Principals and dosage forms of pharmaceutics

Part I. Liquid dosage forms: solutions, emulsions, suspensions, drops

2019

Pharmaceutical Propedeutics

Institute of Pharmaceutical Technology and Biopharmacy

Dosage forms

Medication (medical product) *=*

Active pharmaceutical ingredient (API)+ excipient(s)

+ packaging material

- **Manufacturing/ compounding** - pharmaceutical products
- Pharmaceutical products, which are suitable for direct administration are called as DOSAGE FORM.

Summary

- **Dosage forms** – **its physico-chemical systems**

Liquid dosage forms

Solutions – drops

Disperse systems containing two or more phase – emulsions, suspensions

Injectable products – injections, infusions

Semisolid dosage forms – ointments, suppositories

Solid dosage forms – powders, dusting powders, granules, tablets, capsules

Other dosage forms– patches, nano preparations (liposomes)

Veterinary dosage forms – different applications, dosage forms from human preparations

+ Packaging

Tools for preparation of solutions and other liquid dosage forms

According to health care regulation of 41/2007. (IX. 19.)

- Beakers

- Flasks
  - Erlenmeyer flasks

  - Round bottom boiling flask

- Porcelain volumetric jar (Menzura)
- Glass rods
- Glass funnel with stand
- Boiling ware

Solutions

- Solutions -as a dosage form- are externally or per orally used preparation containing active substance(s) and solvents, which have to be:
- free from sediments,
- clear,
- liquid preparation.

Homogeneous disperse system

Solutions

Advantages

- Solutions are molecularly dispersed systems, they are completely homogenous, and they have the immediate availability for absorption and distribution.
- Solutions also provide a flexible dosage form.
  - they may be used by any route of administration
  - they can be taken by or administered to patients who cannot swallow tablets or capsules
  - doses are easily adjusted

Solutions

Disadvantages

- drugs and chemicals are less stable when in solution than when in dry, solid form
- some drugs are not soluble in solvents that are acceptable for pharmaceutical use
- drugs with objectionable taste require special additives or techniques to mask the taste when in solution
- because solutions are bulkier and heavier than dry, solid dosage forms, they are more difficult to handle, package, transport and store
- oral solutions in containers require measurement by the patient or caregiver. This is often less accurate than individual solid forms, such as tablets and capsules

Solutions

Parts of the solution

- solute: dispersed medium
- solvent: dispersing medium

Mass percentage (%w/w)

- In the solutions the dissolved materials are weighed and the solvent is added to the prescribed mass.
- The solution is given in mass percentage: (%w/w) percent per weight.
- This means the number of grams of solute per 100 g of solution.

Solutions

What to consider during dissolution

- Heat sensitivity of the substances to be dissolved
- The nature of the substance
- The dissolved substance should not separate out from the solution prepared by heating, even after cooling to room temperature

The steps of dissolution

- Find the proper solvent
- Pour the solvent in the bottle (beaker etc..)
- Measure the substance to be dissolved on a balance
- Add the substance to be dissolved to the solvent
- Shake well until it dissolves

Solutions

The order of dissolving

- If there is *no significant* difference in the solubility of the ingredients, we usually dissolve the ingredients according to their *increasing masses*
- If there is *great difference* in their solubility, we perform the dissolution in the order of *increasing solubility*
- If there is a poorly soluble substance that can be dissolved with the help of heating, then we dissolve this substance first in the solvent, heated to the required temperature, and after cooling to room temperature we dissolve the other ingredients
- Volatile or strong-smelling substances are added last
- The ready solution must be shaken and homogenized
- If the solution contains unsolved, extraneous particles, the solution must be filtered

Ph.Hg.VIII.

(8th edition of Hungarian Pharmacopoeia)

- Solutions / pharmaceutical products
- Per oral/ oral liquid preaparations
  (Praeparationes liquidae peroraliae)
- Dermal liquid preparations
  (Praeparationes liquidae ad usum dermicum)

Vaginal solutions
Gargle solutions
Mouth rinse solutions
Solutions applied on oral mucosa
Rectal solutions

Storage

C. It complies with the requirement for the content of H_2O_2.

TESTS

Acidity. To 10 ml add 20 ml of *water R* and 0.25 ml of *methyl red solution R*. Not less than 0.05 ml and not more than 1.0 ml of *0.1 M sodium hydroxide* is required to change the colour of the indicator.

Organic stabilisers. Shake 20 ml with 10 ml of *chloroform R* and then with two quantities, each of 5 ml, of *chloroform R*. Evaporate the combined chloroform layers under reduced pressure at a temperature not exceeding 25 °C and dry the residue in a desiccator. The residue weighs not more than 5 mg (250 ppm).

Non-volatile residue. Allow 10 ml to stand in a platinum dish until all effervescence has ceased. Evaporate the solution to dryness on a water-bath and dry the residue at 100 °C to 105 °C. The residue weighs not more than 20 mg (2 g/l).

ASSAY

Dilute 10.0 g to 100.0 ml with *water R*. To 10.0 ml of this solution add 20 ml of *dilute sulphuric acid R*. Titrate with *0.02 M potassium permanganate* until a pink colour is obtained.

1 ml of *0.02 M potassium permanganate* is equivalent to 1.701 mg of H_2O_2 or 0.56 ml of oxygen.

STORAGE

Store protected from light; if the solution does not contain a stabiliser, store at a temperature below 15 °C.

LABELLING

If the solution contains a stabiliser, the label states that the contents are stabilised. The competent authority may require that the name of the stabiliser be stated on the label.

CAUTION

It decomposes in contact with oxidisable organic matter and with certain metals and if allowed to become alkaline.

01/2005:0396

HYDROGEN PEROXIDE SOLUTION (30 PER CENT)

Hydrogenii peroxidum 30 per centum

DEFINITION

Hydrogen peroxide solution (30 per cent) contains not less than 29.0 per cent *m/m* and not more than 31.0 per cent *m/m* of H_2O_2 (M_r 34.01). One volume of this solution corresponds to about 110 times its volume of oxygen. A suitable stabiliser may be added.

CHARACTERS

A colourless, clear liquid.

IDENTIFICATION

A. To 1 ml add 0.2 ml of *dilute sulphuric acid R* and 0.25 ml of *0.02 M potassium permanganate*. The solution becomes colourless with evolution of gas.

B. To 0.05 ml add 2 ml of *dilute sulphuric acid R*, 2 ml of *ether R* and 0.05 ml of *potassium chromate solution R* and shake. The ether layer is blue.

C. It complies with the requirement for the content of H_2O_2.

TESTS

Acidity. To 10 ml add 100 ml of *water R* and 0.25 ml of *methyl red solution R*. Not less than 0.05 ml and not more than 0.5 ml of *0.1 M sodium hydroxide* is required to change the colour of the indicator.

Organic stabilisers. Shake 20 ml with 10 ml of *chloroform R* and then with two quantities, each 5 ml, of *chloroform R*. Evaporate the combined chloroform layers under reduced pressure at a temperature not exceeding 25 °C and dry the residue in a desiccator. The residue weighs not more than 10 mg (500 ppm).

Non-volatile residue. Allow 10 ml to stand in a platinum dish until all effervescence has ceased, cooling if necessary. Evaporate the solution to dryness on a water-bath and dry the residue at 100 °C to 105 °C. The residue weighs not more than 20 mg (2 g/l).

ASSAY

Dilute 1.00 g to 100.0 ml with *water R*. To 10.0 ml of this solution add 20 ml of *dilute sulphuric acid R*. Titrate with *0.02 M potassium permanganate* until a pink colour is obtained.

1 ml of *0.02 M potassium permanganate* is equivalent to 1.701 mg of H_2O_2 or 0.56 ml of oxygen.

STORAGE

Store protected from light; if the solution does not contain a stabiliser, store at a temperature below 15 °C.

LABELLING

If the solution contains a stabiliser, the label states that the contents are stabilised. The competent authority may require that the name of the stabiliser be stated on the label.

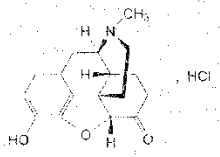
CAUTION

It decomposes vigorously in contact with oxidisable organic matter and with certain metals and if allowed to become alkaline.

01/2005:2099

HYDROMORPHONE HYDROCHLORIDE

Hydromorphoni hydrochloridum



$C_{17}H_{20}ClNO_3$ M_r 321.8

DEFINITION

4,5α-Epoxy-3-hydroxy-17-methylmorphinan-6-one hydrochloride.

Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

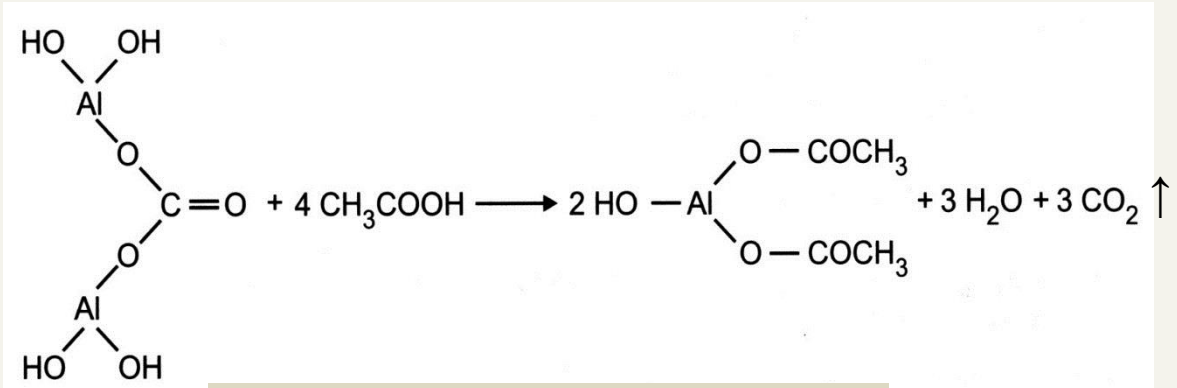
Appearance: white or almost white, crystalline powder.

Solubility: freely soluble in water, very slightly soluble in ethanol (96 per cent), practically insoluble in methylene chloride.

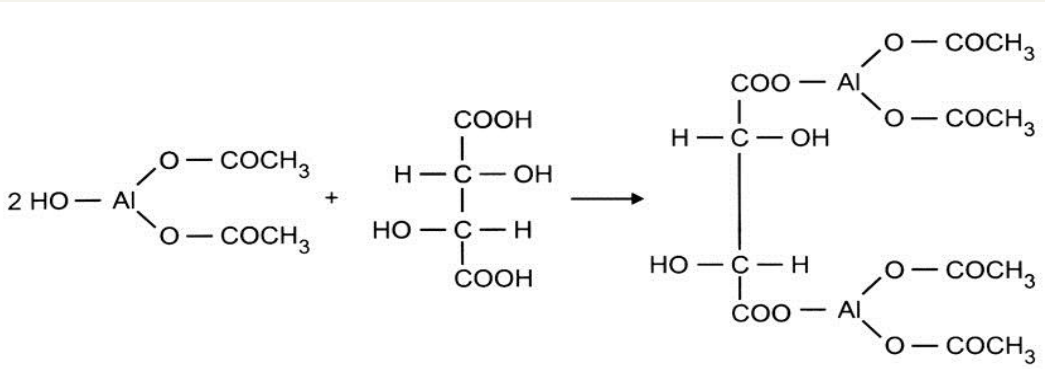
Storage:
Store protected from light; if the solution does not contain stabilizer store at a temperature below 15 ºC

Aluminium aceticum tartaricum solutum (Ph.Hg.VII.) (Burow solution)

$$Al_2(SO_4)_3*18\,H_2O + 3CaCO_3 \rightarrow Al_2(OH)_4CO_3 + 3\underline{CaSO_4}*2H_2O + 10H_2O + 2CO_2\uparrow$$



Creation of basic aluminum acetate



Formation of aluminum acetate tartarate solution

Drops

GUTTAE/ Drops: are intended to use per orally, dispensed to small volumes (drops).

Drops which are applied externally, are termed accoridng to their application:

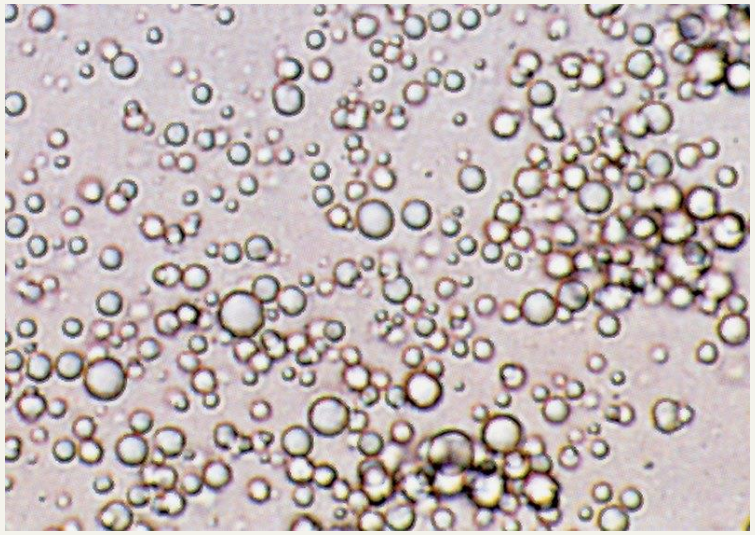
Oculogutta - eye drop
Otogutta - ear drop
Nasogutta - nose drops

Eye drops

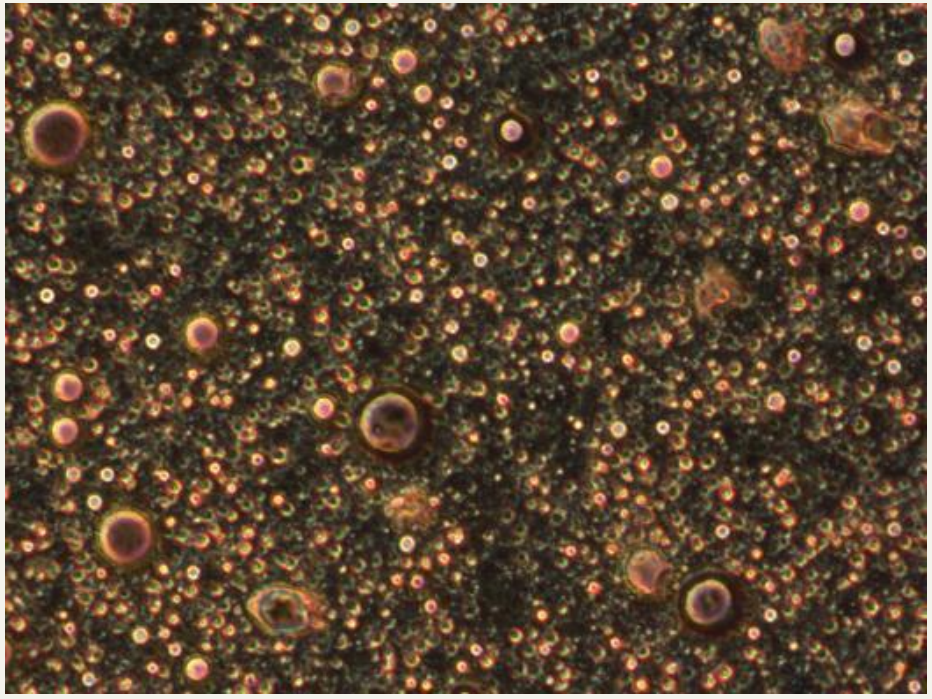
Eye preparations:

- eye drops,
- eye washes,
- powders for preparation of eye drops or eye,
- semisolid ophtalmic preparations (ointments),
- ophtalmic medicated plates

Emulsions



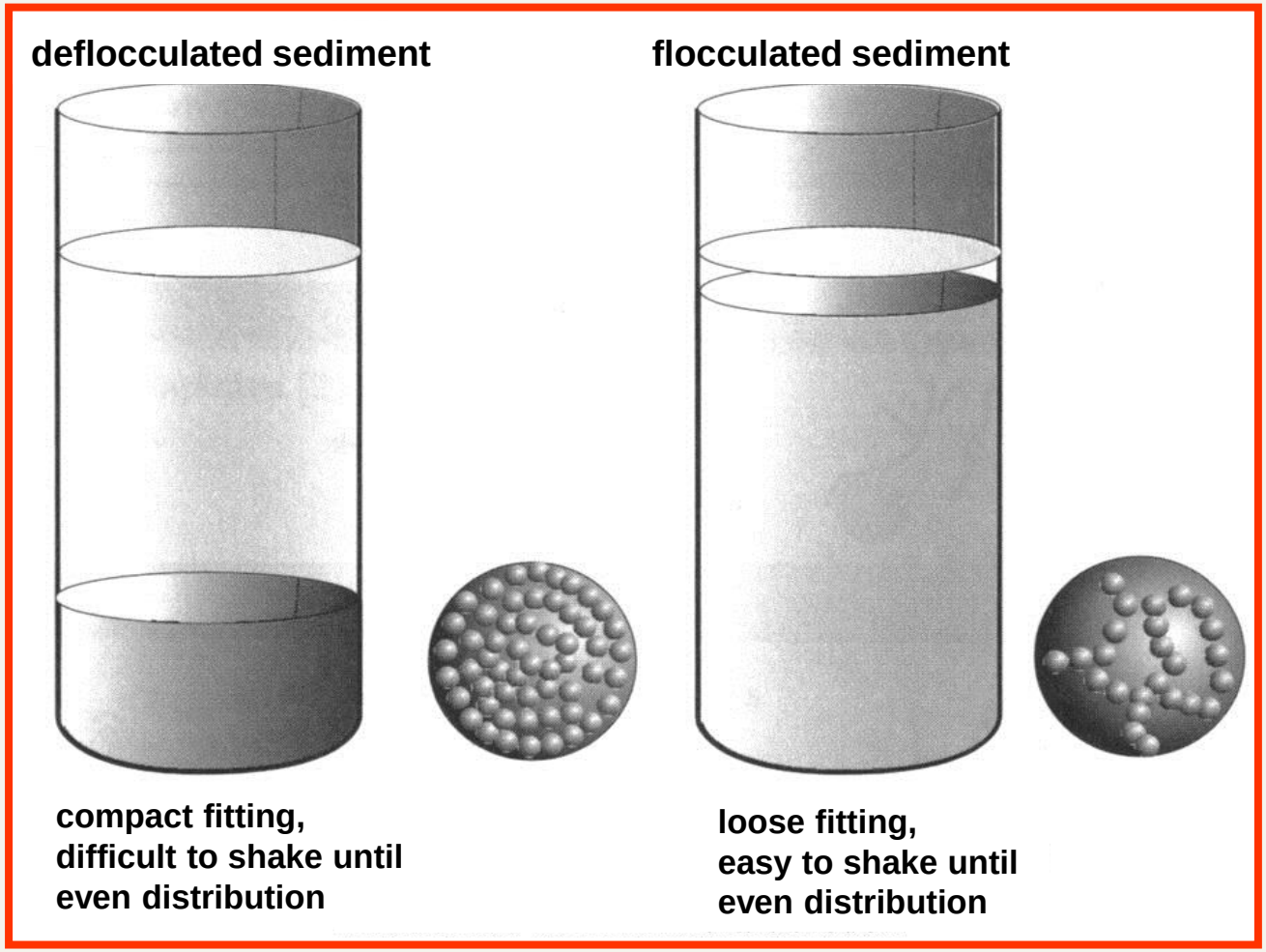
Structure of emulsions:
microscopic picture of milk



Structure of emulsions:
microscopic picture of a hydrophilic ointment

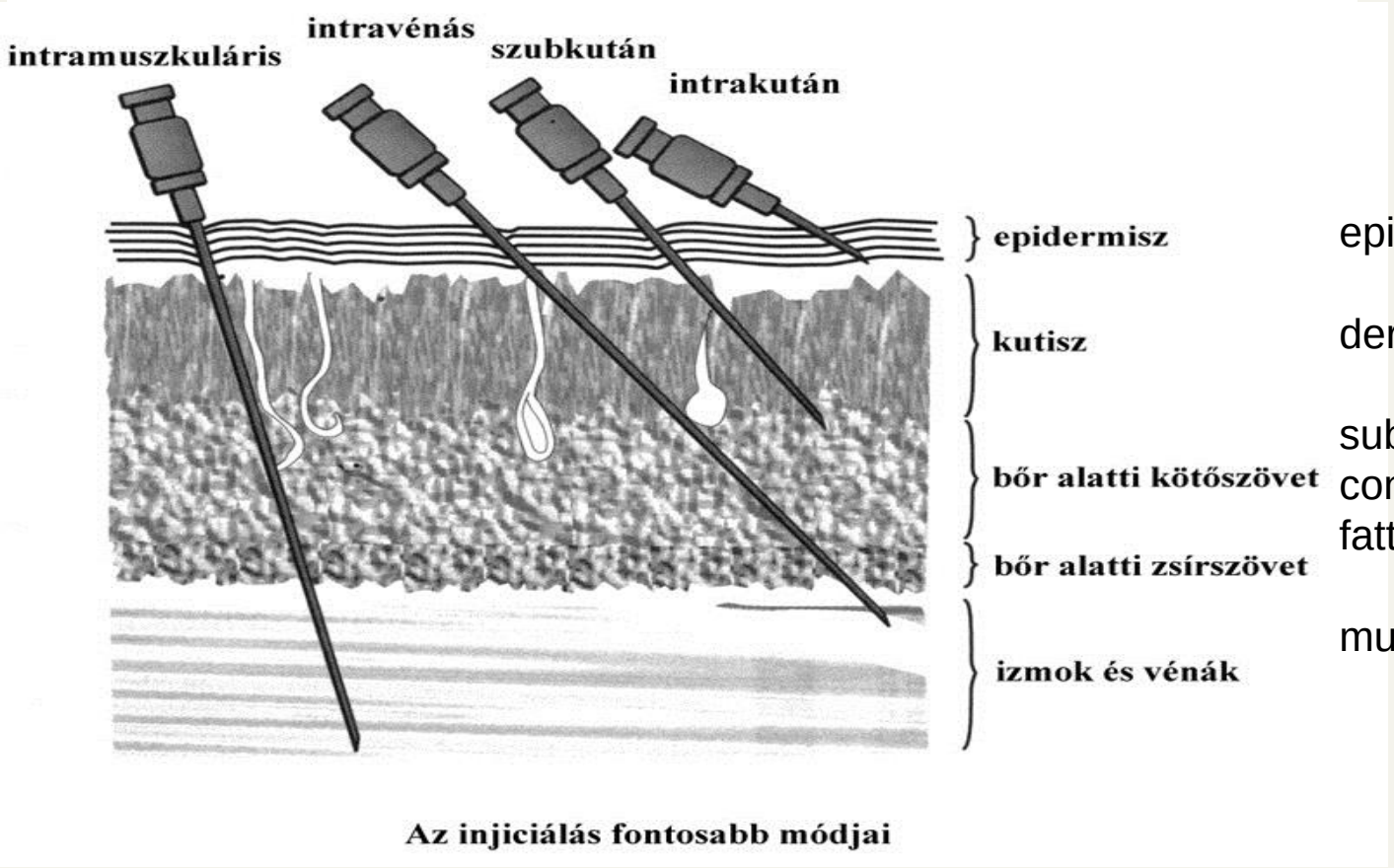
SUSPENSIONS

flocculated and deflocculated sediment



Injections, infusions

intramuscular, intraveneous, subcutaneous, intradermal (intracutaneous)



Az injiciálás fontosabb módjai

epidermis

dermis

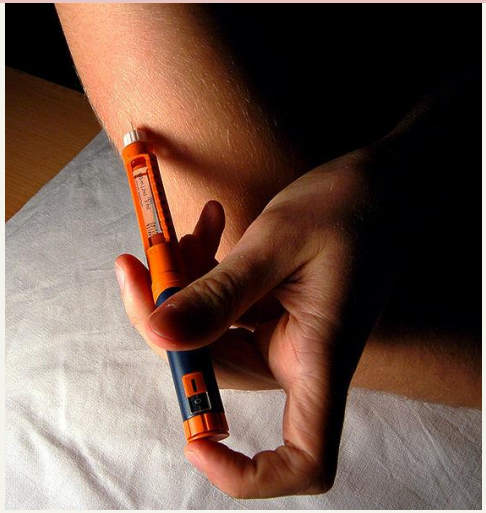
subcutaneous connective tissue and fatty tissue

muscles and veins

Administration of drugs

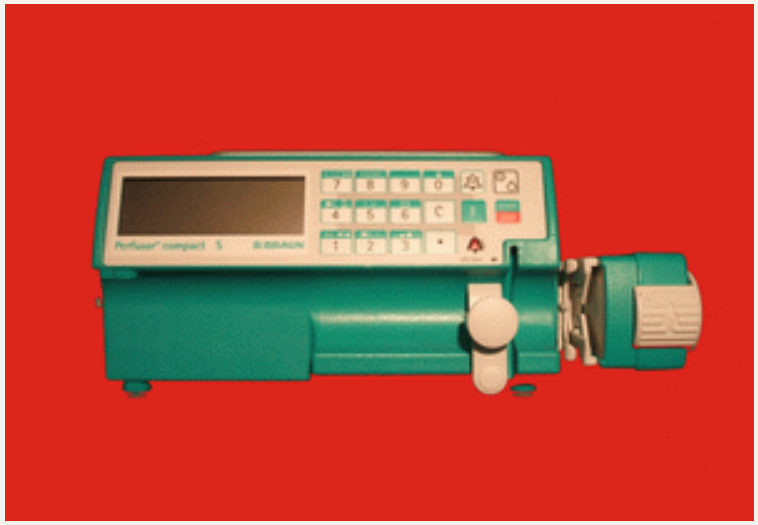
Dosing systems: example administration of insuline

Syringe, needle



Pen

Infusion pump

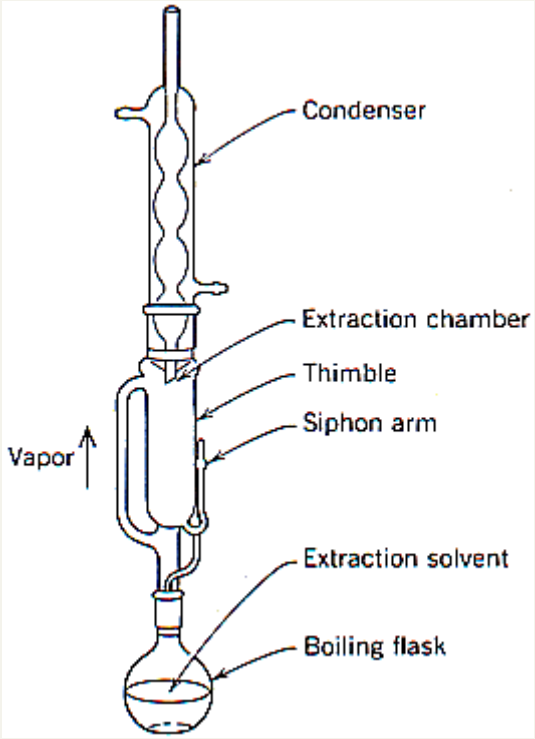


Extracts - EXTRACTA

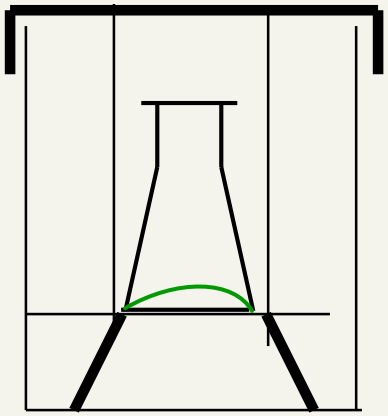
Extracts are liquid, semisolid, solid materials, which are generally gained from solid herbal drugs and materials drerived from animals.

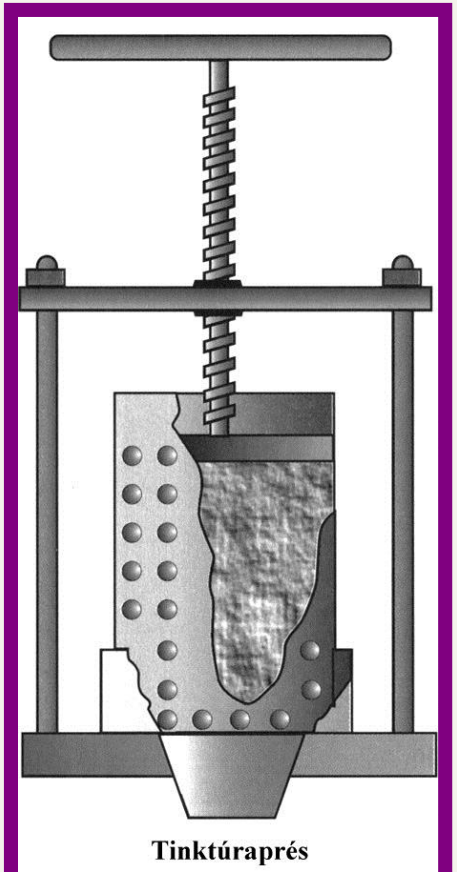
Types according to:

- State of matters:
  - **liquid (liquid extract , tincture)**
  - semisolid(soft ~)
  - solid (dry)
- Types:
  - Standardized extracts (known therapeutical value)
  - „ Quantified extracts” (certain ingredients are in particular concentration interval)
  - other extracts defined by special preparation process and specifications



Schulek pot





Tinktúraprés

THANK YOU FOR ATTENTION!