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Solutions and Syrups	عنوان المحاضرة باللغة الانجليزية
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Pharmaceutical Dosage forms and Drug Delivery Systems By Haward A. Ansel; latest edition.	المصادر والمراجع
Sprowel's American Pharmacy.	

محتوى المحاضرة

Liquid Dosage Forms: Solutions

Factors Affecting Solubility

- Solubility depends on the solvent's ability to overcome solute-solute electronic forces; during dissolution, cohesive forces are replaced by solute-solvent attractions.

General Rules of Solubility

Inorganic molecules

- Monovalent cation + monovalent anion → usually water-soluble (e.g., NaCl, KI).
- One monovalent ion → usually soluble (e.g., BaCl₂, Na₂SO₄).
- Both ions multivalent → often poorly soluble (e.g., CaSO₄, BaSO₄; exceptions exist).
- Alkali metal salts → usually soluble (except Li₂CO₃).
- Ammonium and quaternary ammonium salts → soluble.

- Nitrates, nitrites, acetates, chlorates, lactates → generally soluble (with few exceptions).
- Sulfates/sulfites/thiosulfates → generally soluble (Ca, Ba exceptions).
- Chlorides/bromides/iodides → soluble (Ag^+/Hg^+ exceptions).
- Acid salts of insoluble salts → more soluble than the parent salt.
- Hydroxides/oxides (except alkali metals and NH_4^+) → generally insoluble.
- Sulfides → insoluble except alkali metal salts.
- Phosphates/carbonates/silicates/borates/hypochlorites → insoluble except alkali metals and ammonium.

Organic molecules

- One polar functional group → soluble up to ~5 carbons.
- Branched chains > straight chains in solubility.
- Solubility decreases as molecular weight increases.
- “Like dissolves like”: higher structural similarity → higher solubility.

Preparation of Solutions

- Most pharmaceutical solutions are unsaturated; strengths expressed as % (w/v, v/v, w/w) depending on system.
- Industrially: simple mixing in large vessels with mechanical agitation; heating via thermostatically controlled tanks when needed.

Mixing of Oral Liquids

- Mixing (intensive) vs blending (gentler); aim is a homogeneous product.
- Fluids: Newtonian (easier to mix) vs non-Newtonian.
- Equipment selection:
 - Single-phase: low-shear, high-flow mixers (engulfment).
 - Multiphase: high-shear, low-flow mixers (droplet formation).

Mixing Mechanisms

1. Bulk transport (paddles/blades move large volumes; e.g., LVP kneading).
2. Turbulent mixing (random velocity fluctuations; e.g., syringe-to-syringe).
3. Laminar mixing (viscous systems or gentle stirring).
4. Molecular diffusion (thermal motion at molecular scale).

Oral Solutions & Related Preparations

- Typically include flavorants, colorants, stabilizers, preservatives.
- Note: parabens may partition into flavoring oils, reducing effective aqueous preservative concentration.

Dry Mixtures for Solution

- Used when drug is unstable in water (e.g., penicillin V, cloxacillin, KCl).
- Reconstitute with purified water; stable 7–14 days refrigerated; discard leftovers after therapy.

Oral Rehydration Solutions (ORS)

- For dehydration due to diarrhea (notably in infants).
- Typical per liter: Na⁺ 45 mEq, K⁺ 20 mEq, Cl⁻ 35 mEq, citrate 30 mEq, dextrose 25 g.

Liquid Dosage Forms: Syrups

Definition

- Concentrated aqueous preparations of sugar or sugar substitute, with/without flavoring agents and medicinal substances.

Preparation

- Medicated syrups: combine sucrose, purified water, flavorants, colorants, and therapeutic agent.

Advantages

1. Pleasant vehicle to mask unpleasant taste.
2. Useful for children and elderly.
3. Often alcohol-free (parent-friendly).
4. Any water-soluble, aqueous-stable drug can be incorporated.

Components

1. Sugar: sucrose or substitutes (sorbitol, glycerin, propylene glycol); cellulose polymers as thickeners.
2. Preservatives: benzoic acid 0.1–0.2%, sodium benzoate 0.1–0.2%, parabens total ~0.1%; alcohol may aid solubilization but is usually insufficient alone for preservation.
3. Flavorants
4. Colorants
5. Special agents: solubilizers, stabilizers, thickeners.

Sucrose Details

- USP syrup: 85% w/w sucrose → sweetness, viscosity, stability.
- Specific gravity ≈ 1.313 (100 mL ≈ 131.3 g).
- Practical note: ~ 1 g sucrose per 0.5 mL.

Why Sweetness & Viscosity Matter (H.W. prompt)

- Sweetness aids palatability and adherence.
- Viscosity improves mouthfeel, taste masking, and may slow sedimentation in suspensions incorporated into syrup vehicles.

Types of Syrups

1. Medicated syrups
 - Contain an active pharmaceutical ingredient (API).
 - Example: cough syrups with dextromethorphan, expectorant syrups with guaifenesin.

2. Non-medicated syrups

- Also called flavored vehicles.
 - Serve as pleasant-tasting bases in which medicinal agents can be added.
 - Examples: simple syrup, flavored syrup bases.
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Preservation in Syrups

- High sucrose concentration ($\approx 85\%$ w/v) is inherently self-preserving (little free water available for microbial growth).
 - Lower concentrations require added preservatives, such as:
 - Benzoic acid 0.1–0.2%
 - Sodium benzoate 0.1–0.2%
 - Parabens (methyl-, propyl-, butyl-) $\sim 0.1\%$ total
 - Alcohol (15–20%) sometimes added but usually insufficient alone for preservation.
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Syrup Preparation Methods

1. Solution with heat

- Traditional method: dissolve sugar in water with moderate heating.
- Risk: sugar inversion (sucrose \rightarrow dextrose + fructose) if overheated \rightarrow may cause fermentation.

2. Solution without heat

- Preferred for heat-sensitive ingredients.
- Requires agitation until dissolution is complete.

3. Percolation

- Purified water percolates through a bed of crystalline sucrose → forms syrup.
- Efficient but less common in pharmacy practice today.

4. Addition of medicated liquid to syrup vehicle

- Example: mixing medicated tincture/fluid extract with syrup base.
- Requires clarification (e.g., filtration) to remove incompatibilities or precipitates.

Quality Considerations

- Clarity: syrup should be free from crystals, sediment, or microbial growth.
- Viscosity: should be consistent and stable.
- Flavor and color: should remain unchanged during shelf life.
- Stability: must resist crystallization and microbial contamination.

Examples of Syrups

- Simple Syrup, USP → 85% w/v sucrose solution.
- Syrup of Ipecac (formerly used as an emetic).
- Cough syrups containing expectorants or antitussives.
- Antibiotic syrups (e.g., amoxicillin syrup).