INDUSTRIAL PHARMACY-I

UNIT IV-PARENTERALS

CLASS:26

TOPIC Definition, types, advantages and limitations. Preformulation factors and essential requirements

The USP 24/NF19defines parentral articles as ―those preparations intended for injection through the skin or other external boundary tissue, rather than through the active substances can be administered directly into a blood vessel, organ, tissue, or lesion‖ Parenteral route of drug administration generally includes intravenous (IV), subcutaneous (SC), and intramuscular (IM)route, however, lesser-used routes such as intra thecal, intra arterial, convection-enhanced drug delivery and implants are also included under the broad umbrella of The pharmaceutical convention, however, is to use the term parenteral for those medicines that are administered by means of an injection. Parenteral products are the mainstay of treatment for hospitalized patient. This route of drug delivery offers a plethora of advantages for patients who cannot take medications orally or for those who require rapid onset of action. Parenteral (para–outside enteron-intestine) administration is the introduction into the body of nutrition ,medications ,or other substances other than by the alimentary canal.

Parenteral preparations are defined as solutions, suspensions, emulsions for injection or infusion, powders for injection or infusion, gels for injection and implants. They are sterile preparations intended to be administrated directly into the systemic circulation in human or animal body. They are required, like any pharmaceutical dosage forms, to meet the pharmaceutical quality standards as described in pharma-copeias and to be safe for the intended purpose of use.

In addition to being sterile, parenteral preparations must be pyrogen-free. Sterility can be achieved by different processes of sterilization that should be appropriate to the formulations,4while the pyrogen-free aspect will require, if no depyrogenation process is used during the preparation of the sterile drug products, the use of pyrogen-free pharmaceutical ingredients; drug substances or API (Active Pharmaceutical Ingredient) and excipients. They are usually supplied in single dose glass or plastic containers (PVC nowadays less recommended, or polyolefin) or more and more in pre-filled syringes or pens to facilitate the ease of use.

Parenteral products are unique from any other type of pharmaceutical dosage form for the following reasons: All products must be sterile. All products must be free from pyrogenic (endotoxin) contamination. Injectable solutions must be free from visible particulate matter. This includes

reconstituted sterile powders. Products should be isotonic, although strictness of isotonicity depends on the route of administration. Products administered into the cerebrospinal fluid must be isotonic. Ophthalmic products, although not parenteral, must also be isotonic. Products to be administered by bolus injection by routes other than intravenous (IV) should be isotonic, or at least very close to isotonicity. IV infusions must be isotonic. All products must be stable, not only chemically and physically like all other dosage forms, but also _stable' microbiologically (i.e., sterility, freedom from pyrogenic and visible particulate contamination must be maintained throughout the shelf life of the product). Products must be compatible, if applicable, with IV diluents, delivery systems, and other drug products co-administered.2 Properties Of Parenteral Preparations Parenteral preparations are intended to be administrated through the human or animal body, either by direct injections (for example, bolus intravenous (IV), intramuscular (IM) or subcutaneous (SC)) or by infusion with a controlled infusion rate or by direct implantation through IM or SC. They must meet the following minimum com-pendia criteria:- To be sterile and pyrogen-free

.• To be clear or practically exempt of visible

• particle and to be free from sub-visible particles as required by pharmacopeias EP, USP and JP.

No evidence of phase separation for the emulsions, or aggregates formation for aqueous dispersions such as injectables Mab (monoclonal antibody) preparations.

In case of suspensions, the use of appropriate particle size and any sediment should be readily dispersed upon shaking to give stable formulations and ensure the correct dose to be withdrawn and injected.

Parenteral preparations may require the use of biocompatible excipients that are selected according to the specific application and included at the minimum efficient concentration.

The functionality of these excipients is as follows:- to make the preparation isotonic with respect to blood (glucose/dextrose, mannitol, sodium chloride) to adjust the pH to physiological levels(mineral or organic acids or salts) to prevent the degradation of the drug substances (stabiliser) to ensure or increase the drug substance's solubility to provide adequate antimicrobial preservation (only applicable to multidose preparations).

It must be stressed that excipients should not adversely affect the intended medicinal action of the drug product, nor at the concentration used cause toxicity or undue local irritation

Injections may be classified in six general categories:

- • Solutions ready for injection.

- Dry, soluble products ready to be combined with a solvent just prior to use.
- Suspensions ready for injection.
- Dry, insoluble products ready to be combined with a vehicle just prior to use.
- Emulsions. Liquid concentrates ready for dilution prior to administration

Advantages Of Parenteral Products:-.

These Unconscious patients.

- Uncooperative and unreliable patients
- Onset of action of drugs is faster; hence it is suitable for emergency.

Patients with vomiting and diarrhea.

These are suitable for irritant drugs and drugs with high first pass metabolism.

Drugs are not absorbed oral Drugs destroyed by digestive juice

Disadvantages Of Parenteral Product:-

- Parenteral preparations should be sterile and expensive.
- They require aseptic conditions.
- Cost
- They can‘t easily self- administrated.
- Causes local tissue injury to nerves, vessels,etc.

1. Preformulation Factors

Preformulation is the initial phase in the development of a pharmaceutical dosage form, where the physical and chemical properties of the drug substance are studied to design a stable, safe, and effective formulation. In parenteral products, preformulation is especially critical due to the sterile nature and direct entry into systemic circulation.

Key Preformulation Factors for Parenteral Products

1. **Physicochemical Properties of the Drug**

Solubility: The drug must be soluble in the vehicle chosen for parenteral use. Insoluble drugs may require suspension or emulsions.

pH and Stability: Stability of the drug in solution at various pH values must be assessed. pH affects solubility, stability, and irritation potential.

Partition Coefficient: Determines drug’s lipophilicity/hydrophilicity affecting absorption and formulation strategy.

Molecular Size: Influences absorption and clearance.

Polymorphism: Different crystalline forms may have different solubility and stability profiles.

- **Compatibility Studies**

Interaction of the drug with excipients, vehicle, and container materials must be evaluated to prevent degradation or precipitation.

- **Sterility and Pyrogenicity**

Drug must be free from pyrogens (fever-causing substances). The formulation process should preserve sterility.

- **Stability**

The drug should remain stable under expected storage conditions, including temperature, light, and oxygen exposure.

- **Toxicity and Irritancy**

The drug and excipients should not cause local irritation or systemic toxicity.

- **Viscosity**

Affects ease of injection; excessively viscous solutions are difficult to inject and may cause pain.

2. Essential Requirements of Parenteral Formulations

To be suitable for parenteral use, formulations must meet specific criteria:

A. Sterility: Absolute sterility is mandatory to avoid infections.

B. Pyrogen-Free: Must be free from pyrogens to prevent febrile reactions.

C. Isotonicity: Parenteral solutions should be isotonic or nearly isotonic with body fluids to prevent tissue irritation or damage.

D. Stability: The drug must remain chemically and physically stable throughout shelf life.

E. Clarity and Absence of Particulates: Solutions should be clear and free from visible particles to prevent embolism or irritation.

F. Appropriate pH: pH must be compatible with physiological conditions (usually 4-8) to avoid pain and tissue damage.

G. Non-Toxicity of Additives: All excipients and additives must be non-toxic and compatible with the route of administration.

H. Suitable Packaging: Containers must maintain sterility, be chemically inert, and protect the formulation.

Small volume parenterals

Parenteral emulsions

Dry powders