CHAPTER 10

EXTRACTION

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Abstract

Extraction is a fundamental separation process in pharmaceutical manufacturing, used to isolate desired compounds from natural sources or to purify synthetic products. This technique relies on the principle of differential solubility, where the target compound preferentially dissolves in a selected solvent. Various extraction methods are employed, including liquid-liquid extraction, solid-liquid extraction, and supercritical fluid extraction, each suited to different types of raw materials and target compounds. Factors influencing extraction efficiency include solvent choice, temperature, pH, and contact time. The concept of partition coefficient is explored to understand the distribution of compounds between immiscible phases. Advanced extraction techniques, such as microwave-assisted extraction and ultrasound-assisted extraction, are discussed in the context of improving yield and reducing processing time. Continuous extraction processes, including percolation and Soxhlet extraction, are examined for their applications in large-scale pharmaceutical production. Quality control measures, including assay of extracted compounds and solvent residue testing, are essential to ensure product purity and safety

Keywords: *Solvent extraction, Partition coefficient, Natural product isolation, Purification, Continuous extraction, Process optimization*

Learning Objectives

After completion of the chapter, the student should be able to:

- Define extraction and its applications in pharmaceutical processing.
- Explain the principles and mechanisms of various extraction techniques.
- Describe different types of extraction equipment used in pharmaceuticals.
- Discuss the factors affecting extraction efficiency and yield.
- Explain the concept of solvent selection and its importance in extraction processes.
- Analyze the challenges in extracting different types of pharmaceutical compounds.
- Evaluate methods for optimizing extraction processes in drug development and production.

Extraction 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. Belladonna extract is obtained from the leaves of the plant *Atropa belladonna*. The active ingredient is atropine. Besides atropine starch, lignin, pigments etc. are also present. So, to extract the atropine from the leaves a selective solvent has to be used so that only atropine is soluble in it. Thus, the active ingredient can be separated from the plant.

Source of drugs (active ingredients) may be plant or animal.

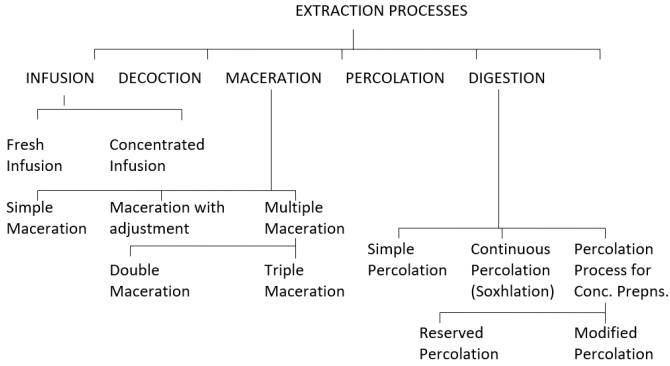
Plant source: Emetine from Ipecac root, reserpine from *Rauwolfia serpentina* root, atropine from Belladonna leaves.

Animal source: Cochineal from insect *Coccus cacti*.

Classification

In this discussion we are concerned primarily with basic extraction procedures for crude drugs to obtain the therapeutically desirable portion and eliminate the inert crude material by treatment with a selective solvent, known as the menstruum.

Let us take some dried leaves (known as the **crude drug)** in a container, add water in it. The active ingredient will come out in the water. Here water, i.e. the solvent of extraction is called **menstruum.** Later the water is filtered. The filtrate is known as the **extract**. The damp crude drugs (damp leaves) are called **marc**. This marc can be expressed i.e., pressed in a chamber to get the residual liquid, which is mixed with the previous extract.



EXTRACTION METHODS

There are several procedures for extraction: e.g maceration, percolation, digestion, infusion, decoction, digestion etc. Most pharmacopoeias generally refer to maceration and percolation for the extraction of active principles from crude drugs.

MACERATION

Principle:

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.

Stoppered container is generally taken to reduce the loss of solvents by evaporation. If the volume of solvent is reduced by evaporation then the extract may become concentrated, which may not be desired.

The drug is allowed to stand for few days

i) to help the solvent to penetrate the cells of the drugs,
ii) to provide the time for partitioning the active ingredient into the solvent and
iii) to transfer the drug out of the cells into the bulk of the solvent.

Frequent agitation is required to reduce the localized concentration around the cells and tissues.

As indicated in the pharmacopoeia the process consists of the following:

Placing the solid materials with whole menstruum in the closed vessel and allowed to stand for 7 days shaking occasionally.

Strained, pressed the marc and the liquid is obtained.

Liquid (i.e the extract) is clarified by subsidence or filtration. The process is normally used for the preparation of tinctures or extracts and menstruum is usually alcoholic, hydroalcoholic (in case of tinctures) or may be aqueous.

1. **Simple maceration** - a process for tinctures made from organized drugs e.g. roots, stems, leaves etc.
2. **Maceration with adjustment** - a process for tinctures made from unorganized drugs such as oleo-resins and gum resins.
3. **Multiple maceration** - a process to prepare concentrated extract. It includes 'Double maceration' and 'Triple maceration'.

SIMPLE MACERATION

Organized drugs having specific cell structures like roots, stems, leaves, flowers etc. are extracted by this procedure.

Apparatus

A wide mouthed bottle or any other container which can be well stoppered can be used for maceration process. A closed container is essential to prevent the evaporation of menstruum which is mostly concentrated alcohol. Otherwise this may lead to variation in strength as no adjustment in volume is made.

Method

Water or alcohol is used as menstruum and the drug menstruum ratio is 1 : 10.

- The drug is placed with the whole of the menstruum in a closed vessel for seven days. During this period shaking is done occasionally.
- After 7 days the liquid is strained and marc is pressed.
- The expressed liquid is mixed with strained liquid.
- It is then filtered to make a clear liquid.
- The **final volume is not adjusted.**

Explanation

1. Shaking of the drug during maceration is essential in order to replace the saturated layers around the drug with fresh menstruum.
2. After straining, the marc is pressed in a filter press, hydraulic press or hand press etc. The marc can be squeezed out of a fine muslin piece, when the quantity of the drug is very small.
3. The pressed liquid is mixed with the strained liquid and then filtered. No final adjustment is made, since the volume of pressed liquid is likely to vary with the process of pressing the marc. If the final adjustment in volume is made, it will give variation in the concentration of active principle although the volume of the final preparation may be the same.
4. Filtration is necessary to remove insoluble cell contents obtained during the pressing of marc.

Examples: The tinctures made by simple maceration process are-

1. Tincture of Orange
2. Tincture of Lemon
3. Tincture of Squill

MACERATION WITH ADJUSTMENT

The process is used for **unorganized** drugs.

Apparatus: Same as simple maceration.

Method:

- In this process the unorganized drug is placed with 4/5 th of the menstruum in a closed vessel for a period of 2-7 days. During this period, shaking is done occasionally .
- After the stated period, the liquid is filtered and the volume is made up by passing the remaining 1 / 5 the of the menstruum through the filter.
- The marc is not pressed.

Explanation

1. The period of maceration is reduced from 7 to 2 days in some cases, because the unorganized drugs behave like simple chemicals that dissolve in the solvent very easily and quickly.
2. 4/5th of the menstruum is used to keep the drug in contact with it in order to take into account the increase in volume after dissolving the soluble matter of the drug. The volume is made up at the end with 1/5th of the menstruum remained.
3. The marc left is a compact gummy matter. It does not retain the menstruum and hence it is not necessary to press the marc.
4. The final volume is made up because all the active constituents of drug get dissolved in the menstruum. Marc is not pressed. hence, there is no change in the concentration of the preparation in case the final volume is made up.

Example

1. Tincture of tolu
2. Compound tincture of benzoin.

MULTIPLE MACERATION

Multiple maceration process is carried out in the same way as simple maceration process, but the menstruum used is divided into two parts in double maceration process and three parts in triple maceration process

Double maceration process:

In this process, the drug is macerated twice by using the menstruum which is divided into two parts in such a manner that the same volume is used for each maceration. The quantity of menstruum required for two macerations are calculated as follows:

Volume of menstruum required for first maceration = (Total volume of menstruum / 2) + Volume to be retained by the drug

Volume of menstruum required for second maceration = Total volume of menstruum - Volume of menstruum used in first maceration

The volume of menstruum to be retained by the drug is determined by experiment, in a test batch of drug by adding a known volume of menstruum to known weight of the drug. After maceration, straining and pressing of the marc, measured volume volume of liquid is obtained. Difference in the volume and the volume used represents the volume retained by the weighable quantity of the drug used.

- In double maceration process, the whole of the drug is macerated for 48 hours with the quantity of the menstruum required for first maceration.
- The liquid is strained and the marc is pressed.
- The marc is macerated again for 24 hours with the remaining menstruum required for second maceration.
- The liquid is strained and and the marc is pressed.
- First and the second liquid is mixed and allowed to stand for 14 days and then filter.

Examples:

The following concentrated infusions are prepared by double maceration process:

1. Concentrated infusion of orange.
2. Concentrated compound infusion of chirata.
3. Concentrated compound infusion of gentian.

TRIPLE MACERATION PROCESS

In this maceration process, the drug is macerated thrice by using the menstruum which is divided into three parts in such a manner that the same volume for three parts in such a manner that the same volume is used for each maceratin.The quantity of menstruum required for three