

Official Solutions:

Are liquid preparations that contain one or more soluble chemical substances dissolved in liquid solvent. The solvent used for preparing official solution is water; other liquids such as alcohol & glycerin are specified in some of monograph.

Uses:

1. For specific therapeutic effect internally or externally.
2. Used as ingredient in compounding of Rx or in the formation of other official preparation.
3. Reagent in various processes.
4. Solvents for certain substances.
5. Coloring agents for pharmaceutical products.

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:

TABLE 1: EXAMPLES OF PHARMACEUTICAL DOSAGE FORMS IN WHICH THE ACTIVE INGREDIENT IS OFTEN CALCULATED AND EXPRESSED ON A PERCENTAGE BASIS

PERCENTAGE BASIS	EXAMPLES OF APPLICABLE DOSAGE FORMS
Weight-in-volume	Solutions (e.g., ophthalmic, nasal, otic, topical, large-volume parenterals), and lotions
Volume-in-volume	Aromatic waters, topical solutions, and emulsions
Weight-in-weight	Ointments, creams, and gels

The symbol % used without qualification (as with w/v, v/v, or w/w) means percent weight in volume for solutions or suspensions of solids in liquids, percent weight in volume for solutions of gases in liquids, percent volume in volume for solutions of liquids in liquids, and weight in weight for mixtures of solids and semisolids.

» 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 applying **heat**, **reducing the particle size of the solute**, **using a solubilizing agent**, and/or **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.

» Pharmacists are able 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**.

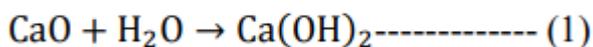
» Pharmacists are aware that certain chemical agents, particularly **calcium salts**, **undergo exothermic reactions** as they dissolve and give off heat. For such materials, the use of heat would actually **discourage the formation of a solution**. The best pharmaceutical example of this type of chemical is **calcium hydroxide**, which is used in the preparation of Calcium Hydroxide Topical Solution, USP.

» 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.

Methods for 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 forming 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**



» **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. E.g., **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 (H₂O₂):

is topical anti-infective using to clean wounds, also used as softening ear wax in certain dilution. H₂O₂ 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:

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:

Anti-coagulants:

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

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.

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% aminoacetic acid in water for injection is used for **irrigating solution in operation such that of prostate (prostatectomy)**.

Physiologic solutions:

Ringer's solution (NF), it is Isotonic solution consists from 6.6% NaCl, 0.3% KCl, 0.33% CaCl₂ 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:

1. Oral solution.
2. Ophthalmic solution.
3. Otic and nasal solution.
4. Topical solution.
5. Parenteral solution.

According to their composition solution may be classified into:

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

Oral solution:

» Most solutions intended for oral administration contain **flavorants and colorants** to make the medication more **attractive and palatable**. When needed, they may also contain **stabilizers** to maintain the chemical and physical stability of the medicinal agents and **preservatives** to prevent the growth of microorganisms in the solution.

» The formulation pharmacist must be wary of chemical interactions between the various components of a solution that may alter the preparation's stability and/or potency. For instance, esters of p-hydroxybenzoic acid (methyl-, ethyl-, propyl-, and butylparabens), frequently used preservatives in oral preparations, have a tendency to partition into certain flavoring oils. This **partitioning effect could reduce the effective concentration of the preservatives** in the aqueous medium of a pharmaceutical product below the level needed for preservative action.

» 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.

Dry mixtures for solution:

» A number of medicinal agents, particularly certain antibiotics, for example, **penicillin V**, have insufficient stability in aqueous solution to meet extended shelflife periods. Thus, commercial manufacturers of these products provide them to the pharmacist in dry powder or granule form for reconstitution with a prescribed amount of purified water immediately before dispensing to the patient.

» The dry powder mixture contains all of the formulative components, including drug, flavorant, colorant, buffers, and others, except for the solvent. Once reconstituted by the pharmacist, the solution remains stable when stored in the refrigerator for the labeled period, usually **7 to 14 days**, depending on the preparation. This is a sufficient period for the patient to complete the regimen usually prescribed. However, in case the medication remains after the patient completes the course of therapy, the patient should be instructed to discard the remaining portion, which would be unfit for use at a later time.

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.

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 **employed as a saline cathartic**.

» 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.

Ophthalmic solutions:

Requirements for ophthalmic solutions:

1. The **sterility** is one of the important considerations in their preparation. Autoclaving in the final container is the preferred method of sterilizing ophthalmic solutions.

2. **Preservatives** suggested for use in ophthalmic solutions include:

- a) **Phenyl ethyl alcohol 0.5%**
- b) **Chlorobutanol 0.5%**
- c) **Benzalkonium chloride 0.01%.**
- d) **Phenyl mercuric nitrate 0.001%**

Ophthalmic solutions that are intended for surgical use must be sterile and must not contain any preservative. Such solution should be packaged in single –use disposable container.

3. Ophthalmic solution should be **isotonic** with lacrimal fluid, although the eye can tolerate tonicity values above and below that corresponding to 0.9% NaCl solution is less likely to produce discomfort or irritation to the eye. The agents which is used to adjust the tonicity of solutions must be compatible with the active medicament.

4. **pH:** The lacrimal fluid has **pH 7.4** ideally ,an ophthalmic solutions should have the same pH as the lacrimal fluid ,this is not usually possible because at this pH many drugs are not soluble in water and most alkaloidal salts are precipitate at this level therefore a pH must be found which represents a compromise between optimum stability and maximum therapeutic effect, and this level must be held by buffers.The buffer system that used should have the pH that is nearest to the physiologic pH of 7.4 and at which precipitation of drug does not occure. The USP and NF give formulas for buffer vehicles which may be used for specific drugs.

5. **Viscosity:** Increase the viscosity of ophthalmic solution offers prolonged contact with the tissue thus enhancing the penetration and therapeutic effect of drug. Thickening agents such as methyl cellulose may be added to increase the viscosity.

Proper packaging:

- Glass containers.
- Plastic containers.
- Fixed and screw dropper

Contact lenses solutions:

- Wetting solutions.
- Cleaning solutions.
- Soaking solutions.
- Combined purpose solutions.

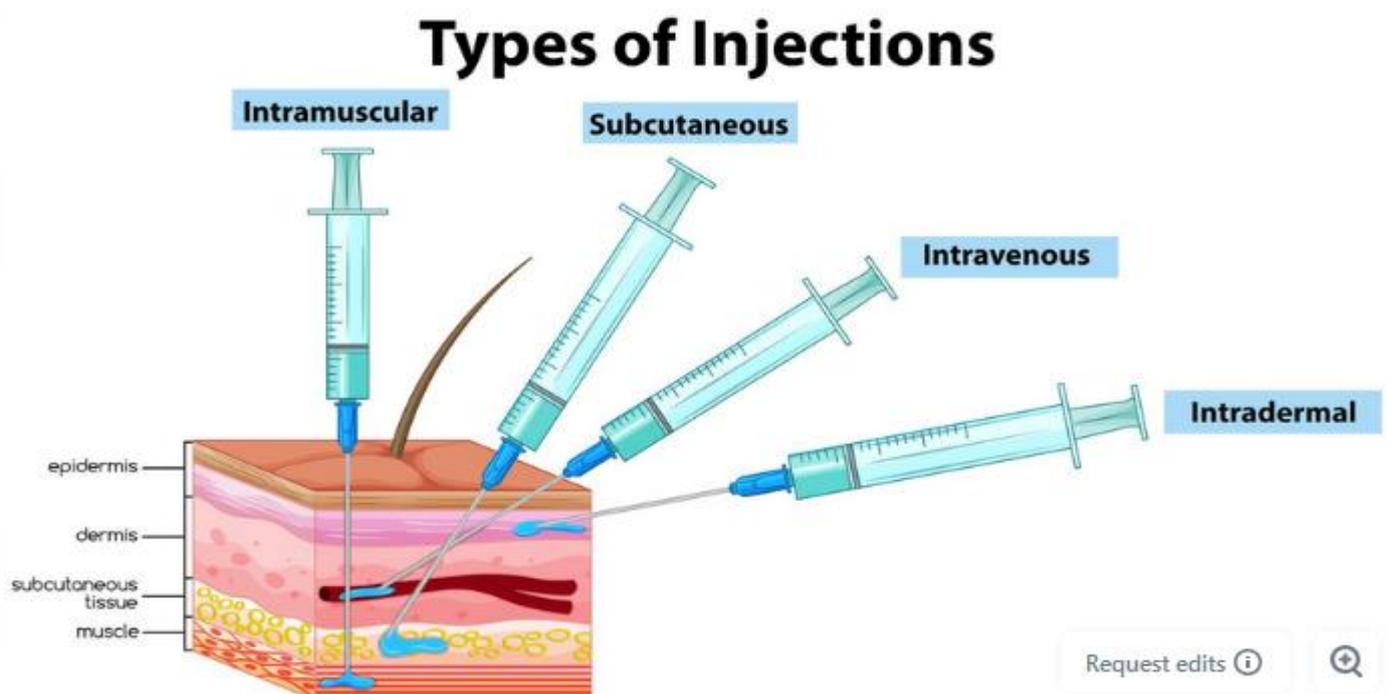
Parenterals:

Parenteral refers to the injectable routes of administration. Parenteral from the Greek words Para + enteron. Meaning “outside of intestine”.

General requirements for parenterals:

- 1. Safety:** solvents (sterile water); but for poorly-water drugs another solvent is added e.g. alcohol, glycol.
- 2. Sterility:** product and container must be sterilized (auto clave), dry heat and filter aid.
- 3. Free from pyrogen:** pyrogen is fever-producing organic substance arising from microbial contamination), is a lipopolysaccharide and endotoxins
- 4. Clarity:** free from particles specially which have a diameter 7.5μ .
- 5. Stability:** should not loss its therapeutic activity
- 6. Isotonicity:** not change the morphology of RBC (no shrinkage or hemolysis).

Types of injections:



1. **Intravenous:** Injected directly into a vein (major or peripheral vein) .Volume unlimited volume (infusion).
2. **Intramuscular:** Injected directly into skeletal muscle (pelvic).Volume (2-5 ml).
3. **Subcutaneous:** Injected directly into alveolar region beneath the layer of the skin.Volume (2 ml).
4. **Intradermal:** Injected between the layer of the skin.Volume (0.2 ml).
5. **Intraspinal:** Injected into spinal canal.Volume (up to 10 ml).
6. **Intra-arterial.**
7. **Intra-articular.**
8. **Intrathecal.**
9. **Intracardiac.**

Advantages and disadvantages of IV injection:

Advantages:

1. Great intensity of response
2. Less irritant.
3. Great stability with some drug.
4. Can be used for large volume .
5. Rapid response.

Disadvantages:

1. Restricted to solution.
2. Cause haemolysis; can be avoid by slow injection.
3. The drug cannot be recovered (it is difficult to get rid of it).

IM Injection

1. It is easier than IV
2. It can be used for solutions, suspensions, and emulsions.
3. The drug will stay in muscle and diffuse slowly so it has slower onset of action.
4. Prolong action.
5. The absorption from this route depends on the release of drug and blood flow.
6. Salt form of the drug absorb faster than free drug.

Subcutaneous injection:

- It is simple to administer.
- Absorption from this route of injection is affected by concentration, solubility and blood flow.
- Example of drug given by this route is **insulin** of two types .**Soluble insulin** show fast absorption but short duration of action .**Insoluble type protamine zinc insulin**, which has slow response or onset but prolong action.

Intradermal:

- Its absorption is slow.
- It is used for **vaccines** and for diagnostic test.

Intraarterial:

- It is used for targeting a drug into organ for **diagnostic test** and **antineoplastic drugs**.

Solutions prepared from tablets:

Halazone tablets for solution USP:

- (4mg of halazone).
- **Uses:**
 1. Disinfectant
 2. For the sterilization of drinking water ,1 or 2 tablets per liter
- The tablets should be labeled to indicate that they are not intended to be swallowed.

Potassium permanganate tablet for solution USP

- 60, 125 and 300 mg of potassium permanganate
- **Uses:** Topical anti-infective.
- Applied topically to the skin and mucous membranes as 0.004 to 1% solution or in a wet dressing

Nasal preparations:

- ☐ These contain adrenergic agents and are employed for their decongestant activity on the nasal mucosa.
 - ☐ Example: **Phenylephrine HCl solution** USP (0.125 to 10%).
 - ☐ Used as vasoconstrictor isotonic solution.
 - ☐ Approximately equal to 0.9% NaCl and buffered to the normal pH range of nasal fluids (pH 5.5 to 6.5) and stabilized and preserved as required.
 - ☐ Certain commercial solutions which are available for both **pediatric and adult** use.
 - ☐ These preparations are best used for **short periods** (no longer than 3 to 5 days).
 - ☐ Patients should advise not to exceed the recommended dosage and frequency of use.
- Examples **phenylephrine** can be used every 3-4 hr while **oxymetazoline** used every 12 hr.

Inhalation solutions:

- ☐ Inhalations are drugs or solutions of drugs administered by the nasal or oral respiratory route either for **local or systemic effect such as salbutamol solution**.