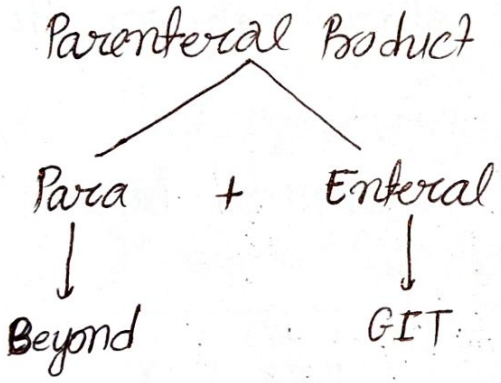
Unit - 4 Parenteral Product :-

→ The Parenteral Dosage form is derrived from two words Para + Enteral.

→ Para means beyond the route and Enteral means: GIT.

→ If any drug is absorb in our blood without Passing through the GIT back they are called Parenteral Product are Parenteral dosage form.



:- Types of Parenteral Product :-

1) Injection
2) Infusion
3) Powder for Injection
4) Concentration Solution for Injection
5) Implants

Property:- In The parenteral dosage form the active medicament is dissolve in a particular solvent which is Pyrogen free and microbes free.

→ And they are incerted in the skin through the injection and directly goes in to the systemic circulation

→ Because the Parenteral dosage form do not contain any kind of disintegration, Dissolution, and absorption process and the drug directly goes into the blood or systemic circulation so their onset of action is quick and immidiate.

→ The parenteral dosage form shows 100% bioavailability. because they donot waste in the First pass metabolism

→ The drug which are very costly and low in conc. they are always given in the parenteral form. because of conjuption or wated money.

(1) Injection:-

→ They are basically a clear solution of active medicament in the solvent which is microbes and Pyrogen free.

→ And they are with the help of Syringe and Niddle incertain inside the blood circulation

(2) Infusion:-

→ Infusions are also Similar to the injection in which the active medicament are dissolve in the water for injection solvent and they are large in volume.

→ Usually 100 to 200 ml and they are with the help of IV set incertain into the Patients.

(3) Powder for Injection :-

→ In this dosage form the active medicament is in sterile and dry form available in a bottle.

→ And the water for injection is added into in and after dissolving they convert into the solution form. and after converting into solution form they are inserted into the body.

(4) Concentrated Solution for injection :-

→ It is very similar to the powder for injection but inthis drug active medicament is sterire in concentrated solution form and after adding the water for injection they are diluted and injected inside the body.

(5) Implants :-

Implants are in a Patch form with active medicament and inserted inside the skin and body and they release the drug for longer duration.

Advantage of Parenteral Product:-

(1) Parenteral Product Shows the immidiate resfonce. because it donot contains the absorption phase.

→ For the very emergency patient oral dosage farmare not effected. for the quick resfonce parenteral product are generally effart.

(2) Those doug which are not affected oraly and metabolised by the first pass metabolism. for those dougs parenteral dosage foom are good.

(3) It is very helpful and good for the unconcious or Noncoperative elderly and infant children.

(4) If any doug is geuen in I.M dose then they have longer duration of action.

(5) For balancing the water level in body IV fluid is insertain.

Disadvantage of Parenteral Product:-

→ (1) These dosage foom we con't taken easily by it self or by family member we should required a trained Person who can inject us.

(2) It caused the severe pain at the site of injection.

(3) It require highly aseeptic Procedure and aseptic area clean sterile room for preparation of parenteral product.

(4) It is very difficult to reverse if any wrong drug or wrong dose is taken.

(5) It is very costly and expensive in nature.

General Requirement for Parenteral Dosage form:-

→ Because the parenteral product are highly sensitive and it should be sterile so there are following requirement are necessary for their Preparation.

1) Stability
2) Sterility
3) Free from Pyrogen
4) Free from foreign Particle
5) Isotonicity
6) Specific Gravity
7) Chemical Purity.

(1) Stability:-

→ The parenteral product should be Physically and chemically inert.

→ It should not be precipitated. It should not create any kind of the chemical reaction.

→ It should not produce any toxic chemical and it should not expire before the expiry date.

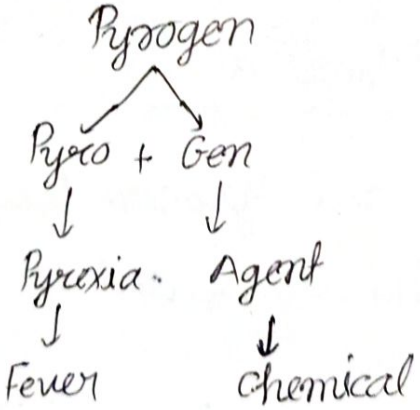
(2) Sterility:

→ The parenteral Product should be 100% Free from the microbes, bacteria, Virus and Pythogens.

- It should be sterile and during the manufacturing of these product environmental condition should be aseptic and sterile.
- After the manufacturing sterility testing must be perform before the dispensing of medicine.

(3) Free from Pyrogen:

- Our Parenteral Product should be free from the Pyrogen which increase the body temp.
- Before dispensing the medicine Pyrogen testing should be applied

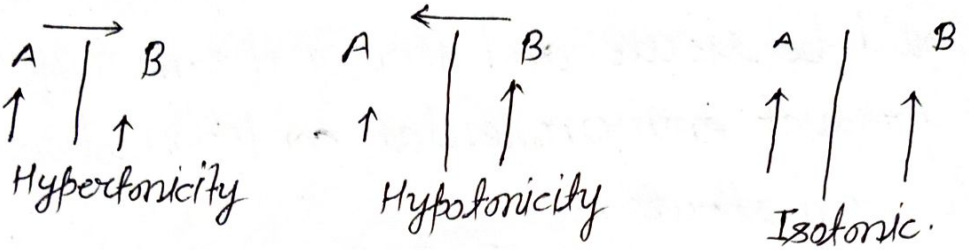


(4) Free from foreign Particle:

- Foreign Particle are those particle which are not active continuent of the medicine and it should be totaly free from the forign particle

(5) Isotonicity :-

→ The parenteral product should be isotonic with the blood and its isotonicity value equals to the 0.9% NaCl solution.



(6) Specific Gravity :-

→ The parenteral product should have the similar specific gravity as per as blood as per as spinal fluid.

(7) Chemical Purity :-

→ It should be chemically pure they are should be no any toxic material is available in the parenteral Product.

∴ Properties of Parenteral Preparation :-

(1) It should be sterile and Pyrogen free.

(2) It should be clear and sterile and No foreign Particle are available.

(3) If the parenteral preparation in emulsion form then there should be no Phase separation.

(4) The excipient which are used in the parenteral Product should be biocompatible with the body and API..

(5) It should be isotonic with the blood as similar to the 0.9% NaCl Solution

(6) It should be the pH of product should be Identical with the blood. it should be equal to the 7.2 to 7.4.

(7) In the case of solution parenteral form the drug API should be 100% soluble in the solid.

(8) In the preparation of Parenteral dosage form Antimicrobial agent or Preservative used for free from microbes.

Formulation of Parenteral Preparation:

(1) API: API are the active Pharmaceutical agent (Ingredient)

(2) Vehicle: (i) Vehicle are the substance which carry the Active Pharmaceutical ingredient within dissolve inside.

⇒ Vehicle are basically used in liquid form it is of two type -

A) Aqueous Vehicle

B) Non Aqueous Vehicle

A) Aqueous Vehicle: If the drug is water soluble then Aqueous vehicle are use as a water.

⇒ But water should be sterile and must be Pyrogen free

⇒ It is of three type.

(i) Water for injection

(ii) Water for injection free from CO_2

(iii) Water for injection free from air.

(B) Non Aqueous Vehicle :-

→ Most of the drug are not stable or Not soluble in the water medium so they are used non aqueous vehicle. For Example :-

		Vehicle
Dimercepol injection	——	Arachis Oil
Hydrocartisome	——	50% Alcohal
Digoxin	——	P.G (Propylene Glycol)

(3) Adjuvants :- (BAS, SSC → Frick)

(A) Buffering Agent :- Because the parenteral product are directly inserted inside the blood so there pH should be balanced.

→ And for maintaing the pH for longer duration buffering agents are use.

Ex :- Citric Acid and Sodium Citrate.
Acetic Acid and Sodium Acetate.

(B) Antimicrobial Agent → Ex - Methyl Paraben zoic Acid
→ Propyl Paraben zoic Acid

(C) Solubelising Agent :- Solubelising agent are used basically to dissolve the 100% API Into the Vehicle.

Ex :- Thiourea Polysorbate and Tween 80.

(D) Stebliser:- Stebliser are used to stable the product. during the entire self life.

Ex- Thiourea, Ascarbic Acid, Sodium metabi Sulphate.

(E) Suspending or Emulsifying Agent :-

Ex-MC, CMC, Gelatin, Acacia.

(F) Chelating Agent :- To remove the heavy metal Particle chelating agent are used

Ex- EDTA.

÷ Processing / Procedure of Parenteral Preparation :-

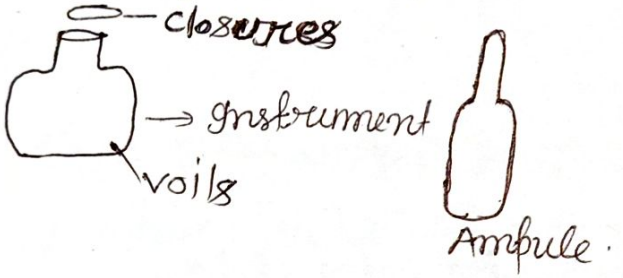
It complete into following nine steps.

(1) Cleaning of Containers, Closures & Equipments.
(2) Collection of Material
(3) Preparation of a Parenteral Products.
(4) Filteration.
(5) Filling
(6) Sealing the Containers.
(7) Sterilization.
(8) Evaluvation.
(9) Labelling and Packaging

(1) Cleaning of Containers, Closures and Equipment:-

→ First of all we collect all the Closures and Containers. like vails and Ampule. and all the instrument which are used in the preparation of parenteral product should be wash and dry sterile properly.

→ It should be wash with the tapped water otherwise it is washed with the hypochloride solution it is used for the washing and dry.



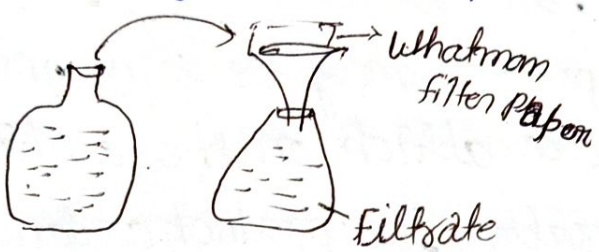
(2) Collection of Material:- After the drying and collection of of the closures and container, now select the API and suitable vehicle solvent and other adjuent material and collect all these material Put in a separate container after sterilization and it should be Pyrogen free.

(3) Preparation of Parenteral Product:- In this step in a large container first of all API is dissolve in the vehicle and after dissolution of vehicle we add different-2 Adjuvants as per the standered operating procedure. and form a drug base.

(4) Filteration

→ Because the parenteral products are directly given into the blood circulation so it should be free from the foreign particles and simple particulate matter.

→ So after the preparation of Parenteral Product it is filtered by using whatman filter paper

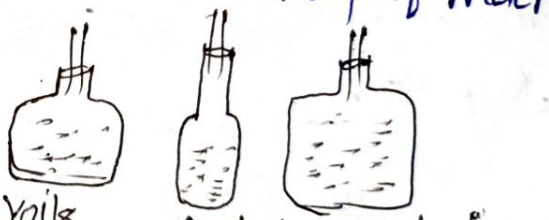


(5) Filling

→ After the preparation And filtration of the parenteral product It should be fill into the appropriate container like Ampule, Voils and Infusion bottle. it can be filled with the help of machine it is of two type-

(i) Semi Automatic Machine.

(ii) Fully automatic Machine.



→ And the amount of Perfomers is already fix.

(6) Sealing the Container

→ Sealing of the container is the next process after the filling and it can be perform by the sealing machine.

→ In the voil container the closure of rubber is available which is sealed from above and alluminium foil is rapped

→ In the ampule sealing the neck of the ampule is heated with flame and after hot heated they can be sealed with the help of Glass or Rod and they do not contain any special type of closure.

(7) Sterilization :-

After the filling and sealing of the container and closure it should be required the sterilization of the container

→ Because during the process may be some microbes or contaminent product are attach on the container.

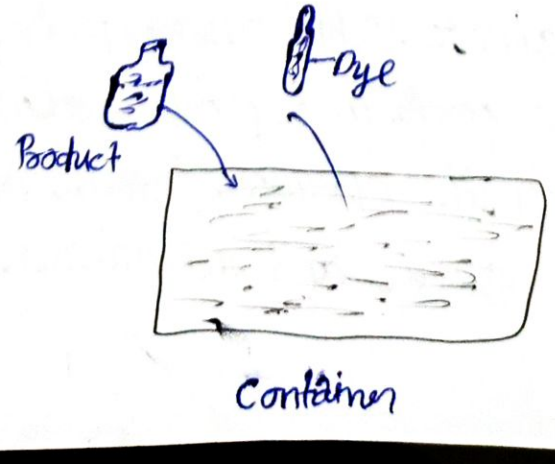
⇒ And after the sterilization the product container is finally free from the microbes.

⇒ And it is basically perform by the moist heat sterilization method.

⇒ In moist heat sterilization method basically autoclave are used and if in the autoclave the containers vails & ampules are for 30 min at 115°C or for 15 min at 121°C.

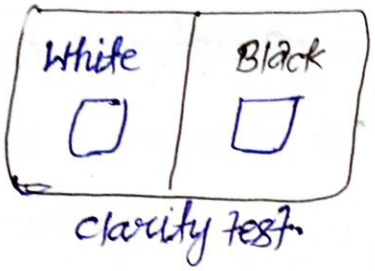
(8) Evaluation :-

(i) Leak test :- Leak test is perform for to evaluvate the proper closing of the container by using the dye solution.



(2) Clarity test:- Clarity test is perform to detect the small particle is present in the parenteral product.

→ And for this we are basically using White and Black background

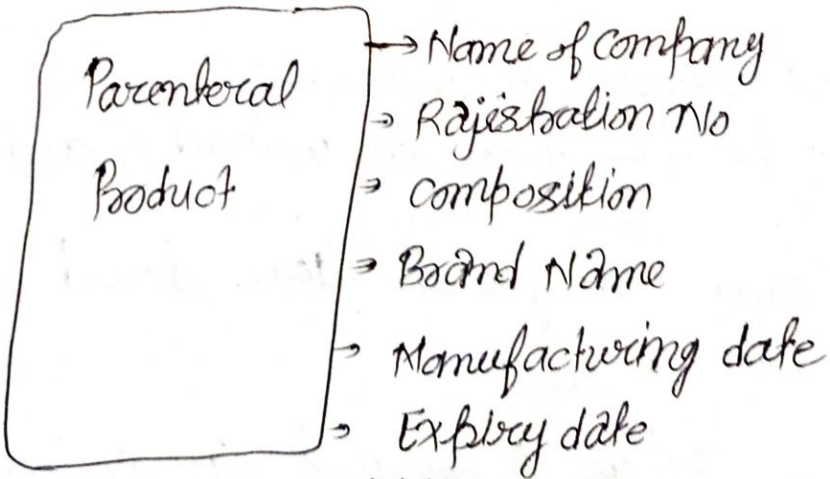


Clarity test.

(3) Content test:-

(9) Labelling and Packaging:-

→ For the preparation of Parenteral Product in last step Labelling and Packaging we write the Name of Company, Rajistration no. Composition, Brand name, Manufacturing date, Expiry date, MRP and give indication on the Product.



÷ Production facilities of Parenteral Preparation ÷

Production Area ÷ The production area of the parenteral preparation require specific facilities due to their aseptic nature.

→ The production area of the parenteral preparation can be deride into five part.

(1) Clean Up Area.
(2) Preparation Area.
(3) Aseptic Area.
(4) Quarantine Area.
(5) Finishing and Packaging Area.

(1) Clean Up area.

→ In this area this is the first area of the Production area of the parenteral Product and where the raw material and the closure and container material are store.

→ It is not aseptic in nature.

→ It should be free from the microbes and foreign particle

→ The wall and ceiling or the floor should be Painted and can be easily clean.

→ They are should be a Exhaust fan to remove the bad air from the room.

→ All the closure and container should be store in the cleanup area. after drying and washing.

(2) Preparation Area :-

- All the instrument should be install in this area. should be of stainless steal.
→ The cealing, floor and walls should be of Plastic Painted.
→ In this area basically we mix the API, Vehicle and make the preparation.
→ After making the preparation the container should be tightly closed.

→

(3) Aseptic Area :-

→ The Aseptic Area is the main area of the parenteral Preparation.
→ Where the preparation are fill into the Ampule and vails.
→ In this area they should be air locked area and 100% sterile.
→ And the person should be which are work inside the this place should be highly trained and completely sterile.
→ And we also allow to minimum moment inside this area
→ In the entrance of this room a HEPA filter of 0.3μ is used to remove the entry of microbes and UV lamp are situated inside the room to kill the microbes.

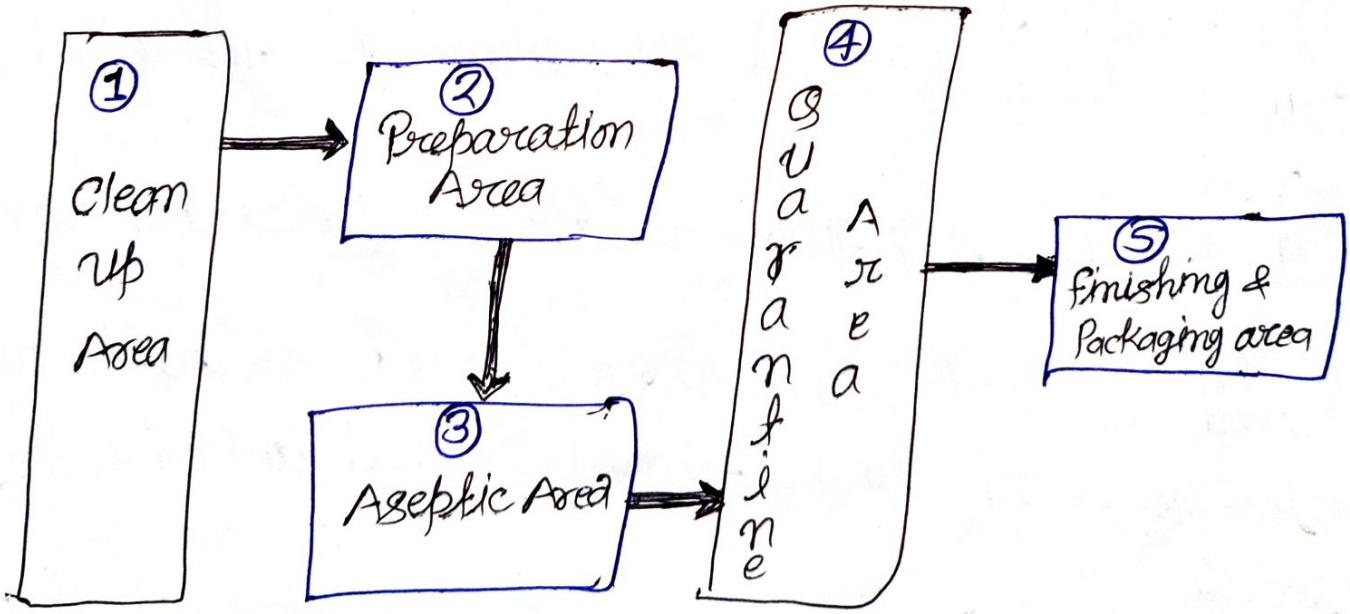
(4) Quarantine Area :-

→ This area is Quarantine Area where is minimum moment of Person is Allow and this area the sample for quality control testing. and all the stocks are store in this area

→ And the sample is sent to the Q.C from this area.

(5) Finishing and Packaging

→ After the Evaluation and Pass of Q.C Test. the product are shift into the finishing & Packaging area where the products are labeling and packaging imperform then after going into the dispatch section then after for the going into the market.



÷ Production of IV Infusion ÷

→ IV Infusion are basically large in volume and given to the patient for the electrolyte and fluid balance in our body.

→ The are prepared by the same method by adding API into the vehicle and proper Adjuvant add.

→ Examples of the IV Infusions are given

(1) Dextrose injection (I.P) Nutrient Replenesher

5%, 10%, 15%, 25% 50%.

(2) Nacl Injection (I.P) 0.9% Nacl – fluid & Electrolyte replacement

(3) Nacl & Dextrose Injection (I.P.) 0.11 – 0.9 % Nacl
2.5% – 25% Dextrose

(4) Sodium Lactate Injection I.P ÷ 1.75 to 1.95% Electrolyte Rep.

(5) Mannitol injection ÷ Diagnostic – Renal function
5%, 10%, 15%, 20%

(6) Mannitol & Nacl (Injection) – Diuretics
5%, 10%, 15%, 20% Mannitol
0.45% Nacl.

(7) Ringer Injection (I.P) 0.86% Nacl
0.03% Kcl
0.33% $CaCl_2$

÷ Opthalmic Preparation ÷

Opthalmic Preparation are those chemical drug which are sterile free of Pyrogen and foreign particle basically used for the eye.

Essential Charectaristics of Opthalmic Preparation ÷

→ It should be free from the foreign particle.

→ The viscosity of the parenteral preparation should be more than water and it should be high because when the viscosity is high then they makes the duration of contect longer on the eye and the better absorption and better effect of drug is produce.

Ex:- Polyvinyl Glycol, Carboxy Methyl Cellulose, & Methyl Cellulose is used.

→ The tonicity of the parenteral preparation should be isotonic with the lacrimal solution of the eye.

→ and its tonicity is maintain up to the range of 0.5% to 2% of NaCl

→ The parenteral preparation pH value should be identical with the pH value of lacrimal solution and the lacrimal pH is about to 7.2 to 7.4 so the parenteral prepation adjusted pH 7.2 to 7.4

→ The parenteral preparation should be 100% sterile because the varrious kind of bacteria and virus can cause the different-2 problems in the eye.

- For example the Pseudomonas Aeruginosa is a bacteria G-ve present in the opthalmic solution. they can cause blindness to the human in twenty to twenty four hours.

→ So the opthalmic preparation should be free from the microbes and they should be sterile after the filling after the preparation and after the packing (Packaging) it should be sterile 100%.

→ For the better absorption of the drug the surface active agent are used for the opthalmic preparation ex- Benzylconium chloride or Polysorbate 20 or Polysorbate 80.

Properties of Opthalmic Preparation:

→ It should be clear.
→ Free from foreign Particle.
→ It should be Pyrogen free.
→ It should be isotonic with the lacrimal solution.
→ Compatible Solvent should be used.

Types of Opthalmic Preparation:

(1) Aquous Eye Drop
(2) Oily Eye Drop
(3) Eye Ointment
(4) Eye lotion.
(5) Paper Strips
(6) Ocusects.
(7) Hydrogel contact lenses.
(8) Collagen Sheilds.
(9) Opthalmic Rods.

Eye drop

→ Eye drop are the clear solution of active medicament in the particular solvent which are microbes and Pyrogen free which are applied on eye. they are called eyedrop.

Types of Eye Drop :- (1) On the basis of solvent eye drops are two types -

(i) Aqueous Eye drop - When solvent is used as water.

(ii) Oil Eye drop - When the solvent is used as the oil.

(2) On the basis of Nature :- On the basis of nature eye drops is of three type -

(1) Solution Eye drop

(2) Suspension Eye drop

(3) Emulsion Eye drop.

Advantage of Eye drops :-

1) Decrease the amount of fluid forming in the eye.

(2) Increase the ability of the eye to drain fluid.

(3) Administering medication for the treatment of eye disorders

(4) preparation for various diagnostic procedures during eye examinations.

(5) There is less risk of side effect than with oral medicines

(6) Used during an examination and Administered as a local anaesthetic Prior to medical Procedure.

Disadvantage of Eye Drops:-

1) A red, irritation.
2) Fatigue or decreased energy.
(3) Skin rash (especially in individuals with known allergy to sulpha drugs.
4) A change in eye color (mostly in hazel or blue to green eyes)
5) Change in taste (especially with a carbonated beverage
16) Increase in thickness and number of eyelashes.
(7) Blurred vision
(8) Head ache.

Ideal Properties of Eye drops:-

→ They should be sterile
→ They should be iso-osmatic with lachrymal secretion
→ They should be free from foreign particles.
→ They should be preserved with a suitable bactericide.
→ They should be remain stable during storage

Preparation of Eye drop:-

1. API
2) Solvent
3) Adjuvent:- 1) Thickening Agent → Methyl Cellulose, Carboxy Methyl Cellulose
2) Buffer → Sod. citrate, Citrate.
3) Antioxidant → Thiosulphate, Sod. Meta Sulphate
4) Wetting Agent → Polysorbate-20 Polysorbate-80
5) Isotonic Agent → 0.9% Nacl.

Step-1 :→ Preparation of bactericidal Vehicle

↓

Step-2 → Preparation of Solution

↓

Step-3 → Clarification

↓

Step-4 → Sterilization

↓

Step-5 → Filling

↓

Step-6 → Packaging

∴ Eye lotion :

→ Eye lotion is a type of sterile aqueous solution. in which basicaly no medicament are used they are available in concentrated solution. and after the dilution they are use for washing the eye.

⇒ Basically it is formulated by different type of salt like - Sodium Chloride,
- Sodium Bicarbonat.

∴ Eye Ointment :

→ Eye ointment is an opthalmic preparation which is in sterile in nature and the are semisolid and they are applied over the eye.

yellow Soft Paraffin – 80g
Liquid Paraffin. – 10g
Wool fat – 10g

∴ Manufacturing Environment ∴

(Same as Parenteteral Preparation)

∴ Evaluvation Test ∴

(i) Sterility Test (same as parenteral)

(ii) Teakage Test. (Same as parenteral)