraction from Liquids:

Extraction from liquids is rather simple, because of availability of solutes. The process is driven initially by partitioning of the solute between the liquid sample and the extractant (mostly a liquid in classical liquid–liquid extraction (LLE), or a sorbent in solid-phase extraction (SPE)), and the only requirement being that the extractant must not be miscible with the sample to ensure isolation of the extract.

Then, as the extraction goes on, diffusion of the solute across the liquid–liquid boundary layer becomes limiting (in case of stirring, diffusion in the bulk phases can be neglected); it mainly depends on solute shape and size, as well as on solvent viscosity.



Extraction from Solids:

Extraction from solid matrices is more difficult. In that case, the compounds of interest must be released from the solid substrate to

achieve their extraction by the solvent; thereby, diffusion inside the solid matrix may be the limiting step. In addition, when solutes are strongly adsorbed onto the matrix, the energy of interaction between the compounds and the matrix must be overcome; besides when the solutes are retained in plant organs or cells, extraction conditions must be strong enough to disrupt the cells; otherwise, the solutes will not be available for the extracting solvent.

The extraction and recovery of a solute from a solid matrix can be regarded as a fve-stage process (Figure 3): (1) desorption of the compound from the matrix active sites; (2) diffusion into the matrix itself; (3) solubilization of the analyte by the extractant; (4) diffusion of the compound in the extractant present within the pore; and (5) transportation to the bulk extractant before final collection of the extracted solute. The obtaining of quantitative and reproducible recoveries necessitates the careful control and optimization of each step; in particular, collection of the extract needs to be carefully controlled as it is often neglected as compared to the extraction step, whereas it may lead to partial losses.

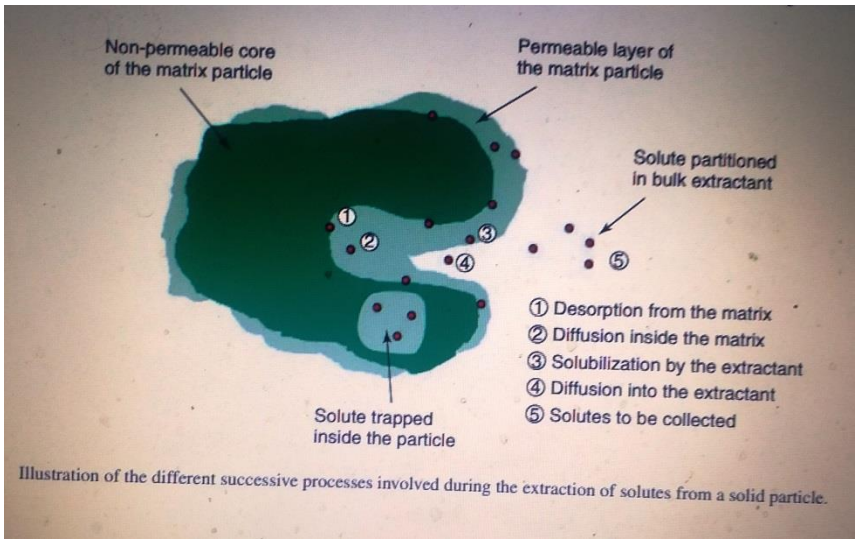


Illustration of the different successive processes involved during the extraction of solutes from a solid particle.

Factors to consider in plant extraction

Several factors need to be considered before optimization of the experimental conditions.

1- Plant Matrix and Extraction method.
2- Particle size of the plant parts
3- Solvent used,
4- The solvent-to-sample ratio.
5- Temperature
6- Extraction time

Plant Matrix and Extraction method

Both fresh and dried sample is used, In most cases, dried sample is preferred because enzymes are absent in dried sample and also grinding of dray sample is easy then fresh. Plant Matrix my be leaves, flowers, Roots, rhizomes, Stems, barks, seeds, …

Different objectives may lead to different extraction techniques and/or methods. The key point is whether the plants to be extracted contain known compounds or unknown structures that are looked for, especially as thermal stability of the solutes may be important. Knowing the **macroscopic structure** of the matrix and **the localization** of the analytes inside is also very useful, especially if they are expected to be contained inside the cellular matrix of the plant material (e.g., essential oil). **Drying** may be recommended as mentioned earlier.

Size reduction (Particle size of the plant parts)

- Usually, the plant material is reduced to a size between 30 and 40 meshes, but this can be changed if the need arises. The objective for powdering the plant material is to rupture its organ, tissue and cell structures so that its medicinal ingredients are exposed to the extraction solvent. Furthermore, size reduction maximizes the surface area, which in turn enhances the mass transfer of active principle from plant material to the solvent. The 30-40 mesh size is optimal, while smaller particles may become slimy during extraction and create difficulty during filtration.
- In addition, to enhance the solute availability, grinding finely the matrix is of prime importance, grinding enables the breaking of some cells, and the subsequent release of solutes contained inside. However, too fine particles may lead to clogging, or to the formation of channels inside the sample that will prevent the solvent to penetrate through the sample matrix.

The choice of extraction procedure depends on the nature of the plant material & the components to be isolated.

- If the constituents are thermos-unstable, extraction methods like cold maceration, percolation are preferred. For thermostable constituents, Soxhlet extraction (if nonaqueous solvents are used) and decoction (if water is the menstruum) are useful.
- Suitable precautions should be taken when dealing with constituents that degrade while being kept in organic solvents, e.g. flavonoids and phenyl propanoids. In case of hot extraction, higher than required temperature should be avoided. Some glycosides are likely to break upon continuous exposure to higher temperature.

- If the extraction time is longer, unwanted constituents may also be extracted. For example, if tea is boiled for too long, tannins are extracted which impart astringency to the final preparation.
- The number of extractions required for complete extraction is as important as the duration of each extraction.

Solvent used

Plant constituents are usually contained inside the cells. Therefore, the solvent used for extraction must diffuse into the cell to dissolve the desired compounds whereupon the solution must pass the cell wall in the opposite direction and mix with the surrounding liquid. Equilibrium is established between the solute inside the cells and the solvent surrounding the fragmented plant tissues.

Modern methods of extraction and isolation of natural products are based on the **polarity** (relative solubility in organic solvents) - **like dissolves like**. This means polar solvents (Methanol, ethanol, and water) dissolve polar molecules, such as glycosides, phenols, saponins and salts. Nonpolar solvents (ether, hexane) dissolve nonpolar molecules such as terpenoids, fats and other organic compounds.

Successful extraction of biologically active compounds from plant material is largely dependent on the type of solvent used in the extraction procedure. According to the pharmacopoeias, ***ethyl alcohol*** is the solvent of choice for obtaining classic extracts such as tinctures and fluid, soft and dry extracts.

The solvent-to-sample ratio is one of important factor for god extraction. The optimum ratio is 1 part of plant sample to 10 part of solvent.

The temperature and extraction time have a considerable effect on the rate of extraction of crude drugs. In general, the extraction increases with increasing temperature and time, but increasing of temperature depends on the nature of the plant material & the components to be isolated.

The ideal solvent for a certain pharmacologically active constituent should:

1. Be highly selective for the compound to be extracted.
2. Have a high capacity for extraction in terms of coefficient of saturation of the compound in the medium.
3. Not react with the extracted compound or with other compounds in the plant material.
4. Have a low price.
5. Be harmless to man and to the environment.
6. Be completely volatile.

EXTRACTION TECHNIQUES FOR PLANT MATERIALS

Basically, one can distinguish the so-called traditional techniques, which have been used for years and modern techniques that have appeared in recent 20years, with a view of reducing both the time and the solvent volume required for the extraction.

- *There are many procedures (methods) for obtaining extracts like:*

1. Infusion
2. Maceration
3. Digestion
4. Decoction
5. Percolation
6. Continuous hot extraction

Infusion

In this method, the plant material (herbal tea) is placed in a pot and wetted with cold or boiling water. Immediately afterwards, boiling water is poured over it, then left to stand covered with a lid, for about fifteen minutes after which the extract (tea) is poured off.

Drug

- Crude drugs of light structure without dense tissues and containing water-soluble constituents.
- The drug may be freshly broken, thinly sliced, cut small or coarsely powdered in order to facilitate the solvent penetration.

Examples: Teas- Senna infusion

Maceration

Maceration is the process of soaking the drug in a solvent with or without the application of heat, until the tissues become softened and the soluble constituents has been dissolved.

Mixing the whole or ground drug with the solvent (drug/solvent ratio: 1:5 or 1:10)Leaving the mixture for several hours to several days with occasional shaking or stirring. The extract is then separated from the plant particles by straining. The procedure is repeated once or twice with fresh solvent. Finally the last residue of extract is pressed out of the plant particles

Digestion: This is a form of maceration in which gentle heat is used during the process of extraction. It is used when moderately elevated temperature is not objectionable. This method is suitable for hard barks or woods which are difficult

for water to penetrate. As a general rule the temperature of the extracting medium should be in the range from 35-40° but not exceeding 50°.

Decoction

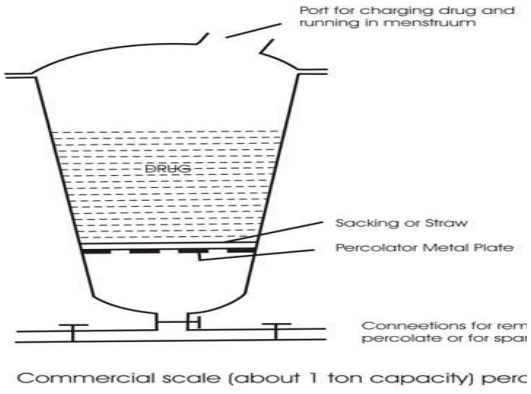
In this process, the crude drug is boiled in a specified volume of water for a defined time; it is then cooled and strained or filtered. This procedure is suitable for extracting water-soluble, heat-stable constituents. The starting ratio of crude drug to water is fixed, e.g. 1:4 or 1:16; the volume is then brought down to one-fourth its original volume by boiling during the extraction procedure. Then, the concentrated extract is filtered and used as such or processed further.

Percolation

Simple percolation: Simple percolation process involves three stages:

Imbibition: Uniform moistening of the raw material with the solvent for a period of 4 hrs. in a separate closed vessel. After imbibition, the drug is packed evenly into the percolator.

Maceration: Sufficient solvent is added to maintain layer above the drug and allowed to stand for 24 h. The 24-h maceration period allows the solvent to diffuse through the drug, solubilize the constituents and leach out the soluble material.



Commercial scale (about 1 ton capacity) perc

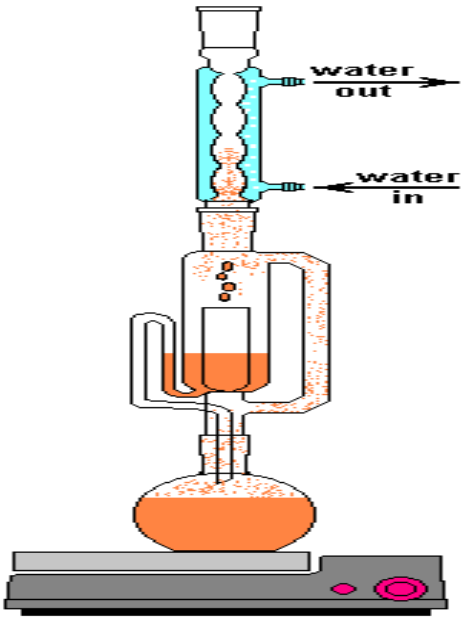
Percolation: The outlet is opened and the solvent is percolated at a controlled rate with continuous addition of fresh solvent. About 75% of the volume of the finished product is collected.

This is the procedure used most frequently to extract active ingredients in the preparation of tinctures and fluid extracts. A percolator (a narrow, cone-shaped vessel open at both ends) is generally used.

Marc: name of the inert fibrous and other insoluble materials remaining after extraction

Continuous hot extraction (Exhaustive Extraction)

In this method, the finely ground crude drug is placed in a porous bag or "thimble" made of strong filter paper, which is placed in chamber E of the **Soxhlet apparatus**. The extracting solvent in flask A is heated, and its vapors condense in condenser D. The condensed solvent drips into the



thimble containing the crude drug, and extracts it by contact. When the level of liquid in chamber E rises to the top of siphon tube C, the liquid contents of chamber E siphon into flask A. This process is continuous and is carried out until the liquid siphoned into flask A is clear.

A Soxhlet extractor is a piece of laboratory apparatus invented in 1879 by **Franz von Soxhlet**. It was originally designed for the extraction of a lipid from a solid material.

The advantage of this method, compared to previously described methods, is that large amounts of drug can be extracted with a much smaller quantity of solvent. This effects tremendous economy in terms of time, energy and consequently financial inputs. At small scale, it is employed as a batch process only, but it becomes much more economical and viable when converted into a continuous extraction procedure on medium or large scale.

Recent Extraction Techniques

Supercritical Fluid Extraction: It is the process of separating using supercritical fluids as the extracting solvent

The supercritical fluid state occurs when a fluid is above its critical temperature (Tc) and critical pressure (Pc), when it is between the typical gas and liquid state. Manipulating the temperature and pressure of the fluid can solubilize the material of interest and selectively extract it.

Carbon dioxide (CO_2) is the most used supercritical fluid. Extraction conditions for **Supercritical carbon dioxide** are above the critical temperature of 31°C and critical pressure of 74 bars. There are many advantages to the use of CO2 as the extracting fluid. In addition to its favorable physical properties, carbon dioxide is inexpensive, safe and abundant. But while carbon dioxide is the preferred fluid for SFE, it possesses several polarity limitations. Organic solvents are frequently added to the carbon dioxide extracting fluid to alleviate the polarity limitations.

Filtration

The extract obtained is separated out from the marc (exhausted plant material) by filtration it through appropriate filter.

Concentration

The filtered liquid extract is subjected to drying to obtain concentrated extract and to remove excess solvents from samples. An important concept that this technique applies is that liquids boil when the vapor pressure is equal to the external pressure or atmospheric pressure.

ISOLATION AND PURIFICATION OF THE CONSTITUENTS

The most difficult operation in phytochemical research is to isolate & purify plant constituents. Mostly it depends upon the physical and chemical characteristics of the compound to be separated.

The physical methods used for the isolation and purification:

- Sublimation
- Distillation
- Fractional liberation
- Fractional crystallization
- liquid – liquid extraction
- Chromatography

DISTILLATION

Distillation is a process of separating the component substances from a liquid mixture by selective evaporation and condensation. It used to separate volatile substances. For a liquid, this process is called **vaporization** and for a solid it is called **sublimation.**

The Process of Distillation

The process of distillation begins with heating a liquid to **boiling point**. The liquid evaporates, forming a **vapor**. The vapor is then cooled, usually by passing it through pipes or tubes at a lower temperature. The cooled vapor then condenses, forming a **distillate**. The distillate is a purified form of the original liquid. When the liquid evaporates, many impurities are left behind, so they are not present in the distillate.

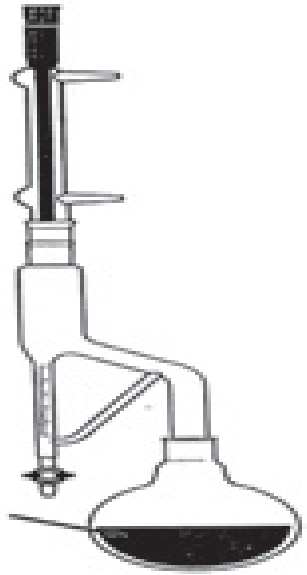
Separation of components from a liquid mixture via distillation depends on the *differences in boiling points* of the individual components. Also, depending on the *concentrations of the components present*, the liquid mixture will have different boiling point characteristics. Therefore, distillation processes depends on *the vapor pressure characteristics of liquid mixtures*.

Chemists use distillation **to purify** compounds in solution or to **separate** mixtures of solutes. For example, different compounds have different boiling points. This property means that a *more volatile* compound will evaporate at a *lower temperature* than a less volatile compound.

Three Types of distillation: Three are three types of distillation:

- Water distillation

- Water and steam distillation
- Direct steam distillation



Clevenger apparatus

Water Distillation: In this method, the material is completely immersed in water, which is boiled by applying heat by direct fire, steam jacket, closed steam jacket, closed steam coil or open steam coil. The main characteristic of this process is that there is direct contact between boiling water and plant material. The laboratory apparatus recommended for trial distillations is the **Clevenger system**.

In water and steam distillation, the steam can be generated either in a satellite boiler or within the still, although separated from the plant material. Direct steam distillation is the process of distilling plant material with steam generated outside the still in a satellite steam generator generally referred to as a boiler.

The Concept of Direct Steam Distillation

-At atmospheric pressure, high-boiling liquids cannot be purified by distillation, since components of the liquid may decompose at the high temperatures required.

-Often the high-boiling substances are essentially insoluble in water, so a separation at lower temperatures can be obtained by *steam distillation*.

- Steam distillation is often used to separate a high-boiling component from small amounts of nonvolatile

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Volatile organic compounds

Plants produce a broad range of volatile organic compounds, with the largest groups being **terpenoids** (compounds with an isoprenoid structure similar to that of the terpene hydrocarbons) Terpenoids contribute to many different scents. For example, the smell of pine trees comes from **pinene**, the smell of ginger is **zingiberene**, whereas **limonene** contributes to the taste and smell of many citrus fruits.

Terpenoids are synthesized through polymerization of C_5 isoprene units. Monoterpenes (composed from two isoprene subunits), diterpenes (composed from

four isoprene subunits), and tetraterpenes (composed from eight isoprene subunits) are produced in the plastids of plants. Volatile oils (are mixture of terpenoids) and terpenoid compounds are obtained from plants by distillation methods.

SUBLIMATION

Sublimation is a technique in which a solid is heated and vaporized, without passing through the liquid phase. The gas is then condensed and collected as a solid. Successful sublimation of material from the crude mixture will result in the formation of crystals on the bottom outside of the cold finger. **Sublimation** is sometimes possible on whole drugs (e.g. isolating caffeine from tea).

FRACTIONAL LIBERATION

Some groups of compounds can be fractionally isolated (liberated) from a mixture.

E.g. A mixture of alkaloid salts in aqueous solution is treated with aliquots of alkali liberates the weakest base first, followed by the liberation of other bases in an ascending order of basicity. If the mixture is shaken with an organic solvent after each addition, then a fractionated series of bases will be obtained.

FRACTIONAL CRYSTALLIZATION

Crystallization is one of the most powerful purification methods and used in isolation of compounds.

The method exploits the differences in solubility of the components of a mixture in particular solvent. The separation of two solutes from the same solution by using either a solvent or a crystallization temperature such that only one solute is supersaturated and crystallizes out. The processes such as concentration, slow evaporation, refrigeration are used for crystallizing the products.

PLANT DRUG FORMS

Phytomedicines

Phytomedicines are drug products made from botanicals; whole extracts, fractions of active plant constituents or pure compounds. They are available in solid and liquid form.

A good example of this is the plant chemical quinine, which was discovered in a rainforest tree (Cinchona ledgeriana) over 100 years ago. For many years the quinine chemical was extracted from the bark of this tree and processed into pills to treat malaria. Then a scientist was able to synthesize or copy this plant alkaloid into a chemical drug without using the original tree bark for manufacturing the drug. Today, all quinine drugs sold are manufactured chemically without the use of any

tree bark. However, another chemical in the tree called quinidine which was found to be useful for various heart conditions couldn't be completely copied in the laboratory and the tree bark is still harvested and used to extract this plant chemical from it. Quinidine extracted from the bark is still used today to produce quinidine-based drugs

- **Crude drugs** generally simply called crude drug.
- **Galenical preparations** including 'instant teas,' and tinctures, ethanolic extracts, essential oils, fatty acids and dried extracts. Medicines prepared according to the formulae of **Galen**.
  - A medicinal preparation composed mainly of herbal or vegetable matter.
  - It is prepared by extraction of crude vegetable drugs (active principles) with suitable solvent(s).
  - The term is now used to denote standard preparations containing one or more active constituents of a plant and made by a process that leaves the inert and other undesirable constituents of the plant un-dissolved.
- **Standardized extracts**, generally with relatively well-established clinical and pharmacological profiles.
- **Non-standardized extracts**, with varying information about quality and, consequently, sometimes uncertain information about clinical efficacy and pharmacological effects
- **Pure compounds**, which are often isolated from botanical drugs (and which are not considered to be herbal medicines)
- **Semithynthetic product**, e.g. etoposide, teniposide, hyoscine butyl bromide etc..

Standardized extracts

An extract is a concentrated preparation of liquid (fluid extract or tinctures) or intermediate (semi-liquid) or solid (dry extract) consistency normally produced from botanical material. Standardized extracts are extracts for which the active constituents (single or groups) are known. They can thus be standardized to a defined content of the active constituent(s) giving a clearly defined amount of an active natural product. Examples include:

- **digitalis leaf extract** (Digitalis folium, foxglove)
- **senna** dry extracts: standardized to 5.5–8.0% hydroxyanthracene glycosides, calculated as sennoside B with reference to dried extract.

- **belladonna leaf** dry extract (Belladonnae folium from Atropa belladonna L., deadly nightshade:(standardized to 0.95–1.05% of alkaloids calculated as hyoscyamine (Eur. Ph.)
- **Ginger**

  Ginger oleoresin, which is widely used in the food industry, is prepared by organic solvent extraction (hexane, acetone, ether, alcohol).

  Powdered ginger root has also been used in the form of capsules to treat motion sickness.

  The newest indication for ginger root is to relieve rheumatic pain and help the mobility of joints.

  The active principles are believed to be gingerols, and extracts are standardized to a certain content of gingerols.
- **Ginseng**

  The ginseng root contain numerous compounds, but the ones considered active are the so-called ginsenosides (about 20).

  They are saponins, glycosides of tetracyclic aglycones.

  It is used as a tonic for invigoration for fatigue and reduced work capacity and concentration and during convalescence.
- **Ginkgo**

  The leaves of the ginkgo *(Ginkgo biloba* L.) contain two groups of pharmacologically interesting compounds, flavonoids (0.5-1%) and terpenes (diterpenes up to 0.5% and sesquiterpenes).

  The ginkgo extract promotes vasodilatation and improves the blood flow in both arteries and capillaries.

  Ginkgo has been the subject of numerous clinical trials for "cerebral insufficiency," and some positive results have been published concerning the use of ginkgo in Alzheimer's disease.

Pure compounds

Artemisinin: Antimalarial properties of extracts of *Artemisia annua* L., a traditional Chinese drug for fevers and malaria. It is an endoperoxide found in the dried aerial parts of the plant. Selectively toxic to various species of *Plasmodium (falciparum, vivax, ovale)* in vitro and in vivo. Synthetic efforts have yielded active derivatives, including *a* and B-artemethers, artether, and artesunate.

Cardiac Glycosides: Two of the *Digitalis* genus, *D. purpurea* L and *D. lanata* Ehrh., are used for the extraction of digitoxin and digoxin. They are still

important drugs in the treatment of heart insufficiency, although synthetic drugs, e.g., B-blockers, are also used.

Morphine: Raw opium is the air-dried latex obtained by incision from the unripe capsules of opium poppy Papaver *somniferum* L. It contains not less than 10.0% morphine and not less than 2.0% codeine. Morphine is the main alkaloid of opium and is known as a powerful analgesic that acts via the central nervous system. Codeine is present in small amounts in opium (about 2%) and can be extracted, but it is usually produced by semisynthesis, i.e., methylation, from morphine.

Diosgenin, obtained from various *Dioscorea* species (yams), is suitable for the manufacture of oral contraceptives and sex hormones.

Hecogenin (plant steroid) provides a practical starting material for the synthesis of corticosteroids.

Taxol and docetaxel *Taxus brevifolia* Nutt are indicated in the therapy of advanced ovarian and breast cancer

Tropane Alkaloids: Tropane alkaloids, mainly atropine and scopolamine, are isolated mainly from *datura stamonium*, *atropa belladonna*, ..

Vinblastine and vincristine are binary indole alkaloids isolated from the aerial parts of the Madagascan periwinkle *(Catharanthus roseus* G. Don syn. *Vinca rosea* L.).

The liquid form include: tinctures, syrups, medicinal oils, medicinal spirits and plant juices. The solid form include: granules, tablets, capsules and lozenges.