SHAMBHUNATH INSTITUTE OF PHARMACY

Third Sessional Examination 2019-20

D.Pharm. 2nd Year

Pharmaceutics-II

Solution to the Paper

Time: - 1hr 30 mins. **Total Marks: – 20**

Paper Code: - 0427 **Roll No: -**

Note: - Attempt any five questions. All Questions carry equal marks.

(5x4=20)

Q.1.Write notes on dialysis fluids.

Ans.

Dialysis Fluids

Dialysis is a process by which the substances are separated from one another due to their difference in diffusibility through membranes. The fluids used in dialysis are known as dialysis fluids. In cases of renal failure, transplantation of kidney or certain cases of poisoning, dialysis is needed to save the patient. In the case of renal failure, it becomes necessary to remove the waste products and to maintain electrolyte balance. This can be done by haemodialysis or intraperitoneal dialysis.

Haemodialysis Haemodialysis is done to remove toxins from the blood. In haemodialysis, the blood from an artery is passed through an artificial dialysing membrane, bathed in dialysis fluid. The dialysing membrane is permeable to urea, electrolytes and dextrose and not to plasma proteins and lipids. So urea which is excess in the blood, pass out in dialysis fluid. After the dialysis, the blood is returned back to the body circulation through a vein. A kidney unit may require more than 1200 litres of solution in a week. So haemodialysis fluid is prepared in concentrated form which can be diluted with deionised water or distilled water before its use.

COMPOSITION OF CONCENTRATED HAEMODIALYSIS FLUID B.P.C.

Dextrose monohydrate	8.0 g
Sodium acetate	19.04 g
Lactic acid	0.4 ml
Sodium chloride	22.24 g
Potassium chloride	0.4 g
Freshly boiled and cooled water to	100 ml

Method : Dissolve dextrose monohydrate, sodium acetate, sodium chloride and potassium chloride in 70 ml of freshly boiled and cooled water. Add Lactic acid. Filter the solution and make up the volume to 100 ml. Pack it in large plastic container. The solution should be stored in a warm place as it is liable to deposit crystals on storage.

One litre of concentrate is diluted with 39 litres of water for each 40 litres required in the artificial kidney.

Intraperitoneal dialysis In this method, the peritoneal cavity is irrigated with the dialysis solution and the peritoneum acts as the semi-permeable membrane thereby the toxic substances normally excreted by kidney are removed. Intraperitoneal dialysis fluid should be sterile and free from pyrogens.

COMPOSITION OF INTRAPERITONEAL DIALYSIS I.P.

Sodium chloride	5.56 g
Sodium acetate	4.76 g
Calcium chloride	0.22 g
Magnesium chloride	0.152 g
Sodium metabisulphite	0.15 g
Dextrose (anhydrous)	17.0 g
Purified water sufficient to produce	1000 ml

Dissolve the ingredients and mix. Filter the solution and place immediately in suitable container and sterilize by autoclaving.

Q.2 Explain the sterility testing in parenterals.

Ans.

STERILITY TESTING

After sterilisation, the test for sterility is the most reliable method for determining whether or not the particular lot of material is sterile. Test for sterility is intended for detecting the presence of viable forms of bacteria, fungi and yeasts in substances, preparations or articles which are required to be sterile as per pharmacopœia.

Principle The test is based on the principle that if bacteria or fungi are placed in a medium which provides nutritive material and water, and kept at a favourable temperature, the organism will grow and their presence can be indicated by a turbidity in the clear medium.

Steps involved in sterility testing

(1) Selection of the sample size.
(2) Selection of the quantity of product to be used.
(3) Method of testing.
(4) Observation and results.

1. Selection of the sample size : Sample must be representative of the whole of the bulk material and lot of final containers. Though mixing is required, while taking the sample from the bulk material, the random sampling is taken from the final containers. I.P. 1996 has recommended the following guide lines for determining the minimum number of items recommended to be tested as given in Table 14.1.

TABLE 14.1

Number of Items in the Batch	*Minimum Number of Items Recommended to be Tested*
1. Injectable Preparations	
Not more than 100 containers	10 per cent or 4 containers whichever is the greater
More than 100 but not more than 500 containers	10 containers
More than 500 containers	2 per cent or 20 containers whichever is the less
2. Ophthalmic and Other Non-injectable Preparations	
Not more than 200 containers	5 per cent or 2 containers whichever is the greater
More than 200 containers	10 containers

Number of Items in the Batch	*Minimum Number of Items Recommended to be Tested*
3. Surgical Dressings	
Not more than 100 packages	10 per cent or 4 packages whichever is the greater
More than 100 but not more than 500 packages	10 packages
More than 500 packages	2 per cent or 20 packages whichever is the less
4. Bulk Solids	
Less than 4 containers	Each container
4 containers but not more than 50 containers	20 per cent or 4 containers whichever is the greater
More than 50 containers	2 per cent or 10 containers whichever is the greater

2. Selection of the quantity of product to be used : Selection of the quantity of product to be used for sterility testing depends mainly on the volume or weight in the container. The minimum samples to be used in each culture medium in the test for sterility are given in Table 14.2.

TABLE 14.2

Quantity of Each Container	*Minimum Quantity to be Used for Each Culture Medium*
For Liquids	
Less than 1 ml	The whole contents of a container
1 ml or more but less than 4 ml	Half of the contents of a container
4 ml or more but less than 20 ml	2 ml
20 ml or more but less than 100 ml	10 per cent of the contents of a container unless otherwise indicated in the monograph
100 ml or more	Not less than half the contents of the container unless otherwise specified
For Solids	
Less than 50 mg	The whole contents of a container
50 mg or more but less than 200 mg	Half the contents of a container
200 mg or more	100 mg

3. **Methods of testing :** Tests for sterility may be carried out by:—
   (a) Membrane filtration method
   (b) Direct inoculation method

(a) Membrane filtration method : The method is preferred in the following cases:—

(i) An oil or oily preparation
(ii) An ointment that can be put into solution
(iii) A non-bacteriostatic solid not readily soluble in culture medium
(iv) A soluble powder or a liquid that possesses bacteriostatic and fungistatic properties
(v) Liquid products where the volume in a container is 100 ml or more

The method involves the filtration of the sample under test through a membrane filter having normal porosity of 0.45µ, and a diameter of approximately 47 mm. After the filtration, the membrane is removed aseptically from the metallic holder and divided into two halves. The first half is transferred into 100 ml of culture media meant for fungi and incubated at 20° to 25°C for not less than seven days. The other half is transferred into 100 ml of fluid thioglycollate medium and incubated at 30° to 35°C for not less than 7 days. Observe the growth in the media.

FLUID THIOGLYCOLLATE MEDIUM

L-cystine	0.5 g
Sodium chloride	2.5 g
Dextrose	5.5 g
Agar	0.75 g
Yeast extract	5.0 g
Pancreatic digest of casein	15.0 g
Sodium thioglycollate	0.5 g
Resazurin	1.0 ml
Distilled water	1000 ml

Method : Mix all the ingredients except thioglycollate and the resazurin, in a mortar. Stir in some hot water. Transfer into a flask and add the remaining water. Make the clear solution by heating in a boiling water-bath. Add the sodium thioglycollate, then 1*N* sodium thioglycollate so that pH of the medium will be 7.1±0.2. Reheat the solution, filter and add the resazurin solution. Transfer into final containers sterilise by autoclaving for 20 minutes at 121°C. Cool promptly to 25°C and store at 20-30°C, avoiding excessive light.

Medium more than three weeks old should not be used. During storage, if more than 30 per cent of the upper portion of the medium has changed to a pinkish colour, it is unsuitable for use.

MEDIUM FOR FUNGI AND AEROBIC BACTERIA
(SOYABEANS-CASEIN DIGEST MEDIUM)

Pancreatic digest of casein	17.0 g
Peptic digest of soyabean meal	3.0 g
Sodium chloride	5.0 g
Dibasic potassium phosphate	2.5 g
Dextrose	2.5 g
Distilled water	1000 ml

Method : Dissolve all the ingredients in the water. Make a clear solution by warming. Cool to room temperature and add sufficient quantity of 0.1*N* NaOH to adjust the pH of the medium between 7.1 to 7.5. Filter and distribute the media into suitable containers. Sterilise in an autoclave at 121°C for 20 mts (at 15 Lb pressure).

(b) Direct inoculation method : In this method the specified quantity of sample under test is drawn aseptically from the container (The quantity of the substance or preparation to be used for the inoculation varies and is given in I.P. 1996) and transferred into a vessel of culture medium. Mix the liquid with the medium and incubate for not less than 14 days. Observe the growth of microorganisms in the medium.

4. Observation and results : The culture medium is examined during and at the end of incubation to find out if there is any microbial growth. The following observations are possible:—

(1) No evidence of growth; hence the preparation being examined passes the test for sterility.

(2) There is evidence of growth. So, re-testing is performed using the same number of samples, volumes to be tested and media as in the original test. If no evidence of microbial growth is then found, the preparation being examined passes the test for sterility.

(3) There is evidence of microbial growth. So, isolate and identify the organism. If they are not readily distinguishable from those growing in the containers reserved in the first test, the preparation being examined fails the test for sterility. They are readily distinguishable from those growing in the containers reserved in the first test. The second re-test is performed using twice the number of samples. The preparation being examined passes the test for sterility in case there is no evidence of microbial growth. In case there is evidence of growth of any microorganisms in the second re-test, the preparation being examined fails the test for sterility.

Q.3 Write notes on additives used in parenteral preparations.

Ans. Additives used in formulation of parenterals:

The formulation of parenteral preparations need careful planning, thorough knowledge of the medicaments and adjuvants to be used. The excess use of adjuvants in parenteral products should be avoided as some of these may interfere with the drug. In the preparation of parenteral products, the following substances are added to make a stable preparation:—

(1) Vehicles
(2) Adjuvants
  (a) Solubilising agents
  (b) Stabilizers
  (c) Buffering agents
  (d) Antibacterial agents
  (e) Chelating agents
  (f) Suspending, emulsifying and wetting agents
  (g) Tonicity factors

1. Vehicles : There are two types of vehicles which are commonly used for the preparation of injections:—

(a) Aqueous vehicles : Water is used as vehicle for majority of injections because water is tolerated well by the body and is safest to

administer. The aqueous vehicle used are:—

(i) Water for injection.

(ii) Water for injection free from CO_2.

(iii) Water for injection free from dissolved air.

Water for injection is a sterile water, which is free from volatile, non-volatile impurities and also from pyrogens.

Pyrogens are by-product of bacterial metabolism. Pyrogens are polysaccharide, thermostable, soluble in water, unaffected by bactericide and can pass through bacteria proof filters.

Pyrogens can be removed from water by simple distillation process using an efficient trap which prevents the pyrogen to enter into the condenser. Immediately after the preparation of water for injection, it is filled into the final container, sealed and sterilised by autoclaving.

Water for injection, contaminated with pyrogens may cause rise in body temperature if injected. Hence, test for pyrogen is done to ensure that water for injection is free from pyrogens.

(b) Non-aqueous vehicles : The commonly used non-aqueous vehicles are oils and alcohols.

Fixed oils, such as, arachis oil, cotton-seed oil, almond oil and sesame oil are used as vehicle. The oily vehicles are generally used when a depot effect of drug is required or the medicaments are insoluble or slightly soluble in water or the drug is soluble in oil e.g., dimercaprol injection by using arachis oil as vehicle.

Ethyl alcohol is used in the preparation of hydrocortisone injection. Hydrocortisone is insoluble in water, hence the solution is made in 50% alcohol. Alcohol causes pain and tissue damage at the site of injection. Therefore it is not used commonly.

Propylene glycol is used as a vehicle in the preparation of digoxin injection. It is relatively non-toxic but it causes pain on s/c or i/m injection.

Sometimes polyethylene glycol and glycerin usually diluted with sterile water are used to prepare solutions for injections. They are used as solvent as well as to increase the stability of certain preparations.

2. Adjuvants : These substances are added to increase the stability or quality of the product. These adjuvants should be used only when it is absolutely necessary to use them. While selecting the additives, care must be taken that they should be compatible both physically and chemically with the entire formulation. They should be added in mini-

mum possible quantity. The following adjuvants are commonly used in preparing the stable parenteral preparations:—

(a) Solubilising agents : These are used to increase the solubility of drugs which are slightly soluble in water. The solubility of drug is increased by using surface active agent like tweens and polysorbates or by using co-solvents.

(b) Stabilizers : The drugs in the form of solutions are more liable to deteriorate due to oxidation and hydrolysis. The stabilizers are added in the formulation to prevent this. The oxidation can be prevented by adding a suitable antioxidant, such as, thiourea, ascorbic acid, sodium metabisulphite, or the product is sealed in an atmosphere of nitrogen or carbon dioxide. Hydrolysis can be prevented by using a non-aqueous vehicle or by adjusting the pH of the preparation.

(c) Buffering agents : The degradation of the preparation which is due to change in pH, can be prevented by adding a suitable buffer to maintain the desired pH. For example, citric acid and sodium citrate, acetic acid and sodium acetate.

(d) Antibacterial agents : These substances are added in adequate quantity to prevent the growth of microorganism during storage. So these substances act as preservatives. Antibacterial agents are added in single dose containers, where parenteral products are sterilised by filtration method, and in multi dose containers to prevent microbial contamination.

(e) Chelating agents : Chelating agent such as EDTA (Ethylene diamine tetra acetic acid) and its salts, sodium or potassium salts of citric acid are added in the formulation, to chelate the metallic ions present in the formulation. They form a complex which gets dissolved in the solvent.

(f) Suspending, emulsifying and wetting agents : The suspending agents are used to improve the viscosity and to suspend the particles for a long time. Methyl cellulose, carboxymethyl cellulose, gelatin and acacia are commonly used as suspending agents. Emulsifying agents are used in sterile emulsions. For this purpose lecithin is generally used. The wetting agents are used to reduce the interfacial tension between the solid particles and the liquid, so as to prevent the formation of lumps. They also act as antifoaming agents to subside the foam produced during shaking of the preparation.

(g) Tonicity factors : Parenteral preparation should be isotonic with blood plasma or other body fluids. The isotonicity of the solution may

Be adjusted by adding sodium chloride, dextrose and boric acid, etc.. in suitable quantities. These substances should be compatible with other ingredients of the formulation.

Q.4. Difference between flocculated and deflocculated suspension.

	Flocculated Suspension	**Deflocculated Suspension**
Sedimented particle	Forms a network like structure	Separate individual particles
Velocity of sedimentation	Fast, fall together	Slow, fall according to size
Boundary	A distinct boundary between sediment and supernatant	No distinct boundary between sediment and supernatant
Supernatent	Clear	Turbid
Suspension	Not pleasing in appearance	Pleasing in appearance
Viscosity	High	Low
Rheology	Plastic & pseudoplastic	Dilatent
Sediment	Loosely packed and doesn't form a cake	Closely packed and form a hard cake
Redispersibility	Easy	Difficult

Q.5. Identification tests of emulsion.

Ans: **TEST FOR IDENTIFICATION OF TYPE OF EMULSION:**

1. **Dilution test**:

In this test the emulsion is diluted either with oil or water. If the emulsion is o/w type and it is diluted with water, it will remain stable as water is the dispersion medium" but if it is diluted with oil, the emulsion will break as oil and water are not miscible with each other. Oil in water emulsion can easily be diluted with an aqueous solvent whereas water in oil emulsion can be diluted with a oily liquid.

2. **Conductivity Test**:

The basic principle of this test is that water is a good conductor of electricity. Therefore in case of o/w emulsion, this test will be positive as water is the external phase. In this test, an assembly is used in which a pair of electrodes connected to an electric bulb is dipped into an emulsion. If the emulsion is o/w type, the electric bulb glows.

(a) o/w type emulsion (b) w/o type emulsion

3. **Dye Solubility Test**:

In this test an emulsion is mixed with a water soluble dye (amaranth) and observed under the microscope. If the continuous phase appears red, it means that the emulsion is o/w type as water is in the external phase and the dye will dissolve in it to give color. If the scattered globules appear red and continuous phase colorless, then it is w/o type. Similarly if an oil soluble dye (Scarlet red C or Sudan III) is added to an emulsion and the continuous phase appears red, then it is w/o emulsion.

4. **Cobalt Chloride Test**:

When a filter paper soaked in cobalt chloride solution is dipped in to an emulsion and dried, it turns from blue to pink, indicating that the emulsion is o/w type.

5. **Fluorescence Test**:

If an emulsion on exposure to ultra-violet radiations shows continuous fluorescence under microscope, then it is w/o type and if it shows only spotty fluorescence, then it is o/w type.

Q.6. Define and classify ointments.

Ans: The ointments are semisolid dosage forms applied for skin or mucous membrane, these are mainly prepared with the hydrocarbons, waxes or polyols these are mainly present more than 50%. The water content and volatile oils are less than 20%.

Classification:

Dermatological ointment: These ointments are applied on the surface of skin. These are again classified into three types based on the site of activity.

a. Epidermic ointments; these types of ointment are exert their therapeutic activity in the **epidermis. eg: ketoconazole ointment.**

b. Endodermic ointments: These are exerting their activity in the **endodermis**. eg; Demodex ointment

c. Didermic ointments: These types of ointments are exerting their activity by enters inter into deeper of skin layers and enter into systemic circulation. **eg; Nitroglycerin ointment.**

Opthalmic ointments: These ointments are mainly used for the treatment of eye problems. The drug enters into the inner layers of the eye. **eg: Moxifloxacin opthalmic ointment**

Rectal ointments: These types of ointments are administered into rectal route. These PEG 400 (Poly ethylene glycol), cetyl alcohol, sterile esters etc for the treatment of bowel problems.

Vaginal ointments: These are mainly used used for the treatment of vaginal infection treatment. **eg: Candicidin ointment**

Nasal ointments; These are mainly used for the treatment of allergic reaction. Comparatively this route is less predominant. The drug directly entered into systemic circulation.**eg; Iprtropium bromide**