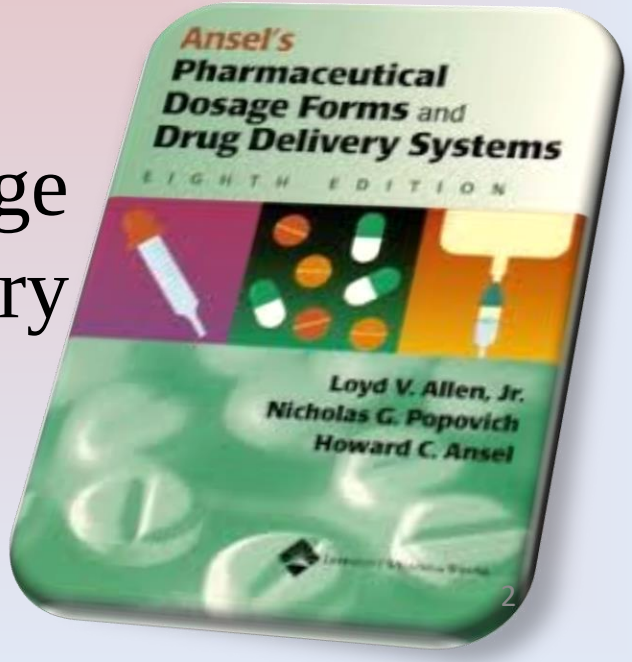
Ministry of Higher Education and Scientific Research
Al- Rasheed University College
Department of Pharmacy

Pharmaceutical Technology for 3rd year students,2018

By:
Dr. Esra`a Ghazy Jabbar
Pharmaceutics PhD.

Pharmaceutical Technology I
Reference of course

- 1- Sprowls American Pharmacy (An introduction to pharmaceutical techniques and Dosage forms) by Lewis W. Ditter.
- 2- Ansels Pharmaceutical Dosage Forms and Drug Delivery Systems by Howard C. Ansel.



Course Syllabus

1- Solubility: Factors affecting solubility; expression of dissolution; dissolution rate versus solubility; preparation of solutions containing non-volatile materials.

2- Official solutions; classification of official solutions; preparation and uses. Definition and methods of clarification; filter aids in clarification.

A/ Aqueous solutions containing aromatic principles; aromatic waters; methods of preparation; stability.

B/ Aqueous solutions containing Non volatile materials.

C- Solution using Mixed solvent Systems (Spirits, elixirs, & Extracted products).

3- Syrups: sugar based syrups; artificial and sorbitol based syrups; stability of syrups.

4- Dispersed systems: their classification; comparisons between different systems: Colloidal dispersions & Coarse dispersions

5- Extraction; maceration and percolation. Tinctures; fluid extracts; extracts of resins and oleoresins.

Liquid dosage forms can be classified

1- For internal use (P.O.) ex., oral suspension and solution

2- for External Use (Topically) ex., lotions or suspension applied to the skin, otic, ophthalmic, or nasal.

3- for injection (Paranterally) ex., subcutaneous injection (Sc.), intramuscular injection (IM.)& intravenous administration (IV.)


solutions

Objectives;

After finishing this chapter, the students will be able to:

1 . Define the various types of oral and topical liquid dosage forms

2 . List the advantages and disadvantages of using liquid dosage forms in immediately compounded prescriptions and in patient therapy.

3 . Compare and contrast liquid dosage forms to solid oral dosage forms.

4 . Define solubility and describe how different factors increase or decrease solute solubility in a given solvent

5 . Evaluate and select a proper solvent and delivery system for a given solute, purpose, and/or patient population

Advantages Vs Disadvantages of liquid dosage forms

Advantages	Disadvantages
1- Used for patients who can not swallow.	1- Has short shelf life due to low stability.
2- Has fast absorption rate.	2- Has less accuracy.
3- more flexible in achieving the proper dosing.	3- Needs special transferring conditions.
4- Best choice for young children and elders.	4- easily infected by microorganisms.
	5- Has special storage requirements.

- ***In physicochemical terms,*** solutions may be prepared from any combination of a solid, liquid, and gas.
- For example, a solid solute may be dissolved in another solid, a liquid, or a gas, and the same being **true** for a liquid solute and for a gas;

- ✓ Nine types of homogeneous mixtures are possible.

- In pharmacy, however, interest in solutions is for the most part limited to preparations of a solid, a liquid, and less frequently a gas solute in a liquid solvent.

- **Solution** : is a homogeneous mixture composed of two or more substances (the solute is dissolved in another substance, known as a solvent).

- ✓ **Concentrated Vs dilute solution**

- ✓ **What is the difference between concentrated & diluted solutions???**

- ✓ **Saturated Vs Unsaturated solutions**

- ✓ **What is the difference between concentrated & diluted solutions???**

➢ ***According to the method of preparation, solutions can be classified into:***

(1) Solutions prepared by simple solution method

Solution prepared by chemical reaction :

3- **Solutions prepared by simple solution with Sterilization:**

4- **Solutions prepared by extraction**.

Different Types of Water , as Defined by the British Pharmacopeia [BP]

Type of water	Use
Purified Water	Used for the preparation of medicines that do not have to be sterile and apyrogenic.
Highly Purified Water	Used for the preparation of medicines where water of high biological quality is needed, except where Water for Injections is required.
Water for Injections	Used for medicines for parenteral administration. Must be pyrogen-free.
Sterilized Water for Injections	Used for medicines for parenteral administration. Water has been sterilized by heat and is suitably packaged.

➢ Examples of Non – Aqueous Solvents used in Pharmaceutical Solutions

Solvent	Use
Alcohols, including polyhydric ones (i.e. those containing more than one hydroxyl group per molecule)	*Ethanol* is the most common organic solvent used in pharmaceutical solutions. It is often used as a co-solvent in oral, topical and parenteral solutions. *Propylene glycol* ($CH_3CH(OH)CH_2OH$) contains 2 hydroxyl groups per molecule. It is often used as a co-solvent in oral, topical, parenteral and otic solutions. *Glycerol* contains 3 hydroxyl groups per molecule. It is widely used as a solvent or co-solvent with water, in oral and parenteral solutions. *Low molecular weight polyethylene glycols* (PEGs) with the general formula $HOCH_2(CH_2CH_2O)_nCH_2OH$. These are used as solvents or co-solvents with water or ethanol. Used in parenteral solutions.
Fixed vegetable oils	Fixed oils are expressed from the seeds, fruit or pit/stone/kernel of various plants. They are non-volatile oils and are mainly triglycerides of fatty acids. Examples include olive oil, corn oil, sesame oil, arachis oil, almond oil, poppyseed oil, soya oil, cottonseed oil, castor oil. Historically, they have been used for intramuscular administration. They are used to a lesser extent now due to their irritancy and the possibility of allergic reactions to certain oils. They are being replaced by synthetic alternatives such as ethyl oleate.
Esters, such as ethyl oleate, benzyl benzoate, ethyl ethanoate	These are used as a vehicle in certain intramuscular injections.
Dimethyl sulfoxide	Used as a carrier for idoxuridine for topical application to the skin.
Glycofurol	Used as a co-solvent in parenteral solutions for intramuscular or intravenous injection.
Ethyl ether	Used as a co-solvent with ethanol in collodions.

- The excipient must be;
  - non–toxic,
  - non-sensitizing,
  - non-irritating, as well as
  - compatible with all the other components of the formulation.

➢Excipients used in Pharmaceutical Solutions

Excipients	Examples of excipients
Co-solvents	Ethanol, glycerol, propylene glycol. The concentration of ethanol should be limited as it exerts a pharmacological action following oral administration.
Flavouring Agents	Used to mask the taste of drugs, many of which have a very unpleasant taste. Synthetic or naturally occurring flavourings such as vanilla, raspberry, orange oil, lemon oil are used for oral solutions. Menthol is used in both oral and nasal solutions. Certain flavours appeal to certain patient populations and certain parts of the world; this must be borne in mind by the formulator. For example, fruit and bubble gum flavours are acceptable to children, whilst mint flavour is not.
Colouring Agents	A colouring agent should correlate with the flavouring agent, e.g. green with mint, red with cherry flavour. Like flavours, colour preference varies between cultures.
Sweeteners	Sucrose, sorbitol, mannitol, saccharin sodium, xylitol, high fructose corn syrup are used to improve the palatability of oral solutions. Sweetened, but sugar-free, preparations containing aspartame are suitable for diabetic patients and are not cariogenic.
Antimicrobial Preservatives	Used to preserve multidose preparations. Examples include benzalkonium chloride, benzyl alcohol, chlorobutanol, thimerosal, combinations of parabens (methyl, propyl, butyl).
Antioxidants	Sodium metabisulphite, sodium sulphite, sodium bisulfate ascorbic acid, used to stabilize solutions.
Chelating Agents	Disodium edentate, used to increase solution stability.
pH Adjusters	Acids, e.g. citric acid, buffers Alkali, e.g. sodium hydroxide, buffers.
Isotonicity Adjusters	Sodium chloride, potassium chloride, mannitol, dextrose, glycerol.
Viscosity Enhancers	Hypromellose, hydroxyethylcellulose, polyvinyl alcohol, povidone, dextran, carbomer 940.

Solubility

- When a solute dissolves, the substance's **intermolecular forces of attraction** must be overcome by forces of **attraction between the solute and the solvent molecules**, in order to break the *solute–solute* and *solvent–solvent* forces to achieve the *solute–solvent* attraction.

- ***Solubility:*** is the maximum concentration to which a solution may be prepared with that solute and that solvent.

- When a solvent at a given temperature has dissolved all of the solute possible, it is said to be ***Saturated***.

➢ Solubility Vs Rate of Solution

➢ **Rate of solution depends on:**

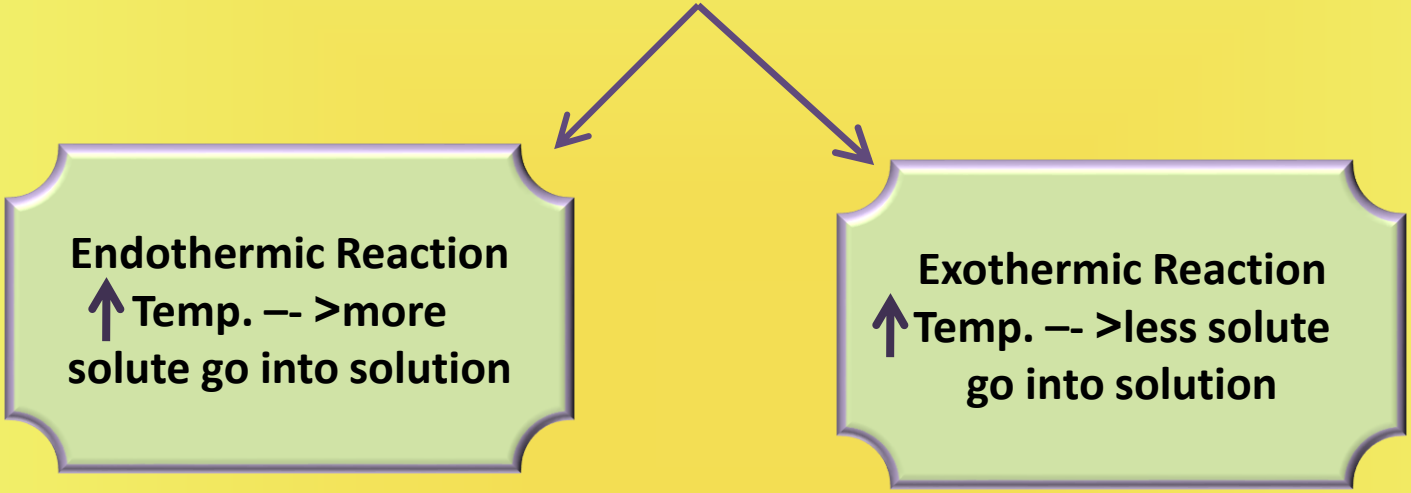
1- **Particle size of the solute**

2- **Agitation**

3- **Temperature:**

➢ Factors that determine the extent of solubility

1- Temperature:



2- Molecular Structure of both Solute & Solvent

- The selectivity of solvent action is dependent on the ability of the solvent to overcome certain **electronic forces** which hold the atoms of solute together and on its ability to act as **solute-solvent biding forces**.

- **The solubility of substances in water is linked to:**

1- The dipole nature of the water molecules.

2-Water is composed of covalent molecules which are described as polar structures with strong dipole characteristics (a negative & positive region)

- **The general criteria for selection of the solvent :**

1- The more nearly solvents & solutes are **alike structurally,** the more rapidly solution takes place.

2- Polar liquids dissolve the electrovalent compounds, but they are poor solvent for non polar substances, (meanwhile, the non polar liquids dissolve the non polar or slightly polar solutes).

In addition, polar liquids should be miscible with other polar liquids & vise versa.

- **The general criteria for selection of the solvent :**

3- Complex organic compounds which have polar & non polar groups in their molecules may **dissolve in polar** liquids, but their ***solubility*** tends to ***decrease*** in proportion to the ***number of non polar groups.***

4- Semipolar liquids, such as ethyl alcohol, possess some of the properties of both polar & non polar solvents.

3- pH :

✓ Most existing drugs are either weak acids or weak bases.

changing the pH of the medium

↓

Increase ionization of the drug increasing drug solubility in an aqueous medium.

Weak Acidic Drugs

$$pH = pKa + \log \frac{S - S0}{S0} \quad \text{.....[Eq. 3]}$$

where; pH = the pH below which the associated free acid will precipitate out of solution because it has low water solubility

(S) is the molar concentration of drug

($S_{0)}$ is the molar solubility of the undissociated species (weak acid).

Weak Basic Drugs

$$pH = pKa\ (pKw\text{-}pKb) + \log \frac{S0}{S - S0} \quad \text{....[Eq. 4]}$$

where; pH = the pH above which the molecular base will come out of solution as a precipitate, ($S - S_0$) is the cation (salt) molar concentration and S_0 is the solubility of the weak base .

4. Effect of other substances on solubility

- ***The solubility of a substance also may depend on ⇒ the types and concentrations of other substances in solution.***

✓ ***solubility of slightly soluble electrolyte ↓ ⟶ by adding second salt contain common ion.***

Ex. If adding NaCl to saturated solution of AgCl ⟶ some of AgCl ppt.

✓ water solubility of nonelectrolyte either ↑or ↓ by ⇒ addition of electrolyte

If:

a. Solubility of nonelectrolyte ↓ → salting out

b. Solubility of nonelectrolyte ↑ → salting in

Solubility Expression :

Description Forms (Solubility Definition)	Parts of Solvent Required for One Part of Solute
Very soluble (VS)	<1
Freely soluble (FS)	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble (SPS)	From 30 to 100
Slightly soluble (SS)	From 100 to 1000
Very slightly soluble (VSS)	From 1000 to 10,000
Practically insoluble (PI)	>10,000

Thanks a lot for your attention