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STERILE DOSAGE FORMS

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Introduction:

- Parenteral preparation are the preparation that are given by other than orally.
- Injections and transfusion fluids are come under the parental preparation.
- Injections should be sterile, isotonic, and free from the foreign particles, such as dust, fibers etc.
- Injections are the sterile solution and suspension of drug in aqueous or oily vehicle meant for introduction in to the body by means of an injectable needle under or through one or more layer of skin or mucous membrane.

- **Advantages of Parenteral Preparation:**

- The drug which are can not be administered by oral route, can administered by this route.
- The patient who are vomiting or suffering form unconscious condition, can not able to take the drugs by orally, can administered by this route.
- The drug action is quick and rapid
- Drug action can be prolonged by modifying the formulation
- Transfusion fluid are also contain nutritive like glucose and electrolytes.

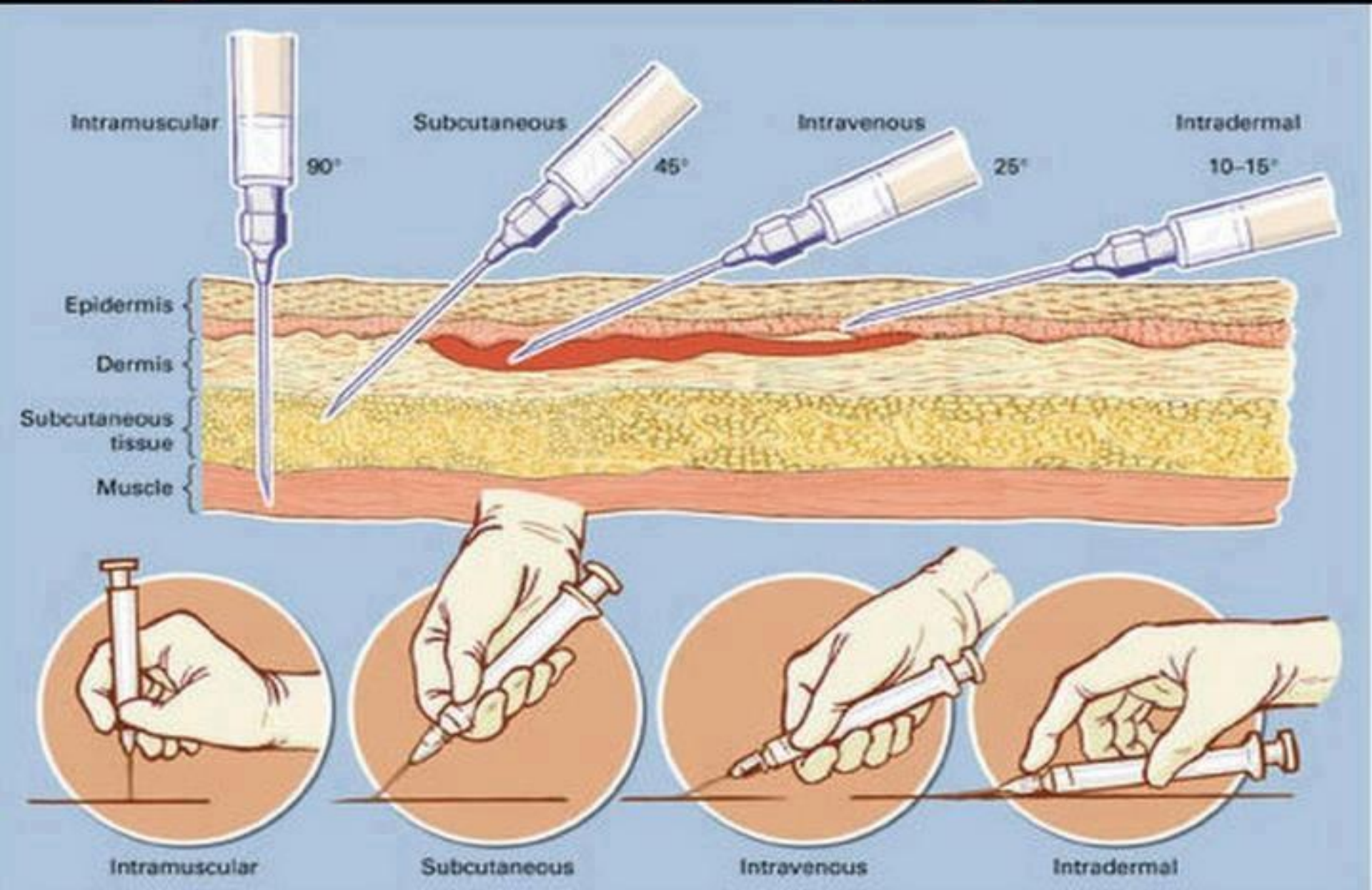
- **Disadvantages:**

- The trained person is required to administer the drug
- Injection causes the pain at the side of injection
- The administration of drug from wrong route of injection may very dangerous.
- The chances of sensitivity reaction or allergic reaction of the drug by an individual.

Route of Administration:

- Intradermal/ Intracutaneous Injection (given between dermis and epidermis layer of skin)
- Hypodermis/ Subcutaneous Injection (given under the skin into subcutaneous tissue i.e. fatty layer)
- Intramuscular Injection (injected deeply into muscular tissue)
- Intravenous Injection (directly into the patient's veins,)
- Intra Arterial Injection (given directly into the arteries)
- Intracardiac Injection (given into the heart muscle or ventricle in an emergency only)
- Intrathecal Injection (surrounding to spinal cord)
- Intracisternal Injection (between first & second cervical vertebrae for withdrawing cerebrospinal fluid)
- Peridural Injection (between the duramater and inner aspect of vertebra)
- Intra-articular Injection (in bones joint)
- Intracerebral Injection (given into Cerebrum)

Angles for inserting injections



- **Types of Parenteral Preparation:**

- Solution or Emulsions of medicament for suitable injections
- Sterile solids
- Sterile Suspension
- Transfusion Fluid

General Requirement for Parenteral Preparation:

Parenteral Products required careful consideration of the following requirement:

- Stability
- Sterility
- Free from Pyrogen
- Free from foreign particles
- Chemical purity
- Isotonicity
- Specific gravity

FORMULATION OF PARENTERAL PREPARATIONS

AQUEOUS VEHICLE:

Water For Injection (WFI) USP

- Highly purified water used as a vehicle for injective preparations which will be subsequently sterilized.
- USP requirement include not more than 10 parts per million of total solids.
- pH of 5.0 – 7.0 .
- WFI may be prepared by either distillation or reverse osmosis.
- Stored in chemically resistant tank.

Bacteriostatic Water For Injection

- This type of water used for making parenteral solutions prepared under aseptic conditions and not terminally sterilized.
- Need to meet USP sterility test.
- It can contain an added bacteriostatic agent when in containers of 30 ml or less.

Sterile Water For Injection (SWFI)

- SWFI containing one or more suitable bacteriostatic agent.
- Multiple-dose containers not exceeding 30 ml.
- They are permitted to contain higher levels of solid than WFI because of possible leaching.
- Used for washing wounds, surgical incisions, or body tissues.

Water Miscible Vehicles

- The number of solvents that are miscible with water has been used as a portion of a vehicle.
- Primarily to affect solubility of drugs and to reduce hydrolysis.

Examples:- Ethyl alcohol, Liquid propylene glycol, Glycerine,

NON – AQUEOUS VEHICLES

- Fixed oils (vegitable origin, liquid, and rancid resistance ,unsaturated, free fatty acid content)

- Peanut oil
- Corn oil
- Cotton seed oil (depo-testosterone)
- Sesame oil
- Soyabean oil
- Ethyl oleate
- Isopropyl myristate.

OTHER ADDITIVES

Anti-bacterial Agents:-

- These are added in multiple dose containers.
- To prevent microorganism growth
- Limitted concenteration of agents are used.

- Phenyl mercuric nitrate and thiomersol 0.01%.
- Benzethonium chloride & benzalkonium chloride 0.01%.
- Phenol & cresol 0.05%.
- Chlorobutanol 0.05%.

Buffers:-

- Added to maintain pH.
- To stabilize a solution from chemical degradation.

Examples:

- Citrate and acetate buffer.
- Sodium benzoate and benzoic acid
- Sodium tartarate and tartaric acid
- Phosphate buffer.

Anti-oxidants:-

- To protect the formulation from oxidation
- Two types

1. Reducing agents

- Ascorbic acid
- Sodium bisulfite 0.01%
- Thiourea

2.Blocking agents

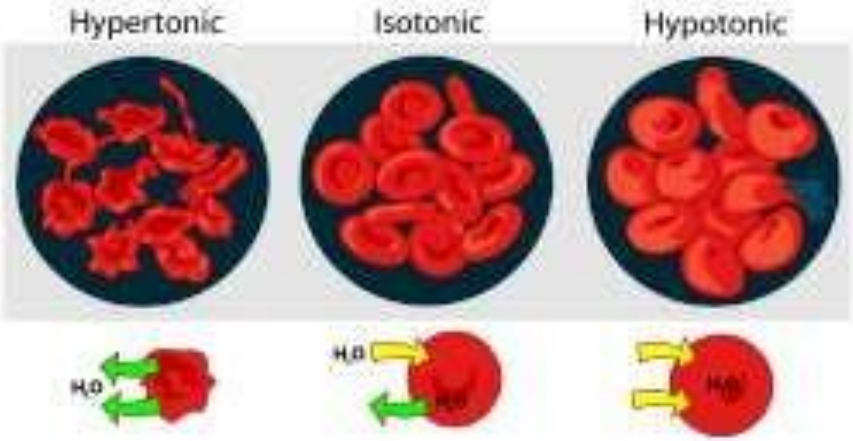
- Tocopherol

Surfactants:-

- **Solubilize the active ingredient**
  - Polyoxythylene sorbitan monooleate & Sorbitan monooleate

Tonicity Agents:-

- Need isotonic solution to avoid destruction of red blood cells, irritation, and tissue damage
- More important for large volumes, rapidly administered, and extravascular injections
- Reduces the pain on injection
  - NaCl & KCl
  - Dextrose
  - Mannitol & Sorbitol



Effect of different solutions on blood cells

Chelating Agent:-

- To remove trace elements that catalyze oxidative degeneration
  - Ethylene diamine tetra acetic acid

Co-solvents:-

- Improve solubility
- Prevent potential for hydrolysis

BULKING AGENTS

- For freeze dried preparations(solids)
  - Mannitol
  - Lactose, sucrose
  - Dextran .

SUSPENDING AGENTS

- CMC,
- Methyl cellulose, Gelatin
- Sorbitol .

EMULSIFYING AGENTS

- Lecithin
- Polysorbate 80

WATER FOR INJECTION (WFI):

- A clear and colorless liquid; odorless.
- Water for injections is pyrogen -free.
- It contains no added substance.
- Water for injections is obtained from potable or Purified water by distillation in an apparatus.
- The distillate is collected and stored in conditions designed to prevent growth of microorganisms and to avoid any other contamination.

- **Evaluation of Parenteral Preparation:**
  - **Sterility Test**
  - **Clarity Test**
  - **Leakage Test**
  - **Pyrogen Test**
  - **Assay**

- **Sterility Test:**

- All the Parenteral preparation are supplied in sterile form.
- The sterility test is strictly carried out under the aseptic condition in order to avoid accidental contamination.
- The Sterility test is must be carried out either by,

i. Membrane Filtration Method

ii. Direct Inoculation Method

- Steps of Sterility Testing:

- Selection of sample size
- Selection of quantity of product to be used
- Method of testing
- Observation and result

- **Clarity Test:**

- Clarity test id performed to ensure that the Parenteral products are free from foreign particles.

- Each Parenteral prepares is passes form the clarity test.

- **Leakage Test:**

- This test is performed only for the ampoules which have been sealed by the fusion.
- Leak test is performed in the vacuum chamber, the ampoules are dipped in methylene blue in vacuum chamber i.e. Leak test apparatus.
- Then vacuum is applied.
- When vacuum is released the color solution will entered with defective sealing
- The presence of dyes in the ampoule, confirm the leakage and hence rejected.

- **Pyrogen Test:**

- These test is perform for the check the presence or absence of pyrogen in the Parenteral Preparation.
- These test is involves the measurement of the rise in body temperature of rabbits following intravenous injection in marginal ear vein of a sterile solution of Parenteral preparation is examined.

- **Assay:**

- Assay is performed according to the method is given in the monograph of that Parenteral Preparation in pharmacopeia.

- Assay is done to check the quantity of medicament present in that preparation

- A= abc

a (absobtivity), b (pathlength), c (Concentration)