

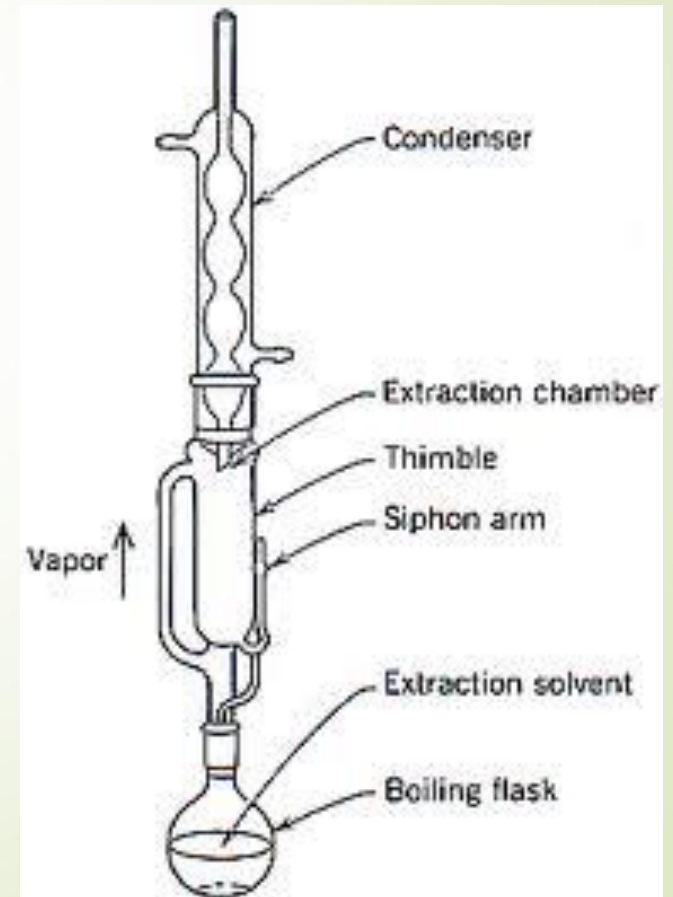
Pharmaceutical Extraction

PHM 2010
Introduction to Pharmaceutical
Technology

2022

EXTRACTION (extractio);


The act of drawing one part out of a compound
Derivation from an original; lineage; descent



EXTRACTION;

- ▶ Extraction, as the term is used pharmaceutically, involves the separation of medicinally active portions of **plant or animal tissues** from the inactive or inert components by using selective solvents in standard extraction procedures.

- ▶ The products obtained from plants are relatively **impure liquids, semisolids, or powders** intended only for oral or external use.

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- Extraction products include classes of preparations known as:
 - Decoctions
 - Infusions
 - fluid extracts,
 - Tinctures
 - pilular (semisolid) extracts
 - powdered extracts.
 - Such preparations popularly have been called galenicals, after Galen, the 2nd century Greek physician.

Extraction for pharmaceutical purposes;

1- To take the essence of drugs using a solvent or to remove certain substances from drugs

Liquid–liquid extraction, also known as partitioning, is a separation process consisting of the transfer of a solute from one **solvent** to another, the two solvents being immiscible or partially miscible with each other

Extraction for pharmaceutical purposes;

2. Extraction of Crude Drugs

-Extraction of active agents from plants, separate unwanted compounds and concentrate the active compound


Alkaloids, tannins, glycosides, oils, resins, oleoresins, essential oils

-Extraction of excipients from plants,

Pectins, mucilages, gums, starches, sugars



Extracts can be classified due to:

- Solvent used;
 - Aqueous extracts
 - Alcoholic extracts
 - Etheric extracts
 - Hydro-alcoholic extracts
 - Etheric-alcoholic extracts
 - Their consistency
 - Preparation method
 - Extraction of dried drogs
 - Extraction of dissolved substances in liquids
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Extraction of dissolved substances in liquids

Explained by «Nernst Distribution Law (1891) or Partition Law»

- This law determines the relative distribution of a component that is soluble in two liquids, these liquids being immiscible or miscible to a limited extent.
- The Nernst distribution law states that, “at equilibrium, the ratio of the concentrations of a third component in two liquid phases is constant.”

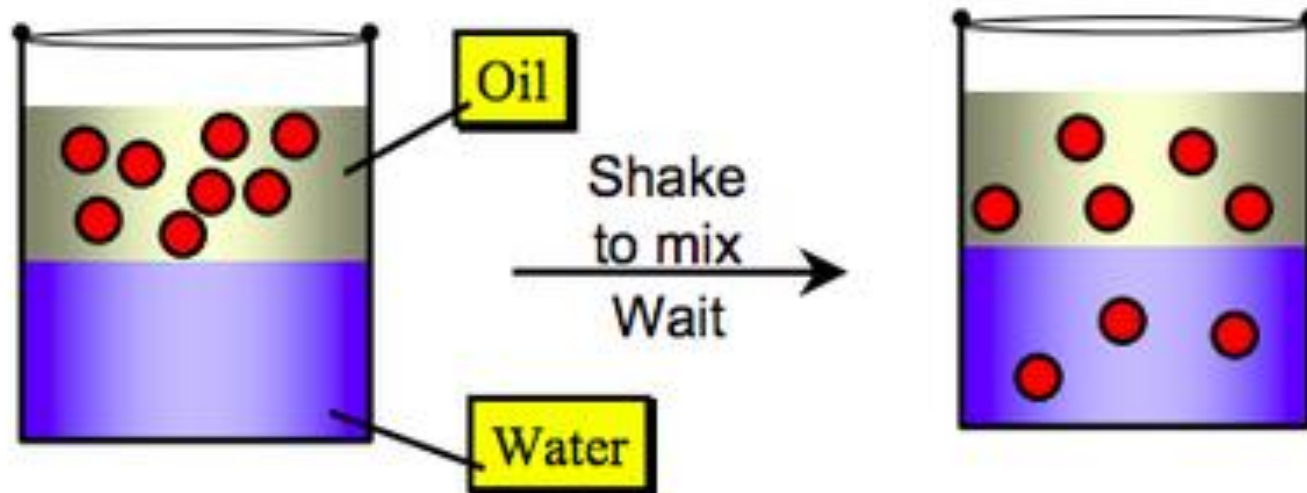


Fig. 2 Partition Coefficient - a substance added to a mixture of oil and water will dissolve in each. At equilibrium the chemical potential (free energy) will be the same in both phases.

The partition coefficient is determined by measuring the concentration of drug in the oil and water phases

- Partition Coefficient = $PC = \frac{[Drug]_{oil / fat}}{[Drug]_{water}}$
- *i.e.* $PC = (\text{Concentration of Drug in Fat/Oil}) / (\text{Concentration of Drug in Water})$

Extract types according to their consistency

Liquid Extracts

Extracts containing 1 part by weight of the substance in equivalent weight or volume. Contains more than 35-40% water

Soft Extracts


Extracts having a consistency between liquid and dry extract.. Obtained by partial evaporation of the solvent used. Contains 15-16% water

Dry Extracts

Solid extracts obtained by evaporation of the solvent used by vacuum drying under $< 60^{\circ}\text{C}$ temperature.. Contains $< 5\%$ water



Extraction methods

- Mechanical extraction
 - Extraction by distillation
 - Extraction with solvents
 - Supercritical fluid extraction
- 



Mechanical extraction

1. An incision is made on alive plant using a sharp blade allowing a thick fluid to leak out. The product is then scraped off.

Opium, balsam, gum, resin

2. Herbal samples are crushed with press using pressure.

Almond oil, peanut oil, cottonseed oil, cocoa butter

Black mulberry, lemon fruit juices

Extraction with distillation

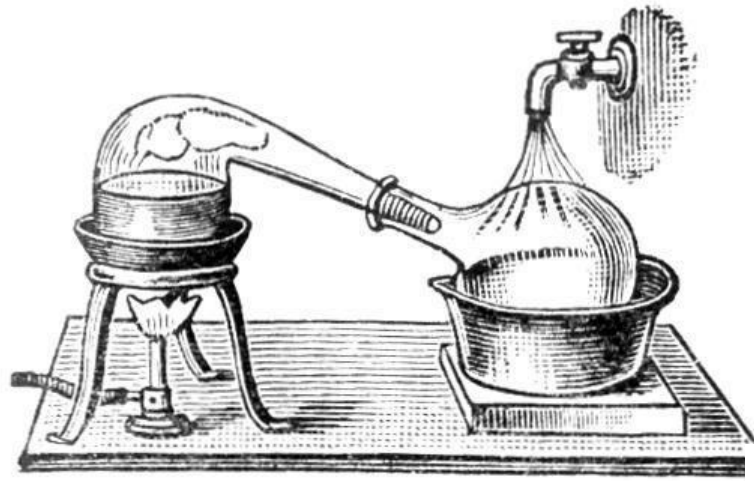
Distillation;

The process of physically separating one or more components with a different boiling point in a mixture.

In pharmaceutical technology

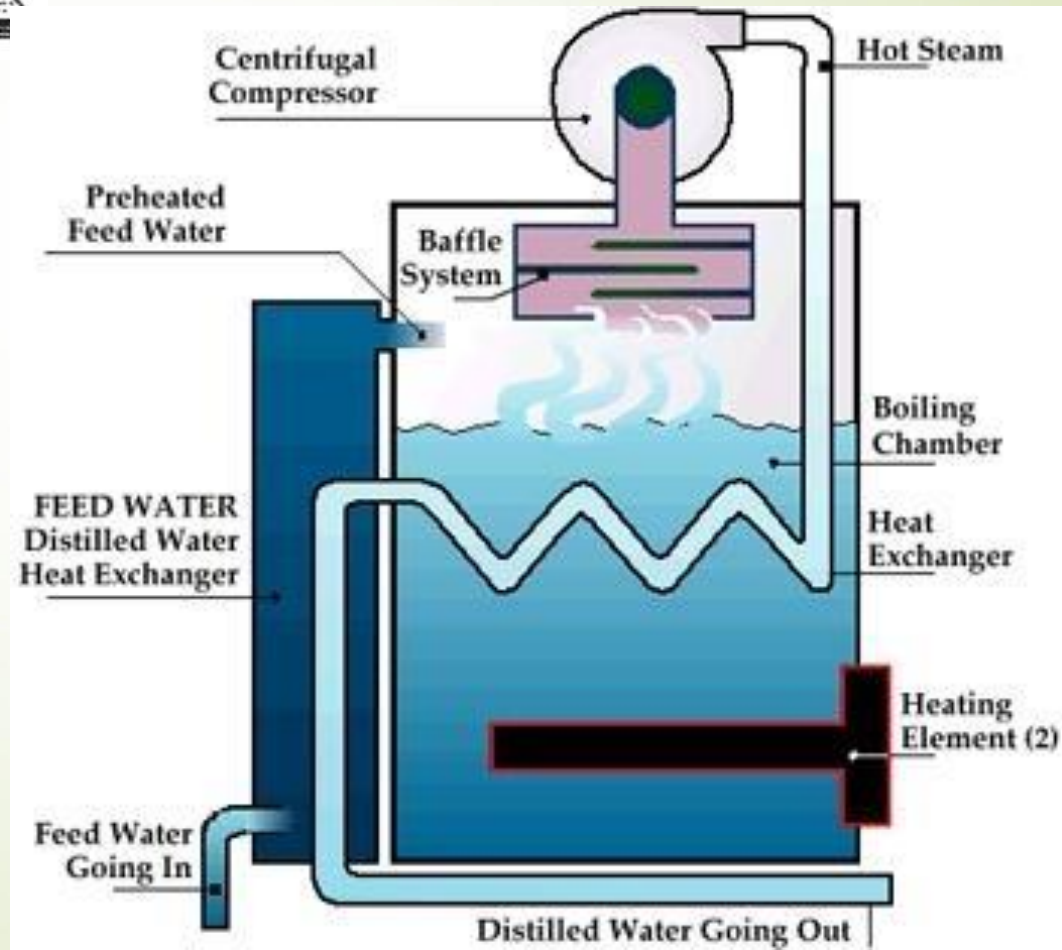
- * It is used for obtaining pharmaceutical grade water
- * Applied to plants containing volatile and easily evaporable active agents

Essences (essential oils), some aromatic waters



- ▶ Plants samples such as leaves, barks, roots, fruits and flowers are used

- Direct distillation
- Distillation with water vapor





Direct Distillation


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- Small amount of water is added on the distillation container containing plant pieces.
- The vessel is heated at the bottom.
- Obtained water vapor carries the volatile material.
- The mixture is concentrated by cooling.
- The product is collected in the collection container.

Distillation with water vapor;

- Water is added on the distillation container containing plant pieces.
- Water vapor obtained in a separate place is transferred to this container.
- With the aid of the heat of the water vapor, the volatile material evaporates and drains with water vapor.
- The product is cooled and collected.

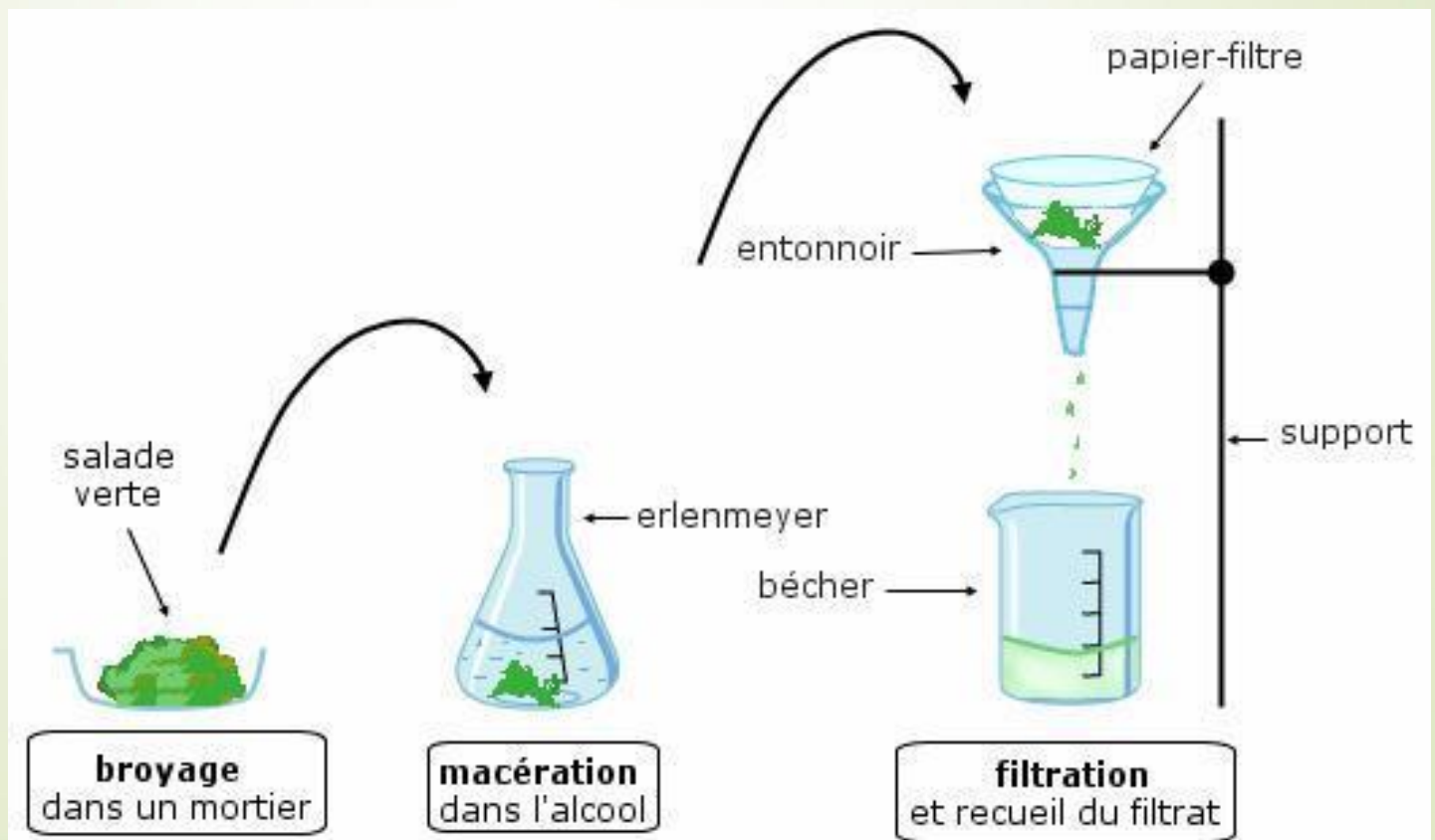




Extraction methods using solvents

- Maceration
 - Dimaceration
 - Decoction
 - Infusion
 - Digestion
 - Percolation
- 

Maceration

This is a process that consists of maintaining contact between the plant and a liquid for a period of time. It is conducted at room temperature. It consists of immersing a plant in a liquid (water, oil, alcohol, etc.)



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- The solid ingredients are placed in a stoppered container with prescribed solvent and allowed to stand for a period of at least 3 days in a warm place with frequent agitation, until soluble matter is dissolved.
 - The mixture is filtered and, after most of the liquid has drained, the residue on the filter is washed with sufficient quantity of the prescribed solvent or solvent mixture
 - The filtrates are combined
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Dimaceration

The solid ingredient is subsequently subjected to maceration twice.

1st maceration lasts for 6 hours - 2 days,

Bitter tasted ingredients can be found

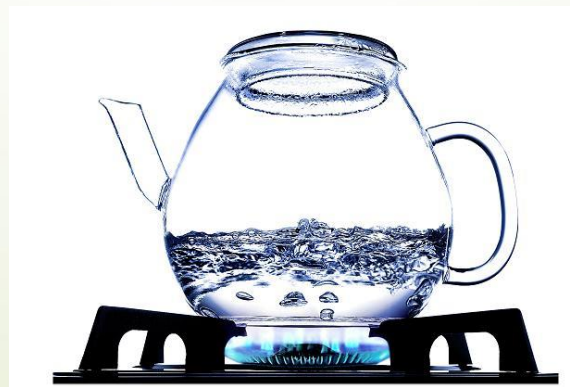
2nd maceration lasts for 12 hours - 3 days

Etheric oils can be found

Extracts of belladonna, cinchona, gentian, henbane, opium, carrageenan are examples


Decoction

- This once popular process extracts water soluble and heat stable constituents from crude drugs, by:
- boiling in water for a certain time,
- cooling,
- Straining and
- passing sufficient cold water through the drug to produce the required volume.





Infusion

- An infusion is a dilute solution of the readily soluble constituents of crude drugs.
 - Fresh infusions are prepared by macerating the solids for a short period of time with boiling water.
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Digestion

This is a form of maceration in which gentle heat (40-60°C) is used during the process of extraction.

It is used when moderately elevated temperature is not objectionable and the dissolving efficiency of the solvent is increased thereby.



Percolation

It is a continuous extraction method performed by passing a solvent that can dissolve the active material inside the drug of appropriate fineness.

«Percolators» are used:

- different shape and size
- glass, porcelain, enamel or stainless steel

The product obtained is called «percolate».

Percolation has 5 stages:

- The drug is brought to the appropriate size.
- It is mixed with small amount of solvent and allowed to stand for a while before filling into the percolator. Thus, the dry drug is swelled.
- A small piece of cotton is placed on the bottom of the percolator and the moistened drug is filled into the percolator without being compressed. The filter paper and cotton are placed on top of the drug.
- The solvent is poured from the top and the system is allowed to macerate for a while.
- The product is removed from the bottom by opening the tap of the percolator.



Advanced Extraction Methods

(a)

Conventional Extraction Methods

MACERATION



Powdered crude sample mixed with solvent

INFUSION



Powdered crude sample mixed with cold or boiling water

DIGESTION



Powdered crude sample mixed with solvent and macerated with gentle heat

DECOCTION



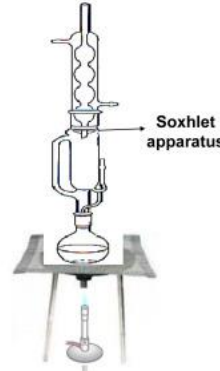
Powdered crude sample mixed with water and boiled

PERCOLATION



Powdered crude sample mixed with solvent is extracted in a percolator

SOXHLET

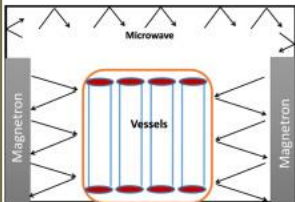


Powdered crude sample mixed with solvent and heated inside the apparatus for a specific period of time

(b)

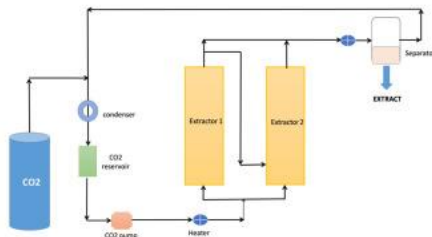
Advanced Extraction Methods

MAE



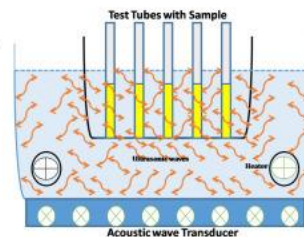
Sample mixed with organic solvent and heated by microwaves through ionic conductance and dipole rotation

SFE



Sample extracted by using CO₂ as a solvent which depends on the critical point

UAE



Sample extracted by using organic solvent which under ultrasonic wave forms cavitation bubbles

- supercritical fluid extraction (SFE)
- microwave assisted extraction (MAE)
- ultrasonic assisted extraction (UAE)



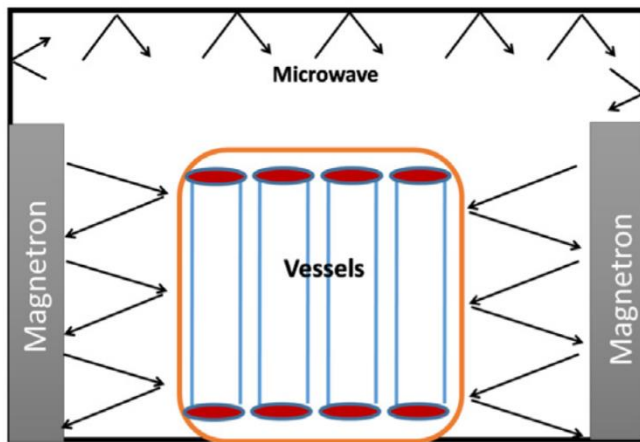
These techniques are known for their

- ▶ short extraction time,
- ▶ reduced volume of organic and hazardous solvents,
- ▶ very simple to perform,
- ▶ achieving a higher extraction yield with lower energy consumption.

These extraction techniques are defined as **green extraction** as they use alternative solvents, reduce energy consumption and ensure the safety and high quality of the extract.

microwave assisted extraction (MAE)

MAE



Sample mixed with organic solvent and heated by microwaves through ionic conductance and dipole rotation

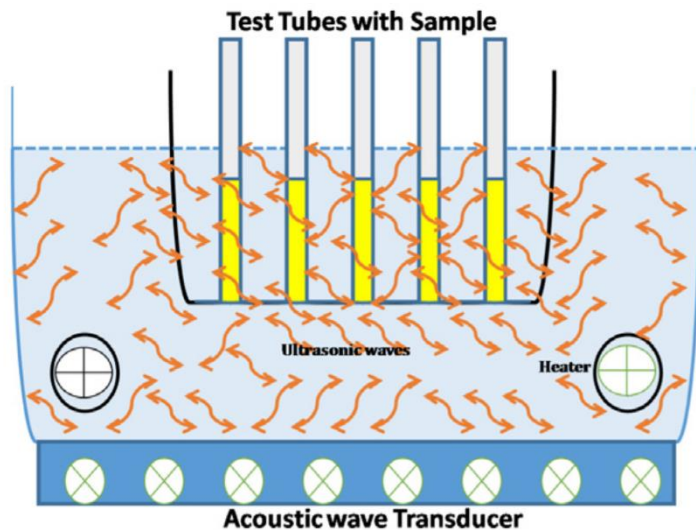
- Electromagnetic radiation is used to heat the sample by continuous dipole rotation (dielectric heating) and by the frictional resistance to the ion flow, both of which induce an increase in thermal energy
- The most commonly used type is the extraction in a closed vessel under controlled pressure and temperature,
- The second type of MAE consists of an open extraction vessel under atmospheric pressure conditions and the maximum temperature that can be reached based on the solvent boiling point.

microwave assisted extraction (MAE)

- The extraction efficiency under microwave depends on the nature of both solvent and sample.
- The solubility of the different compounds to be extracted can be maximized by fixing the solvents mixture ratio and controlling the temperature/ power.
- MAE has a number of advantages, including the extraction of both volatile (solvent extraction) and non-volatile (dry extraction) compounds.

ultrasonic assisted extraction (UAE)

UAE



Sample extracted by using organic solvent which under ultrasonic wave form cavitation bubbles

UAE uses ultrasonic energy (>20 kHz) for extraction using either ultrasonic bath and/or ultrasonic probe.

It works on the principle of making cavitation bubbles which collapse and produce higher shear, which results in complete extraction.

Supercritical fluid extraction

It is the process of separating the active substances from solid, semi-solid or liquid matrix using supercritical fluids.

► At a certain, material-dependent temperature, the density of the gas phase will be equal to the density of the liquid, so that there will no longer be a phase boundary between the liquid and gas phase, and both are now indistinguishable (this is called a supercritical fluid).

Supercritical fluid extraction

- It can diffuse through solids like a gas, and dissolve materials like a liquid.
- **Supercritical CO₂** is the most commonly used liquid.

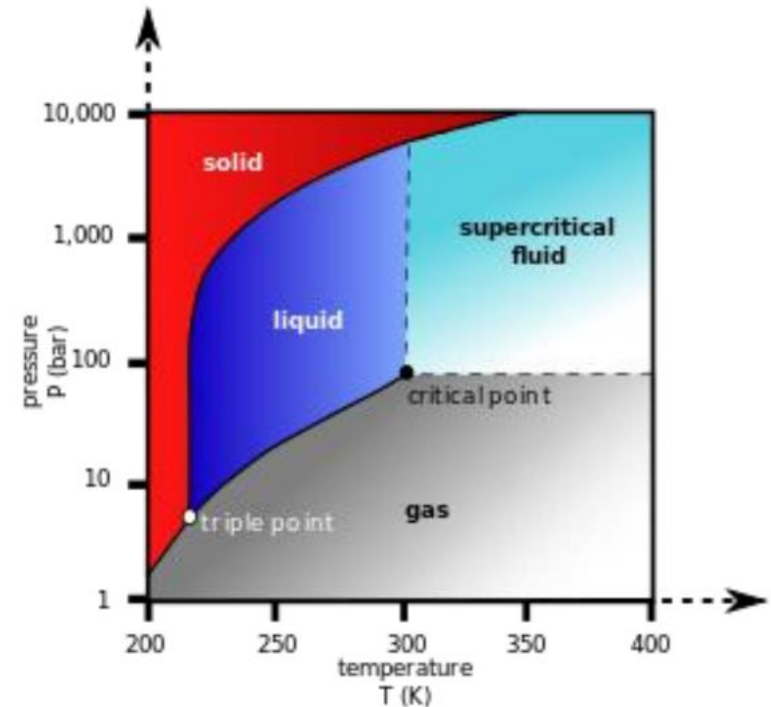
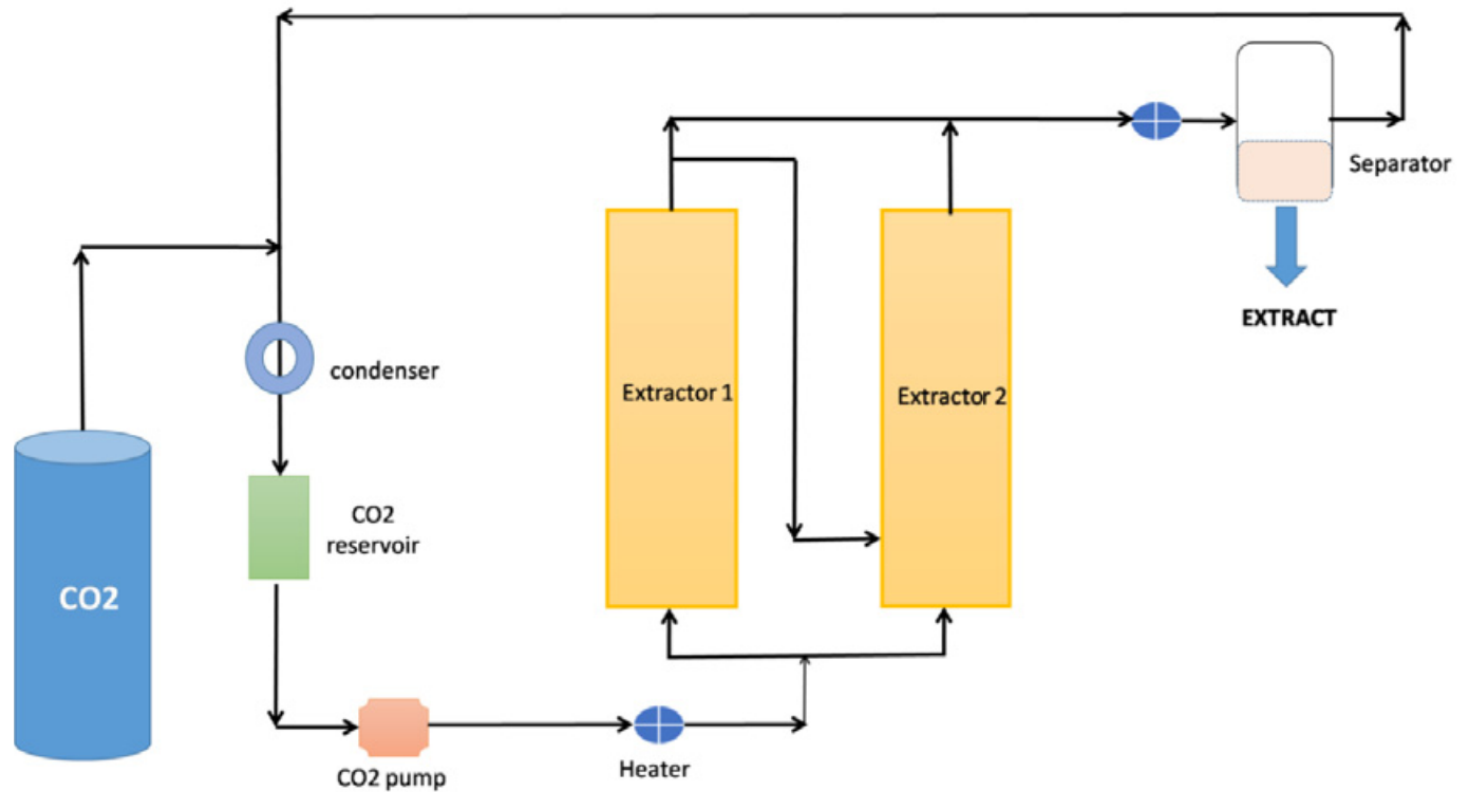




Figure 1.1 Carbon dioxide pressure- temperature [1]

SFE



Sample extracted by using CO₂ as a solvent which depend on the critical point

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- SFE involves use of gases, usually CO₂ for the extraction process. The critical point that is the optimum temperature and pressure at which the substance can vaporize is very important in SFE, which is more profitable over the classical extraction methods considering the environment. It is the most technologically advanced extraction system and finds widespread application in environmental, chemical, food, agriculture, pharmaceutical and nutraceutical industries
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Pharmaceutical preparations prepared by extraction

- Decoctions: Rataniae, Saponaria
- Infusions: Tilia, Digitalis
- Alcoholates: Garus
- Elixirs: Garus
- Tinctures: Belladon, Ipeca, Opium tincture
- Extracts: Opium extract, Kaskara sagrada liquid extract



Alcoholates

- Aromatic fragrant preparations prepared by initial maceration and subsequent distillation of crude drugs in ethyl alcohol for a certain period of time.
- Alcohol content is high

Garus alchoolate (Alchoolat de Garus)

Elixirs

- Clear and sweet preparation consisting of a mixture of alcohol and water.



Tinctures

- ▶ Tinctures are defined in the USP as alcoholic or hydroalcoholic solutions prepared from vegetable materials or from chemical substances, an example of the latter being Iodine Tincture.
- ▶ The USP, specifically, describes two general processes for preparing tinctures, one by percolation and the other by maceration.
- ▶ Belladonna Tincture, USP, is prepared by percolation. Compound Benzoin Tincture, USP, and Sweet Orange Peel Tincture, USP, are prepared by the maceration procedure.