Chapter - Manufacturing

Additives of Parenterals

The parenterals contain several additives and stabilizers of highest purity

1. **Preservative and stabilizers:** These preserve the drug and make product stable, parenterals are liable to degradation on decomposition and hydrolysis,Antioxidants are used to prevent-oxidative degradation,Hydrolysis can be prevented by PH adjustment where water is avoided as vehicle Eg-EDTA,antioxidant like sodium sulphide

2. **Buffering agent ;** These are used to maintain the PH of parenteral products during storage and to prevent the degradation. Eg- Acetate, Citrates, Phosphates.

3. **Anti-oxidants;** To prevent oxidative degradation of parenterals products antioxidants are added Eg sodiam bisulphite (0.1%),Sodiam metabisulphite,Sodiam thiosulphate,thiourea,acetone.

4. **Antimicrobial agents** ; These are used to prevent microbial growth essential in multidose container,during withdrawal of dose, the product may be contaminated hence to maintain the sterility of the product the following antimicrobial agent are added in adequqte preparation

Cresol 0.05%
Benzalkonium chloride 0.001%
Chlorobutanol 0.5%
Phenyl mercuric nitrate 0.002%

5. **Tonicity contributors;** The tonicity of solution is adjusted by using susbtances which must be compatible with other ingredients of the preparation.Eg- Sodaim chloride, Borax .

\6 **Wetting,suspending and emulsifying agents**

Agent	**Use**	**Examples**
Wetting agent	Used in suspension to maintain the particle size	Sorbitan trioleate,tween-80
Suspending agent	To prevent flocculation of suspended particles and used in parenteral suspensions	Sodium CME,Methyl cellulose, sodium citrate
Emulsifying agent	For emulsification	Lecithin

Handling of containers

After cleaning, the wet containers are more liable to contaminate than dry one , hence these wet container should be protected by Laminar air flow of clean, air covered with a stainless steel box and dry it and sterilized.

Type of glass to prepare container is;

1. Type I Borosilicate glass
2. Type II Treated soda lime glass
3. Type III Soda lime glass

Principle involved in hydrolytic resistance test for glass ; Glass containers very easily yield alkali ions to aqueous preparations as parenterals solutions are stored for long period and large volume parenterals are in contact with glass, a considerable amount of alkali is extracted. Therefore ,hydrolytic resistance test is a limit test used for estimation of the quantity of alkali yielded to a solution

General method of Preparation of Syrup

Syrups are concentrated aqueous preparation of sugar with or with out added flavouring agent and medicated syrup

Most of the syrup contain sugar preservative and colouring agent, flavouring agent and may be solublizer and stabilizer.

General method of production of syrup involve.

1. Dissolving o all water soluble ingredients excepts sucrose.
2. Addition of sucrose followed by soebitol
3. Paraben may be added from paraben concentration
4. Flavouring agent is added.
5. Making the volume and cooled and filtered

For hydro alcoholic syrup procedure involve.

1. Dissolve all alcohol soluble ingredients in alcoholic solvent
2. Water soluble ingredients to be dissolved in water.
3. With continue agitation add aqueous solution to alcoholic solution

The following equipment's are of Drugs and cosmetic rules 1940 for manufacture of syrup

1. Mixing and storage tank
2. Vacuum or gravity tank
3. Water,steam or deionisor

Bulk concentration

Many solutions and semisolid which can be used as pharmaceutical aid or after dilution are compounded in bulk and as concentration called as bulk concentrates,
The bulk compounded liquid orals includes syrups, elixirs, suspension, emulsion,.The semisolid which are compounded in bulk includes emulsion and ointment.

Advantages of liquid orals

1. It is convenient for use.
2. It gives rapid onset of action
3. It provides good compliance to patient
4. It mask the unpleasant taste

Disadvantages of liquid orals

1. It is unstable
2. It causes oxidation when exposed to air
3. It is costly as compared to solid dosage form
4. I t is not handled easily

Procurement of stores

Centralised purchases for the entire hospital of all the items are done either by a purchase officer or purchase committee.Decentralised purchases are done by the user department ,where pharmacist purchase,compound,dispense and manufacture drug in the hospital.

1. Supplier; To deliver goods to his representative.
2. Accountant department; Regarding cost center to be charged
3. Purchase section; To retain if for his department file
4. Department for which purchase requisitioned is originated; It originates when the copy match with purchase requisite form to check for accuracy
5. Two copies for receipt section of stores; Out of which one is used once the goods arrive for checking& other when the goods are back ordered
6. A copy for history which the purchase section to a certain rates and other things in future

Method of procurement of medicament's in stores

The centralised purchase department by an officer has to issue purchase order, follow them up,institute procedures and invite quotations and maintain purchase record
The decentralised purchase made either by a junior medical officer or pharmacist have to carry out.

A) Direct purchase from wholesaler/manufacture
B) Institute procedure for bid inviting
C) Emergency purchase from local market
D) Entry in to rate contract

Source of purchase store; Each hospital has to select sources of supplies very carefully. The list of suppliers with their full address and telephone number is maintained by the pharmacist.

Purchase requisition; Once the specifications are drawn purchase requisition is prepared. The requisition carry the description of items ,their packaging their prize, their quantity.The original requisition is send to the administrative head of department,once app[roved by the administrative head it is send to the purchase officer.

Purchase order; After the receipt of purchase requisition,purchase officer/pharmacist prepare a detail purchase order in a period form. When the specification, prize and quantities are spelled out systematically and several copies are prepared and given to

1.Supplier
2. Accountant department
3. Purchase section.
4. Department from where purchase requisition originated
5. Two copies for receipt section of stores
6. A copy for history with purchase action.

Receipt of goods; When the ordered articles arrive, the quantities and prices are checked and compared with purchase order. If the part of the goods are returned to the supplier,immediately a ‘’Good return note’’ is prepared with the copy going to supplier,other to the concerned department.Against return a credit note may be obtained from the supplier, supplies received entered on the purchase record register.

Tender system purchasing in hospital ; Tenders of bids are invited fro several suppliers , the lowest bidder is selected for applying the order .Rate contracts given to the bidder bind him to supply at an agreed rate. A specified total quantity,against purchase order re lase from time to time till an agreed quantity contact is over, it ensure assured supply at an assured time of an assured quality.

For bulk drugs for regular medicine it is better to have a rate contract with a penal of supplier/single supplier.Rate contracted product need stricter testing in terms of quality.The quality is measured analytically as well as clinically, when in house quality testing laboratory is not available the samples must be send either to a reputed private or government laboratory

Testing raw materials ; Testing of raw materials is the most important step in the manufacturing of pharmaceutical product,To get the quality product one has to use the quality raw material .Hence the raw material is of great significance in quality control

All the statements in the monograph given under heading ‘’standard’’ constitute the standard for the official substances and a substance is not of

pharmacopocial quality unless it compiles with all requirements stated under ‘’standard’’