BRIEF ABOUT PARENTERALS

- para: outside
- enteron: intestine (i.e. beside the intestine)
- defined as sterile drug, solution or suspension that is packaged in a manner for suitable administration by hypodermic injection either in the form prepared or after addition of a suitable solvent or suspending agent.
- Parenteral products are injected through the skin or mucous membranes into the internal body compartments.
- These are the preparations which are given other than oral routes.
CONTENTS:
- Definition
- Introduction
- Advantages
- Disadvantages
- Routes of administration
- Formulation of product (SVP)
- Packaging
- Sterilization
- Special product of parenterals
DEFINITION:

According to USP: “an injection that is packaged in containers labeled as containing 100 ml or less”
INTRODUCTION:

- All the sterile products packaged in vials, ampoules, cartridges, syringes, bottles or any other container that is 100ml or less fall under the class of SVP.

- Ophthalmic products packaged in squeezable plastic containers, although topically applied to the eye rather than administered by injection, also fall under the classification of Small Volume Injections (SVI) as long as the container size is 100ml or less.

- SVP aqueous solutions can be administered by intravenous route because of local irritation. Small volume parenteral products can be formulated and packaged in several ways and include a wide variety of products like:
ADVANTAGES

- Quick onset of action.
- Suitable for the drugs which are not administered by oral route.
- Useful for unconscious or vomiting patients.
- Useful for patients who cannot take drugs orally
- Useful for emergency situations.
DISADVANTAGES

- Pain on injection.
- Difficult to reverse an administered drug’s effects.
- Sensitivity or allergic reaction at the site of injection.
- Requires strict control of sterility & non pyrogenicity than other formulation.
- Only trained person is required. Require specialized equipment, devices, and techniques to prepare and administer drugs.
- More expensive and costly to produce.
ROUTES OF ADMINISTRATION:

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  Three primary routes of parenteral administration are commonly employed
- Subcutaneous
- Intramuscular
- Intravenous
FORMULATION OF SVP:

- **Aqueous vehicle:**
  - **1. Water For Injection (WFI) USP:** Highly purified water used as a vehicle for injectable preparations which will be subsequently sterilized.
  - USP requirement include not more than 10 parts per million of total solids.
  - pH of 5.0 to 7.0 WFI may prepared by either distillation or reverse osmosis.
  - Stored for less than 24hr at RT or for longer times at specific temperatures. Should be meet USP pyrogen test It may not contain any added substances.
  - Stored in chemically resistant tank.
**Bacteriostatic Water for Injection (BWFI):** 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 30ml or less.
Sterile Water for Injection USP SWFI containing one or more suitable bacteriostatic agents. Multiple-dose containers not exceeding 30 ml. They are permitted to contain higher levels of than WFI because of the possible leaching of glass container. Sterile Water for Irrigation. Wash wounds, surgical incisions, or body tissue
Water-miscible vehicles:
primarily to effect solubility of drugs and/or
reduce hydrolysis.

Non-aqueous vehicles:

Fixed oils (vegetable origin, liquid, and rancid
resistance, unsaturated, free fatty acid
content) – Peanut oil – Corn oil – Cotton seed
oil (depo-testosterone) – Sesame oil –
Soybean oil (source of fat in intralipid) – Ethyl
oleate – Isopropyl myristate
ADDITIVES IN PARENTERAL PRODUCTS

Antimicrobials Agents;
Required to prevent microorganism growth
Limited concentration of agents -
Phenylmercuric nitrate and Thiomersol 0.01%
Benzethonium chloride and benzalkonium chloride, Phenol or cresol 0.5% -
Chlorobutanol 0.5%

Buffers;
Added to maintain pH Results in stability
Effective range, concentration, chemical effect
e.g Citrate and Acetate buffer, and Phosphate buffer
Tonicity Adjusters

- Electrolytes: NaCl
- Non electrolytes: Glucose, Mannitol, Glycerine
- Ex. Of isotonic: Dextrose injection 5% & NaCl injection 0.9%
- Not important in IM & SC
- Important in ID, intraspinal
- Tonicity can be measurement by: osmometer, Fragility point
- **Surfactant:** Polysorbate ethers
- **Suspending agent:** Methyl cellulose, CMC, PVP
- **Emulsifiers:** Lecithin
- **Chelating agents:** Disodium EDTA
- **Complexing agent:** 2-OH propyl b-cyclodextrane
- **Protein stabilisers:** Amino acids, pvp
- **Antioxidants:** Ascorbic acid, Cysteine
PACKAGING:

- packaging materials: Glass, Plastic, Rubber
- Sealing Ampoules: Ampoules are unique in that the primary and secondary seal are the same.
- Ampoules are sealed by melting a portion of glass in a flame.
- Pull seal – Slow, Reliable, powder or other types with wide opening Roll or Tip seal
Sealing of Bottles, Cartridges and Vials

Primary seal consisting of a tight rubber or plastic closure and secondary seal that holds the primary seal in place. Secondary seals are usually aluminum caps that are crimped on to a threadless container.
STERILIZATION

- Steam sterilization
- Dry heat sterilization
- Sterilization by filtration
- Gas sterilization
- Sterilization by ionizing radiation
SPECIAL TYPES OF PARENTERALS

- Suspension
- Emulsion
Parenteral suspension is a dispersed, multiphased, heterogeneous system of insoluble solid particles intended principally for intramuscular and subcutaneous injection. Because a delicate balance of variables is required in order to formulate a suitable product, a suspension is one of the most difficult parenteral forms to prepare. Such a product must not cake during shipping and storage and should be easy to suspend and inject through an 18 to 21 gauze needle throughout its shelf life.
To achieve these goals it is necessary to control the crystallization, particle size reduction, and sterilization of the drug substance.

Suspension give prolong drug release. Particle size of drug should be small and uniform.

Suspension require following additives wetting agent, suspending agent, buffering agent, preservative, antioxidant, ionicity agents.
EXAMPLE OF INGREDIENTS USED IN AQUEOUS PARENTERAL SUSPENSIONS

- Suspending agent
- Gelatin, mannitol, povidone
- Surfactants
- Lecithin, polysorbate 80.
- Solubilizing agents
- Propylene glycol
- PH adjustment
- Citric acid, sodium citrate.
Two basic methods are used to prepare parenteral suspension:

1. Sterile vehicle and powder are combined aseptically.

2. Sterile solutions combined and crystal formed in situ.
Problem encountered in suspension formulation are

- Settling and caking.
- Polymorphic transformation.
- Crystal growth.
An emulsion is a heterogenous dispersion of one immiscible liquid in another.

This inherently unstable system is made possible through the use of an emulsifying agent, which prevent coalescence of the dispersed droplet.

Parenteral emulsion are rare because it is necessary (and difficult) to achieve stable droplet of less than 1 micron meter to in prevent emboli in blood vessels and it is not usually necessary to achieve an emulsion for drug administration.

Formulation options are severely restricted through a very limited selection of stabilizers and emulsifiers primarily due to the dual constraints of autoclave sterilization and parenteral injection.
Problems encountered in emulsion formulation

1. Creaming and cracking

2. Rancidity in oil phase

3. Partitioning of preservative between oil and water phase
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Thank You