

# Pharmaceutical Technology I

## Lecture 1

1/10/2019

### Definition and classification of dispersed systems

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References: text books

Lewis W. Dittert, "American pharmacy", Lippincott. company, 1974.

Ansel's Pharmaceutical dosage forms and drug delivery systems

10<sup>th</sup> edition by Howard C. Ansel. Sinko. Wolters Kluwer,

Lippincott Williams &Wilkins. Philadelphia. 2014.

Suggested References:

British Pharmacopeia BP

United stated Pharmacopeia USP

Martin Physical pharmacy

# Lecture 1

## Dispersed system

- Dispersed system is a mixture of two phases (dispersed phase and dispersion medium), which consist of dispersed part of one or two substances in a dispersion medium.
- The dispersed phase may called solute or internal phase, while the dispersion medium called solvent or external phase.

# Classification of dispersed systems

1. According to physical state of both phases dispersed system can be classified into nine types as:

Dispersed phase	Dispersion medium		
	Solid	liquid	Gas
Solid	S / S	S/L	S/G
Liquid	L / S	L / L	L/G
Gas	G/S	G/L	G/G

Solid in liquid and liquid in liquid is the most used in pharmaceutical preparations

- 2.** According to the interaction between the two phases, dispersion system can be classified as
- lyophilic dispersion e.g. sugar in water, alcohol in water, and
  - lyophobic dispersion e.g. benzene with water, oil with water.
- 3.** According to the particle size of the dispersed phase, dispersion can be divided into:
- molecular dispersion
  - colloidal dispersion and
  - coarse dispersion.

- Molecular dispersion can be defined as a homogenous system of two or more substances; this system may be called **true solution**, because the solute completely dissipated into solvent.
- Whereas other dispersions are heterogeneous system-as exemplified by **suspension** and **emulsion**-where the dispersed phase, typically a particle of some type, is physically distinguishable from the medium in which it is dispersed.

## **Molecular dispersions**

1. Molecular dispersion is a true solutions of a solute phase in a solvent.
  2. The dispersed phase (solute) is in form of separate molecules homogeneously distributed throughout the dispersion medium(solvent).
  3. The molecule size is less than 1 nm.
- ❖ The examples of molecular dispersions:
1. air (a molecular mixture of Oxygen, Nitrogen and some other gases),
  2. electrolytes (aqueous solutions of salts),
  3. metal alloys solid solution.

## Colloidal dispersion (colloids)

1. Colloids are micro-heterogeneous dispersed systems, in which the size of the dispersed phase particles is within the range 1 - 1000 nm.
  2. The colloids phases can not be separated under gravity, centrifugal or other forces. Dispersed phase of colloids may be separated from the dispersion medium by micro-filtration.
- ❖ The examples of colloids:
1. milk (emulsion of fat and some other substances in water),
  2. fog (aerosol of water micro-droplets in air),
  3. Silica aerogel monolith,
  4. Alumina aerogel monolith

## **Coarse dispersions (suspensions)**

1. Coarse dispersions are heterogeneous dispersed systems, in which the dispersed phase particles are larger than 1000 nm.
2. Coarse dispersions are characterized by relatively fast sedimentation of the dispersed phase caused by gravity or other forces. Dispersed phase of coarse dispersions may be easily separated from the continuous phase by filtration.



# Solutions

- In pharmaceutical term, solutions are "liquid preparations that contain one or more chemical substances dissolved in a suitable solvent or mixture of mutually miscible solvents".
- pharmaceutical solutions may be classified according to their intended uses into:
  1. Oral solution
  2. Otic solution
  3. Ophthalmic solution
  4. Nasal solution (e.g. normal saline nasal drop)
  5. Topical solutions

❖ Other solutions, because of their composition or use, may be classified as other pharmaceutical dosage forms.

1. For example, aqueous solution containing sugar are classified as **syrops**. Whereas, sweetened hydroalcoholic solutions are termed **elixirs**.
2. On the other hand solutions of aromatic materials are termed **spirits** if the solvent is alcohol and **aromatic water** if the solvent is aqueous

- ❖ Solutions prepared by extracting active constituents from crude drugs are termed **tincture** or **fluid extracts**, depending on their method of preparation and concentration. **Tinctures** may also be solutions of chemical substances dissolved in alcohol or in a hydroalcoholic solvent.
- ❖ Certain solutions prepared to be sterile and pyrogen free and intended for parenteral administration are classified as **injections**.



- The preferred dosage form is solution but sometimes we use suspension instead of solution because:
  1. To get more stability
  2. To change the drug taste
  3. Large quantity of the drug will be in the dispersed form and not precipitate.

- ❖ Solutes other than the medicinal agent are usually present in orally administered solutions.
- These additional agents usually are included to provide **color, flavor, sweetness** or **stability**.
- In formulating or compounding a pharmaceutical solution, the pharmacist must use information on the solubility and stability of each solute present with regard to the solvent or solvent system employed.

# Types of solutions

- **Solution of solid in liquid**

Most of true solutions are example of solid in liquid solution.

- **Solubility:**

- The solubility of an agent in a particular solvent indicates the maximum concentration to which a solution may be prepared with that agent and that solvent.

- When excess of solid (solute) is shaken with liquid (solvent) for a period of time a maximum amount of it will be dissolved, the solvent is then saturated by solute resulting in saturated solution at a given temperature.

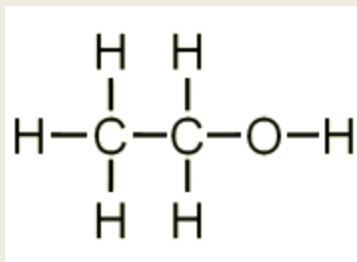
# Factors affecting solubility of solid in liquid

1. Temperature: the effect of temperature is not always the same, there are three different cases:
  - a. Endothermic system: most chemicals absorb heat when they are dissolved and are said to have a positive heat of solution, resulting in increased solubility with an increase in the temperature.
  - b. Exothermic system: a few chemicals have a negative heat of solution and exhibit a decrease in solubility with a rise in temperature e.g. methyl cellulose, NaOH and  $\text{Ca}(\text{OH})_2$ .
  - c. Neither exothermic nor endothermic system: which means that the solubility of the compound at low temperature is the same when the temperature is high e.g. NaCl.



- ## 2. Effect of molecular structure of solute and solvent (like dissolves like)
- The more nearly solute and solvent are alike molecular structure the greater the solubility of one in the other.
  - In general it may be stated that the polar solvents like water will dissolve salts and other electrolyte readily
  - but they are poor solvents for non polar substances. On other hand, non polar liquids are required for non polar solutes.
  - Polar liquids may act as solvent when solute are capable of H-bond formation with solvent e.g. water and alcohol of low MWt.
  - As the MWt of alcohol increased, resulted in decrease polarity and decrease the solubility in water.

- Polar liquids should be miscible with other polar liquids. Conversely non polar liquids dissolve only slightly in polar solvents, but they dissolve readily in solvents that are non polar.
- Complex organic compounds which have polar and non polar groups in their molecules may dissolve in polar liquids, but their solubility in such solvents tends to decrease in proportion to the number of non polar groups
- Semipolar liquids, such as ethyl alcohol possess some of properties of both polar and nonpolar solvents.



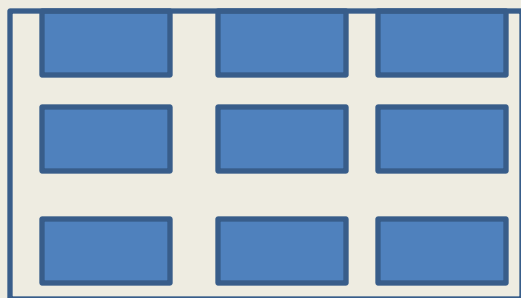
Ethyl alcohol or ethanol have

- 5 non polar carbon–Hydrogen bond
- 1 C-C bond (non polar)
- C-O bond & H-O bond (polar)

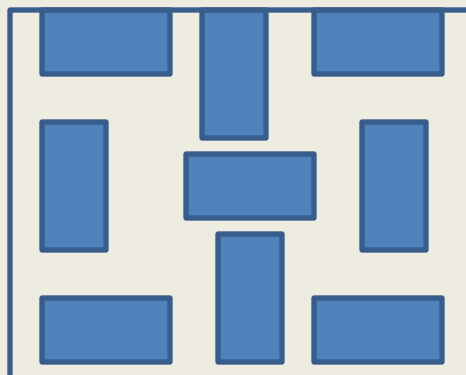
So it is considered as good solvent for some polar and non polar substances due to the presence of distinct polar and non polar regions

3. Effect of nature of solute: the solutes suffer from polymorphism, hydrates, solvates.
- **Polymorphism:** it is a phenomenon that the compound exists in more than one form which has the same chemical structure but different physical properties like melting point, solubility, absorption and therapeutic activity.
  - Some polymorph is inactive, so pharmacist should aware about this phenomenon.

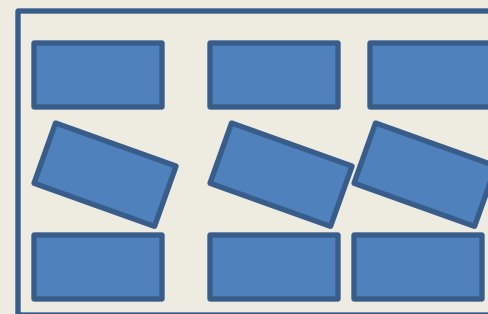
- Q. why solute suffers from polymorphism?
- polymorphism takes place because different arrangement of molecules in crystal.



Polymorph 1



Polymorph 2



Polymorph 3

- Example of drug shows polymorphism chloramphenicol, it exists in more than one polymorph; one active and other not active.
- Various techniques are used in determining crystal properties, the most widely used methods are hot stage microscopy, thermal analysis, infrared spectroscopy and X-ray diffraction.

- **Hydrates**: compounds contain water in their crystals.
- **Solvates**: compounds contain other solvent than water in their crystals.
- The anhydrous form of the compound is more soluble than hydrate form of the same compound, while the solvate of the same compound is more soluble than non-solvate form in water.
- Hydrate may be monohydrate, dihydrate and trihydrate.
- Example of hydrate: Ampicillin trihydrate it contains three molecules of water.

Q. Why the anhydrous form of the same drug is more soluble than the hydrous form?

Answer: due to the presence of water within the crystal, so the hydrous form will be busy with its own water of crystallization to form hydrogen bond. While anhydrous is not busy so it can form hydrogen-bond with the external phase (solvent) e.g. the water.

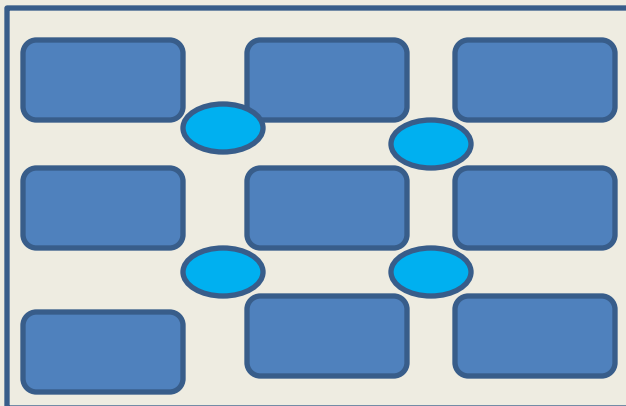
Q. Anhydrous form has a faster dissolution rate than the hydrate.

Answer: In hydrate, water could bond between two drug molecules via hydrogen bond and tie the lattice and hence slow down its dissolution rate.

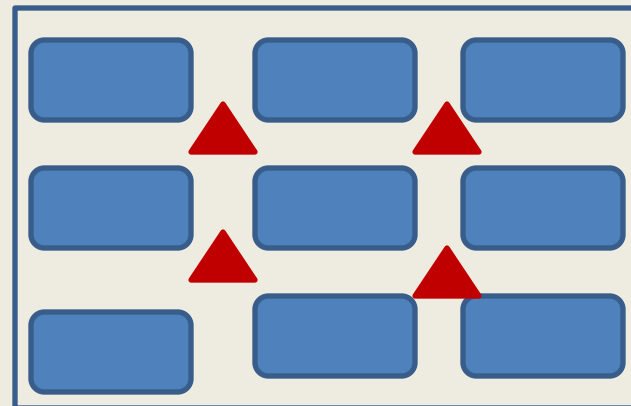


Q. why the solvate form of the same drug is more soluble than non-solvate form in water?

Answer: This is because the compound contains solvent such as ethanol, which has a tendency to interact with the external water, so as a result, it make crystals more soluble.



Hydrate



Solvate