Index No:.....

UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

THIRD BPHARM PART I EXAMINATION – JANUARY 2026

PH 3113 ANALYTICAL CHEMISTRY - SEQ

TIME: TWO HOURS

INSTRUCTIONS

- There are **four** questions in parts **A, B** and **C** in this SEQ paper.
- Answer **all** questions.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.
- Use illustrations where necessary.

PART A

01.

1.1 Discuss the major sources of impurities in pharmaceutical manufacturing. (***30 marks***)

1.2 Describe the concept of process validation in pharmaceutical manufacturing and describe its key elements. (***30 marks***)

1.3 Discuss the key parameters of analytical method validation in pharmaceuticals. (***40 marks***)

PART B

02.

2.1 In titrimetric analysis, "primary standards" are crucial to ensure accurate and reliable results.

2.1.1 How would you define a primary standard? (***05 marks***)

2.1.2 Give five factors that a substance should possess to be a primary standard. (***10 marks***)

2.2 A student carried out a titration of 25.00 mL portion of an unknown concentration of acetic acid with 0.5020 mol dm^{-3} of previously standardized NaOH. This titration required 18.80 mL of NaOH to neutralize the acetic acid solution.

2.2.1 Sketch a pH curve for this titration considering the pH in the Y-axis and the volume of NaOH in the X-axis indicating 2, 6, 10 and 14 on the Y-axis scale. (***10 marks***)

2.2.2 Indicate the equivalence point and the buffering zone (if any) on the titration curve drawn in part 2.2.1. (*10 marks*)

2.2.3 Select the most suitable indicator that can be used in this titration, from the three indicators; methyl red (pK_{In} = 5.00), thymol blue (pK_{In} = 1.65) and phenolphthalein (pK_{In} = 9.10). Give <u>one</u> reason to justify your answer. (*10 marks*)

2.2.4 Assume that the student has suddenly stopped the above titration after the addition of 9.40 mL of NaOH, calculate the pH of the solution in the titration flask (pK_a of acetic acid = 4.76). (*20 marks*)

2.3 A Na_2CO_3 solution is contaminated with a small amount of $NaHCO_3$. This solution was titrated with HCl to determine the concentration of each component of the solution. First, 50.00 mL portion of this solution was titrated with 0.1200 mol dm^{-3} HCl solution, which required 14.50 mL to reach the phenolphthalein endpoint. Another 50.00 mL portion of this solution was titrated with the same HCl solution using methyl orange as the indicator. It was required 32.50 mL to reach the endpoint.

Note: No any other components in the solution to react with HCl except Na_2CO_3 and $NaHCO_3$.

2.3.1 Give balanced chemical equations involved in these titrations. (*10 marks*)

2.3.2 Calculate the concentrations of Na_2CO_3 and $NaHCO_3$ in the above solution. (*25 marks*)

PART C

03.

3.1 Formation of precipitate is a crucial step in gravimetric analysis and precipitation titrations.

3.1.1 What are the main phases in precipitate formation? (*10 marks*)

3.1.2 Briefly explain the methods that can be used to maximize the final phase in precipitate formation. (*20 marks*)

3.1.3 Suppose that a saline sample is given to you to determine its NaCl concentration using a precipitation titration method. If the medium is found to be slightly acidic, propose a suitable argentometric titration method for this analysis. (*20 marks*)

3.2 The effectiveness and selectivity of EDTA titrations are heavily dependent on the pH of the solution.

3.2.1 Show that at pH 2 formation of the FeY^- complex is favorable, but that of the AlY^- complex is not (log K_{FeY} = 25.1, log K_{AlY} =16.1, and $\alpha_{y4-} = 7.6 \times 10^{-14}$ at pH 2).

(***25 marks***)

3.2.2 A 50.00 mL aliquot of a solution containing Fe^{3+} and Al^{3+} was buffered to pH 2 and titrated with 0.0500 mol dm^{-3} EDTA using salicylic acid as the indicator (purple → yellow), requiring 24.82 mL to reach the end point. The pH of the titration mixture was then adjusted to 5 and 50.00 mL of 0.0500 mol dm^{-3} EDTA was added in excess. The resulted solution was titrated with 0.0411 mol dm^{-3} Fe^{3+}, requiring 17.84 mL at the salicylic acid indicator. Calculate the molar concentrations of Fe^{3+} and Al^{3+} in the solution mixture. (***25 marks***)

04.

4.1 Consider the potentiometric titration of 50.00 mL of 0.0500 mol dm^{-3} Sn^{2+} with 0.1000 mol dm^{-3} Tl^{3+}. Both the titrand and the titrant are prepared in 1.0 mol dm^{-3} HCl.

The titration reaction is:

$$Sn^{2+}(aq) + Tl^{3+}(aq) \rightleftharpoons Tl^{+}(aq) + Sn^{4+}(aq)$$

Titration curve points can be calculated with the Nernst equation using standard electrode potential of the two half-reactions that form the complete redox reaction.

In $HClO_4$, the formal potential (the E^0 values) for the reduction of Tl^{3+} to Tl^+ is 0.77 V and that for the reduction of Sn^{4+} to Sn^{2+} is 0.139.

4.1.1 What is the volume of Tl^{3+} needed to reach the equivalence point? (***10 marks***)

4.1.2 What is the potential of the indicator electrode at the:

4.1.2.1 half-equivalence point (50% of titration)? (***10 marks***)

4.1.2.2 equivalence point (100% of titration)? (***05 marks***)

4.1.2.3 200% titration? (***05 marks***)

4.2 Diazotization titrations are used for determination of alpha drugs, sulphanilamide, chlorophenol, procaine etc. Giving relevant chemical equations, briefly explain:

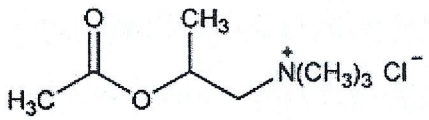
4.2.1 the principle of diazotization titrations. (***15 marks***)

4.2.3 the indicator used in diazotization titration. (***10 marks***)

4.3

4.3.1 In the preparation of the 0.1 M perchloric acid in nonaqueous titrations, amount of acetic anhydride added should be optimum. Explain why. (***10 marks***)

4.3.2 The following procedure was carried out to determine the % of methacholine chloride in a commercially available tablets. Dried methacholine chloride tablets (4 g) was dissolved in a mixture of 50 mL of glacial acetic acid and 10 mL of acetic anhydride. After adding 10 mL of mercuric acetate solution and one drop of crystal violet indicator it was titrated with 0.1 M perchloric acid to a blue-green end point reaching at 56.00 mL. A blank titration was required 1.70 ml of perchloloric to reach the end point.



(methacholine chloride, MW 195.69 g mol^{-1})-

4.3.2.1 Write titration equation. (***10 marks***)

4.3.2.2 Show that 1 mL of 0.1 M perchloric acid is equivalent to 19.57 mg of methacholine chloride. (***05 marks***)

4.3.2.3 Why acetic anhydride and mercuric acetate are added? (***10 marks***)

4.3.2.4 Calculate % w/w of methacholine chloride in the used tablets. (***10 marks***)

@@@@@@@@@@@@@@@@@@@@