

Pharmaceutical Quality Management

ASSAY OF ALKALOIDAL **DRUGS**

By:

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ALKALOIDS:

- ▶ Alkaloids are the natural organic compounds that contain nitrogen in a complex molecular structure, biosynthetically derived (at least in parts) from various amino acids, exert significant pharmacological activity and are basic in nature.
- ▶ OR Natural, organic, nitrogenous substances that are more or less alkaline in nature.
- ▶ OR Basic, natural compounds that pose a profound pharmacological activity and contain nitrogen in their molecule

➤ **Purpose of Assay:**

Assay of alkaloids is generally performed for purposes of:

- Standardization
- Proof of purity
- Commercial evaluation
- Pharmacological purposes
- ***Important considerations:*** Alkaloidal substances are the organic chemical compounds that are difficult to extract. These are present in comparatively small quantities and in many cases, these are destroyed by improper manipulations. The assays are conducted using immiscible solvents such as chloroform, ether or amyl alcohol except where the properties of the alkaloids sought necessitate a special method (e.g. as for morphine in opium).

➤ **Chemical nature of alkaloids:**

- insoluble or slightly soluble in water
- soluble in organic solvents which are immiscible with water
- Salts of alkaloids are soluble in water

This character makes it possible to separate the alkaloid by partitioning

➤ **Preparation of drugs for assay:**

- The drug should be pulverized to the required finesse-required mesh
- Care should be taken to avoid the loss of water during the pulverization

➤ **Weighing for assay:**

The accuracy should be within 10 mg for quantities equal to 5g or over

➤ **Extraction of Drug:**

- Extraction of the drug Extraction is based on the basicity of alkaloids and on the fact that they normally occur in plants as bases/salts (i.e. on the solubility of bases and salts in water and organic solvents).
- Plants also contain some other materials which can interfere with extraction such as large amounts of fat, waxes, terpenes, pigments and other lipophilic substances (e.g. by forming emulsions) –avoided by defatting the crushed herb (using petroleum ether and hexane) .

Extraction method normally depends on the raw material, the purpose of extraction & the scale on which is to be performed.

- The alkaloid bearing drugs are extracted with one of the following methods
 1. Maceration
 2. Percolation
 3. Continuous extraction

❖ Maceration

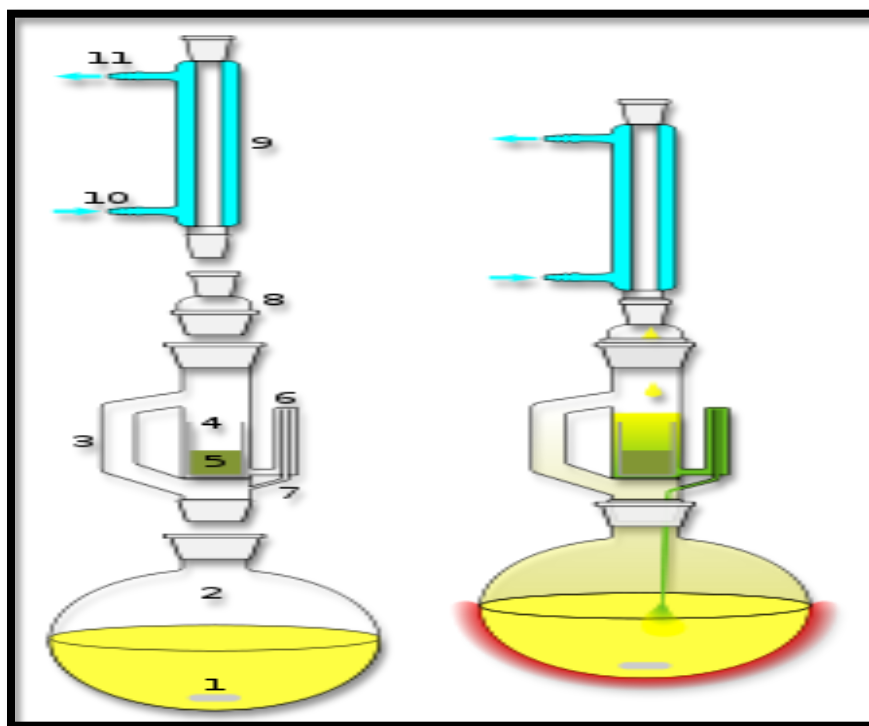
- Accurately weighed powdered drug is dipped in a specified amount of solvent or mixture of solvents
- Then made it alkaline with ammonia TS solution and mix well and allow to macerate for 12 -24 hours with occasional shaking
- Afterwards allow the solvent to settle
- Decant and aliquots of which are used for analysis

❖ Percolation

- Place accurately weighed powdered drug in a suitable container, saturate with suitable solvent for 5min
- Make it alkaline with Ammonia solution, mix thoroughly and put in percolator
- Allow the drug to macerate for 10-12 h
- Percolate it slowly until percolate is alkaloid free
- Determine the completeness of the extraction process by evaporating about 4ml of last percolate to dryness, dissolving the residue in 0.5ml of approximately 0.5N acid and adding a drop of mercuric iodide solution (valser's reagent); not more than a slight turbidity is produced.

❖ Continuous extraction

- Counter current extraction using soxhlet extractor



1: Stirrer bar 2: Still pot (the still pot should not be overfilled and the volume of solvent in the still pot should be 3 to 4 times the volume of the soxhlet chamber) 3: Distillation path 4: Thimble 5: Solid 6: Siphon top 7: Siphon exit 8: Expansion adapter 9: Condenser 10: Cooling water in 11: Cooling water out

Procedure of Continuous extraction:

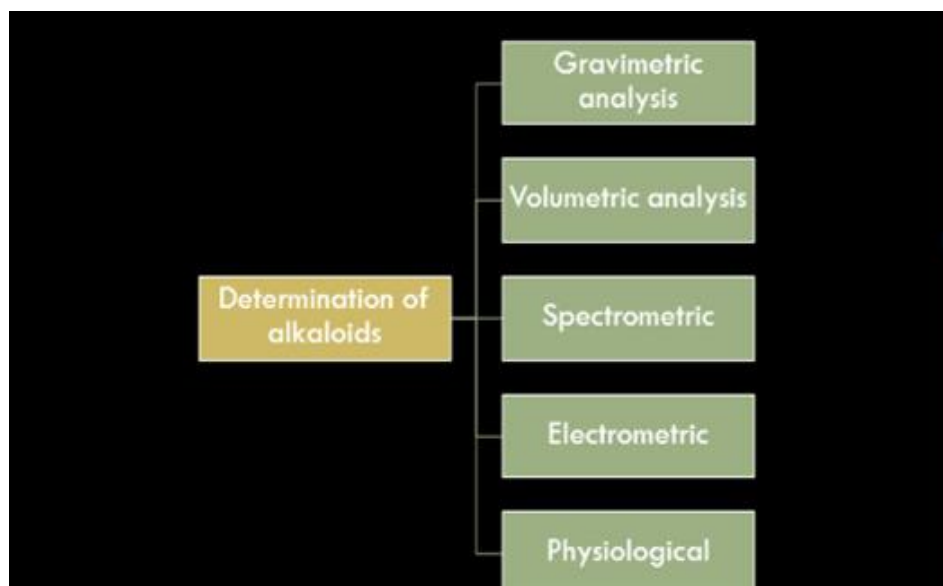
- The solvent is heated to reflux. The solvent vapour travels up a distillation arm, and floods into the chamber housing the thimble of solid. The condenser ensures that any solvent vapour cools, and drips back down into the chamber housing the solid material. The chamber containing the solid material slowly fills with warm solvent. Some of the desired compound dissolves in the warm solvent. When the Soxhlet chamber is almost full, the chamber is emptied by the siphon. The solvent is returned to the distillation

flask. The thimble ensures that the rapid motion of the solvent does not transport any solid material to the still pot. This cycle may be allowed to repeat many times, over hours or days.

1. Purification

- Take the aliquot, and extract with dilute acid
- Then make the acid part alkaline and extract with some immiscible solvent
- Purification of the alkaloids is thus achieved by any of the following methods;
 - Crystallization
 - Removal of associated alkaloids using chemical methods
 - Using immiscible solvents (repeated extraction of alkaloid from aqueous and organic solvent)

Determination of alkaloids:



2. Determination of alkaloids

- Evaporate the alkaloidal solution to dryness by steam or with a current of air
- Soften the residue with 1 ml neutral ether or alcohol
- Add a volume of standard acid and warm gently to make complete solution
- Add the volume of water to make 25 ml
- Titrate the excess of acid by a standard alkali using methyl red as an indicator
- If alkaloidal residue is to be weighed, dry it at 105°C to a constant weight
- If solvent is chloroform
- Remove the traces with few ml neutral ether or alcohol followed by evaporation

❖ Special treatment

➤ Use of adsorbent:

- for fluidextracts and tinctures having alkaloidal drugs, it is necessary to evaporate them to dryness
- To facilitate evaporation and reduce loss, extracts are added on an adsorbent-previously acid or alkali washed-then made neutral by washing with water and dried before use

➤ Emulsions:

- Avoid shaking of immiscible solvent with water
- If emulsion forms, add excess of either of the solvents
- It will results in the break down of emulsion

- Emulsion can also be broken down by adding anhydrous sodium sulphate