TYPES OF PARENTERAL DOSAGE FORMS

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OBJECTIVES OF THE LECTURE

• What are various types of parenteral formulations?

• What are features of particular parenteral formulations and how these are prepared?

• What are advantages / disadvantages of particular parenteral formulations?
TYPES OF PARENTERAL PREPARATION:

• Most common types of parenteral preparations includes:

  – SOLUTIONS

  – EMULSIONS

  – SUSPENSIONS

  – DRY POWDER FOR SOLUTION/SUSPENSION
Features of parenteral solutions

• Most common
• Prepared by dissolving the drug and preservative, adjusting the pH and sterile-filtering the resultant solution through a 0.22 μm membranes filter.
• May include alcohols, glycols, or other non-aqueous solvents.
• Most solutions have the viscosity and surface tension very similar to water.
• Some solutions may be viscous e.g. streptomycin and ascorbic acid injection.
• Drug solutions that resist heat, are terminally autoclave sterilized after filling; this assures product sterility and package.
**TYPES OF PARENTERAL PREPARATION: SOLUTIONS**

(A) Single-dose vials  
(B) Multidose vials  
(C) Ampules  
(D) Large-volume bottles or bags used for intravenous administration
TYPES OF PARENTERAL PREPARATION: EMULSIONS

- Initially parenteral emulsions were developed as a source of calories and essential fatty acids, as intravenous TPN / hyper alimentation.
- Later it evolved as a promising parenteral delivery system for lipophilic substances such as medicinal fats, oils, fatty acids, fat soluble vitamins.
- The dispersed droplets are 0.5-1.0 μm in diameter.
- This corresponds to the size of the chylomicra; which are the natural transport systems for fat through the blood stream.
Types of Parenteral Preparation: Emulsions

Advantages of Parenteral Emulsions

✓ Some drugs show more stability, efficacy or safety in the emulsion form.

✓ The anti-inflammatory activity of dexamethazone palmitate parenteral emulsion is 5-6 times of dexametnazone solution parenteral.

✓ Diazepam as parenteral emulsion showed lower toxicity than the solution form.

✓ Physostigmine salicylate emulsion is more stable than the solution form.

✓ Improved Stability and Solubility clarithromycin, all-trans-retinoic acid, sodium phenobarbital,
Disadvantages of Parenteral Emulsion:

- Manufacturing process is very difficult because you are dealing with individually sterilized ingredients and under aseptic procedure.
- Sterilization is difficult, because heat influence stability of heat labile oils and filtration is impossible.
- Emulsion is unstable system, upon storage may result in increased globule size due to coalesce and this is very dangerous because it would cause thrombosis if injected intravenously.
- Long term emulsion therapy may lead to overloading syndrome (fever, anemia, hepato-spleeno-megaly)
TYPES OF PARENTERAL PREPARATION: EMULSIONS

- **Aqueous Phase:** It is usually WFI, to which additives are required to adjust osmolarity using glycerin, sorbitol, xylitol, sodium chloride or dextrose.

- **Oily Phase:** Natural vegetable oils such as sesame, linseed, peanut, olive or cotton seed or soya bean oils are used as oily phase for parenteral emulsions.

- **Emulsifiers:** Natural Lecithin (a mixture of phosphatides) are the most safest parenteral emulsifiers. They are very stable towards hydrolysis and oxidation.

- Other emulsifiers and stabilizers that are suitable for pararentral emulsions are polysorbate 80, gelatin, methylcellulose and serum albumin.
TYPES OF PARENTERAL PREPARATION: EMULSIONS

Key Process Parameters:
- Rate of mixing
- Temperature
- Rate of cooling
- Pressure
- Number of cycles
- Sterilization duration
TYPES OF PARENTERAL PREPARATION: EMULSIONS
TYPES OF PARENTERAL PREPARATION: SUSPENSIONS

• Formulated for unstable & poorly soluble drugs.
• Provides more prolonged drug actions.
• Contain 0.5-5% solid (however certain antibiotic parenteral suspensions such as procaine penicillin G may contain up to 30% solids).
• Particle size is usually less than 5μm.
• They are limited to SC, IM and intraarticular routes as IV administration of a suspension may result in vasoocclusion.
Requirement for an ideal Parenteral suspensions should have good syringeability and injectability to be properly administered.

- **Syringeability**: refers to handling characteristics of suspension while withdrawing it from the container to a syringe. Where clogging and foaming may occur.

- **Injectability**: refers to suspension characteristics during injection (the required pressure for injection and aspiration).

- Both terms depend on viscosity and particle characteristics of the suspension.

- Cake formation shouldn’t occur during its shelf life.

- Re-suspension of drug particles should occur easily with mild shaking.
TYPES OF PARENTERAL PREPARATION: SUSPENSIONS

- General steps in manufacturing:
  - Sterilization and milling of active ingredient (s).
  - Sterilization of vehicle.
  - Aseptic wetting and dispersion of the active ingredient (s).
  - Aseptic milling of the bulk suspension.
  - Aseptic filling of the bulk suspension in suitable containers.
TYPES OF PARENTERAL PREPARATION: SUSPENSIONS

• **Advantages of suspension:**
  
  – suitable for insoluble drugs
  
  – increased stability
  
  – possible depot action

• **Disadvantages:**
  
  – difficult formulation and manufacturing
  
  – patient discomfort.
  
  – difficult dose uniformity.
  
  – Setteling and cake formation
TYPES OF PARENTERAL PREPARATION: SUSPENSIONS
Due to instability in water, many drugs are formulated as drug powders to be reconstituted prior to administration. eg. Penicillins, barbiturates, benzocain.

Sterile water for injection is supplied with dry powders to make “solutions / or suspensions for injections”.

The obtained solution / suspension will meet with all the requirements of solution / suspension for parenteral.

Reconstituted solutions can be given by IV or IM route, however suspension is forbidden for IV administration.
METHODS OF PREPARING A STERILE DRUG POWDER:

- Sterile recrystallization:
  - The drug is dissolved in a solvent and the obtained solution is sterilized through 0.22 μm membrane filter.
  - A sterile anti-solvent is then added to crystalize the drug particles, which is filtered and dried aseptically.

  Advantages: Flexible and economic.

  Disadvantage: variations from batch to batch and contamination.
METHODS OF PREPARING A STERILE DRUG POWDER:

**Lyophilization:**

- It is a process of separating a solid substance from solution by freezing the solvent and evaporating the ice under vacuum.
- Drug solution is sterile filtered into sterile trays which are aseptically loaded into a freeze dryer.
- The solution is then frozen at -50°C and then dried by vacuum to separate the drug powder.

- **Advantage:** Removal of water at low temperatures.
- **Disadvantage:** Biological molecules are damaged by the stress associated with freezing, and drying.
- Costly, time consuming.
METHODS OF PREPARING A STERILE DRUG POWDER:

*Spray Drying:* The solution of the drug is sprayed into a dry chamber where it comes in contact with a hot steam of a sterile gas (80-100 °C).

- **Advantage:**
  - Simple, Economical, scalable, faster.
  - Coating of particles during drying prolonged release.

- **Disadvantage:**
  - High processing temperatures and high shear forces can easily damage drugs.
  - Higher level of drug losses than freeze drying.
  - Limited solvent choice for a given drug.
  - Cannot prepare product directly in vials or plates.
TYPES OF PARENTERAL PREPARATION: DRY POWDER..
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Types of parenteral preparation: Dry powder.

Procedure of reconstitution

1. Clean the rubber diaphragm of the medication vial and the diluent vial with an alcohol swab.
2. Unpack the desired syringe, pull the plunger to fill the barrel with air equal to the desired amount of diluent.
3. Inject the air into the vial of WFI to create positive pressure and to ease withdrawal.
4. Invert vial and withdraw the desired amount of WFI.
5. Inject the WFI into the medication vial and withdraw the syringe and needle.
6. Invert & Shake the vial to mix well.
7. Positive pressure may be created in the freshly mixed medication vial for easy withdrawal (step 3).
THANK YOU FOR ATTENTION

GOOD LUCK ..