SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES

COIMBATORE-641035

UNIT I - SUB TOPIC: PHARMACEUTICAL ANALYSIS - PUZZLES

Introduction to Pharmaceutical Analysis-Preparation and Standardization of Solutions:

In analytical chemistry, particularly in pharmaceutical and quality control settings, the preparation and standardization of molar (M) and normal (N) solutions are essential for accurate titrations and assays. Molarity is moles per liter, while normality is equivalents per liter, depending on the reaction (e.g., for dibasic oxalic acid, N = 2M). Below, I present hypothetical case studies inspired by standard laboratory procedures from educational and pharmaceutical guidelines. These cases simulate real-world applications, such as drug purity testing or reagent quality assurance. Each case includes key steps, formulas, and calculations.

The puzzles at the end are based on these case studies, drawing from scenarios involving calculations, procedures, and troubleshooting.

Case Study 1: Preparation of 0.1 M Oxalic Acid Solution in a Pharmaceutical Quality Control Lab

In a pharma lab testing aspirin purity, a 0.1 M oxalic acid solution (primary standard) is prepared for standardizing NaOH used in acid-base titrations. Oxalic acid ($H_2C_2O_4 \cdot 2H_2O$, MW 126.07 g/mol) is dibasic, so for normality, N = 2M.

Procedure:

- Weigh a clean, dry watch glass and record its weight.
- Add approximately 3.15 g of oxalic acid crystals to the watch glass and weigh accurately.
- Transfer to a 250 mL volumetric flask using a funnel.
- Rinse the watch glass and funnel with distilled water, adding rinsings to the flask.
- Dissolve the crystals by swirling with ~100 mL distilled water.
- Make up to the 250 mL mark with distilled water and mix thoroughly.
- No further standardization is needed as it's a primary standard, but verify by titrating against a known NaOH if required.

Calculation for Weight:

- For 0.1 M in 250 mL: Weight = (Molarity × MW × Volume in L) / 1 = (0.1 × 126.07 × 0.25) = 3.15175 g.

This solution was used to confirm NaOH strength for batch release.

Case Study 2: Standardization of 0.1 N Sodium Hydroxide Solution in an Industrial Water Treatment Facility

At a water treatment plant, 0.1 N NaOH is standardized against oxalic acid for pH adjustment processes. NaOH (MW 40 g/mol) is monobasic, so N = M.

Preparation:

- Dissolve ~4.2 g NaOH pellets in ~100 mL distilled water in a 1 L volumetric flask.
- Cool, make up to 1 L with distilled water, and let stand for 1 hour.

Standardization:

- Weigh ~0.5 g potassium hydrogen phthalate (KHP, MW 204.23 g/mol, primary standard) dried at 120°C.
- Dissolve in 75 mL CO_2-free water in a conical flask.
- Add 2 drops phenolphthalein indicator.
- Titrate with NaOH until permanent pink endpoint.
- Reaction: KHP + NaOH → KNaP + H_2O.
- Equivalent: 1 mL 0.1 N NaOH ≡ 20.423 mg KHP.

Calculation:

- Normality (N) = (Weight of KHP in g × 1000) / (Equivalent weight of KHP × Volume of NaOH in mL) = (0.5 × 1000) / (204.23 × V), where V is burette reading.

In the case, 24.5 mL NaOH was used for 0.5 g KHP, confirming ~0.1 N.

Case Study 3: Preparation and Standardization of 0.1 M Hydrochloric Acid in a Clinical Chemistry Lab

In a hospital lab for electrolyte analysis, 0.1 M HCl is prepared and standardized. HCl (MW 36.46 g/mol, conc. ~37%, density 1.19 g/mL) is monobasic, N = M.

Preparation:

- Add ~8.5 mL conc. HCl to ~100 mL water in a 1 L volumetric flask (add acid to water).
- Cool, make up to 1 L with water, and let stand for 1 hour.

Standardization:

- Weigh ~0.5 g tromethamine (THAM, MW 121.14 g/mol) dried at 105°C.
- Dissolve in 50 mL water.
- Add 2 drops bromocresol green indicator.
- Titrate with HCl to pale yellow endpoint.
- Equivalent: 1 mL 0.1 M HCl ≡ 12.114 mg THAM.

Calculation:

- Molarity (M) = (Weight of THAM in mg) / (121.14 × Volume of HCl in mL).

In the scenario, 41.2 mL HCl titrated 0.5 g THAM, yielding ~0.1 M.

Case Study 4: Preparation and Standardization of 0.1 M Sodium Thiosulphate in a Food Testing Lab

In a food lab detecting iodine in salts, 0.1 M $Na_2S_2O_3$ (MW 248.18 g/mol) is prepared and standardized. In iodometry, equivalent weight = MW (1 electron transfer), so N = M.

Preparation:

- Dissolve ~25 g $Na_2S_2O_3 \cdot 5H_2O$ and 0.2 g Na_2CO_3 in ~100 mL water in a 1 L flask.
- Make up to 1 L and let stand.

Standardization:

- Weigh ~210 mg $K_2Cr_2O_7$ (MW 294.18 g/mol) dried at 120°C.
- Dissolve in 100 mL water in a stoppered flask.
- Add 3 g KI, 2 g $NaHCO_3$, 5 mL HCl; stand in dark 10 min (liberates I_2).
- Titrate with $Na_2S_2O_3$ to yellowish green.
- Add 3 mL starch; titrate to blue discharge.
- Reaction: $6\ Na_2S_2O_3 + K_2Cr_2O_7 + 7\ H_2SO_4 \rightarrow 3\ Na_2S_4O_6 + K_2SO_4 + Cr_2(SO_4)_3 + 7\ H_2O$ (via I_2 intermediate).
- Equivalent: 1 mL 0.1 M $Na_2S_2O_3 \equiv 4.903$ mg $K_2Cr_2O_7$.

Calculation:

- Molarity (M) = (Weight of $K_2Cr_2O_7$ in mg) / (49.03 × Volume of $Na_2S_2O_3$ in mL).

In the case, 20.5 mL $Na_2S_2O_3$ was used for 210 mg $K_2Cr_2O_7$, confirming ~0.1 M.

- Why is oxalic acid considered a primary standard in this experiment?
- Calculate the weight of oxalic acid required to prepare 250 mL of 0.1 M solution.
- What would happen if the watch glass was not dried before weighing the sample?
- Why is KHP used as a primary standard for NaOH?
- If 0.5 g KHP required 24.5 mL of NaOH, calculate the normality of NaOH.
- Why should acid always be added to water, not the reverse?
- Calculate the molarity of HCl if 0.5 g THAM required 41.2 mL of acid.
- Write the overall redox reaction occurring in the titration process.
- Calculate the molarity if 210 mg $K_2Cr_2O_7$ required 20.5 mL $Na_2S_2O_3$.
- Why must burettes and pipettes be rinsed with the solution to be used before titration?
- How do parallax errors affect titration accuracy, and how can they be avoided?