Pharmaceutical Technology

Official solutions

Preparation of Solution

- Most pharmaceutical solutions are unsaturated with solute. Thus, the amounts of solute to be dissolved are usually well below the capacity of the volume of solvent employed.
- The strengths of pharmaceutical preparations are usually expressed in terms of percent strength, although for very dilute preparations, expressions of ratio strength may be used.
- These expressions and examples are shown in the following table:

EXPRESSION	ABBREVIATED EXPRESSION	MEANING AND EXAMPLE
Percent weight in volume	% w/v	Grams of constituent in 100 mL of preparation (e.g., 1% w/v = 1 g constituent in 100 mL preparation)
Percent volume in volume	% v/v	Milliliters of constituent in 100 mL of preparation (e.g., 1% v/v 1 mL constituent in 100 mL preparation)
Percent weight in weight	% w/w	Grams of constituent in 100 g of preparation (e.g., 1% w/w = 1 g constituent in 100 g preparation)
Ratio of strength to weight in volume	-:— w/v	Grams of constituent in stated milliliters of preparation (e.g., 1:1,000 w/v = 1 g constituent in 1,000 mL preparation)
Ratio of strength to volume in volume	-:— v/v	Milliliters of constituent in milliliters of preparation (e.g., 1:1,000 v/v = 1 mL constituent in 1,000 mL preparation)
Ratio of strength to weight in weight	-:— w/w	Grams of constituent in stated number of grams of preparation (e.g., 1:1,000 w/w = 1 g constituent in 1,000 g preparation)

- Some chemical agents in a given solvent require an extended time to dissolve.
- To hasten dissolution, a pharmacist may employ one of several techniques, such as

1. applying heat,
2. reducing the particle size of the solute,
3. using a solubilizing agent, and/or
4. subjecting the ingredients to vigorous agitation.

- Most chemical agents are more soluble at elevated temperatures than at room temperature or below because an endothermic reaction between the solute and the solvent uses the energy of the heat to enhance dissolution.

- However, elevated temperatures cannot be maintained for pharmaceuticals, and the net effect of heat is simply an increase in the rate of solution rather than an increase in solubility.

- An increased rate is satisfactory to the pharmacist because most solutions are unsaturated anyway and do not require a concentration of solute above the normal capacity of the solvent at room temperature.

- Pharmacists are reluctant to use heat to facilitate solution, and when they do, they are careful not to exceed the minimally required temperature, for many medicinal agents are destroyed at elevated temperatures and the advantage of rapid solution may be completely offset by drug deterioration.

- If volatile solutes are to be dissolved or if the solvent is volatile (as is alcohol), the heat would encourage the loss of these agents to the atmosphere and must therefore be avoided.
- Pharmacists are aware that certain chemical agents, particularly calcium salts, undergo exothermic reactions as they dissolve and give off heat. For such materials, the use of heat would actually discourage the formation of a solution.
- The best pharmaceutical example of this type of chemical is calcium hydroxide, which is used in the preparation of Calcium Hydroxide Topical Solution, USP.

- Calcium hydroxide is soluble in water to the extent of 140 mg/100 mL of solution at 25°C (about 77°F) and 170 mg/100 mL of solution at 15°C (about 59°F).
- Obviously, the temperature at which the solution is prepared or stored can affect the concentration of the resultant solution.

- In addition to or instead of raising the temperature of the solvent to increase the rate of solution, a pharmacist may choose to decrease the particle size of the solute.
- This may be accomplished by comminution (grinding a solid to a fine state of subdivision) with a mortar and pestle on a small scale or industrial micronizer on a larger scale.

Official Solutions

- Official solutions are liquid preparations that contain one or more chemical substances dissolved in liquid solvent, and are mentioned in one of pharmacopeia i.e., USP, BP, NF. For example, Iodine solution (NF). The solvent may be water, sometimes glycerin or alcohol or mixture of solvents.
- Official solutions are differentiated by their active constituents, method of preparation, their strength and potency, mode of administration, and their uses.

Uses of official solutions

1. As therapeutic solution (internally or externally)
2. In compounding of other prescriptions.
3. As a reagent in various processes.
4. As a solvent for certain substances
5. As coloring agent for pharmaceutical product.

- There is no uniform method for preparation of official solution but each group of solutions is prepared by specific method.
- According to method of preparation it can be classified into:

Preparation of Solution

1. Solution prepared by simple solution.
2. Solution prepared by chemical reaction.
3. Solution prepared by simple solution with sterilization.
4. Solution prepared by extraction.

- The first method is the easiest method and simplest method of preparation. Sometimes if a solution could be prepared by simple solution and by chemical reaction, then solution prepared by simple solution is preferred.
- This is because chemical reaction is not easy method; it involves using many reagents resulting in many compounds hard to be purified. It contains all the products of the reaction that have taken place during the method of preparation.

- However, there is still some substances can be form solution by both simple solution and chemical reaction. For example $Ca(OH)_2$ solution which known as lime water is prepared according to simple solution by dissolving $Ca(OH)_2$ in water and by chemical reaction by shaking lime CaO with un excess of water as shown in Equation 1

$$CaO + H2O \longrightarrow Ca(OH)2 \text{ ---------- (1)}$$

- Although simple solution is preferred, sometimes chemical reaction has to be chosen for the following reasons:

1. The pure solute may not dissolve from a solid state in other way than chemical reaction for example; Aluminum subacetate which is used as astringent used in wet dressing of eczema.
2. The active constituent is not obtained or not readily usable in a form other than that of solution e.g. formaldehyde solution (active constituent is gas). Formaldehyde solution (formalin) used as disinfectant.

- Hydrogen peroxide solution (H_2O_2): is topical anti-infective using to clean wounds, also used as softening ear wax in certain dilution. H_2O_2 solution liberates 10 times its volume oxygen hence; it is called 10 volume peroxide.

3. Some by products are desired like Mg citrate, which is used as cathartic.

Examples of solution prepared by simple solution

- **Amaranth solution USP 1%**: prepared by dissolving amaranth in purified water. It is used as coloring agent to impart color to clear liquid preparation.
- **Gentian violet solution USP 1%**: gentian violet in hydroalcoholic solution (10% alcohol v/v). It is used as topical local anti-infective it is used topically in undiluted form in infections caused by gram-positive bacteria or by certain parasitic fungi.
- **Iodine solution NF**: it is used as local anti-infective for skin and surgical disinfectant.
- **Tolnaftate solution USP 1%** in a non aqueous homogeneous vehicle of polyethylene glycol 400.
- **Clindamycin phosphate topical solution**: used in treatment of acne vulgaris.

Solutions prepared by extraction

- **Solutions prepared by extraction:** for example epinephrine solution (adrenalin chloride USP) diluted to 1:1000 in purified water.
- It is prepared with the help of hydrochloric acid; it is used as vasoconstrictor to increase blood pressure, to prevent hemorrhage and to prolong action of local anesthetic for dentistry purposes.

Solution prepared by simple solution with sterilization

A. **Anti-coagulants:**

1. Heparin solution USP sterile solution of 75,000 units of sodium heparin in sodium chloride injection.

It is used 30 ml for 500 ml of whole blood.

2. Citrate, phosphate, dextrose solution: it is sterile solution consist from 3% citric acid, 26.3% sodium citrate, 2.22% sodium biphosphate and 25.5% dextrose. All these contents dissolve in water for injection; this solution is used as anti-coagulant for storage of whole blood. About 70 ml of this solution should be used for 500 ml of whole blood.

B. **Irrigating solution**: it is used to flush or bathe wounds or surgical tissues, should be sterilized because is used for sensitive areas of the body.

- Example of irrigating solution aminoacetic acid sterile solution (NF): it consists from sterile solution of 1.5 and 15%.
- 15% requires dilution aseptically before use.
- 15% aminoacetic acid in water for injection is used for irrigating solution in operation such that of prostate (prostatectomy).

C. **Physiologic solutions:**

- Ringer's solution (NF), it is Isotonic solution consists from 6.6% NaCl , 0.3% KCl, 0.33% $CaCl_2$ diluted in purified water.
- It cannot be used as parenteral solution, because its solvent is purified water (not water for injection).
- Ringer's could be considered as irrigating and physiologic solutions, and used as solvent for compound used topically for delicate membrane, use to keep living tissues to reverse all reflexes for a period of time.
- Ringer's solution, sometimes called trichloride solution (Isotonic solution of trichloride).

According to the pharmaceutical used solution may be classified into:

- Oral solution.
- Ophthalmic solution.
- Otic and nasal solution.
- Topical solution.
- Parenteral solution.

According to their composition solution may be classified into:

- **Syrups** (Aqueous solution containing sugar).
- **Elixer** (sweetened hydroalcoholic solution).
- **Spirits** (solution of aromatic material with alcohol solvent).
- **Aromatic water** (solution of aromatic material in water as solvent).
- **Tinctures or fluid extract** (prepared by extracting active constituent from crude drug).

- Oral solutions, syrups, elixirs, spirits, and tinctures are prepared and used for the specific effects of the medicinal agents they carry.
- In these preparations, the medicinal agents are intended to provide systemic effects.
- The fact that they are administered in solution form usually means that they are soluble in aqueous systems and their absorption from the gastrointestinal tract into the systemic circulation may be expected to occur more rapidly than from suspension or solid dosage forms of the same medicinal agent.

Oral Solutions

- The pharmacist may be called on to

1. dispense a commercially prepared oral solution;
2. dilute the concentration of a solution, as in the preparation of a pediatric form of an adult product;
3. prepare a solution by reconstituting a dry powder mixture; or
4. extemporaneously compound an oral solution from bulk ingredients.

- Knowledge of the solubility and stability characteristics of the medicinal agents and the solvents employed in the commercial products is useful to the pharmacist for informing the patient of the advisability of mixing the solution with juice, milk, or other beverage upon administration.

Examples of oral solutions

1. **Oral Rehydration Solutions**

- Rapid fluid loss associated with diarrhea can lead to dehydration and ultimately death in some patients, particularly infants.
- During diarrhea, the small intestine secretes far more than the normal amount of fluid and electrolytes, and this simply exceeds the ability of the large intestine to reabsorb it. This fluid loss, which occurs mostly from the body's extracellular fluid compartment, can lead to a progressive loss of blood volume culminating in hypovolemic shock.

- Oral rehydration solutions are usually effective in treatment of patients with mild volume depletion, 5% to 10% of body weight. These are available OTC and are relatively inexpensive, and their use has diminished the incidence of complications associated with parenterally administered electrolyte solutions.

- A liter of typical oral rehydration solution contains 45 mEq Na^+, 20 mEq K^+, 35 mEq Cl^-, 30 mEq citrate, and 25 g dextrose.
- These formulations are available in liquid or powder packet form for reconstitution. It is important that the user add the specific amount of water needed to prepare the powder forms. Furthermore, these products should not be mixed with or given with other electrolyte containing liquids, such as milk or fruit juices.

2. **Magnesium Citrate Oral Solution**

- Magnesium citrate oral solution is a colorless to slightly yellow clear effervescent liquid having a sweet, acidulous taste and a lemon flavor. It is commonly referred to as citrate or as citrate of magnesia.
- The solution is prepared by reacting official magnesium carbonate with an excess of citric acid, flavoring and sweetening the solution with lemon oil and syrup, filtering with talc, and then carbonating it by the addition of either potassium or sodium bicarbonate.

- The solution provides an excellent medium for the growth of molds, and any mold spores present during the manufacture of the solution must be killed if the preparation is to remain stable.
- For this reason, during the preparation of the solution, the liquid is heated to boiling (prior to carbonation); boiled water is employed to bring the solution to its proper volume; and boiling water is used to rinse the final container. The final solution may be sterilized.

- The solution is employed as a saline cathartic, with the citric acid, lemon oil, syrup, carbonation, and the low temperature of the refrigerated solution all contributing to the patient's acceptance of the large volume of medication.
- For many patients, it is a pleasant way of taking an otherwise bitter saline cathartic.