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A Review on Parenteral Products

[1]mr. Nilesh .S. Mhaske, [2]miss Rajeshwari .D. Pawar
Assistant Professor, Department of Pharmaceutics, Dr.Vithalrao Vikhe Patil Foundation's College of Pharmacy, Vilad Ghat, Ahmednagar, Maharashtra, India-414111
Student, Department of Pharmaceutics, Dr.Vithalrao Vikhe Patil Foundation's College of Pharmacy, Vilad Ghat, Ahmednagar, Maharashtra, India-414111

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ABSTRACT:-
The parenteral route of administration is the most effective route of drug delivery. In parenteral drug delivery major progress has been done in the field of formulation technologies so as to provide a targeted and sustained release of drug in predictable manner. Parenteral product must be essentially free from biological contamination. Most are injected or placed into the body tissue and do not pass through liver before entering bloodstream. This route of administration maintain its value due to special advantages like quicker onset of action in case of emergency ;target drug quickly to desired site of action , prevention of first pass metabolism. This review article deals with the general introduction, evaluation and also deals with the novel system in drug delivery to overcome problem associated with conventional parenteral drug delivery system.
Keywords: Parenteral product, sterilization, Route of administration.

I. INTRODUCTION:-

Sterile products are dosage form of therapeutic agents that are free of viable microorganism. Principally these include parenteral, ophthalmic and irrigating preparations. The term derived from Greek work 'para' means outside and 'Enterone' means intestine. Parenteral products are unique among dosage forms of drugs because they are injected through the skin or mucous membrane into internal body compartments. The parenteral product must be exceptionally pure and free from physical, chemical and biological contaminants. Parenteral are sterile solutions or suspensions of drug in aqueous or oily vehicle that are given by other than oral routes.

Definition:-Parenteral preparations are sterile, pyrogen free liquids or solid dosage forms packaged in either single dose or multidose containers.

Advantages:-

- Rapid onset of action.
- Useful in emergency situations.
- Useful for patients who cannot take drugs orally.
- Provide sustain drug delivery.
- Target drug delivery.
- Complete bioavailability [upto 100%].
- Prolonged drug action is possible.
- Drug which is unstable in GIT can be given.

Disadvantages:-

- Pain on injection
- Difficult to reverse an administered drug effect.
- Sensitivity or allergic reaction at site of injection.
- More expensive and costly to produce.
- Trained person is required.
- Required specialized equipment device and technique to prepare and administer drugs.
- Requires strict control of sterility and non-pyrogenicity than other formulation.

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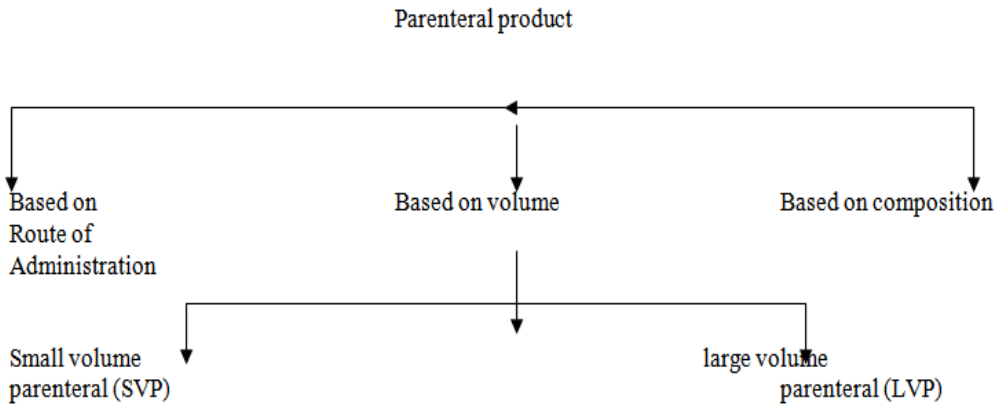
Types of parenteral :-



A. Based on route of Administration :-

1. Intramuscular - Muscle
2. Subcutsneous –under the skin
3. Intradermal-Into the skin
4. Intravenous-vein
5. Intraarticular- joints
6. Intraosseous-bone
7. Intrathecal-spinal fluid
8. Intracardiac-heart
9. Intraspinal –spinal colum
10. Intracerebral-brain
11. Intraarterial-Arteries
12. Endotracheal-down the trachea
13. Intrasynovial-joint fluid area

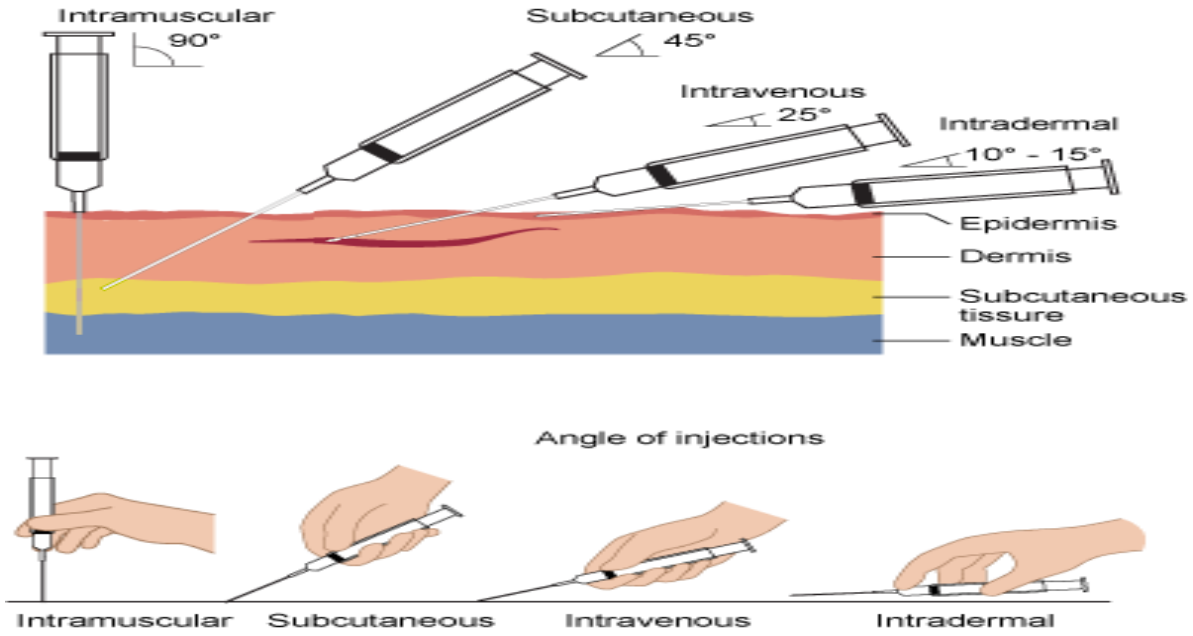


Fig no-1 Route of Administrations

B.Based on volume:-

1.Small volume parenteral – An injection that is packed in containers labeled as containing 100 ml or less.

Eg- solution ,suspension,emulsion,dry powders

2.Laege volume parenteral- LVP as product in container labeled as containing more than 100 ml of single dose injection intended for administration by IV infusion .

These are injected directly into blood stream (IV preparation) poured into open body cavities and surgical area or introduced into body cavity,they must be sterile,non pyrogenic and free from particulate matter .

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C.Based on composition-
These product can be administered by Intra or extra vascular routes.
These LVP are packed into either glass or plastic container of 1 lit. capacity.

General Requirements For Parenterals :-
1. Sterility
2. Free from pyrogens
3. Free from particular matter
4. Isotonicity
5. Specific gravity
6. Chemical purity
7. Stability

Consideration in Parenteral Preparations:-
1. Vehicle:-
- The vehicles should be pharmacologically inert,non-toxic, compatible with blood, maintain solubility of drug
- Chemically and physically must be stable.
- Pyrogen and microbe free
- Not affected by PH.
- Non aq.may be used to drug of limited water solubility.
- It must be safe in amount administered.
- Eg.fixedoils,peanutoil,Ethyloleate.

2**.Preservatives:-**
- It is a substance that prevents or inhibit microbial growth and extends the shelf life of drug products.

1.Antimicrobial preservative
2.Anti-oxidants
3.Buffer
4.Chelating agents
5.Cryoprotectants
6.Inert gas
7.Surfactant and solubilizing agents
8.Tonicity modifiers
9.Viscosity modifiers

3.Antioxidant:-
- To protect formulations from oxidation .
- There are 2 types-
- a. Reducing agents-eg. Thiourea , Ascorbic acid,Sodium bisulfate 0.01%
- b.Blocking agents-eg. Tocopherol
- Added to maintain PH for solubility ,stability and pain reduction.

4.Cryoprotectants:-
- Prevent and stabilize denaturation of proteins from effect of freezing.
- Sugar-sucrose,lactose,glucose,trehalose,
- Polyols-glycerol,mannitol,sorbitol
- Amino acid- glycine,alaning,lysine
- Polymers-PEG,dextran,PVP

5.Lyoprotectants:-
- Substance which protect drug especially proteins from degradation during drying .
- Sugar-mannitol, lactose, maltose, maltodextrin, trehalose, sucrose
- Amino acid-glycin,histadine,arginine

6.Solubilizing agents and surfactants:-
- Substance are used extensively in parenteral suspension for wetting powders and provide acceptable syringe ability.(eg- steroid ,fat soluble vitamins)
- Must be purified ,sterile,pyrogen free.
- In limited volume depending on route and type.
- Should not vehicles must have special purity and other std. to assure sterility,stability,and safety
- Eg-sodium state,fixed vegetable oil,PEG,alcohol

Importance of Isotonicity:-
- Need an isotonic solution to avoid destruction of RBC,irritation and tissue damage.
- More important for large volumes,rapidly administered and extravascular injections.
- Reduce pain on injections.
- Nacl and KCL .
- Dextrose
- Mannitol and Sorbitol
- Tonicity modifiers:- To minimize the tissue damage and irritation reduce hemolysis and prevent electrolyte imbalamce,product should be isotonic
- Dextrose (4-5.5%) Nacl(0.5-0.9%)and sodium sulfate (1-1.6%) is used to adjust tonicity.

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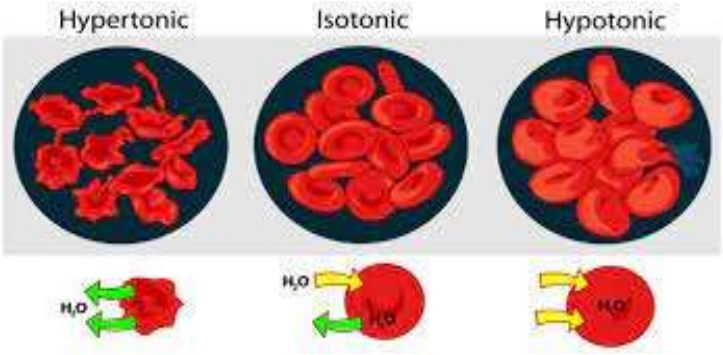

Fig no-2 Importance of Isotonicity

Formulations :-
A.Opthalmic preparations
B.Freeze-dried product
C.Long acting formulations:-
1.suspension
2.Emulsion
3.Sterile powders:
a.Sterilerecrystalization
b.Lyophilization
c.Spray drying

Production Procedure:-
Production process includes all the steps from accumulation and combining of ingridients of formula to enclosing of product in individual container for distribution.
SOP's are very important.

Flow chart:

Dispensing of raw materials and excipients

⇩

Washing and depyrogenation of vials, sterilization of rubber stoppers

⇩

Manufactuing

⇩

Filtration through 0.2 micro under sterile nitrogen Pressure

⇩

Filling into vials through online 0.2 micro cartridge

⇩

Sealing of vials, visual inspection

⇩

Labelling and packaging

⇩

Final product analysis and release

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Opthalmic Preparations:- Ophthalmic preparations are of 3 types:
1.Eye Drop
2.Eye Ointment
3. Eye Lotion

1. OphthalmicDrop: Ophthalmic drop are sterile aq./oily solution essentially free from foreign particles, suitably compounded and packaged for instillation into the eye.
Dose-5 to 10 ml
Types of drug supplied in eye drops form are :- Antiseptic,Anesthetics,Antiinflamatories,Mydratics ,Miotics and Diagnostics aids.

INGRIDIENTS	EXAMPLES
1.VEHICLE	Water/non aq.vehicle
2.THICKENING AGENT	Methylcellulose,CMC,PEG
3.BUFFER	Borate buffer,phosphate buffer, citrate buffer.
4.TONICITY MODIFIER	Nacl,boric acid
5.ANTIOXIDANTS	Sodium metabisulphite &sodium thiosulphate
6.PRESERVATIVES	Phenyl/mercuric nitrate
7.CHEALATING AGENTS	Disodium edentate

Method of preparation:-
1.Dissolution
2.Sterilization
3.Addition of excipients
4.Make up the volume
5.Filling and packaging
6.Sterilization
7.Labelling

Ophthalmic Ointment:-Ophthalmic ointments are sterile semisolid dosage form meant for administration into the eye.

Method of preparation:-
1.Dissolution
2.Sterilization
3.Addition of base and excipients
4.Filling and packaging
5.Sterilization
6. Labelling
Eg . Chloramphenicol eye ointment , chlortetracycline eye ointment

Filling and sealing:- The filtered product is filled into final container such as ampoules,vials and transfusion bottles

- Ampules used for single dose and vials used for filling multidose
- On small scale filling is done by manually by using hypodermic syringe and needle.
- On large scale filling is done by automatic filling machine.
- Filling operations is carried out in aseptic precautions.
- During filling the ampules ,the care should be taken that solution be filled below the neck og ampules.
- Sealing should be done immediately after filling.
- Ampoules are sealed by manually by rotating neck of ampule in flame of Bunsen burner on small scale.
- Ampules are sealed by ampule sealing machine is used in which tip of ampule is used to fused to seal it on large scale.
- Rubber closure must fit opening of container snugly enough to produce seal.
- A faster hand method involves picking up closure and inserting it into vials by means of tool connected to vacuum line.

Sterilization and packaging;-
1. Sterilizationof product:- This process is applicable to manufacture of certain pharmaceuticals and biological that is thermobile .
The rate of drying depend on the thermal conductance of frozen product .
Freeze driers are usually operated by an automatic control system.The product is usually processed until there is less than 1%moisture in dried material.
Eg. Multiple vitamin combinations,antibiotics,hormones,tissue section.
Equipment and containers should be cleaned.
Glassware and metalware is automatically conveyed ,usually in an inverted position through series of rigorous , high pressure treatment including hot detergent,hot tap water and final rinse with distilled water.

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2.Packaging of product:-It is important part of product
It must be particularly dignified,neat and attractive appearance if it is to convey to user the quality ,purity and reliability.
The packaging should be protect the product against the physical damage during shipping,handling and storage.

Storage and Distribution:- The storage and distribution as important as production .
Opthalmic preparations should maintain their integrity throughout their production.
WFI(water for injection) should not be held for more than 24 hrs at room temperature before it is used ,but if held at 80^0 C .
The distribution may be by direct withdrawal from tank or in large plants through pipe system.

Quality control test for parenteral product:-
1. Pyrogen test:
a.LAL test b. Rabbit test
2. Sterility test
3.Leakage test

1. Pyrogen test: -Detection of endotoxins via LAL test and rabbit test
Pyrogens are product of metabolism of micro organism gram negative bacteria produce MOA potent pyrogen.
When these pyrogen introduce in body produce fever with acne.
The test performed to detect presence of pyrogen is

a. LAL test:-
LAL reagent ⟶ it is lysate of ameboytes obtained from horseshoe crab only
It is in vitro test.

Combination of 0.1ml of test sample with LAL reagent (incubate for 1hr at 37 □C)
⇩
Mixer is analyzed for presence of gel clot
⇩
Positive test indicates presence of endotoxins.

b. Rabbit test :-

Inject the solution on rabbit ear vein
⇩
The temperature sensing probe into rectum cavity at depth 7.5cm
⇩
Warm test solution at 37 C
⇩
Initially performed on 3 rabbit

Interpretation:-

When no one rabbit shows risk of temperature 0.5 □C then solution is non-pyrogenic.
⇩
If test fail then take on 5 Rabbit
⇩
Out of 8 rabbit not more than 3 rabbit show temperature rise the solution is non-pyrogenic.

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2.**Sterility test** :- It is most important and essential characteristics of parenteral product . Sterility means complete absence of all riable micro-organism.
a.Direct transfer test
b.Membrane filtration test

a**. Direct transfer test:-** It involve the direct incubation of required volume of sample in two test tube containing culture medium ,FTM,SCDM.

b**.Membrane filtration method:-**Filtration of sample through membrane filter 0.22 micron diameter 47 mm with hydrophobic characteristics.

Limits of membrane filtration:-

No,of article in batch (injectable)	No.of articles to be tested
Not more than 100 article	10% / 4 article
More than 100 but not more than 500	10
More than 500	2% of 20 article
For large volume parenteral	2 % of 20 article

Interpretation – No visible evidence of microbial growth in culture medium.

3. Leakagetest:-It is desirable that all the parenteral preparation which are filled in ampoules must be hermetically sealed.
The ampoules are immersed in 1% methylene blue solution in a vacuum chamber under negative pressure. When the vaccum is released the coloured solution will enter those ampoules having defective sealing.The presence of dye in the ampoule confirms the leakage and hence rejected.
Containers and Closure:-Containers are in close contact with product .

Glass conytainers traditionally have been used for sterile product .many of which are closed with rubber stopper.

Interest in plastic containers have been increasing and such containers are being used for commercial Opthalmic preparation and IV solution.
Requirements for containers and closure:
1.It should not yeild foreign substance to product.
2.It should be transparent to allow visual inspection of content in it.
3. It should not have any adverse effect on the product.
4.It should be compatible with the product .
5.It should prevent diffusion in or across the walls of container and closure.

Types of contsiners:-
1.Airtight container
2.Hermetically sealed container
3.Light resistant container
4.Multi dose container
5.Sealed container
6.Single dose container
7.Tamper –evident container
8.Tightly –closeed container
9.Well- closed container.

Containers and closure used for parenteral product:-
1.Glass
2.Plastic
3.Metal
4.Rubber

Test for Glass container:-
a.Hydrolytic resistance test
b.Glass grain test
c. Surface glass test
d.Surface etching test
e. Light transmission test
f. Arsenic test

a.Hydrolytic resistance test: This test is performed to determine whether amount of alkali that is leached from glass container is in specified limit or not.
The leaching of alkali is accelerated by autoclaving and amount of alkali leached is determined by titrating it with acid.There are two test ,test 1 is done on type I and type II glass containers to check whether the hydrolytic resistance is because of only surface treatment.
Procedure:
Test1- Remove the debris from the containers and rinse the containers by distilled water.

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In case of ampoulrd fil the ampoules to its maximum capacity with the distilled water and then seal them.In case of vials and bottles ,fill them till 90% of their volume and cover with borosilicate dishes or glass foils.
Placed container in autoclave and rinse the temperature from 100^0 to 121^0 over 20 min,maintain temperature of 121^0 for 60 min and reduce temperature from 121^0 to 100^0 over 40 min.
Remove the container ,cool them and carry out further titration within one hr.
Combine liquid from containers,take volume of liquid as given and add 0.15ml of methyl red solution for each 50. ml of liquid.
Titrate with 0.01 M HCL and note the endpoint.
Conduct one blank titration using same amount of distilled water and determine different .the result shall be less than value given.
Test2- Runse the container twice with water and then fill completely with 4% v/v solution of hydrofluric acid .
Allow to stand at room temperature for 10 min.
Empty containers and rinse carefully 5 times with water.
Carry out procedure described under Hydrolytic resistance.Compare result with given limiting value.
For type I glass value obtained with hydrofluric acid –treated containers are closely similar to those stated for type Iand type II glass.
For type II g;ass value obtained with hydrofluric acid –treated containers greatly exceed those given for type II glass.

B. Glass grain test:-Rinse containers with purified water and dry in oven.
Wrap the glass in paper and crush to produce not more than 30ml pieces.Place sample in special morter and pestle and crushed it.
Pass it through the sieve no 25 and 40 .Again passed through sieve no 50 .Repeat crushing and seiving till two fractions are obtained between 25-40 mesh and 40-50 mesh size. Wash sample by several times with acetone and dry in oven.
Weigh 10 gm of 2 fractions of grain in 2 conical flask and add 50 ml of free water keep one sample as blank with water.Close the flask with borosilicate disc or aluminium foil and autoclave at 121 ± for 30 min.To content the flask add 0.05ml methyl red solution and titrate with 0.02 M HCL colour changes.
Calculate the difference in sample and blank readings.

c.Surface glass test:- Test is similar to hydrolytic resistance test I as per IP 2018 .Only difference is volume of test liquid used for test.
d.Surface itching test:- This test similar to hydrolytic resistance test2 as per IP .The surface etching test is used in addition to surface glass test to determine whether container is surface treated or has hydrolytic resistance.

e.Test for Arsenic for glass container :-The glass container for aq. Parenteral preparation should comply with this test..Wash the ampoules with distilled water .
Prepare test solution as that of hydrolytic resistance to produce 50ml. Pipette 10ml of solution and add 10 ml of nitric acid and evaporate it till the solution dry in water bath. Dry it in the oven and add 10 ml of hydrazinemolybdate reagent.
Reflux it in water bath for 20 min,cool it and determine absorbance at 840 nm as blank.
The absorbance of test solution should not exceed absorbance obtained by repeating determination using 0.1ml of arsenic std. solution in place of test solution.

f . Light transmission for glas and plastic container ;- This test design to measure amount of light transmitted by either transporant or translucent glass or plastic material used for pharmaceutical containers.
Place section in spectrophotometer with its cylindrical axis parallel to plane of slit so that light beam is normal to surface of section. Measure transmittance at intervals of about 20nm in region of 290-450 nm.

Test of Plastic containers for parenterals preparations :-
1. Leakage test
2. Collapsibility test
3. Clarity and colour of solution
4. Acidity or alkalinity
5. Light absorption
6. Reducing substance
7. Transparency

1 . Collapsibility test : This test is applicable to containers which are to be squeezed in order to remove contents.Acontainer by collapsing inward dusring use should yield .90 % of its nominal contents at required rate of flow at ambient temperature.

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2. Clarity and colourof solution :- This test is conducted with the special solution 's'.
Solution: Fill the container to its nominal capacity with water and close it. Heat it in the autoclave at the temperature121± 2^0 C. is reached within 20 to 30 min and maintain at this temperature for 30 min . use the solution atleast 4 hrs after preparations.
Blank : Prepare a blank by heating water in borosilicate glass.the solution S should be clear and colourless.

3.Acidity or Alkalinity :- The solution S is equivalent to the 4 % volume of container and add 0.1 ml of phenopthalein solution .The solution should be colourless.When 0.4 ml of 0.01 M NAOH is added to this solution ,the solution turns pink in colour.When 0.8ml of 0.01 M HCL and 0.1 ml of methyl red then solution become orange – red or red.

4.Light absorption :-The light absorption in range 230 to 360nm of solution S using blank should not more than 0.20 ml

5.Reducing substance :-To 20 ml of solutions adde increase ml of dilute H_2 SO_4 and 20 ml of 0.002 M $KMNO_4$ .Boil it for 3 min and cool it. Add 1 gm of potassium iodide and then immediately vtitrate with the 0.01 M sodium thoisulphate by using 0.25 ml of starch solution as indicator .Carry out titration using 20ml of blank .The difference between the titration values is not more than 1.5 ml

6. Transparency:-Fill container previously for preparations of solution S to its nominal capacity with 1 in 200dilution of std. suspension for container made from polyethylene or polypropylene. For containers of other materials use a 1 in 400 dilutions. The cloudlness of suspension is perceptible when viewed through container and compared with similar container filled with water.

Test of plastic containers for ophthalmic preparations :-
1.Leakage test
2.Collapsibility
3. Clarity of aqueous extract
3.Non- volatile residue
5.Sytemic injection
6.Intracutaneous test
7.Eye irritation test

1. Eye irritation test : This tets is designed to evaluate response to instillation of extract of material under examination in eye of rabbit.Naclinjectionand vegetable oil are used as extracting media for plastic container. The 3 healthy albino rabbits are selected .In one eye 100 uḷ of sterile water for injection is instilled and in other 100 uḷ of the prepared extract is instilled.
The eyes of rabbit are examined for presence of irritation for 23,48 and 72 hrs .The requirements of test are met if sample extract shows no significant irritation response during observation period over that with blank extract.

Test for metal containers for eye ointment ;-
Select sample of 50 tubes and clean each tube by blowing .Fill the tube with suitable molten eye ointment base, close the open end of each tube by double fold and allow filled tubes to cool overnight at temperature of 15^0 to 20 ^{0} C.

Using heated bacteriological metal filter with 4.25 cm filter paper, filter the opintment by removing it from tube.The ointment melts in the heated filter.The application of suction helps for easy filtration of molten base.

Remove filter paper ,dry it, examine by magnifying glass.Note the no .of all metal particles 1 mm in length and longer the no. in range 0.5 mm to less than 1 mm and no .in range 0.2 mm to less than 0.5mm . Calculate average no. of metal particles counted in each of three ranges.

Give each metal particle detected on filter paper a score as follows and add scores together. The lot of tubes passes the test if total score is less than 100 points; if total score is more than 150 points the lot fails the test. If the total score is between 100 to 150 , the test is repeated on further sample of 50 tubes and lot passes test if sum of total score in two test is less than 150 points.

Test for Rubber closure:-
1.Appearance of solution
2.PH of aq. Extract
3.Light absorption
4.Reducing substance
5.Residue on evaporation
6.Sterilization test
7.Fragmentation test
8.Self- sealability
9.Biological test

Preparation of sample :-Wah closure vigorously by 0.2 %w/v solution of an anionic surface active agent and rinse with water. Place a no.of washed

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closure corresponding to surface area of about 100 cm² in suitable container and add 200 ml of water per 100cm² surface area of closure and weigh. Heat it in autoclave so that temperature of 119˚ to 123˚ is reached within 20 to 30 min and maintain at that temperature for 30 min.
Make up original weigh with water for injection after cooling .Separate solution from closure by decantation. Prepare a similar blank using 200ml of water for injection.Dry the treated closure at 64˚ to 66˚ C at pressure not exceeding 0.7 kPa for 24 hrs.

1.Appearance of solution :- Solution A is not more opalescent than opalescence std. and not more intensely coloured than reference solution.
2.PH of aqueous extract :- To 20ml of A add 0.1 ml of bromothymol blue solution. Not more than 0.3ml of 0.01M NAOH or 0.3 ml of 0.01 M HCL is required to change the colourof solution to blue or yellow respectively.
3.Light absorption :-Filter solution A through membrane filter with nominal pore size od 0.5 Um and reject first few ml of filtrate . Measure light absorption of filtrate in range 220 to 360 nm ,using blank solution .The absorbance should not more than 2.0 ;if necessary dilute the filtrate before measurement and correct result for dilution.
4.Residue on evaporation :- Evaporate 50 ml of solution A to dryness on water bath and dry at 105 ˚C.The residue weighs not more than 4 mg.
5.Sterilization test:- The prepared closures sample shall not often or become tacky and there shall be no visual change in closure.

6.Fragmentation test :- This test is applicable to closure intended to be pierced by hypodermic needle. For closure that are intended to be used for aqueous preparation place a volume water corresponding to nominal volume minus 4ml in each of 12 clean vials. Close vials with prepared sample of closure .Secure with the cap and allow to stand for 15 hr.

For closure that are intended to be used for dry preparations .close 12 clean vials with prepared closure .using lubricated long level hypodermic needle with an external diameter of 0.8 mm fitted to clean syringe ,inject 1 ml of water into vials and remove 1ml of air,carry out this operation for 4 time for each closure ,piercing each time at different site.
Pass the liquid in vials through filter with nominal pore size of 0.5 Um .Count no.of fragments visible to naked eye.The total no.of fragments should not more than 10 except in case of butyl rubber closure where total no.of fragments should not be more than 15.

7.Self -sealability :-This test is applicable to closure intended to be used with multidose containers.Fill 10 suitable vials with water to nominal volume close vials with prepared closure and secure with cap .For each closure use new hypodermic needle with an external diameter of 0.8 mm and pierce the closure 10 times ,piercing each time at different site.

Immerse vials upright in 0.1 %w/v solution of methylene blue and reduce the external pressure and leave vials immersed for 30 min. Rinse outside of vials .none of vials should contain any trace of coloured solution.

8.Biological test :-This test is similar to biological test of plastic container. The only difference is preparations of sample extract which is discussed below.

Sample extract preparation : To intact closure, sterile normal saline is added as extracting medium and it is autoclaved at 121˚ ± 0.1 ˚C for 60 min. the extract is decanted after cooling and used for intravenous and subcutaneous injections.

Novel Innovation in pharmaceutical industry :-
Automation / Labor saving technique by which process performed with minimal human assistance.It can be done at various levels of mfg. system such as handling of raw matter,semi finished good ,finished goods,during production process.
Laboratory robotics provides automation in areas .such as sample preparation and handling ,wet chemistry procedure , laboratory process control and instrumental analysis.
Advantages-
Better quality
2.Minimize total labor cost
3.General accuracy , more output , greater speed
4. Improve better working condition
Disadvantages-
1.Huge investment
2.It can creat unemployment
3.Continuous power supply

Clean in place (CIP) :-Cleaning method used in industry to clean vessels , interior surface of pipes, filter, equipment, fitting without disassembly.
A typical system that produce purified water may require.

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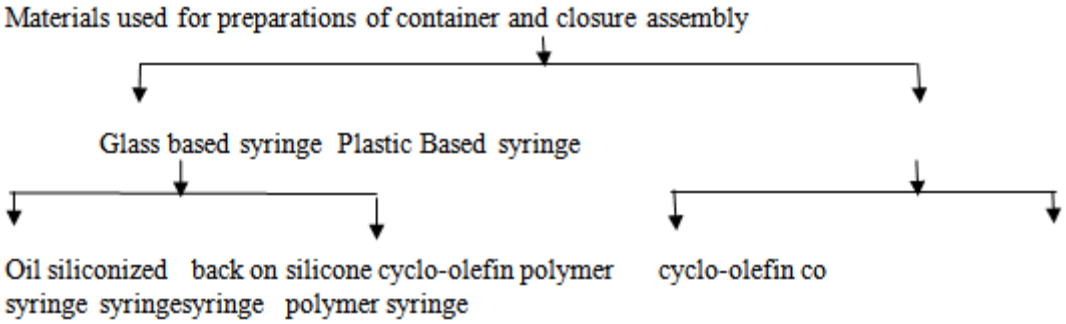
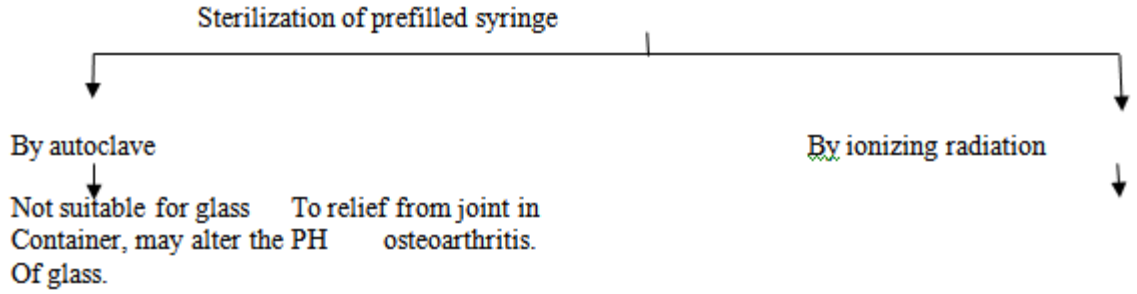
1.Pre- treatment
2.Final treatment
3. Polishing step

Sterilization in place (STP) :-It is timed sterilization of upstream and downstream biopharmaceutical production train using clean stream.

A. Prefilled syringe :-Aprefilled syringe is single dose packet of parenteral drug to which a needle has been fixed by mfg. Prefilled syringe assure delivery to particulate free solution and accommodate volume. Range from – 0.25 to 5.0 ml .Purpose of prefill 1.Primary pack
2.To give appropriate amount of medication to patient



Filling process in prefilled syringe : Hyaluroncontruct mfg. (HCM) patented method of syringe filling envolve, vaccume filling couped with online vaccume stoppering, known as bubble free filling.
Sterilization of prefilled syringe



B.Needle free injection :-Needle free injection technology encompasses a drug delivery through the sking using any of forces as ;orentzs shock waves ,pressure by gas/ electrophoresis.
It give the free from unnecessary pain but also a drug in solid pellets can also administered.

Advantages:
1.Prevent skin puncture
2. Fast drug delivery
3.Better drug stability
4.Avoid effect of needle shearing
5. Eliminate needle phobia
6. Self administration
7. Improve immune response

Disadvantages:
1. Complex and expensive
2. All systemare not fitted into size
3. Need for personnel training and maintance

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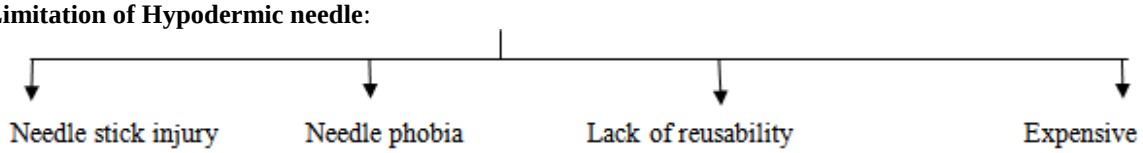
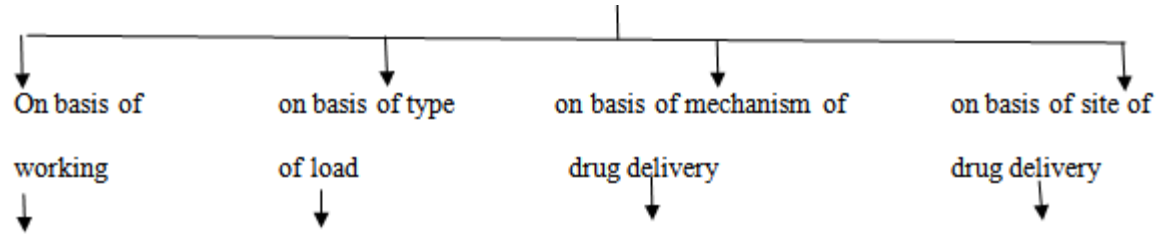
Limitation of Hypodermic needle:

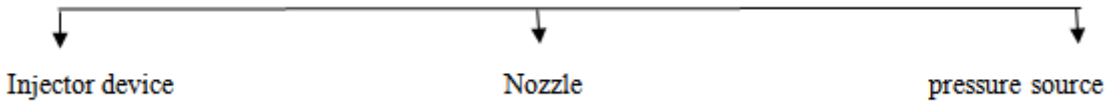


Classification: -



1.spring system 1. Liquid 1.nano patches 1.intradermal injector
2.laser powdered 2. Powder2. sand paper assisted 2. intramuscular inector
3.energy propelled 3.projectile delivery 3. subcutaneous injector
System 3. lontophoresis enabled
4.lorentz force 4. micro needle
5.gas propelled
6.shock wave

Components of needle free injection: -



-Drug chamber -it serves the passage for drug -for drug
-it fires drug particles at a typical deliveryforce fully
Speed of 100 m/s with a depth of 2mm -by pushing punger
Most common arifice 0.127 mm it provide the necessary
pressure

MOA:-Entire needle less devices operate by same principle of creating a high pressure (>10 MPa) jet of liquid (velocity 100 m/sec) containing drug penetrating to skin.
In general needle free technology works by forcing liquids medication at high speed through a timming orifice that is held against the skin .
This create an ultrafine steam of high pressure fluid that penetrate the skin without the use of needle.

C. Powdered jet :-Ajet injector is type of medical injecting syringe device used for a method of drug delivery known as jet injection.
Mechanism:
1.Compressed gas as power source
2.Adrug compartment containing particulate drug formation
3. A nozzle to direct the flow of particles.

D. Form ,Fill, Seal Technology :-It is automated computer technique to prepare sterile product like IV infusion bottles.
1.Form- Formation of container
2.Fill – Filling of container with content
3. Seal – Sealing of container
a.Pre-sterilization of machine
b.Production in aseptic chamber
c.Post – production cleaning.

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II. CONCLUSION:-

The parenteral route of Adminisration is the most effective route for the delivery of active pharmaceutical substance specially drugs cannot be taken orally.The above practice work describes that manufacturing of parenteral products,filling,sealing,strorage conditions,evaluation test.It is more important to manufacture good quality of parenteral products.

Quality control should be a fundamental segment of parenteral products manufacturing.All the test which are performed are essential and have its own importance in parenteral production.All of these tests ensure that product meet its quality which has been judged to satisfactory also.

All the detailed information about the parenteral products and its manufacturing are given in the above practice work .

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