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B. Pharm. Sem-I
Pharmaceutical Analysis-I (AS-2501)
Model Answer

Section A:

(12 x 2 = 24)

1. Short Questions

1.1

Ans Potassium ferricyanide, Diphenylamine

1.2

Ans Benzoic acid, Oxalic acid.

1.3

Ans Drying is the term used when temperature is below 250 °C and ignition for temperature between 250 °C and 1200°C.

1.4

Ans It means the condition when weighing of sample after drying and ignition gives constant weight for any number weighing.

1.5

Ans Relative supersaturation = $[Q-S]/S$ Where Q is the total concentration of substance that is to be precipitated and S is the equilibrium solubility.

1.6

Ans pH may be defined as negative logarithm of hydrogen ion concentration.

Buffer may be defined as solution which resists the change in pH on addition of small amount of acid or base.

1.7

Ans In Mohr's method, $AgNO_3$ (in burette) is titrated with NaCl (taken from pipette) while in Volhard method, $AgNO_3$ (taken from pipette) is titrated with NH_4CNS (in burette). Nitric acid and nitrobenzene are used in Volhard method while they are not used in Moh's method.

1.8

Ans pH range is 8.3 to 10; colour change is colorless to pink.

1.9

Ans Molarity = $\frac{\text{Weight of the substance (in gm/litre)}}{\text{molecular weight of substance}}$

1.10

Ans Normality = $\frac{\text{weight of the substance (in gm/litre)}}{\text{equivalent weight of substance}}$
Strength = Normality / Equivalent weight

1.11

Ans 0.63 g of oxalic acid to be dissolved in 100 ml of Distilled water.

1.12

Ans It means the condition when no turbidity is seen on adding few drops of precipitant from sides of beaker wall carefully to the solution with settled precipitate.

Section B: Long Questions:

(14 x 4 = 56)

2.

Ans

Sampling:

The sample which is weighed for quantitative analysis is very small. It is necessary to take a representative sample correctly to ensure that results. The samples should be homogeneous and in the form of powder.

Dissolution:

To dissolve the sample, take a clean beaker and transfer the weighed sample completely to the beaker. Add sufficient water to the sample to get a clear solution.

Formation of Precipitate:

For ideal precipitant, it should react with analyte to form the precipitate which can be easily filtered. Precipitations are generally carried out in resistant glass beaker with slow addition of dilute solution of precipitant with sufficient stirring. This reaction should be carried out in hot solution. The precipitant which forms a precipitate having the least solubility should be chosen.

Completeness of Precipitation:

The completeness of precipitation is checked by adding a few drops of precipitant from sides of beaker wall carefully to the solution with settled precipitate. If no turbidity is seen at the edge, precipitation is complete. It is always advisable to check the completeness of precipitation before filtration.

Filtration:

In this operation, precipitate is separated from mother liquor. Various types of filter medias are used for this purpose. The choice of filter media is based on the nature of precipitate, cost of media, and the heating temperature required for drying. The filtering medias used in gravimetric analysis are:

1. Filter paper
2. Filter pulp
3. Filter mats
4. Permanent porous filter discs

1. Filter paper: Quantitative filter papers used in gravimetric analysis should have very low ash content. Manufacturers of filter papers generally give the average ash per paper. This value also can be estimated by igniting the several filter papers in the crucible. Lower values of ash content are usually achieved by washing with hydrochloric and hydrofluoric acid during its manufacture. Circular filter papers with 7.0, 9.0, 11.0, 12.5 cm diameter are available. They are available in different degrees of porosities. The filter papers made are generally of three

degrees of porosities. One for gelatinous and coarse particles, second for medium size particles and third for very fine precipitates. The speed of filtration also varies for these papers. It is fast for first, medium for second and slow for third type of filter paper mentioned above. Filter papers of quantitative work are treated with nitric acid have greater mechanical strength very low ash content and are more resistant to acids and alkalis.

Whatman filter papers are generally available for this purpose and are used in gravimetric analysis.

They are available under different grades and their pore diameters in (μ) microns are given below:

Fast speed	Medium speed	Slow speed
No. 31	No. 30	No. 32
(4.6)	(2.2)	(1.1)
No. 41	No. 40	No. 42
(4.1)	(2.4)	(1.1)
No. 54	No. 52	No. 50

Whatman filter paper No. 30, 31, 32 and 50, 52, 54 are generally cheap No. 42 filter is generally useful for very fine particles while No. 41 is used for gelatinous precipitates.

Size of filter paper is based on the bulk of the precipitate and not the volume of the solution to be filtered. The precipitate should occupy one third of its capacity. In addition, funnel should match the size of filter paper.

2. Filter pulp: For filtration of gelatinous precipitates quantitative filter papers cannot be used as the pores as the pores tend to be clogged by the precipitate. For filtration filter pulp is used instead of filter papers. Filter pulp can be prepared by macerating the filter paper torn into pieces of with hot distilled water. Whatman filter clipping (ashless) are also used for this purpose. Filter pulp tablets are also available and are easily disintegrable in case of filtration by this filter pulp. The bulk of filter pulp should be equal to that of the gelatinous precipitate. Addition of filter pulp is made immediately before filtration and after the precipitation.

The precipitate along with filter pulp is transferred to crucible when it is still wet and drying is completed in the crucible. For very fine particles which are difficult to coagulate can also be filtered by using filter pulp.

3. Filter mats:

a) Gooch crucibles: Gooch first employed a filter mat of purified asbestos supported inside the platinum crucible. The bottom of the crucible was perforated with numerous small holes. Afterward idea was extended to porcelain and then to silica crucibles. All crucibles of this type are called Gooch crucibles. Generally, porcelain variety is used by beginners. Asbestos used in generally long fibered, white, silky and anhydrous. It is prepared by boiling it with HCl. Asbestos for Gooch crucibles are available in market. They are generally used under suction. The crucibles can be dried to constant weight. For temperature up to 250°C , electric oven can be used. Electrically heated muffle furnace is used for drying at higher temperature. The asbestos normally tends to lose weight above 250°C . It is generally useful for precipitates that require heating up to 250°C .

b) Munroe crucibles: A platinum Gooch crucible containing mat was first used by Munroe. Because of high cost of platinum, Munroe crucible are not used for routine analysis. The main advantages of these crucibles are resistance to chemical, filtration of finest particles, rapidity of filtration and heating to a very high temperature.

c) Glass fibre discs: inexpensive glass fibre discs are available for use instead of asbestos mat. A circle of glass fibre filter paper may be placed in a coarse porosity filter crucible for rapid filtration. Glass fibres are made

from fine borosilicate glass fibres. They possess the main features as having excellent retention property with rapid filtration, unaffected by chemical reagents and heating up to 500°C.

4. Permanent porous filter discs: in these types, there is no preparation of filter mat as in case of Gooch crucible. Best example of this is sintered glass crucibles.

- a) **Sintered glass crucibles:** these crucibles are made of resistant glass i.e. pyrex and have porous disc of sintered glass fused in the body of the crucible. These filter discs are of various porosities. They are G₁, G₂, G₃, G₄ types. Their pore sizes are 100-200 microns, 40-50 microns and 5-10 microns respectively. The crucibles G₁ type is used for coarse particles while G₄ type for very fine particles. The crucibles are of two types tall form and the low, wide form.

The main features of sintered glass crucibles are their resistance to chemicals and ease of drying and cleaning.

These crucibles can be heated to 200°C. If heated above 430°C, permanent strains are produced and they soften above 610°C.

- b) **Silica crucibles:** if drying of precipitate is done above 200°C, silica crucibles can be used. These are similar to sintered glass crucibles but are made up of (pure fused silica). They are G₁, G₂, G₃, G₄ types. These crucibles can be used for drying of precipitate up to 1000°C. These crucibles are resistant to chemical agents but are affected by phosphate, strong alkalis and hydrofluoric acid.
- c) **Porcelain crucibles:** The porcelain crucibles are glazed inside and outside. The bottom of it consists of a plate of porous porcelain. These crucibles are available in different sizes and porosities. They can be heated to relatively higher temperature. The heating should be gradual at higher temperature to avoid cracking of filter plate. Porcelain crucible should not be heated directly in the flame.

A new crucible should be washed with concentrated hydrochloric acid and then with distilled water. Always care should be taken to avoid clogging of filter discs.

Washing of precipitate:

After filtering the precipitate, the impurities on the surface of precipitate can be removed by washing of precipitate. In addition, mother liquor which is entrapped with precipitate is also removed by washing. Many precipitates are not washed with water, but with washing solution. Ideal washing solution should have no solvent action on precipitate but should dissolve foreign matter easily.

The washing solutions are of following type:

- a) **Washing with the solution of precipitant:** in this case the precipitant is washed with dilute solution of precipitant. Ex lead sulphate precipitate washed by dilute sulphuric acid.
- b) **Washing with the solution of electrolyte:** when pure water is used for washing the precipitate, many precipitates may be peptized i.e. Converted to colloidal state. The washing is done with electrolyte solution.

- c) **Washing with substances which suppress the hydrolysis of precipitate:** sometimes precipitates undergo the hydrolysis leading to increase in solubility. It can be prevented by washing the solution which suppresses hydrolysis. Ex. washing of MgNH_4PO_4 precipitate with dilute solution of ammonia.
- d) **Washing with water:** if the precipitate is very stable and there is no effect of solubility or no effect leading to peptisation or no effect leading to hydrolysis to precipitate, the precipitates can simply be washed with distilled water. Ex. Washing the precipitate of BaSO_4 with water.

Drying and ignition of precipitate:

The main object of drying is to convert the precipitate to a weighed form having constant composition. It is heated to remove water and remove the adsorbed electrolyte from washing solution. Drying or ignition process will depend on nature of precipitates and filtering media used for the purpose. Drying is the term used when temperature is below 250°C and ignition above 250°C and below 1200°C . Drying is possible for precipitates filtered on filter paper, Gooch crucible, sintered glass or porcelain crucibles. Ignition is done by heating with appropriate burner or crucible can be placed in electrically heated muffle furnace.

'Heating to constant weight' is an important aspect. It will be significant only when period of heating, cooling of covered crucible and weighing are repeated.

3.

Ans

Mixed Indicator

In some cases, the pH range is very narrow and the colour change over this range must be very sharp. This is not possible with ordinary acid-base indicators. The result may be achieved by use of the suitable mixture of indicators. Example: A mixture of equal parts of neutral red (0.1% solution in alcohol) and methylene blue (0.1% solution in alcohol) gives a sharp colour change from violet-blue to green in passing from acid to alkaline solution at pH 7. another example of mixed indicator is a mixture of phenolphthalein (3 parts of 0.1% solution in alcohol) and alpha-naphtholphthalein (1 part of 0.1% solution in alcohol) passes from pale rose to violet at pH 8.9.

Universal Indicator

By suitably mixing certain indicators the color change may be made to extend over a considerable portion of the pH range. Such mixtures are usually called "Universal indicators". They are not suitable for quantitative titrations but may be employed for the determination of the approximate pH of a solution by colorimetric method.

For example, dissolve 0.1 g of phenolphthalein, 0.2 g of methyl red, 0.3 g of methyl yellow, 0.3 g of bromothymol blue and 0.5 g thymol blue in 500 ml of absolute alcohol and add sufficient sodium hydroxide solution until the color is yellow. The colour changes are:

At pH 2 colour is red;

At pH 4 colour is orange;

At pH 6 colour is yellow;

At pH 8 colour is green;

At pH 10 colour is blue.

Several universal indicators are available commercially as solutions and as the test papers and are used in calorimetric determination of pH.

4.

Ans

Assay of sodium chloride injection by Mohr's method:

Sodium chloride injection (I.P.) (sodium chloride infusion) is a sterile solution of sodium chloride in water for injection and contains 0.9 percent w/v of sodium chloride (limits, 0.85 to 0.95 per cent NaCl). It is assayed (I.P. 1996), by Mohr's method using an appropriate volume of the injection.

Procedure Transfer to a conical flask an accurately measured volume equivalent to about 0.25 g of sodium chloride. Add about 50 ml of water, and titrate with 0.1 N silver nitrate, using solution of potassium chromate as indicator.

Calculation

$$\text{Per cent (w/v) purity} = \frac{V1 \times N1 \times 0.005845}{0.1 \times V2} \times 100$$

V1 = volume of silver nitrate solution

N = normality of silver solution

V2 = volume of the sample

Assay of sodium chloride injection by Volhard's method:

The assay of the sodium chloride injection is now carried out by Volhard's method. An appropriate volume of the injection, diluted with water is treated with a measured volume of standard silver nitrate solution in the presence of nitric acid and nitrobenzene. The excess of silver nitrate is determined by titration with standard ammonium thiocyanate solution using ferric ammonium sulphate as indicator.



1000 ml of N/10 silver nitrate are equivalent to 1/10 NaCl.

Procedure Transfer to a glass stoppered flask an accurately measured volume equivalent to about 0.25 g of sodium chloride and 50 ml of water. Add 50.0 ml of 0.1N silver nitrate, 3ml of nitric acid, 5ml of nitrobenzene, and 2ml of ferric ammonium sulphate solution and shake well. Titrate with 0.1N ammonium thiocyanate until colour becomes reddish yellow.

Each ml of 0.1N silver nitrate is equivalent to 0.005844 g of NaCl.

$$\text{Per cent (w/v) purity} = \frac{(V1 \times N1) - (V2 \times N2) \times 0.005844}{0.1 \times V3} \times 100$$

V1 = volume of silver nitrate solution

N1 = normality of silver nitrate solution

V2 = volume of ammonium thiocyanate solution

N2 = normality of ammonium thiocyanate solution

V3 = volume of the sample

5.

Ans

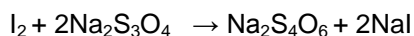
Assay of Iodine Solution (Weak and Strong)

Iodine occurs in the form of bluish black solid, having a metallic lustre and a characteristic penetrating odour. It is soluble in 2950 parts of water. Weak and strong iodine solutions are prepared by dissolving iodine in aqueous solution of potassium iodine. Weak iodine solution (I.P. 1966) contains 2.0 per cent w/v of I (limits, 1.95 to 2.05) and 2.5 per cent w/v of KI (limits, 2.45 to 2.55). Strong iodine solution (I.P. 1966) contains 10.0 per cent w/v of I (limits 9.5 to 10.5) and 6.0 per cent w/v of KI (limits, 5.7 to 6.3).

The assay of iodine solution involves double titration. In the first titration free iodine content is determined by titration with 0.1N sodium thiosulphate solution. In the second titration the acidified solution is titrated with potassium iodate (KIO₃) solution for estimation of total iodine and potassium iodide.

In the first titration iodine is reduced to sodium iodide (NaI) and sodium thiosulphate is oxidised to sodium tetrathionate (Na₂S₄O₆).

The decolouration of iodine solution marks the end point.



1000 ml of N/10 sodium thiosulphate are equivalent to 1/10 I.

Procedure Dilute 10 ml with 20 ml of water, and titrated with 0.1N sodium thiosulphate.

Each ml of 0.1N sodium thiosulphate is equivalent to 0.01269 g of I.

Calculation

$$\text{Percent (w/v) of iodine} = (V_1 \cdot N \cdot 0.01269 / 0.1 \cdot V_2) \cdot 100$$

V₁ = volume of sodium thiosulphate solution

N = normality of sodium thiosulphate solution

V₂ = volume of the sample

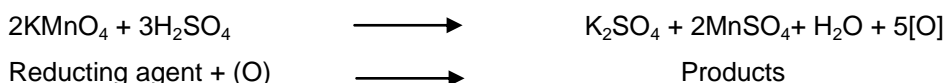
6.

Ans

Potassium permanganate, KMnO₄ is one of the useful and versatile oxidants. Its solution is fairly stable. It is readily available at a moderate cost and acts as a *self indicator* in most titrations. It was first introduced in volumetric analysis by **F. Marguerette** in 1840 for the titration of ferrous iron.

Titration is usually carried out in the acid medium with consequent reduction of permanganate ion to manganous ion (Mn²⁺). Among the three mineral acids available, only sulfuric acid is most suitable for use with potassium permanganate because it does not act on permanganate ion in the dilute solutions.

In the presence of dilute sulfuric acid, potassium permanganate reacts with reducing agents according to the key equation:



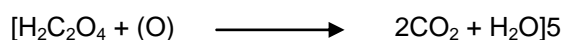
As the titration proceeds potassium sulphate and manganese sulphate accumulate, but at the dilution used, gives colourless solution because K_2SO_4 and $MnSO_4$ are colourless solution. As soon as the oxidation is complete and potassium permanganate is in excess, the solution become pink. In other words, potassium permanganate acts as its own indicator known as a self-indicator. Thus in potassium permanganate titrations the use of external indicator is unnecessary as it itself is a self indicator.

Potassium permanganate is not a primary standard because

- i. It cannot be obtained in pure state,
- ii. It undergoes decomposition, in the presence of impurities to MnO_2 , on standing.

Estimate the strength of the given sample of $KMnO_4$ solution in g/litre. Prepare a standard solution of N/10 oxalic acid.

Principle: In this method given in 1912 by Mebride, a solution of oxalic acid acidified with dilute sulphuric acid is titrated slowly with potassium permanganate at a temperature between 60-70 °C until a permanent is as follows:



Procedure: It involves the following steps:

- i. *Preparation of N/10 oxalic acid:* weigh out accurately $63 \times 1/10 = 1.575$ g of pure oxalic acid crystals in weighing bottle or a watch glass. Transfer it to a 250 ml measuring flask. To this add 50 ml of distilled water and dissolve the crystals of oxalic acid by shaking gently and then make up the solution up to the mark on it with more of distilled water. Again, shake the flask gently up and down to ensure thorough mixing.
- ii. *Titration of $KMnO_4$ with oxalic acid:* rinse the burette with potassium permanganate solution and fill it up to a convenient mark. One should be sure that nozzle of the burette should not contain air bubbles but filled with the $KMnO_4$ solution only. Pipette out 20 ml of the given standard solution of oxalic acid (N/10) into a titration flask and add to it a test tube of dilute, sulphuric acid. Heat the flask on a wire gauze to 60-70 °C, i.e., to a temperature which is just unbearable to touch by hand. Note the initial reading of the burette by nothing the upper meniscus. Run the potassium permanganate solution slowly in small amounts at a time into the hot solution and shake till the end point is reached. The end point is a change of colourless solution to a just permanent pink solution. Note the final reading of the burette by nothing the upper meniscus only.

7.

Ans

Very pure reagents of high stability are used in preparation of standard solution. In such cases the accurate weight of reagent is taken, dissolved and diluted to exact known volume and concentration is calculated on theoretical basis. This method has some limitation such as all the results depend on single measurement and single weighing. The substances of high purity used in preparation of standard solution are known as primary standard substances.

Primary standard substances:

Primary standard substances should satisfy the following requirements:

1. It must be easy to obtain, to purify, to dry and to preserve in pure state.
2. It should be 100.00% pure although 0.01 to 0.02% impurity is tolerable if accuracy known.
3. It should be stable to atmospheric condition. It should not decompose or be hygroscopic, or deliquescent.
4. It should show a high equivalent weight in order to reduce the effect of weighing errors. In weighing a greater amount of substance, the relative error will be smaller than that for a small amount.
5. The reaction with standard solution should be stoichiometric and practically instantaneous.
6. The reaction to be amenable to use simple indicator to determine the end point of the titration.
7. There should not be any difference between end point and theoretical equivalence point i.e. titration error should not be there.
8. It should be readily soluble under the condition in which it is to be employed.
9. It should not have water of hydration so that the composition of solid does not change with variation in relative humidity.

It is not always possible satisfy all the requirements of a primary standard but the requirement mentioned above should be met at all times as closely as possible. In practice ideal primary standard are difficult to obtain and hence, a compromise between above requirement is usually necessary.

The commonly used primary standard substances are:

Acid base titration: Sodium carbonate, potassium hydrogen phthalate, succinic acid, benzoic acid, oxalic acid, adipic acid.

Redox Titration: Potassium dichromate, potassium bromate, potassium iodate, sodium oxalate.

Precipitation titration: Sodium chloride, potassium chloride, potassium bromide, silver nitrate AR.

Complexometric titration: Various pure metals such as zinc magnesium, manganese and salts such as lead nitrate calcium's carbonate etc.

As the number of primary standard substances is limited, a substance with less but known purity is used in standardization process. These substances are known as secondary standards

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