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EXTRACTION

Extraction:

- Extraction is the method of removing active constituents from a solid or liquid by means of liquid solvent.
- The separation of medicinally active portions of plant or animal tissues from the inactive or inert components by using selective solvents.
- In this method the wanted components are dissolved by the use of selective solvents known as menstrum & undissolved part is a marc.

After the extraction unwanted matter is removed.

Extracts are prepared by using ethanol or other suitable solvent.

- **Extract :** Extracts can be defined as preparations of crude drugs which contain all the constituents which are soluble in the solvent.

Marc: Solid residue obtain after extraction

Menstruum: Solvent used for extraction

Type of extracts

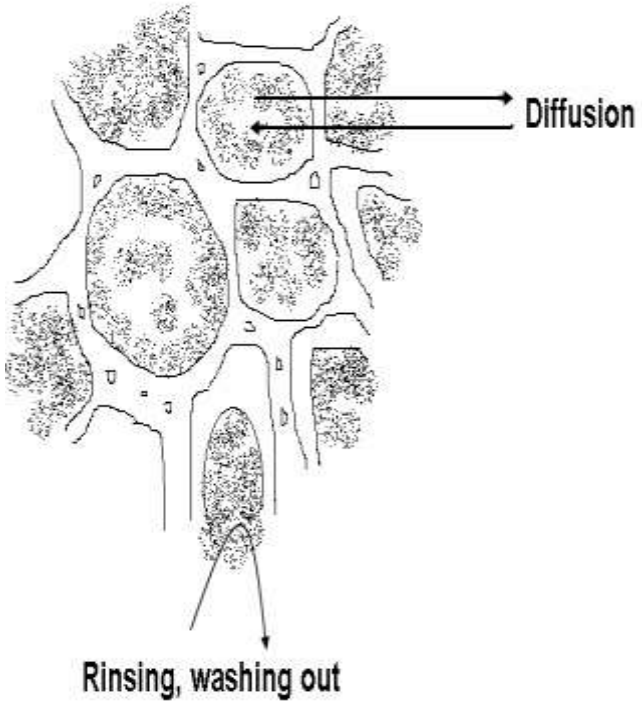
- Dry extract (Tab, cap.)

  E.g. belladonna extract
- Soft (Ointment, suppository)

  E.g. glycerrhiza extract.
- Liquid : As tincture.

¬Dissolution of extractive substances out of disintegrated cells.

¬ Dissolution of extractive substances out of intact plant cell by diffusion (requires steeping and swelling)



- ¬ Penetration of the solvent into the plant cells and swelling of the cells.
- ¬ Diffusion of the dissolved extractive substances out of the cell.

¬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

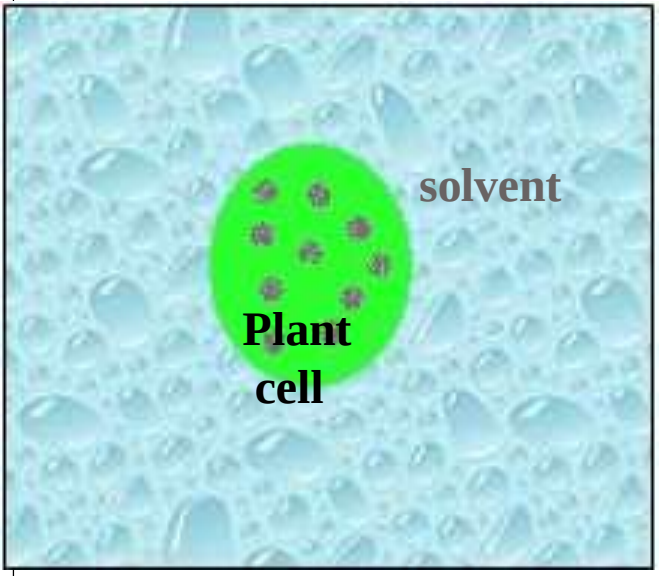
.

¬An equilibrium is established between the solute inside the cells and the solvent surrounding the fragmented plant tissues

Ideal properties of the solvents :

1. Be highly selective for the compound to be extracted.
2. Not react with the extracted compound or with other compounds in the plant material
3. Have a low price.
4. Be harmless to man and to the environment.
5. Be completely volatile.
6. Should not mix up with water.
7. Should have the big capacity in relation to extractive.
8. The density of solvent should be difference from water density.
9. Should have the minimum viscosity.

Mechanism of Extraction :



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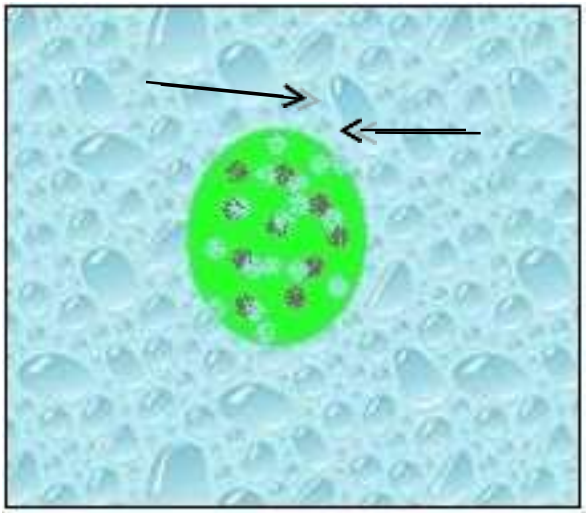

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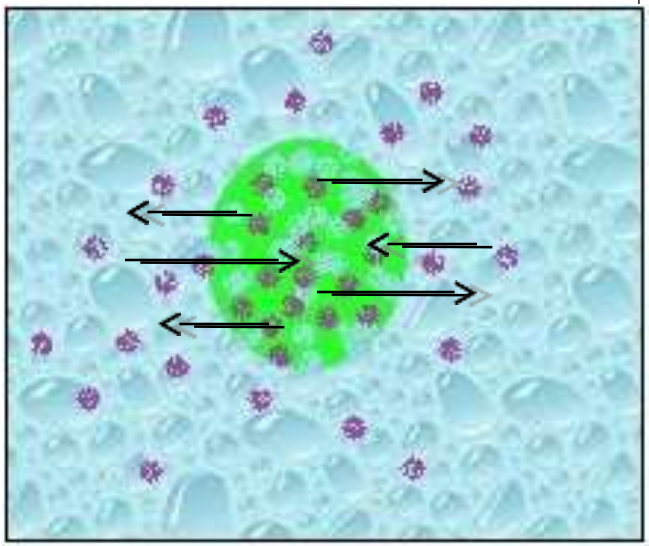

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Factors affecting extraction process :

- Nature of drug
- Solvent
- Temperature
- pH
- Particle size

Methods of extraction :

- Infusion
- Decoction
- Digestion
- Maceration
- Percolation
- Continues hot extraction
- Supercritical fluid extraction
- Counter current extraction
- Microwave assisted extraction
- Ultrasonication-Assisted Extraction:

Infusion :

Fresh infusions are prepared by macerating the crude drug for a short period of time with cold or boiling water. These are dilute solutions of the readily soluble constituents of crude drugs.

Types of Infusion :

- Fresh Infusion : e.g. Infusion of orange
- Concentrated Infusion : e.g. Concentrated infusion of Quassia

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.

e.g. Tea , Coffee

Digestion:

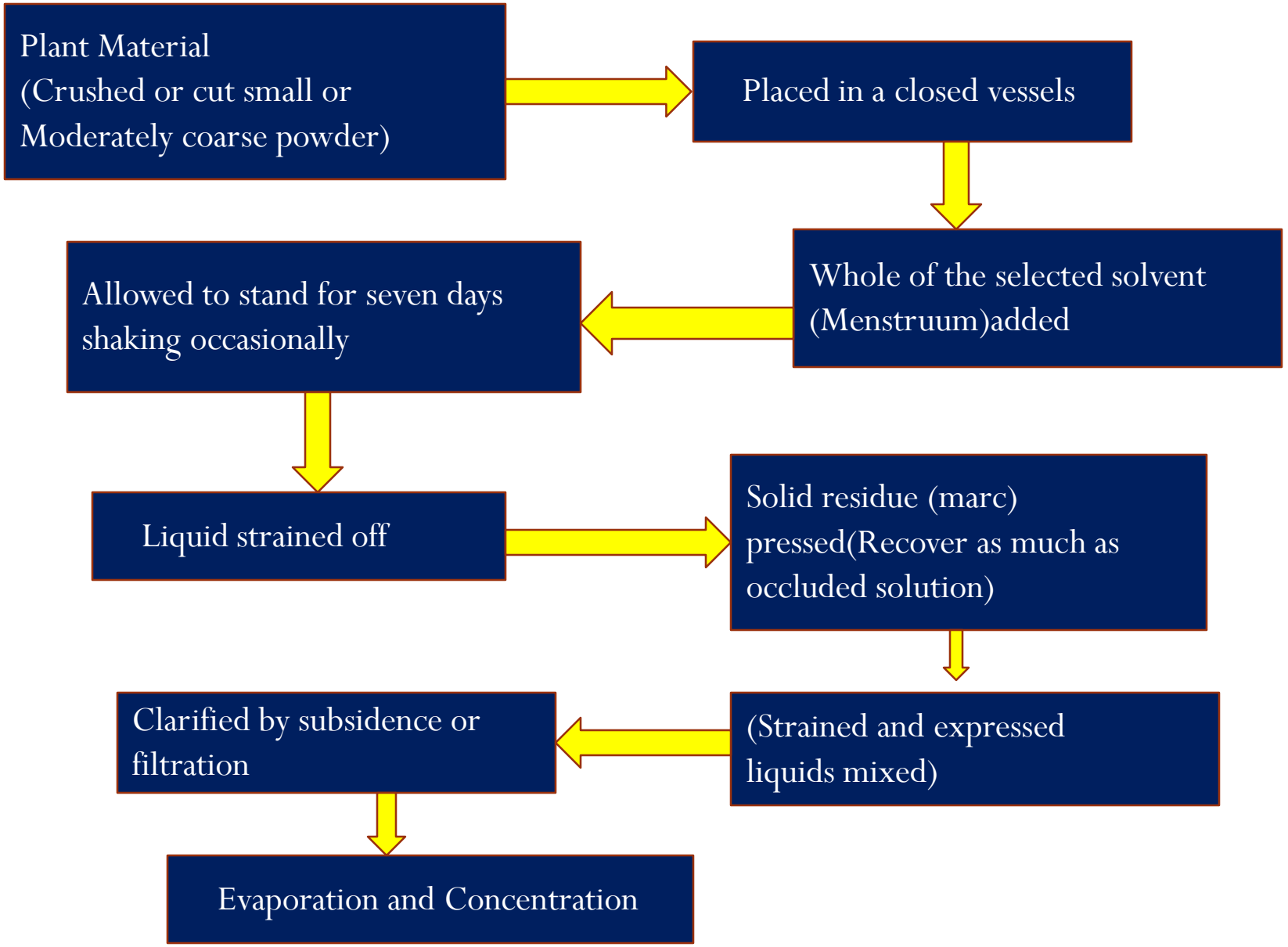
- This is a form of macerationin which gentle heat is used during the process of extraction.
- It is used when moderately elevated temperature is not objectionable. The solvent efficiency of the menstruum is thereby increased.

  e.g. Extraction of Morphine

Maceration :

In this process solid ingredients are placed in a stoppered container with the whole of the solvent and allowed to stand for a period of at least 3 days (3 - 7 days) with frequent agitation, until soluble matter is dissolved. The mixture is then strained (through sieves / nets), the marc pressed and the combined liquids clarified (cleaned by filtration) or by decantation, after standing.

Process of maceration :



Types of maceration :

- Simple maceration: for organized and unorganized Crude drug

e.g. i) Tincture of Orange

ii) Tincture of Lemon

iii) Tincture of Squill

- Double maceration : Concentrated infusion of orange
- Triple maceration: The maceration process may be carried out with help of heat or stirring

e.g. i) Concentrated infusion of Quassia

ii) Concentrated infusion of Senna

¬*SIMPLE MACERATION*:-

¬INTRODUCTION:-

The extraction of the drug with a solvent with several daily shakings or stirrings at room temperature.

- In this type of maceration, organized drug are used.

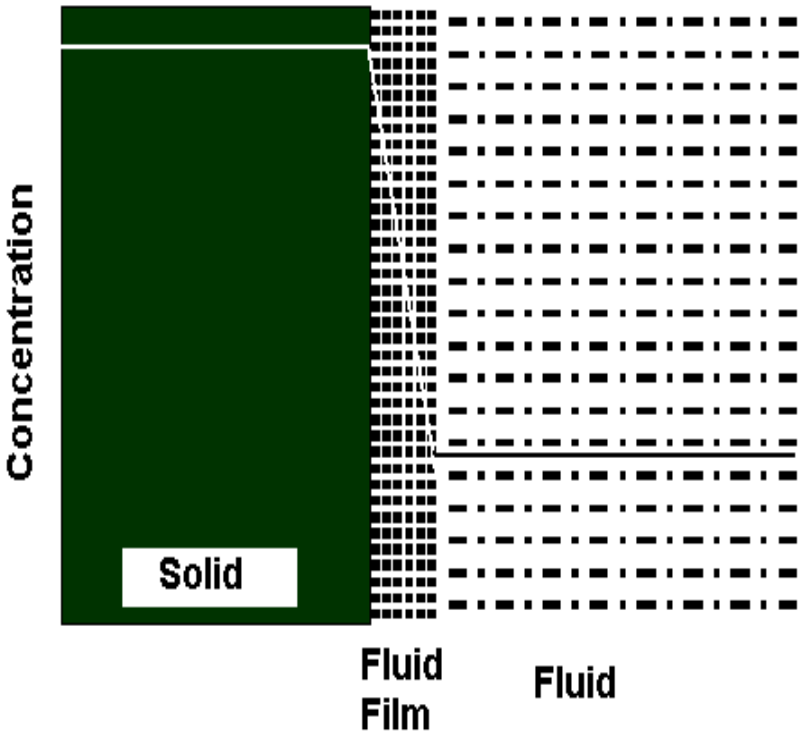
TYPES:-

1.Kinetic maceration: is carried out at room temperature, like simple maceration, the difference being that the material is kept in constant motion.

2.Vortical (turbo) Extraction:-The drug is stirred in the menstrum with a high-speed mixture or homogenizer

THEORY:-

The extraction of the drug with a solvent with several daily shakings or stirrings at room temperature.



Where,

weight of solute diffusing = W

Diffusion coefficient = D

Surface area = A

Concentration of solute at interface=C1

Concentration of solute in bulk = C2

Thickness of boundary layer = L

Time = θ

$$W = \frac{DA\,(C1-C2)\,\theta}{L}$$

¬THEORIES OF MACERATION:-

- Schoenemann's Diffusion theory

The rate of extraction depends on the rate of diffusion

- Boucher et al., Soaking theory

Not only the rate of diffusion but also the rate of dissolution of the substances in the solvent critically affect the rate of extraction

- _Karnowsky's Capillary velocity Theory

It represents the rate of extraction as a function of the rate of flow in the capillaries.

- Schultz & Koltz theory of maceration

$$C = am^q$$

c= Concentration in the macerate (kg/m^3)
m= weight of solvent used per unit quantity of drug (kg/kg)
a and q are constants

Factors affecting Maceration

Concentration gradient (C1-C2) is affected by several factors

1.Solid/solvent ratio: Yield decreases with constant quantity of solvent and increasing proportion of drug material.

2.Dissolution from disintegrated cells: Particle size

3.Steeping and swelling of plant material: Capillary dilation and increase in diffusion rate (Mucilage)

4.Diffusion from intact plant cell: Solvent must be able to solublilize substances

5.Temperature: increase solubility (diffusion coefficient), and decrease the viscosity

6.pH value: Influence the selectivity of extraction (qualitative and quantitative)

7.Interaction of dissolved constituents with insoluble support material of plant

8.Degree of lipophilicity

9.Effect of addition of surfactants, salts and co-solvents

¬MODIFIED MACERATION:-

¬*INTRODUCTION:-*

- In this type of maceration unorganized drug are used which have no cellular or tissue structure.

  eg. Gum, Resins, Gum-resins, Oleo gum-resins.

- Here, unorganized drugs are used because in short time complete reaction not takes place. Because of no cellular structure in unorganized drugs, soluble components are directly exposed to menstrum so the process is quicker.
- Here the whole procedure is like simple maceration but the final product is not collected by pressing the marc but it is adjusted to the definite volume.

¬MULTIPLE MACERATION-

- The aim of multiple maceration is to achieve maximum extraction by using proteins of the total volume of menstrum for successive maceration.
- The volume of menstrum calculated as follows:-

¬VACUUM MACERATION:-

- It employs a designed maceration vessel with arrangement for connecting it to vacuum line.
- Modification increase its permeability of cell walls considerably & facilitates extraction in much shorter time

Merits

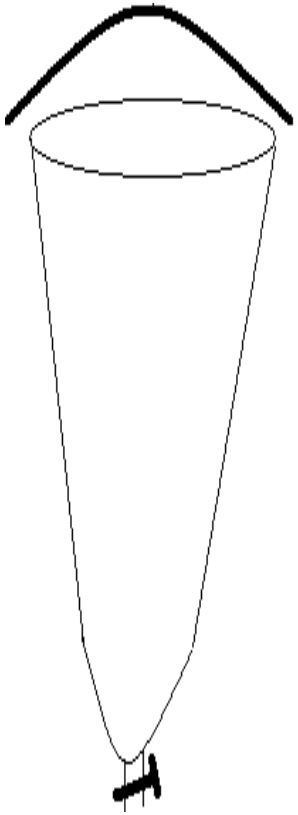
- Small sample size.
- Strong swelling properties or high mucilage.
- Energy saving process.

Demerits

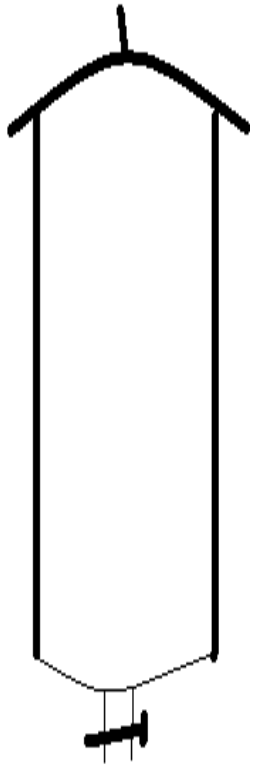
- Not exhaustively extract the drug.
- It is very slow process.
- Solvent required is more.

¬Percolation :

- It is continuous downward displacement of the solvent through the bed of crude drug material to get extract.
- Most frequently used to extract active ingredients in the preparation of tinctures and fluid extracts.
- It is the method of short successive maceration or process of displacement
- A percolator (a narrow, cone-shaped vessel open at both ends) is generally used.



conical



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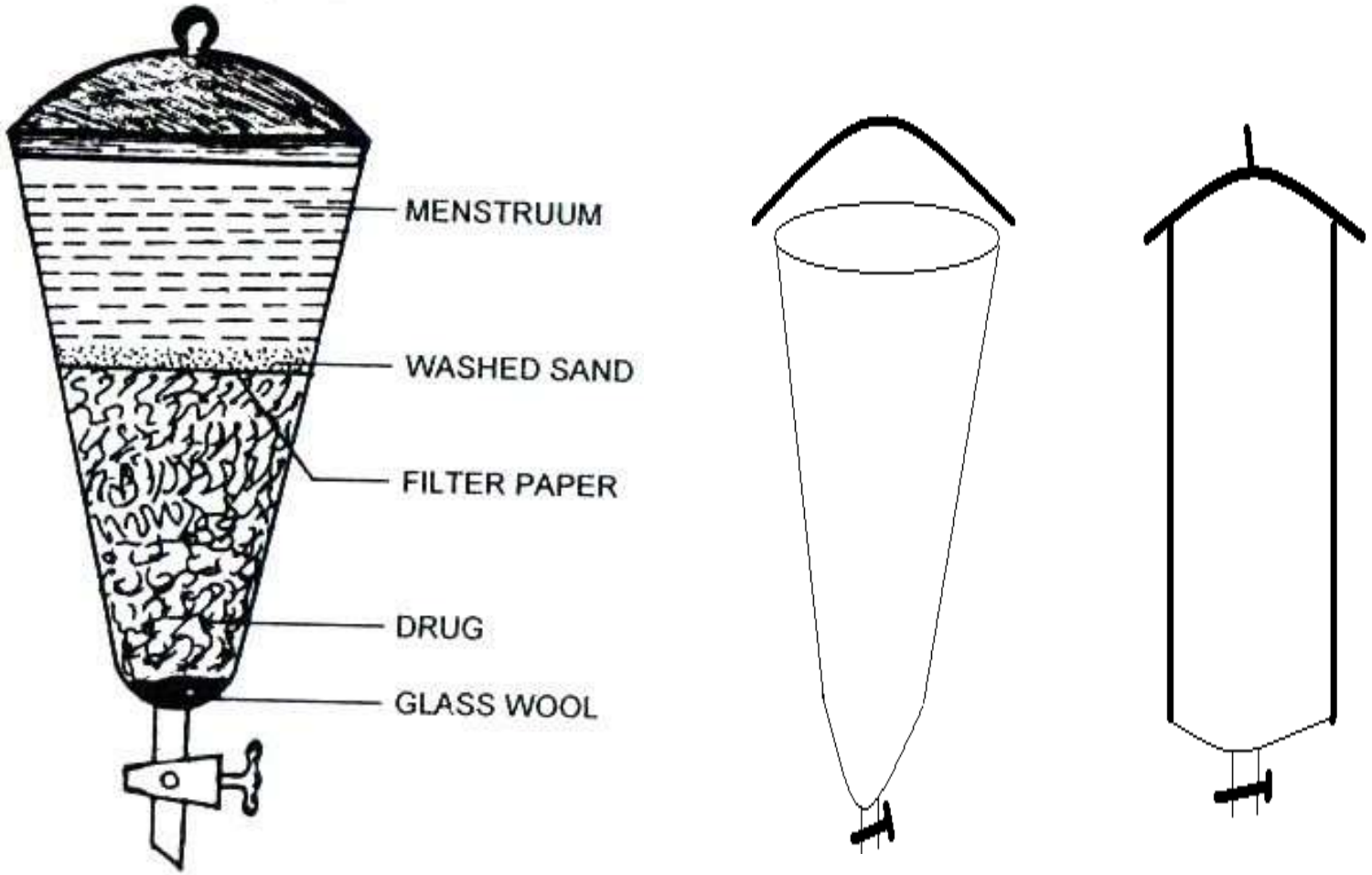

MENSTRUUM
WASHED SAND
FILTER PAPER
DRUG
GLASS WOOL

Steps in percolation :

- **1. Size reduction:** The drug to be extracted is subjected to suitable degree of size reduction, usually from coarse powder to fine powder.
- **2. Imbibition:** During imbibition the powdered drug is moistened with a suitable amount of menstruum and allowed to stand for four hours in a well closed container.
- **3. Packing:** After imbibition the moistened drug is evenly packed into the percolator.
- **4. Maceration:** After packing sufficient menstruum is added to saturate the material. The percolator is allowed to stand for 24 hours to macerate the drug.
- **5. Percolation:** The lower tap is opened and liquid collected therein is allowed to drip slowly at a controlled rate until 3/4th volume of the finished product is obtained.

Types of Percolation :

1.Simple Percolation :

Drug → Imbibition → Maceration → Percolation and collect the percolate i.e.3/4th of the volume of finished preparation

200gms — For 4 hours — For 24 hours

e.g. i) Tincture of Belladonna

ii) Compound tincture of cardamom

2. Modified Percolation :

- Repeated maceration is more effective than simple.
- Multiple maceration – Solvent divided into equal multiple time considering the solvent retained by plant tissue.
- Used to prepare concentrated preparation.

Reserved percolation:

- In this case the extraction is done through the general percolation procedure.

- At the last, the evaporation is done under reduced pressure in equipment like a Climbing evaporator to the consistency of a soft extract (semi solid) such that all the water is removed.

- This is then dissolved in the reserved portion which is strongly alcoholic and easily dissolves the evaporated portion with any risk of precipitation.

Merits :

- Requires less time than maceration.
- Extraction of thermolabile constituents can be possible.

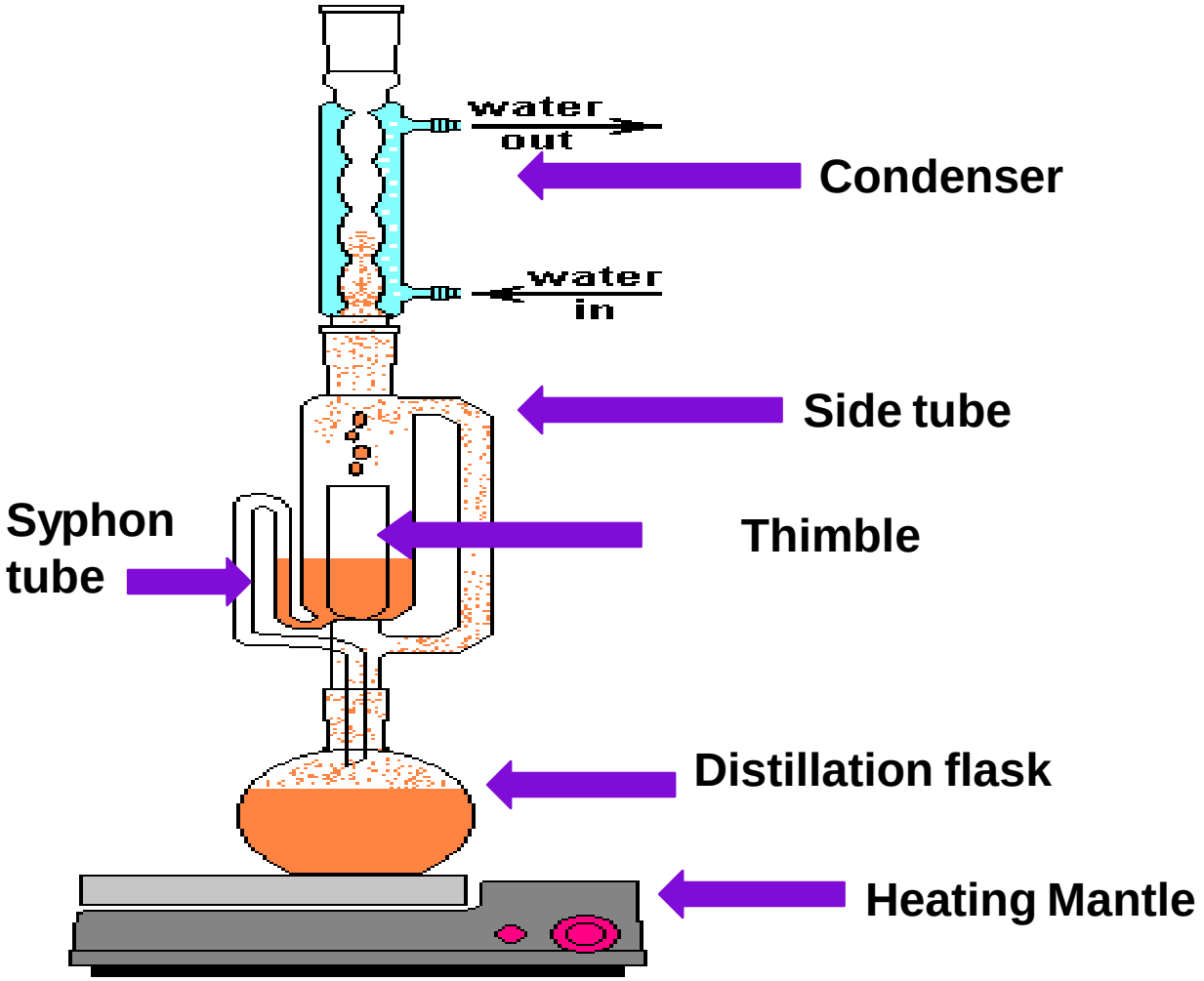
Demerits :

- Requires more time than soxhalation.
- More solvent is required.
- Skilled person is required.

Maceration Vs Percolation

Maceration	Percolation
•Time consuming and also extraction is not complete	• short time and more complete extraction
•Not required skilled operator	•Skilled operator is required
•For certain substances which are very less soluble in solvent and requires only prolonged contact with solvent.	•Special attention should be paid on particle size of material and throughout process.
•Suitable method for less potent and cheap drugs	•Suitable method for potent and costly drugs

Soxhalation



- THE SOXHLET EXTRACTOR Continuous extraction of a component from a solid mixture.
- Boiling solvent vapors rise up through the larger side-arm. Condensed drops of solvent fall into the porous cup, dissolving out the desired component from a solid mixture.
- When the smaller side-arm fills to overflowing, it initiates a siphoning action.
- The solvent, containing the dissolved component, is siphoned into the boiler below residual solvent then drains out of the porous cup, as fresh solvent drops continue to fall into the porous cup.
- . . . and the cycle repeats . . .

Merits :

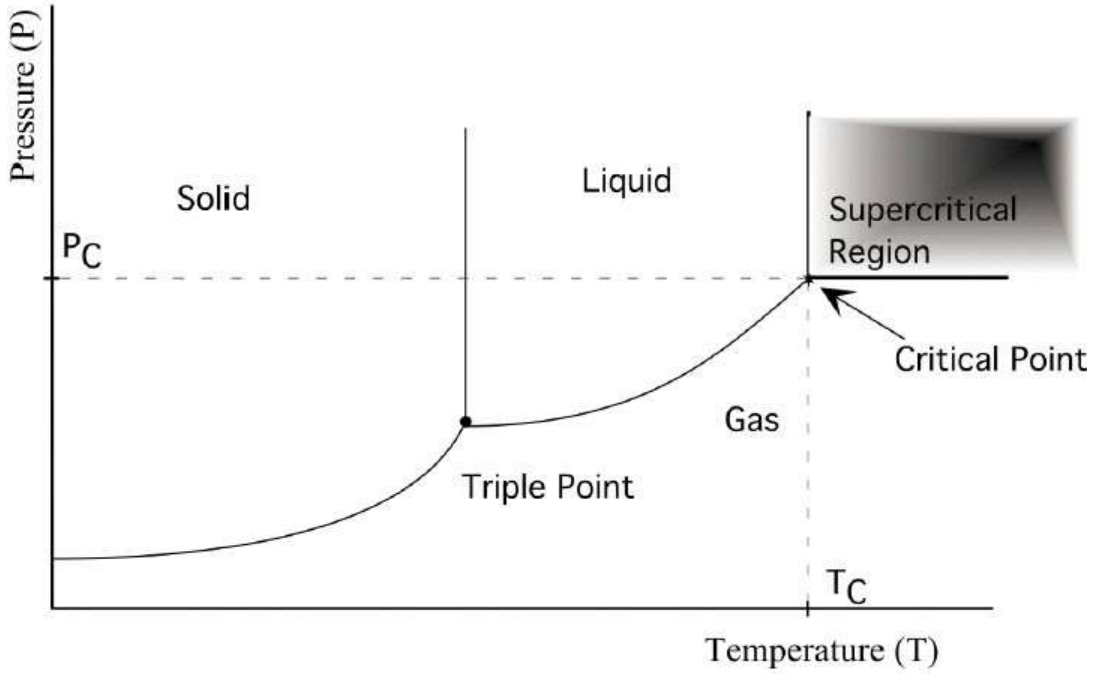
- Large amount of drug can be extracted with much smaller quantity of solvent.
- Tremendous economy in terms of time, energy & ultimately financial inputs.
- Small scale used a batch-process.
- Becomes more economical when converted into continuous extraction.
- Procedure on large scale.

Demerits :

- Physical nature of drug.
- Solvent.
- Chemical constituent of drug.

Supercritical Fluid Extraction

- For every substance, there is a critical temperature (Tc) and pressure (Pc) above which no applied pressure can force the substance into its liquid phase. If the temperature and pressure of a substance are both higher than the Tc and Pc for that substance, the substance is defined as a **supercritical fluid.**



Properties of SCFs :

- At the critical point, the density of the gas and liquid phases is the same; there is no distinction between the phases. i.e. between those of the pure liquid and gas.
- Supercritical posses densities that are liquid-like and
- Transport properties that are gas-like.
- These offers good penetrative ability and good extractive ability.

Choice of SCFs solvent :

- Good solving property,
- Inert to the product,
- Easy separation from the product,
- Cheap,
- Low CP because of economic reasons,
- Carbon dioxide is the most commonly used SCF, due primarily to its low critical parameters (31.1°C, 73.8 bar),
- non-toxicity.

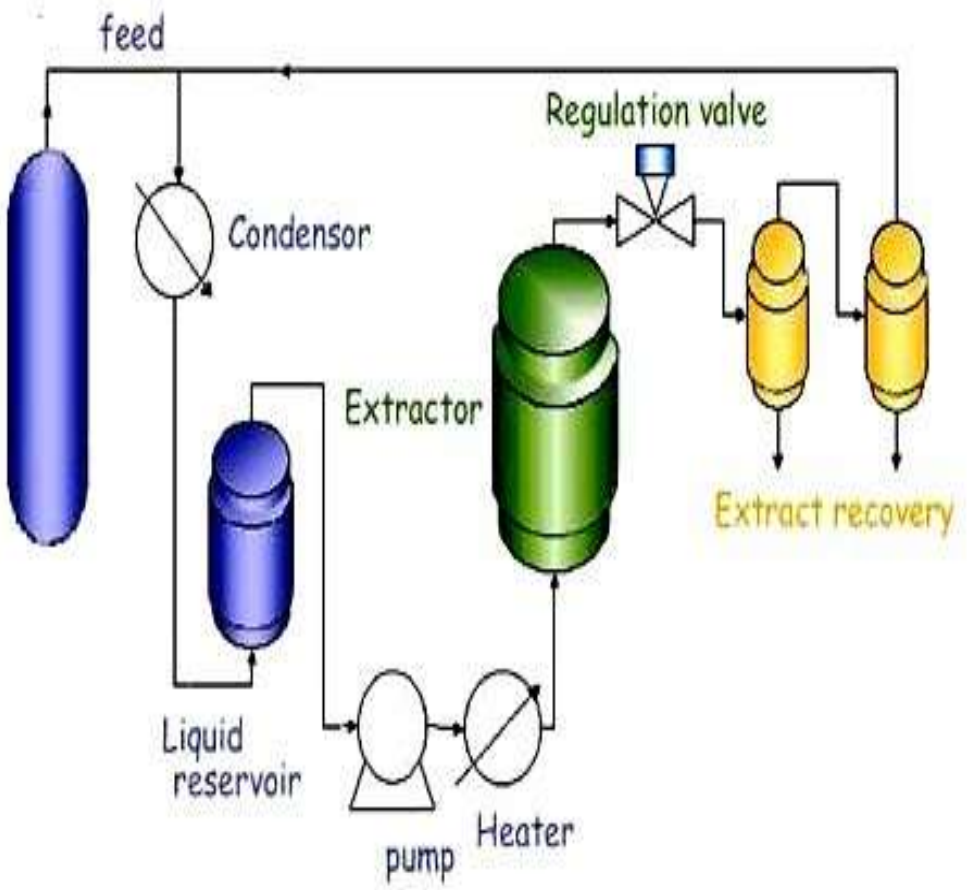
- However, several other SCFs have been used in both commercial and development processes. The critical properties of some commonly used SCFs are ;

Fluid	Critical Temperature (K)	Critical Pressure (bar)
Carbon dioxide	304.1	73.8
Ethane	305.4	48.8
Ethylene	282.4	50.4
Propane	369.8	42.5
Propylene	364.9	46.0
Trifluoromethane (Fluoroform)	299.3	48.6
Chlorotrifluoromethane	302.0	38.7

Supercritical Fluid Extraction Process :

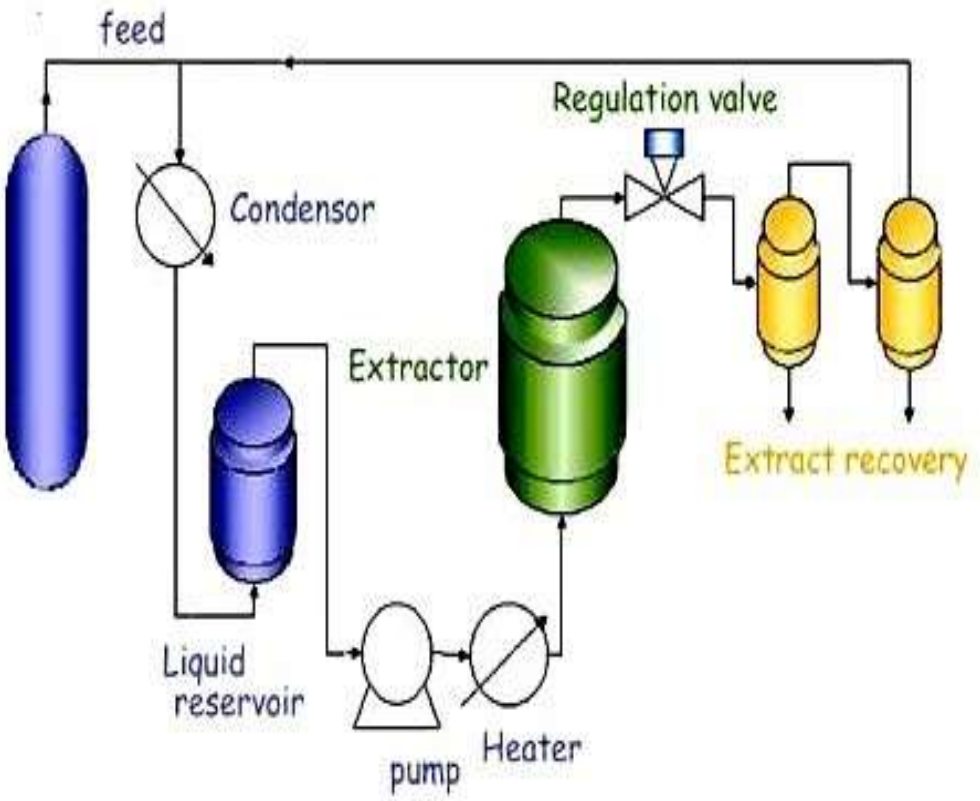
- The oldest typical and most common supercritical fluid extraction from solids is performed as a batch process, with a continuous flow of SCF.

- An extraction medium (going to be SCF) stored in the feed tank and liquid SCF is pumped from a reservoir ; it is heated and pressurized to reach the supercritical conditions



Supercritical Fluid Extraction Process :

- Supercritical SCF enters the extraction chamber where contact with crude drug bed occurs and the more volatile substances are dissolved into the supercritical fluid.
- Solute and SCF leave extractor and extract is precipitated in separators, where SCF becomes gaseous.
- Gas is recycled by condensation before returning to liquid reservoir.



Advantages of Supercritical Fluid Extraction :

- Dissolving power of the SCF is controlled by pressure and/or temperature.
- SCF is easily recoverable from the extract due to its volatility.
- Non-toxic solvents leave no harmful residue.
- High boiling components are extracted at relatively low temperatures.
- Separations not possible by more traditional processes can sometimes be effected.
- Thermally labile compounds can be extracted with minimal damage as low temperatures can be employed by the extraction.

Disadvantages of Supercritical Fluid Extraction :

- Elevated pressure required.
- Compression of solvent requires elaborate recycling measures to reduce energy costs.
- High capital investment for equipment.

Applications of Supercritical Fluid Extraction :

- Recovery of organics from oil shale
- Separations of biological fluids
- Bioseparation
- Petroleum recovery
- Crude dewaxing
- Coal processing (reactive extraction and liquefaction)
- Selective extraction of fragrances, oils and impurities from agricultural and food products
- Pollution control
- Combustion and many other applications.

Counter-Current Extraction

- A liquid-liquid extraction process in which the solvent and the process stream in contact with each other flow in opposite directions.
- Screw extractors and carousel extractors are the two type of equipments used for Counter-Current Extraction.

Counter-Current Extraction PROCESS

- In counter-current extraction (CCE), wet raw material is pulverized using toothed disc disintegrators to produce fine slurry.
- The material to be extracted is moved in one direction (generally in the form of fine slurry) within a cylindrical extractor where it comes in contact with extraction solvent.
- The further the starting material moves, the more concentrated the extract becomes.
- Finally, sufficiently concentrated extract comes out at one end of the extractor while the marc (practically free of visible solvent) falls out from the other end.

Advantages :

1. A unit quantity of the plant material can be extracted with much smaller volume of solvent as compared to other methods like maceration, decoction, and percolation.
2. CCE is commonly done at room temperature, which spares the thermolabile constituents from exposure to heat which is employed in most other techniques.
3. As the pulverization of the drug is done under wet conditions, the heat generated during comminution is neutralized by water. This again spares the thermolabile constituents from exposure to heat.
4. The extraction procedure has been rated to be more efficient and effective than Continuous hot extraction.

Applications :

1. DNA purification:
2. Food Industry:
3. Ex. Citrus oils, Unsaturated fatty acids, and squalene tocopherol.

   An important application is citrus oil processing,

   An important subject in perfumes and food industries.

Microwave-assisted Extraction :

- Microwaves are electromagnetic radiations with a frequency from 0.3 to 300 GHz (Camel, 2001).
- In order to avoid interferences with radio communications, domestic and industrial microwaves generally operate at 2.45 GHz (Fig. 1). Owing to their electromagnetic nature, microwaves possess electric and magnetic fields which are perpendicular to each other.
- The electric field causes heating via two simultaneous mechanisms, namely, dipolar rotation and ionic conduction

- Microwave-assisted extraction offers a rapid delivery of energy to a total volume of solvent and solid plant matrix with subsequent heating of the solvent and solid matrix, efficiently and homogeneously.
- Components of the sample absorb microwave energy in accordance to their dielectric constants.
- When plant material is immersed inside a microwave transparent solvent, the heat of microwave radiation directly reaches to the solid without being absorbed by the solvent, resulting in instantaneous heating of the residual moisture in the solid.
- Heating causes the moisture to evaporate and creates a high vapour pressure that breaks the cell wallof substrate and releases the content into solvent.
- The extracting selectivity and the ability of the solvent to interact with microwaves can be modulated by using mixtures of solvents.
- One of the most commonly used mixtures is hexane-acetone.

Collection of the essential oil. The oil is separated from water simply by decantation.

High definition video system for visual control of process.

Icon-driven programs provide full control of the extraction method parameters.

Samples are placed in dedicated easy-to-handle glass modules. Loading/unloading of samples are immediate and easy.

Microwave labstation, microprocessor controlled with infrared automatic temperature system.

Special lab-grade water chiller for optimal extraction performance (option)

Mobile module for flexibility of use (option)

Advantages of Microwave Assisted Extraction :

- It reduces solvent consumption,
- It has a shorter operational time,
- It possess moderately high recoveries,
- Has a good reproducibility and minimal sample manipulation for extraction process.

Disadvantages of Microwave Assisted Extraction:

- A n additional filtration or centrifugation is necessary to remove the solid residue during MAE.
- Furthermore, the efficiency of microwaves can be very poor when either the target compounds or the solvents are non-polar, or when they are volatile.

Applications of Microwave-Assisted Extraction:

- MAE can extract nutraceuticals products from plant sources in a faster manner than conventional solid–liquid extractions.
- MAE (80% methanol) could dramatically reduce the extraction time of ginseng saponin from 12 h using conventional extraction methods to a few seconds.

- **Biologically active compounds extracted by microwave-assisted Technique**
  - Extraction of taxanes from *Taxus brevifolia* needles,
  - Azadiractin related limonoids from **Azadirachta indica** seed kernels,
  - Extraction of glycyrrhizic acid from *Glycyrrhizia glabra* roots,
  - Extraction of artemisinin from *Artemisia annua*.
- A higher microwave temperature and a short extraction time are more effective in extracting anti-oxidative phenolic compounds from tomato using MAE.
- MAE was proven as a potential alternative to traditional methods for extraction of phenols such as chlorogenic acids from green coffee beans.

Ultrasonication-Assisted Extraction:

- The procedure involves the use of ultrasound waves, which have frequencies higher than 20 kHz, have great effects on extraction yield and kinetics.

- UAE involves ultrasonic effects of acoustic cavitations. Under ultrasonic action solid and liquid particles are vibrated and accelerated and, because of that solute quickly diffuses out from solid phase to solvent
- Ultrasound assisted extractors are ultrasonic baths or closed extractors fitted with an ultrasonic horn transducer. The mechanical effects of ultrasound induce a greater penetration of solvent into cellular materials and improve mass transfer.

Advantages of Ultra sonicated extraction:

- It is an inexpensive, simple and efficient alternative to conventional extraction technique.
- It include the increase of extraction yield and faster kinetics.
- It reduce the operating temperature allowing the extraction of thermolabile compounds.
- Compared with other novel extraction techniques such as microwave-assisted extraction, the ultrasound apparatus is cheaper and its operation is easier.

Disadvantages of Ultra sonicated extraction:

- The active constituents of medicinal plants through formation of free radicals and consequently undesirable changes in the drug molecules.

Applications:

- Used to extract nutraceuticals from plants such as essential oils and lipids dietary supplements.

  e.g. oils from almond, apricot and rice bran

- Extraction of saponinfrom ginseng, the observed total yield and saponin yield increased by 15 and 30%, respectively

- extracts. It was found that rice bran oil extraction can be efficiently performed in 30 min under high-intensity ultrasound either using hexane or a basic aqueous solution.

- Extraction rates of carvone and limonene by ultrasound-assisted extraction with hexane were 1.3–2 times more rapid than those by the conventional extraction depending on temperature

SOLVENTS

- *Petroleum ether* :- Fixed oils, Phytoglycerols.
- *Benzene*:- Fixed oils, Phytosterols.
- *Chloroform*;- Alkaloids
- *Acetone:-* Phytosterols
- *Ethanol:-* Carbohydrates, Glycosides
- *Saponin:-* Phenolics, Tannins, proteins, Amino acids
- *Water:-* Proteins, Amino acids, Glycosides, Gums, Mucilages, Carbohydrates

¬properties of ideal solvent:

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 human being and to the environment.
6.Be completely volatile.

¬ DIFFICULTIES:-

- Different active constituents like alkaloids, glycosides, tannins, terpenoids, resins oils etc requires advanced knowledge of phytoconstituents which help in selection of method.
- Different forms of insoluble matters may affect the extraction process.

  eg. Cellulose, proteins etc. in many drugs only the active constituent is not soluble material but along with it large proportion of unwanted material is solubilized. In such situations, a solvent chosen is as selective as possible.
- Wet vegetable material is an excellent medium for microbial growth and it may leads to loss of active substances and solvent must have suitable preservative action.