Types of Pharmaceutical Solutions

- Aromatic waters
- Syrups
- Elixirs
- Linctus
- Mouthwashes and gargles
- Nasal solutions
- Ear drops
- Enemas
- Other externally used preparations

Classification of Solutions by Administration Route

- Oral Solutions
- Topical Solutions
- Oromucosal Solutions
- Rectal Solutions
- Ophtalmic, otic and nasal solutions
- Irrigation Solutions
- Inhalation Solutions
- Lens Solutions

Aromatic waters

Aromatic waters are clear aqueous solution saturated with volatile Oils (e.g. rose oil, Peppermint oil), or other **aromatic** or volatile substances eg. camphor. Their odours and taste are of those of the drugs or volatile substances from which they are prepared.

Preparation:

1) *Distillation method: Water vapor distillation is performed. The distillate obtained by this method is called hydrolate. After obtaining the hydrolate, it is filtered through the filter paper.*

2) Simple dissolution of essential oils in water: Prepared by mixing essential oil directly with solvent.

3) *The method of dissolving essential oils using an excipient or dispersing agent:*

1. Method	***VOLATILE OIL***	***ADSORBENT (Talc)***	**Mix with water by shaking**	**Set aside**	**Filter**		
2. Method	***VOLATILE OIL***	***ALCOHOL***	**Mixing with water**	***TALK addition***	**Shake**	**Set aside**	**Filter**

Purified talc used in this process serves two purposes:

1. That of dispersing the volatile substances so as to make it more completely soluble in water.
2. Aids the filtration from excess of volatile oil as ordinary filter paper will not hold back finely dispersed particles, especially oils. The talc is a good adsorbent and the undissolved volatile material is adsorbed and prevented from passing through the filter

Stability of Aromatic Waters:

- Excessive exposure to light and to changes in temperature cause aromatic waters to loose some of their desirable characteristics.
- Since the solutes are volatile materials loss of aroma occurs on prolonged exposure to the hot atmosphere.
- Since aromatic waters are saturated solutions, lowering the temperature causes separation of the aromatic component, thus producing cloudiness.
- To avoid as far as possible the presence of microorganisms the water used for preparing aromatic water should be recently boiled, distilled water, as that ordinary distilled water is usually contaminated by the presence' of such micro-organisms. No preservative should be added to aromatic waters.
- Prepared aromatic waters should be freshly used. By time evaporation, decomposition or turbidity may be observed and if so: preparation should be discarded.
- However, there are also aromatic waters that can be stored for a long time.

Lemonade

- Lemonades are preparations that contain organic or inorganic acids and sweetened with sucrose or syrups. They can be used as active substance or carrier.

- Since the amount of sucrose is as low as 10%, they are fermented and molded in a short time. Fermentation results in carbon dioxide, lactic acid and citric acid. Therefore it should be prepared fresh and consumed in a short time.

Lactic Acid Lemonade (Limonade Lactique, Limonade)

Lactica - T.K.1954

Rx

Lactic acid	1 k
Distilled water	89 k
Syrup Simplex	10 k

Preparation: Lactic acid is dissolved in water and mixed with simple syrup and 100 grams of lemonade is prepared.

Potions

- Solutions or colloidal preparations containing one or more active agents
- They contain syrup and aromatic substances.
- Because they contain a small amount of sugar, they have low stability.
- They are prepared in small amounts to be consumed within one or two days

Potion Cordiale, Potio Cordialis (TK 1954)

Rx

Mint water	45p
Melissa water	45p
cinnamon water	45p
citrus flower water	45p
Sytup Simplex	20p

Elixirs

- Elixirs are clear, sweetened hydroalcoholic solutions intended for oral use and are usually flavored to enhance their palatability.
- Nonmedicated elixirs are used as vehicles
- Medicated elixirs are used for the therapeutic effect of the active agents they contain
- They may contain glycerine and syrup
- In addition to alcohol and water, the elixirs may contain glycerin and syrup as solvent.

Elixirs

- They are less sweet and viscous compared to syrups
- Flavorings are added to increase palatability
- Coloring agents are added to improve their appearance
- Alcohol percentage: 10-12 % (self -preserving)

: Antimicrobial agent is not required

Disadvantage: Alcohol (for children and adults who choose to avoid alcohol)

- The powder and granüle forms of elixirs are also present which can be hydrated just before use.

Fenobarbital Eliksiri (Phenobarbital Elixir – U.S.P. XXVII)[13]

Rx

Fenobarbital	4	g
Portakal esansı	0.75	g
Amarant çözeltisi	10	mL
Alkol	150	mL
Gliserin	450	mL
Basit şurup	150	mL
Su y.m.	1000	mL

Hazırlanışı: Formüldeki maddeler tartılır. Fenobarbital çözülür. Diğer maddeler ilave edilir. Hipnotik olarak kullanılır.

Syrups

- Syrups are concentrated solutions of sugar in water or other aqueous liquids.
- Flavoring and active agents (±)
- Their density is always greater than one.
- Polyols such as glycerin and sorbitol are also added to the syrups to prevent crystallization, correct the taste and alter the solubility.

Sirupus Simplex (BP 2002)

Sugar		667 g
Purified water	q.s.	1000 g

Syrup (USP 27)

Sugar		850 g
Purified water	q.s.	1000 ml

Inversion
Caramelization
Fermentation
Mould growth

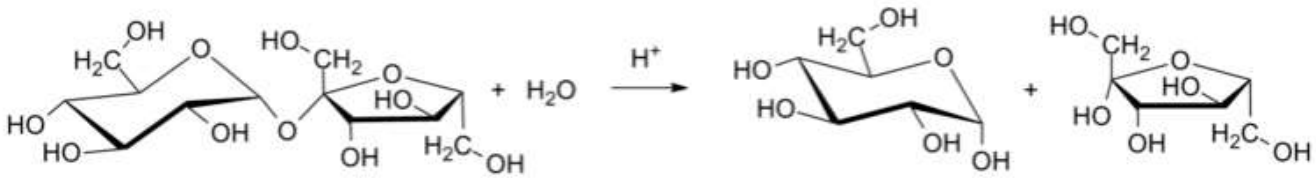
- Sugar (disaccharide)

hydrolysis

inversion reaction (high temperature, acidic pH)

Glucose

Fructose (invert sugar)



$C_{12}H_{22}O_{11}$ (sucrose) + H_2O (water) → $C_6H_{12}O_6$ (glucose) + $C_6H_{12}O_6$ (fructose)

•Invert sugar properties:

•More susceptible for fermentation and microbial growth.
•Tend to darken in color.
•But decrease oxidation of other drugs (fructose formed is reducing sugar)
• Fructose is sweeter than sucrose.
•The rate of inversion process is enhanced by the medium acidity.
•Overheating cause caramelizaltion of sucrose (amber color)
•Syrups cannot be sterilized by autoclaving without caramelization (amber color).

Preparation of Syrups

- solution with heat,
- solution by agitation
- addition of sucrose to a liquid medication or flavored liquid
- percolation

Solution with Heat—

- This method is a suitable preparation method, if the constituents are not volatile or degraded by heat, and when it is desirable to make the syrup rapidly.
- Purified water is heated to 80–85°C, and then removed from its heat source Sucrose is added with vigorous agitation. Then, other required heat-stable components are added to the hot syrup, the mixture is allowed to cool, and its volume is adjusted to the proper level by the addition of purified water.
- In instances in which heat labile agents or volatile substances, such as flavors and alcohol, are added, they are incorporated into the syrup after cooling to room temperature.

Agitation without Heat—

- This method is used in cases in which heat would cause degradation or volatilize formulation constituents.
- On a small scale, sucrose and other formulation ingredients may be dissolved in purified water by placing the ingredients in a vessel of greater capacity than the volume of syrup to be prepared, allowing intense agitation without spillage.
- This process is more time consuming than Solution with Heat, but the product has greater stability.

Addition of Sucrose to a Liquid Medication or Flavored Liquid—

- This method is often used with fluid extracts or tinctures.
- Syrups made in this way develop precipitates, because alcohol is often an ingredient of the liquids used, and the resinous and oily substances solubilized by the alcohol precipitate when water is added.
- A modification of this process entails mixing the fluidextract or tincture with the water, allowing the mixture to stand to permit the separation of insoluble constituents, filtering and then dissolving the sucrose in the filtrate. It is obvious that this procedure is not permissible when the precipitated ingredients are the valuable medicinal agents.

Percolation—

- In the percolation method, either purified water or the source of the medicinal component is passed slowly through a bed of crystalline sucrose, thus, dissolving it and forming a syrup. This latter method really involves two separate procedures: first, the preparation of the extractive of the drug, and then the preparation of the syrup. To be successful in using this process, technique is critical:
- 1) the percolator used should be cylindrical or semi-cylindrical and cone-shaped as it nears the lower orifice;
- 2) a coarse granular sugar must be used, otherwise it will coalesce into a compact mass, which the liquid cannot permeate.

Oramucosal solutions

- Oromucosal solutions are solutions that contain antiseptic, local anesthetic or astringent active agents and aromatic excipients which are applied in the oral cavity. They are simple or mixed, aqueous or concentrated solutions with good fragrance and flavor.

- Externally used for local effect. Their labels should indicate their preparation and administration (dilution, spreading, rinsing, mouthwash) information.

Mouthwashes

- Mouthwashes are aqueous solutions, often in concentrated form,, containing one or more active ingredients and excipients. In these preparations, alcohol, glycerin and water are generally used as solvents. The ideal pH should be between 6.5-7.0.

- Mouthwashes can be used for two purposes:
  - therapeutic
  - cosmetic.

- Therapeutic rinses or washes can be formulated to reduce plaque, gingivitis, dental caries, and stomatitis. Cosmetic mouthwashes may be formulated to reduce bad breath through the use of antimicrobial and/or flavoring agents.

- Antimicrobials
- Colorants
- Synthetic sweeteners
- Surfactants

Gargles

Gargles are aqueous solutions frequently containing antiseptics, antibiotics, and/or anesthetics used for treating the pharynx and nasopharynx by forcing air from the lungs through the gargle held in the throat; subsequently, the gargle is expectorated. Many gargles must be diluted with water prior to use.

- Antiseptic, antibiotic, anesthetic
- Colorants
- Synthetic sweeteners

Rx

Sodium chloride		2 g
Sodium bicarbonate		1 g
Saccharine sodium		0.01 g
Mint essence		1.25 g
Distilled water	q.s.	250 ml

Used as an antiseptic.

Collutoire

- These preparations are locally applied on the lesions of oral or throat mucosa. Antiseptic and local anesthetic active agents are used.

- Solvent (glycerin, alcohol or water)
- Colorants
- Synthetic sweeteners

Methylene Blue Collutorio

Rx

Methylene blue		0.6 g
Glycerine		30 g
Distilled water	q.s.	50 ml

Methylene blue is dissolved in a few drops of water.
Glycerine is added and mixed.
Used as an antiseptic on gums and mouth mucosa.

Rectal Solutions
Enemas

- Enamas are rectally administered preparations in aqueous or oily solution, emulsion or suspension form. They are used for various purposes and grouped under 3 groups according to their use.

1) Evacuation enemas: Enema preparations which are employed to evacuate the bowel

2) Retention enemas: Enema preparations which are employed to influence the general system by absorption, or to affect a local disease. They may possess anthelmintic, nutritive, sedative, or stimulating properties, or they may contain radiopaque substances for roentgenographic examination of the lower bowel.

Enemas

Starch Enema (Remington 20th ed.)

Rx

Micronized wheat starch		30.0 g
Purified water	q.s.	1000.0 ml

Phosphate Enema I (BP 99)

Rx

Sodium dihydrogen phosphate (dihydrate)		160 g
Disodium hydrogen phosphate (dodecahydrate)		60 g
Purified water (freshly boiled)	q.s.	1000 ml

Irrigation Solutions-Lavages

- Irrigation solutions are sterile, non-pyrogenic solutions used to wash or bathe surgical incisions, wounds, or body tissues. Because they come in contact with exposed tissue, they must meet stringent USP requirements for sterility, total solids, and bacterial endotoxins. These products may be prepared by dissolving the active ingredient in Water for Injection.

- Sterile water for irrigation: It is like water for injection. Does not contain antimicrobial agent. It is stored in glass or plastic packages larger than 1 liter.

- Packaging:
  - They are packaged in single-dose containers, preferably Type I or Type II glass, or suitable plastic containers, and then sterilized.
- A number of irrigations are described in the USP:
- Acetic Acid Irrigation for bladder irrigation,
- Dimethyl Sulfoxide Irrigation for relief of internal cystitis,
- Glycine Irrigation for transurethral prostatic resection,
- Ringer's Irrigation for general irrigation,
- Neomycin and Polymyxin B Sulfates Solution for Irrigation for
- infection, and Sodium Chloride Irrigation for washing wounds.

Inhalation solutions

- These are solutions used in the bronchial and nasal symptoms to provide comfort to the patient. Their effect can be local or systemic. They are administered via aerosols or nebulizers for inhalation. They are prepared in sterile water or sodium chloride solution and contain an inert, propellant gas.

Collodion

- *Collodion*, a 4.0 percent (w/v) solution of pyroxylin (cellulose dinitrate) in a mixture of 75 percent (v/v) ether and 25 percent (v/v) ethyl alcohol, is also a cellulose-based, lyophilic colloidal system.
- They are applied to the skin by means of a soft brush or other suitable applicator and, when the ether and ethanol have evaporated, leave a film of pyroxylin on the surface.
- There are two basic types: flexible and non-flexible.
- Non-flexible collodion is often used in theatrical make-up. When applied to the skin, it shrinks as the solvent evaporates, causing wrinkles and is used to simulate old age, or scars.

Collodion

- Flexible Collodion is often used as a surgical dressing or to hold dressings in place. When painted on the skin, collodion dries to form a flexible nitrocellulose film. While it is initially colorless, it discolors over time. It is applied on the skin and cracks in the skin. Elastic Collodion is prepared to prevent sticking and solidification of collodion on the skin.
  - Do not apply on open wounds

Collodions

Collodion (USP 27)

Pyroxylin		40 g
Ether		750 ml
Alcohol		250 ml

Flexible Collodion(USP 27)

Camphor		20 g
Castor oil		30 g
Collodion	q.s.	1000 g

Salicylic Acid Collodion(USP 27)

Salicylic Acid		100 g
Flexible Collodion	q.s.	1000 g

Lens solutions

- Wetting solutions
- Cleaning solutions
- Disinfection solutions
- Storage solutions
- Artificial tear solutions
- Multi Purpose Solutions

Lens Type	Polymeric Structure	Lens Properties	Solutions
Hard, hydrophobic	Polymethyl methacrylate	Low gas permeability Low water content Normal wettability	Wetting Solution Incubation Solution Cleaning Solution Artificial Tear Solution
Soft, hydrophilic	Hydroxyethyl methyl methacrylate	Low gas permeability High water content Good wettability	Disinfection Solution Cleaning Solution
Soft, hydrophobic	Silicone rubber	High gas permeability Low water content Low wettability	Wetting Solution Incubation Solution Cleaning Solution
Hard, hydrophilic	Cellulose acetate butyrate	Good gas permeability Good wettability	Wetting Solution Incubation Solution Cleaning Solution Artificial Tear Solution

Properties of contact lenses

- İdeally-soft
- Not irritating
- Must have a specific gas permeability (Oxygen permeability)
- Should not lose transparency over time (Eg: Should not lose transparency by absorbing large amounts of antimicrobial agents)
- It should have a certain water holding capacity and should not cause the eye to dry
- Must be easily wettable

Properties of contact lens solutions

- Must be sterile and isotonic
- Not irritating
- In terms of wettability, their surface tension must be low
- Contain preservative

Wetting Solutions

They are used to cover hydrophobic surfaces of polymethyl methacrylate, silicone, acrylate and other hard lenses to provide a hydrophilic property.

- Viscous agent
- Surfactant

cellulose derivatives, polyvinyl alcohol, polyvinyl prolidone, polyethylene glycol

- Preservatives (sorbic acid)

Cleaning Solutions

- To remove
  - Loosely bound foreign matter
    - Cell debris
    - Mucus, lipid , protein
    - Cosmetic or other surface contaminat
  - Majority of micro-organisms

- Surfactants
- Buffers
- Osmolality adjusting agents
- Preservatives
- Water

Rx

Stabilized papain	10.0 mg
Polyethylene glycol	3350 4.0 mg
Sodium chloride	44.7 mg
Sodium carbonate (anhydrous)	31.0 mg
Disodium edetate	8.0 mg
L-cysteine hydrochloride-monohydrate	10.0 mg
Tartaric acid	20.0 mg
Sodium borate	19.1 mg

For 1 Tablet

Disinfection Solutions

- FDA approved
- Have appropriate disinfection properties
- Isotonic
- sterile solution
- Does not interfere with the lens material,
- Does not change the physical, chemical and optical properties of the lens.

Two different disinfection solutions are available:

a) Heat disinfectants: Isotonic saline containing no preservative is placed in the lens container and heated to a certain temperature.

b) Cold disinfection solutions: Lenses are either incubated in a compatible solution (thiomersol or chlorhexidine) or hydrogen peroxide solutions are used.

Storage Solutions

- It is a solution which is used for incubating/storing lenses and providing water absorption of hard lenses. They should include appropriate preservatives for ophthalmic solutions.
- Also contains other materials such as chlorhexidine and benzalkonium chloride, water-soluble polymers and sodium edetate.

Catalase	550 IU
Thiomersal	0.01 mg
Sodium chloride	8.5 mg
Disodium edetate	1 mg
Disodium hydrogen phosphate	2.1 mg
Sodium hydrogen phosphate	0.9 mg
Distilled water	1 ml

Artificial Tear Solutions

- They are especially used in hard lenses. They are similar to tear contents. They are also known as wetting solutions.

Multi Purpose Solutions

- They have the common properties of storage, wetting and disinfection solutions. The lenses cleaned with the cleaning solution are stored in this solution.

Rx

Polyquerternium-1	0.001 mg
Sodium citrate (dihydrate)	0.56 mg
Sodium chloride	0.516 mg
Citric acid (monohydrate)	0.021 mg
Disodium edetate (dihydrate)	0.05 mg
Distilled water	1ml

Spirits

- Spirits, sometimes known as essences, are alcoholic or hydroalcoholic solutions of volatile substances. Like the aromatic waters, the active ingredient in the spirit may be a solid, liquid, or gas.

- Spirits may be used pharmaceutically as flavoring agents
  - As flavoring agents, they are used to impart the flavor of their solute to other pharmaceutical preparations.
- Medicinally for the therapeutic value of the aromatic solute.
  - For medicinal purposes, spirits may be taken orally, applied externally, or used by inhalation, depending upon the particular preparation.
  - When taken orally, they are mixed with a portion of water to reduce the pungency of the spirit.
- Depending on the materials utilized, spirits may be prepared by simple solution, solution by maceration, or distillation.
- The spirits still listed in the USP/NF are aromatic ammonia spirit, camphor spirit, compound orange spirit, and peppermint spirit.

Preparation of large volume solutions

Equipment:

- Tanks
- Heating units
- Mills
- Filters

- stainless steel
- teflon coated surfaces
- Clean, if necessary - sterile
- Filtering through filters
- High quality pure water should be used

Filling of large volume solutions

- weight → Slow and Simple
- pressure → With pressure pumps / semi-automatic
- vacuum → Large volume solutions / fully automated

- Jacketed Tanks
- Tubes that can carry large quantities of liquid
- Closed systems to prevent turbulence → Foaming during filling
- Prevention of contamination (outfit, gloves and mask)

Stability of Solutions

- Ready-to-use solutions usually have a shelf life of 1-5 years.
- The drugs in the form of solutions undergo decomposition easily and rapidly in terms of stability.
- Their chemical stability is lower than solid dosage forms.
- interaction (chemical) reactions between active substance - solvents and excipients.
- External factors such as: Heat, light, air, oxygen, moisture, packaging material, microorganisms may cause degradation.
- Warnings should be written on the label:

  «Keep in a cool place» or «Keep in refrigerator» or «Protect from light»

- EXAMPLE: For the solutions with volatile solvents:
  - «Store in tightly closed containers, keep away from heat»

Physical Changes:

Increased viscosity or crystallization due to evaporation of solvent in the formulation.

Chemical Changes:

To prevent hydrolysis;

1) The product should be prepared at an appropriate pH range in which hydrolysis chance will be the lowest . (Eg. Novokain solutions are stable at pH 3-6.)
2) The solvent type can be changed.
3) Addition of surfactant
4) Chemical structure can be modified
5) Prodrug or salt-ester derivatives may be preferred.
6) Protect from catalysts such as heat, light and metals.
7) With the addition of chelating agent such as EDTA, heavy metals in the medium can be removed.

Oxidation: The process of reacting the active substance with oxygen.

Adrenalin, Vitamin A, B12, D, E, C, tetracycline (antibiotic), hormone and iron compounds.

- Addition of antioxidants
- Freshly distilled water is preferred.
- If necessary, the water is boiled and the dissolved O_2 is removed.
- N_2 gas is passed.
- It causes oxidation of metals.
- Addition of EDTA.
- Light-protective packaging is selected.
- The storage temperature is reduced.

Microbial Changes

Add preservatives or minimize the chance of microbial growth.