GPAT Pharmaceutics

Sample Paper – 10

Duration: 36 Minutes **Maximum Marks: 100**

Instructions

- This paper contains **25** Multiple Choice Questions (Single Correct Answer), modelled on the Pharmaceutics portion of **GPAT** entrance.
- Each correct answer carries **+4 marks**. There is **a penalty of −1 mark** for each incorrect answer. Unattempted questions carry no marks.
- Only **one** option is correct per question.
- Syllabus: **GPAT Pharmaceutics — Analytical Methods, Instrumental Analysis, Pharmaceutical QA/QC.**
- Personal calculators, mobile phones, and electronic gadgets are strictly prohibited. A simple on-screen calculator is provided in the CBT interface; rough sheets are supplied at the centre.

Q1. Karl Fischer (KF) titration is the pharmacopoeial method of choice for determining water content in pharmaceutical drug substances and excipients. Both coulometric and volumetric KF methods are based on the Bunsen reaction: $I_2 + SO_2 + H_2O + 3\,\text{base} \rightarrow 2\,\text{HI} \cdot \text{base} + SO_3 \cdot \text{base}$. For a highly sensitive test on an anhydrous drug powder expected to contain approximately **0.01% w/w** water (trace moisture level), which KF method is MOST appropriate?

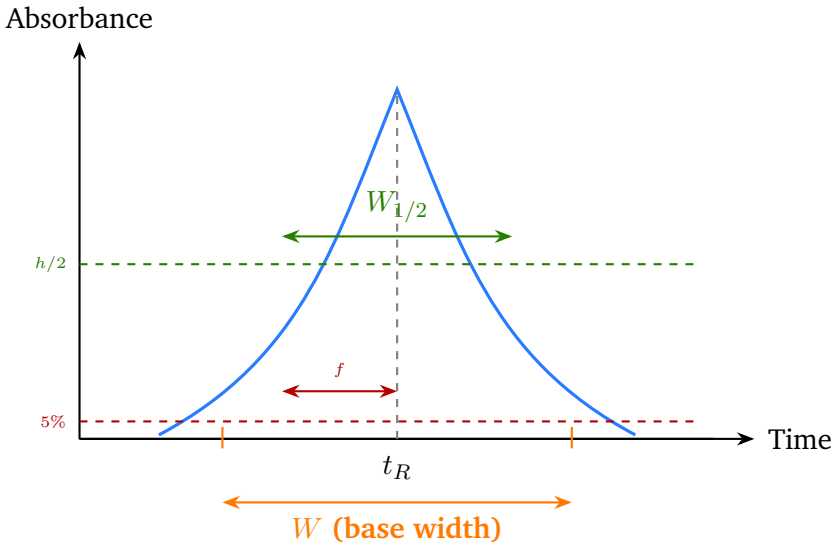
(A) Volumetric KF in which iodine-containing Karl Fischer reagent is delivered from a burette; suitable for samples containing 0.1–100% water

(B) Coulometric KF in which iodine is generated electrochemically at constant current directly in the titration cell; suitable for trace moisture 0.001–0.1% w/w

(C) Volumetric KF using a single-component anhydrous methanol-based reagent to prevent side reactions with aldehyde or ketone groups in the matrix

(D) Karl Fischer back-titration: excess standard iodine solution is added and the surplus iodine is back-titrated with sodium thiosulfate

Q2. The figure below shows a chromatographic peak with the baseline tangent construction (base width W), the width at half peak height ($W_{1/2}$), and the front half-width at 5% height (f) used for the USP tailing factor.



When W is the peak width at the **base** obtained by tangent extrapolation (as shown), the number of theoretical plates N for the HPLC column is correctly calculated by:

(A) $N = 5.545\left(\frac{t_R}{W}\right)^2$ — coefficient 5.545 applied to the base width W

(B) $N = 16\left(\frac{t_R}{W_{1/2}}\right)^2$ — coefficient 16 applied to the half-height width $W_{1/2}$

(C) $N = 16\left(\frac{t_R}{W}\right)^2$ — coefficient 16 applied to the base width W

(D) $N = \left(\frac{t_R}{W_{1/2}}\right)^2$ — no scaling coefficient applied

Q3. In HPLC method validation, the resolution R_s between two adjacent chromatographic peaks is defined as:

$$R_s = \frac{2(t_{R2} - t_{R1})}{W_1 + W_2}$$

where t_{R1}, t_{R2} are retention times and W_1, W_2 are the corresponding base widths. For the quantitative determination of *closely eluting impurities* in a drug substance, which value of R_s represents **complete baseline separation** as recommended by the USP for related substances methods?

(A) $R_s = 1.0$ — approximately 4% peak overlap; only the minimum detectable separation

(B) $R_s = 1.2$ — partial overlap present; marginal resolution acceptable only for main peak assay without impurity calculation

(C) $R_s = 1.5$ — conventional baseline resolution with $< 0.1\%$ overlap; adequate for most quantitative methods

(D) $R_s = 2.0$ — complete separation with no measurable overlap; USP-recommended criterion for related substances/impurity quantitation

Q4. The capacity factor (retention factor) k' quantifies how much more time an analyte spends in the stationary phase compared to the mobile phase, relative to an unretained compound:

$$k' = \frac{t_R - t_0}{t_0}$$

An analyte elutes at $t_R = 8.5\,\text{min}$; an unretained void-volume marker elutes at $t_0 = 1.7\,\text{min}$. What is k', and does it fall within the generally recommended range for HPLC separations?

(A) $k' = 4.0$; within the acceptable range $1 < k' < 10$ — well retained with practical run time

(B) $k' = 5.0$; outside the acceptable range — the analyte elutes too close to the void, risking interference

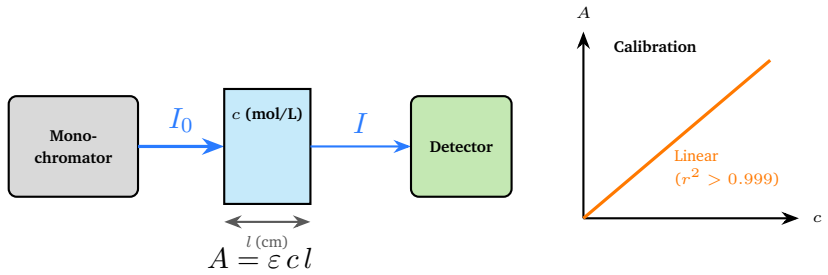
(C) $k' = 4.0$; outside the acceptable range — the acceptable range for HPLC is $0.5 \leq k' \leq 2.0$

(D) $k' = 6.8$; within the acceptable range $1 < k' < 10$ — correctly calculated from the raw data

Q5. The Beer-Lambert law relates absorbance A to concentration c and path length l:

$$A = \varepsilon \cdot c \cdot l = \log\left(\frac{I_0}{I}\right)$$

where ε is the molar absorptivity ($\mathrm{L\,mol^{-1}\,cm^{-1}}$). The figure shows a spectrophotometer cuvette (left) and a linear calibration plot (inset).



A drug solution of molar concentration $c = 2.0 \times 10^{-5}\,\mathrm{mol/L}$ gives an absorbance $A = 0.480$ in a 1 cm cell at 254 nm. What is the molar absorptivity ε?

(A) $\varepsilon = 12\,000\,\mathrm{L\,mol^{-1}\,cm^{-1}}$
(B) $\varepsilon = 24\,000\,\mathrm{L\,mol^{-1}\,cm^{-1}}$
(C) $\varepsilon = 48\,000\,\mathrm{L\,mol^{-1}\,cm^{-1}}$
(D) $\varepsilon = 9\,600\,\mathrm{L\,mol^{-1}\,cm^{-1}}$

Q6. Laser diffraction (e.g., Malvern Mastersizer) measures the angular distribution of scattered light to characterise particle size distributions. The result is reported as a *volume-weighted* distribution, with key percentile parameters: D_{10}, D_{50}, D_{90}, and the volume-weighted mean $D[4,3]$. The **span** of the distribution is calculated as $(D_{90} - D_{10})/D_{50}$. In this context, D_{50} represents:

(A) The volume-weighted mean diameter $D[4,3]$ (De Brouckere mean), equal to the fourth moment divided by the third moment of the volume distribution

(B) The 90th percentile diameter: 90% of the total particle volume lies below this size

(C) The median particle diameter on a volume-weighted basis: 50% of the total particle volume consists of particles *smaller* than this diameter

(D) The surface area–weighted mean diameter $D[3,2]$ (Sauter mean), used primarily for characterising spray droplets and powders for dissolution

Q7. The BET (Brunauer-Emmett-Teller) method measures specific surface area of pharmaceutical powders, granules, and porous materials by nitrogen gas adsorption at 77 K. The BET equation is linearised as:

$$\frac{P}{V(P_0 - P)} = \frac{1}{V_m C} + \frac{(C-1)}{V_m C} \cdot \frac{P}{P_0}$$

A linear plot of $P/[V(P_0 - P)]$ vs. P/P_0 over the range $0.05 \leq P/P_0 \leq 0.35$ yields a slope and intercept. From which primary parameter is the specific surface area (m^2/g) subsequently calculated?

(A) The total pore volume V_p (mL/g) measured at $P/P_0 = 0.99$, representing the maximum amount of nitrogen adsorbed

(B) The BET constant C (dimensionless), which reflects the heat of adsorption of the first nitrogen monolayer relative to the heat of liquefaction

(C) The inflection pressure P/P_0 at which the adsorption isotherm transitions from monolayer to multilayer adsorption

(D) The monolayer volume V_m ($mL_{STP}\,g^{-1}$), derived from the slope and intercept of the BET linear plot, from which $S = V_m N_A a_{N_2}/22414$ is calculated

Q8. DSC-based purity determination (USP general chapter $\langle 891 \rangle$) exploits the effect of dissolved impurities on the melting behaviour of a drug substance. According to the van't Hoff equation applied to fractional

melting:

$$T_{\text{peak}} = T_0 - \frac{\Delta H_f}{R\,T_0^2} \cdot X_{\text{im}}$$

where T_0 is the ideal (pure) melting point, X_{im} is the mole fraction of impurity, and ΔH_f is the molar enthalpy of fusion. What is the **primary** observable change that impurities cause in the DSC melting endotherm of an otherwise pure drug?

(A) Both a depression of the melting onset temperature *and* broadening (widening) of the endothermic peak, both effects increasing in proportion to the mole fraction of impurity

(B) Appearance of a distinct second endothermic peak at a lower temperature, corresponding to the melting of a eutectic mixture of drug and impurity

(C) An exothermic recrystallisation event appearing just before the main melting endotherm, indicating solid-state phase transformation driven by impurity migration

(D) An elevation (increase) of the melting onset temperature caused by lattice energy stabilisation from the impurity occupying crystal defect sites

Q9. Thermogravimetric analysis (TGA) continuously records sample mass as a function of temperature (or time) under a controlled atmosphere. In the TGA thermogram of a drug **monohydrate** ($\text{MW}_{\text{drug}} = 340\,\text{g/mol}$), a mass loss step of approximately 5.0% is observed centred near 100 °C, with the DTG (derivative TGA) peak at 98 °C. This mass loss is MOST consistent with:

(A) Thermal decomposition of a labile functional group (e.g., ester or carbonate linkage) in the drug molecule, occurring at temperatures above the melting point

(B) Loss of water of crystallisation (dehydration), releasing 1 mole of water per mole of monohydrate; expected mass loss $\approx 18/340 \times 100\,\% \approx 5.3\,\%$ at 80–120 °C

(C) Sublimation of the drug API from the solid phase directly to the

vapour phase, typically observed above 150 °C for most crystalline solids

(D) Evaporation of residual granulation solvent (e.g., ethanol or isopropanol) trapped as channel solvate in the crystal lattice

Q10. Several colligative-property and scattering techniques are available for molecular weight determination of pharmaceutical polymers: membrane osmometry, static light scattering, viscometry, and gel permeation chromatography (GPC/SEC). Membrane osmometry measures the osmotic pressure π that develops across a semipermeable membrane (which the solvent permeates but the polymer cannot). Using the van't Hoff relationship $\pi/c = RT/M_n$ for an ideal dilute polymer solution, membrane osmometry is the technique of choice for measuring which molecular weight average?

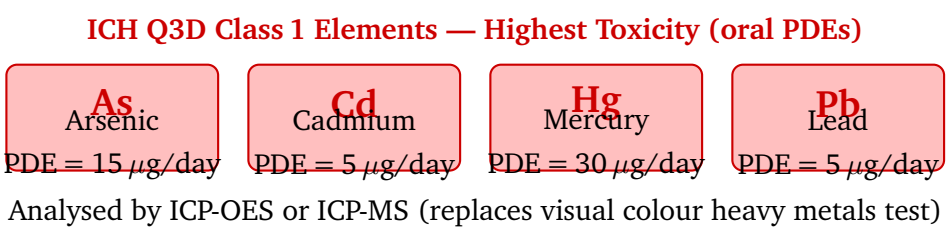
(A) Weight-average molecular weight M_w, because osmotic pressure is proportional to total polymer mass in solution

(B) Z-average molecular weight M_z, the third moment of the molecular weight distribution, measured by sedimentation equilibrium

(C) Number-average molecular weight M_n, because each polymer chain (regardless of size) contributes equally to the colligative osmotic pressure

(D) Viscosity-average molecular weight M_v, because the osmotic pressure at the membrane reflects the hydrodynamic volume of swollen polymer coils

Q11. ICH Q3D classifies elemental impurities (heavy metals) in pharmaceutical products into three classes based on toxicity and natural occurrence. The figure below highlights the four **Class 1** elements (highest toxicity concern) with their oral Permitted Daily Exposures (PDEs).



According to ICH Q3D, which of the following is a **Class 1** elemental impurity with an oral Permitted Daily Exposure (PDE) of **5 μg/day**?

(A) Arsenic (As) — Class 1, oral PDE = 15 μg/day
(B) Mercury (Hg) — Class 1, oral PDE = 30 μg/day
(C) Cobalt (Co) — Class 2A (moderate probability of occurrence in pharmaceutical products)
(D) Lead (Pb) — Class 1, oral PDE = 5 μg/day

Q12. The Total Aerobic Microbial Count (TAMC) is a key microbiological quality attribute tested in pharmaceutical products per USP $\langle 2021 \rangle$ and Ph. Eur. 2.6.12. The choice of growth medium and incubation conditions is strictly defined. Which combination of agar medium and incubation temperature/duration is specified by USP $\langle 2021 \rangle$ for the TAMC test?

(A) Casein soya bean digest agar (CSDA) incubated at 30–35 °C for not less than 5 days
(B) Sabouraud dextrose agar (SDA) incubated at 30–35 °C for not less than 5 days
(C) MacConkey agar incubated at 37 °C for 24–48 hours (selective for Enterobacteriaceae)
(D) R2A agar incubated at 20–25 °C for 7 days (used for pharmaceutical water microbiology, USP $\langle 1231 \rangle$)

Q13. A pH meter requires two-point calibration using primary standard buffers before measuring the pH of an unknown sample. Best practice requires that the measurement pH lies *between* the two calibration buffers. Standard buffers available in the laboratory include: potassium tetroxalate (pH 1.68), potassium hydrogen phthalate (KHP; pH 4.00), phosphate buffer (pH 6.86), and borax (pH 9.18) — all at 25 °C. For measuring a

drug solution at approximately pH 5.5, which combination of standard buffers is MOST appropriate?

(A) Potassium tetroxalate (pH 1.68) and KHP (pH 4.00) — pH 5.5 lies above both standards
(B) KHP (pH 4.00) and phosphate buffer (pH 6.86) — pH 5.5 is bracketed between these two standards, giving optimal two-point calibration
(C) Phosphate buffer (pH 6.86) and borax (pH 9.18) — pH 5.5 lies below both standards
(D) KHP (pH 4.00) and borax (pH 9.18) — the bracketing range of 5 pH units is too wide for accurate interpolation at pH 5.5

Q14. An Ostwald (Ubbelohde) capillary viscometer is used to determine the kinematic viscosity of a pharmaceutical liquid. The instrument is calibrated by measuring the efflux time t of a reference liquid (water, $\nu_{\text{water}} = 0.8931\,\text{mm}^2/\text{s}$ at 25 °C) and calculating the instrument constant C ($\text{mm}^2\,\text{s}^{-2}$). For any test liquid with efflux time t seconds, kinematic viscosity ν is calculated from:

(A) $\nu = \eta/\rho$, where dynamic viscosity η is determined independently using a rotational rheometer and ρ is the density measured by pycnometry
(B) $\nu = \eta \times \rho \times t$, combining all three measured parameters to correct for head pressure and gravitational effects
(C) $\nu = C \times t$, where C is the instrument calibration constant ($\text{mm}^2\,\text{s}^{-2}$) and t is the efflux time (s) measured for the test liquid
(D) $\nu = (t_{\text{sample}}/t_{\text{water}}) \times \nu_{\text{water}}$, normalising efflux time against that of water without requiring an instrument constant

Q15. Dissolution method validation is performed per USP $\langle 1092 \rangle$ and ICH Q2(R1) to demonstrate that the method reliably quantifies drug release from the dosage form. Multiple validation characteristics are assessed, including accuracy, precision, linearity, specificity, and range. In the context of dissolution method validation, **accuracy** is typically assessed by:

(A) Measuring the %RSD of UV absorbance across six replicate injections of the same standard solution to confirm instrument repeatability

(B) Constructing calibration curves at five concentration levels and confirming the correlation coefficient $r^2 > 0.99$ to demonstrate linearity

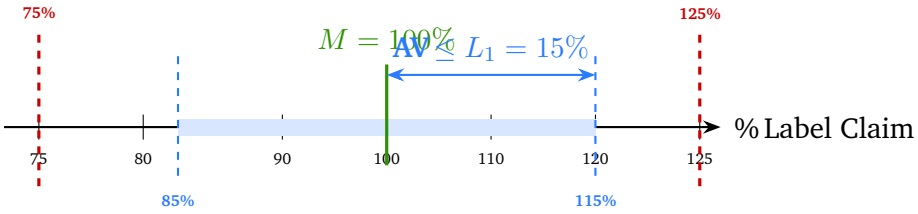
(C) Evaluating dissolution profile changes when pH of the medium, paddle speed, and temperature are varied at $\pm$ limits (robustness/ruggedness)

(D) Adding accurately weighed quantities of drug substance (corresponding to 80%, 100%, and 120% of the dissolution specification) to the dissolution medium and measuring percentage recovery by the HPLC assay method

Q16. USP $\langle 905 \rangle$ (Uniformity of Dosage Units) defines the Acceptance Value (AV) as:

$$\text{AV} = |M - \bar{X}| + ks$$

where M is the reference value (100% for most products), $\bar{X}$ is the sample mean, $k = 2.4$ for $n = 10$ units, and s is the sample standard deviation. The figure below illustrates the AV limits on a % label claim number line.



At **Stage 1** of the USP $\langle 905 \rangle$ content uniformity test ($n = 10$ units), the Acceptance Value (AV) must not exceed:

(A) $L_1 = 15\%$ — the Stage 1 and Stage 2 acceptance limit; pass if AV $\leq 15\%$ and no individual unit is $< 75\%$ or $> 125\%$ of label claim

(B) $L_2 = 25\%$ — the Stage 2 reject limit; only if AV exceeds this value does the batch fail outright

(C) 10% — a tighter internal specification used for immediate-release tablets but not the official USP limit

(D) 5% — the limit applied only to narrow therapeutic index drugs under a company-specific specification

Q17. Dynamic light scattering (DLS) measures particle size of nanoparticles and colloids by analysing fluctuations in scattered light intensity. By default, DLS instruments report an intensity-weighted (z-average) size distribution. Practitioners frequently observe that the intensity-weighted mean diameter is larger than the number-weighted mean diameter for the same sample. Why does the **intensity-weighted** distribution systematically **overestimate** particle size compared to the number-weighted distribution?

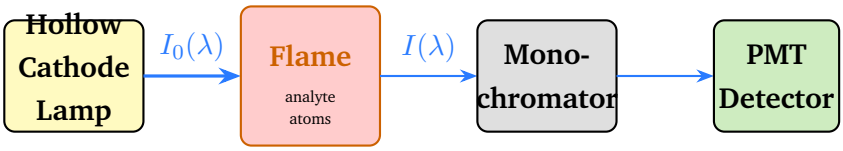
(A) Because larger particles sediment to the bottom of the measurement cuvette more rapidly, generating longer-duration signal bursts that are weighted more heavily in the autocorrelation function

(B) Because scattered light intensity is proportional to the *sixth power* of particle diameter ($I \propto d^6$, Rayleigh regime), so even a trace population of large particles or aggregates contributes disproportionately to the intensity-weighted distribution

(C) Because the Stokes-Einstein equation ($d_H = k_B T / 3\pi\eta D$) is only valid for spherical particles, introducing a systematic positive bias for irregularly shaped particles when converting diffusion coefficient to hydrodynamic diameter

(D) Because the DLS autocorrelation function analysis algorithm assumes a perfectly monomodal size distribution, and any degree of polydispersity forces the cumulants fitting to report an artificially inflated mean diameter

Q18. In atomic absorption spectroscopy (AAS), the sample is atomised in a flame (air-acetylene or nitrous oxide-acetylene) or in a graphite furnace, and the analyte atoms absorb radiation at element-specific resonance wavelengths. The figure below shows the key optical components of a flame AAS instrument.



$A = \log(I_0/I) = \varepsilon\, c\, l$ **(Beer-Lambert)**

In this system, the **primary role** of the hollow cathode lamp (HCL) is to:

(A) Atomise the sample solution by providing a high-temperature plasma (6000–10000 K) that dissociates all chemical bonds in the analyte matrix

(B) Amplify the initial signal from the flame through resonance ionisation, increasing sensitivity by converting neutral analyte atoms to ions

(C) Emit extremely narrow, element-specific spectral emission lines at the resonance wavelength of the analyte element, enabling selective atomic absorption measurement

(D) Provide a broad white-light continuum source so that absorbance can be measured simultaneously across multiple elements without changing the lamp

Q19. An Abbe refractometer measures the critical angle of total internal reflection to determine the refractive index n of a liquid. For aqueous sucrose solutions, the Brix scale (°Bx) is defined as % w/w sucrose. The refractive index of pure water at 20 °C is $n = 1.3330$, and the refractive index increases by approximately 0.00143 per degree Brix at 20 °C. A pharmaceutical sucrose syrup gives a reading of $n = 1.3620$ at 20 °C. What is the approximate sucrose concentration?

(A) Approximately 10.2 % w/w sucrose ($n \approx 1.3476$ at 20 °C)

(B) Approximately 13.7 % w/w sucrose ($n \approx 1.3526$ at 20 °C)

(C) Approximately 16.8 % w/w sucrose ($n \approx 1.3570$ at 20 °C)

(D) Approximately 20.3 % w/w sucrose: $\Delta n = 1.3620 - 1.3330 = 0.0290$; °Bx $= 0.0290/0.00143 \approx 20.3$

Q20. Specific optical rotation $[\alpha]_D^T$ is used to assess chiral purity of pharmaceu-

tical active ingredients (amino acids, steroids, antibiotics). It is defined as:

$$[\alpha]_D^T = \frac{100\,\alpha}{l \times c}$$

where α is the observed rotation (degrees), l is the path length (dm), and c is the concentration (g/100 mL). A solution of a chiral drug ($c = 5.0$ g/100 mL, $l = 2$ dm) shows an observed rotation $\alpha = +5.2^\circ$ at 25 °C, 589 nm (sodium D-line). What is the specific optical rotation $[\alpha]_D^{25}$?

(A) $[\alpha]_D^{25} = +52^\circ$, calculated as $100 \times 5.2/(2 \times 5.0) = 520/10 = +52^\circ$
(B) $[\alpha]_D^{25} = +26^\circ$ (dividing only by path length, omitting the concentration factor in the denominator)
(C) $[\alpha]_D^{25} = +104^\circ$ (multiplying by concentration rather than dividing, giving twice the correct value)
(D) $[\alpha]_D^{25} = +5.2^\circ$ (using the observed rotation directly without applying the specific rotation normalisation formula)

Q21. Cylinder-plate (agar diffusion) bioassay is the classical pharmacopoeial method for determining the biological potency of antibiotics (e.g., erythromycin against *Bacillus subtilis*; polymyxin B against *Staphylococcus aureus*). Potency is expressed in International Units (IU/mg) by comparing inhibition zone diameters against a reference standard. It is sometimes stated that a cylinder-plate bioassay can detect biologically active forms of an antibiotic that HPLC may miss. This is because:

(A) Agar diffusion bioassays are inherently more sensitive than UV detection, capable of quantifying antibiotic concentrations below the HPLC quantitation limit of 0.01 μg/mL
(B) The microbiological inhibition assay responds to *any* chemical species capable of inhibiting microbial growth, including active metabolites, enantiomeric impurities, biosynthetically related analogues, and degradation products with retained activity, regardless of their UV absorption or chromatographic retention characteristics
(C) HPLC mobile phases (e.g., acetonitrile/0.1% TFA) chemically degrade labile antibiotic functional groups before UV detection, whereas

the aqueous agar environment preserves full biological activity throughout the assay

(D) The cylinder-plate method requires no sample preparation, eliminating potential losses during liquid-liquid extraction or solid-phase extraction steps that routinely reduce HPLC recovery to below 80%

Q22. Thin-layer chromatography (TLC) is widely used in pharmaceutical analysis for identity confirmation, purity assessment, and reaction monitoring. The retardation factor R_f is defined as:

$$R_f = \frac{\text{distance travelled by spot}}{\text{distance travelled by solvent front}}$$

In a TLC experiment on silica gel 60 F_{254} plates with a chloroform:methanol (9:1) mobile phase, a compound travels **3.6 cm** from the origin while the solvent front travels **9.0 cm**. What is the R_f value?

(A) $R_f = 0.25$
(B) $R_f = 0.30$
(C) $R_f = 0.40$
(D) $R_f = 0.60$

Q23. Fluorimetry (spectrofluorimetry) measures the intensity of light emitted by a fluorescent analyte at a wavelength longer than the excitation wavelength. Fluorimetry is often described as 100- to 1000-fold more sensitive than UV-Vis absorption spectrophotometry for fluorescent compounds. The **primary** reason for this superior sensitivity is:

(A) Fluorescent compounds inherently possess higher molar absorptivities (ε) than non-fluorescent compounds, generating a larger primary absorbance signal at the same concentration

(B) Excitation monochromators in fluorimeters provide a narrower effective spectral bandwidth (≤ 0.1 nm) than conventional UV-Vis spectrophotometers, substantially reducing stray light contributions to the background signal

(C) Fluorescence emission always occurs in the visible range (400–700 nm),

where photomultiplier tube (PMT) detectors are intrinsically more sensitive than in the UV region used in standard absorbance measurements

(D) The emission detector is positioned at 90° to the excitation beam; fluorescence signal is measured against an essentially dark (near-zero) background rather than as a small decrease in a large transmitted beam, yielding a far superior signal-to-noise ratio

Q24. The USP tailing factor T_f quantifies peak asymmetry in HPLC and is a key system suitability parameter. It is defined as:

$$T_f = \frac{W_{0.05h}}{2\,f}$$

where $W_{0.05h}$ is the total peak width at 5% of peak height, and f is the distance from the peak maximum to the *leading edge* of the peak, both measured at 5% of peak height. A chromatographic peak has $W_{0.05h} = 0.44\,\text{min}$ and $f = 0.18\,\text{min}$. What is T_f, and what does it indicate about peak shape?

(A) $T_f = 1.22$; slight tailing, within the USP system suitability acceptable range ($T_f \leq 2.0$), calculated as $0.44/(2 \times 0.18)$

(B) $T_f = 0.82$; slight fronting (leading peak), indicating adsorption-site overloading or column void formation

(C) $T_f = 2.44$; excessive tailing exceeding the USP acceptable limit of 2.0, leading to system suitability failure

(D) $T_f = 1.54$; moderate tailing, calculated by using $W_{0.05h}/f$ without the factor of 2 in the denominator

Q25. During a UV-Vis stability study of a drug in solution, a series of spectra is recorded at different time points as the drug degrades. As shown in the figure described below, all spectra in the series pass through a single common point (isosbestic point) at one particular wavelength, regardless of the extent of degradation. This observation MOST directly confirms that:

(A) The degradation follows strictly pseudo-first-order kinetics, with a rate constant directly determinable from the change in absorbance at the isosbestic wavelength over time

(B) The molar absorptivity (ε) of the parent drug molecule is independent of temperature, pH, and ionic strength under the experimental conditions, ensuring a stable baseline

(C) The degradation product is UV-transparent (non-absorbing at all wavelengths), and only the parent drug molecule contributes to the measured absorbance at any wavelength

(D) Exactly two absorbing species are present (parent drug and a single degradation product), with no accumulation of any absorbing intermediate; the total absorbance at the isosbestic wavelength remains constant as the mole fraction of parent drug decreases

Detailed Solutions

Q1.

Solution

Concept — Karl Fischer (KF) Water Determination: Both KF methods are based on the Bunsen reaction consuming iodine and water in a 1:1 molar ratio. The key difference is *how* iodine is introduced:

- **Volumetric KF:** iodine is present in a pre-formed reagent solution delivered from a burette. Suitable for samples containing **0.1–100% w/w** water; minimum sample size ≈ 1 mg water.
- **Coulometric KF:** iodine is generated *in situ* at the anode electrochemically ($2\,I^- \rightarrow I_2 + 2e^-$) at a constant current. 1 mole I_2 requires exactly 2 Faradays; the amount generated is determined by integrating the current. Suitable for **0.001–0.1% w/w** water (μg levels).

Step 1 — Identify the moisture level: The sample contains $\approx 0.01\%$ w/w water — within the coulometric range (0.001–0.1%) and below the reliable range of volumetric KF ($> 0.1\%$).

Step 2 — Select the method: Coulometric KF is the only method with sufficient sensitivity for trace moisture determination at the μg level.

Why other options are wrong:

- Option A: Volumetric KF is designed for moisture $> 0.1\%$; at 0.01% the titration volume would be too small to measure accurately.
- Option B: Coulometric KF with electrochemical iodine generation is correct for trace moisture. **Correct.**
- Option C: Single-component anhydrous reagents address ketone/aldehyde side reactions but do not address the sensitivity limitation; the method is still volumetric.
- Option D: Back-titration adds excess iodine then back-titrates; this is a volumetric approach and suffers the same sensitivity limitation as A.

Final Answer: Trace moisture (0.01%) requires coulometric KF $\Rightarrow$ B

Answer: (B) Go Back to Q1

Q2.

Solution

Concept — Number of Theoretical Plates: For a Gaussian peak, the column efficiency N can be calculated from two equivalent expressions, depending on where the width is measured:

$N = 16\left(\frac{t_R}{W}\right)^2$ (base width by tangent) OR $N = 5.545\left(\frac{t_R}{W_{1/2}}\right)^2$ (width at half heigh

Step 1 — Identify which width is used: The question specifies W = peak width at the **base** by tangent extrapolation. The correct formula uses the coefficient **16** with W.

Step 2 — Cross-check the coefficient: For a Gaussian peak: $W = 4\sigma$ and $W_{1/2} = 2.355\sigma$. Substituting $W = 4\sigma$: $N = (t_R/\sigma)^2 = (t_R/(W/4))^2 = 16(t_R/W)^2$. Substituting $W_{1/2} = 2.355\sigma$: $N = (t_R/\sigma)^2 = (2.355\,t_R/W_{1/2})^2 = 5.545(t_R/W_{1/2})^2$. **The coefficients 16 and 5.545 are not interchangeable.**

Why other options are wrong:

- Option A: Uses coefficient 5.545 with W (base width) — wrong coefficient for base width formula.
- Option B: Uses coefficient 16 with $W_{1/2}$ (half-height width) — the 16 coefficient applies only to the base width W, not $W_{1/2}$.
- Option C: $N = 16(t_R/W)^2$ — correct coefficient with correct width. **Correct.**
- Option D: Missing the scaling coefficient entirely; the formula $N = (t_R/W_{1/2})^2$ gives $N/5.545$, grossly underestimating efficiency.

Final Answer: W at base requires coefficient 16 $\Rightarrow N = 16(t_R/W)^2 \Rightarrow$ C

Answer: (C) Go Back to Q2

Q3.

Solution

Concept — Resolution and Peak Separation: Resolution R_s between two peaks quantifies the degree of physical separation. Key threshold values for symmetric Gaussian peaks:

- $R_s = 1.0$: $\approx 4\%$ peak overlap; peaks are partially merged.
- $R_s = 1.5$: $\approx 0.1\%$ overlap; "baseline resolution" by classical definition; adequate for most quantitative methods with correction.

- $R_s = 2.0$: essentially complete separation ($< 0.01\%$ overlap); USP recommendation for related substances/impurity methods where even trace impurities must be quantified without interference.

Step 1 — Identify the USP requirement for impurity methods: For closely eluting impurities that must be quantified (e.g., process impurities, degradants), the USP specifically recommends $R_s \geq 2.0$ to ensure that the impurity peak is fully resolved and its area accurately integrated without contribution from the main peak tail.

Why other options are wrong:

- Option A: $R_s = 1.0$ is the *minimum detectable* resolution, not suitable for quantitative impurity measurement.
- Option B: $R_s = 1.2$ still has significant overlap; adequate only for main peak assay where impurities are not separately quantified.
- Option C: $R_s = 1.5$ is baseline resolution but the USP requirement for *related substances methods* is the stricter $R_s \geq 2.0$.
- Option D: $R_s = 2.0$ is the USP criterion for complete separation in related substances methods. **Correct.**

Final Answer: $R_s = 2.0 \Rightarrow$ complete separation for impurity quantitation $\Rightarrow$ D

Answer: (D) Go Back to Q3

Q4.

Solution

Concept — Capacity Factor (Retention Factor) k': k' measures the relative amount of time the analyte spends in the stationary phase versus the mobile phase. $k' = 0$: unretained (elutes with void). Acceptable range: $1 < k' < 10$; optimal $2 \leq k' \leq 8$. $k' < 1$: poor resolution (near void); $k' > 10$: excessively long run time.

Step 1 — Calculate k':

$$k' = \frac{t_R - t_0}{t_0} = \frac{8.5 - 1.7}{1.7} = \frac{6.8}{1.7} = 4.0$$

Step 2 — Check the range: $k' = 4.0$ lies within the acceptable range $1 < k' < 10$. The analyte is well retained (4 times the void time) and the run time is practical (8.5 min).

Why other options are wrong:

- Option A: $k' = 4.0$, within range 1–10. **Correct.**
- Option B: $k' = 5.0$ is the wrong calculation; $6.8/1.7 = 4.0$, not 5.0. Also, 5.0 would still be within range, making the description wrong.
- Option C: $k' = 4.0$ is the correct value, but the stated acceptable range of $0.5 \leq k' \leq 2.0$ is incorrect; the HPLC acceptable range is $1 < k' < 10$.
- Option D: $k' = 6.8$ is incorrect; k' is calculated as $(t_R - t_0)/t_0 = 6.8/1.7 = 4.0$, not 6.8.

Final Answer: $k' = 6.8/1.7 = 4.0$; within acceptable range 1–10 $\Rightarrow$ A

Answer: (A) Go Back to Q4

Q5.

Solution

Concept — Beer-Lambert Law and Molar Absorptivity: $A = \varepsilon \cdot c \cdot l$. Rearranging: $\varepsilon = A/(c \cdot l)$. ε (L mol^{-1} cm^{-1}) is an intrinsic molecular property at a given wavelength; it is independent of concentration and path length.

Step 1 — Substitute the given values:

$$\varepsilon = \frac{A}{c \times l} = \frac{0.480}{2.0 \times 10^{-5}\,\text{mol/L} \times 1\,\text{cm}} = \frac{0.480}{2.0 \times 10^{-5}} = 24\,000\,\text{L mol}^{-1}\text{cm}^{-1}$$

Step 2 — Verify the linear range: $A = 0.480$ is within the Beer-Lambert linear range ($A = 0.1$–1.0), confirming that the concentration is in the linear zone of the calibration curve.

Why other options are wrong:

- Option A: 12 000 $= 0.480/(4.0 \times 10^{-5})$ — uses twice the stated concentration; computational error.
- Option B: 24 000 $= 0.480/(2.0 \times 10^{-5})$ — correct calculation. **Correct.**
- Option C: 48 000 $= 0.480/(1.0 \times 10^{-5})$ — uses half the stated concentration; computational error.
- Option D: 9 600 — would require $c = 0.480/9600 = 5.0 \times 10^{-5}$ mol/L, not the given 2.0×10^{-5} mol/L.

Final Answer: $\varepsilon = 0.480/(2.0 \times 10^{-5}) = 24\,000\,\text{L mol}^{-1}\,\text{cm}^{-1} \Rightarrow$ B

Answer: (B) Go Back to Q5

Q6.

Solution

Concept — Laser Diffraction Percentile Diameters: In laser diffraction (volume-weighted) particle size analysis:

- D_{50} = **median** on the cumulative volume distribution: 50% of the *total volume* of particles lies below this diameter.
- D_{10} = 10th percentile volume; D_{90} = 90th percentile volume.
- $D[4,3]$ (De Brouckere mean) = volume-weighted mean; different from D_{50} unless the distribution is symmetric.
- $D[3,2]$ (Sauter mean diameter, SMD) = surface area–volume mean; $D[3,2] = 6/(\rho \cdot S_{BET})$ for non-porous spheres.

Step 1 — Distinguish D_{50} from $D[4,3]$: D_{50} is a *percentile* (median), not a *mean*. It equals the diameter at which the cumulative volume distribution curve crosses 50%. $D[4,3]$ is the volume-weighted mean and will exceed D_{50} for positively skewed (right-tailed) distributions.

Why other options are wrong:

- Option A: Describes $D[4,3]$, not D_{50}.
- Option B: Describes D_{90} (90th percentile), not the 50th.
- Option C: D_{50} is the volume-weighted median: 50% of total volume consists of particles smaller than D_{50}. **Correct.**
- Option D: Describes $D[3,2]$ (Sauter mean), not D_{50}.

Final Answer: D_{50} is the volume-weighted median particle diameter $\Rightarrow$ C

Answer: (C) Go Back to Q6

Q7.

Solution

Concept — BET Specific Surface Area Calculation: The BET linear plot (slope $= (C-1)/(V_m C)$; intercept $= 1/(V_m C)$) allows determination of V_m (monolayer volume at STP per gram of solid). The specific surface area is then:

$$S_a = \frac{V_m \times N_A \times a_{N_2}}{22\,414}$$

where $N_A = 6.022 \times 10^{23}\,\text{mol}^{-1}$, $a_{N_2} = 0.162\,\text{nm}^2$ (cross-sectional area of one N_2 molecule at 77 K), and 22 414 mL/mol is the molar volume of an ideal gas at STP.

Step 1 — Extract V_m from the BET plot: From slope (m) and intercept (b): $V_m = 1/(m+b)$; $C = (m/b) + 1$. Only V_m (not C) enters the surface area formula directly.

Why other options are wrong:

- Option A: Total pore volume V_p at $P/P_0 = 0.99$ characterises mesopore volume but is not used to calculate specific surface area.
- Option B: BET constant C reflects the heat of adsorption; it is a secondary parameter that does not appear in the surface area formula.
- Option C: The inflection pressure is a qualitative feature of the isotherm shape but is not a measured quantity used in the BET equation.
- Option D: V_m (monolayer volume) is derived from the BET linear plot and is the primary parameter from which S_a is calculated. **Correct.**

Final Answer: Specific surface area is calculated from V_m obtained via the BET linear plot $\Rightarrow$ D

Answer: (D) Go Back to Q7

Q8.

Solution

Concept — Van't Hoff Freezing-Point Depression Applied to DSC Purity: In DSC-based purity analysis (USP ⟨891⟩), the drug acts as the solvent and the impurity as the solute. The van't Hoff equation predicts:

$$T_{\text{peak}} = T_0 - \frac{\Delta H_f}{R T_0^2} \cdot X_{\text{im}} \qquad \Rightarrow \qquad \Delta T_{\text{depression}} \propto X_{\text{im}}$$

Additionally, impurities broaden the melting peak because the eutectic behaviour causes the drug to melt over a temperature range (not a sharp point), with the lowest-melting eutectic fraction melting first and the purer fraction melting last. Both effects increase with impurity concentration.

Step 1 — Identify the two observable changes: (1) **Onset temperature depressed** below the pure drug melting point. (2) **Peak width increased** (broader endotherm) due to progressive melting over a range rather than a sharp transition.

Step 2 — Confirm the fractional melting analysis: Purity is determined from the slope of a $1/F$ vs. T_m plot, where F is the fraction melted at temperature T_m. This exploits the broadening to extract X_{im} quantitatively.

Why other options are wrong:

- Option A: Depression and broadening of the melting endotherm. **Correct.**
- Option B: A distinct second peak would indicate a separate eutectic melt; DSC purity analysis applies only to high-purity drugs ($> 98.5\%$) where no separate eutectic peak is visible.
- Option C: An exothermic event before melting would indicate recrystallisation; this is unrelated to impurity-induced depression.
- Option D: Impurities lower (depress) the melting point, never raise it; lattice energy stabilisation is not an impurity effect.

Final Answer: Impurities depress onset temperature and broaden the melting endotherm $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q8

Q9.

Solution

Concept — TGA Events and Temperature Ranges:

- Dehydration of hydrate: 50–150 °C; gradual, broad mass loss; mass loss $\approx 18n/M_{\text{drug}} \times 100\%$ where n = number of water molecules per formula unit.
- Residual solvent loss: 50–120 °C (overlapping with dehydration but characteristic of the solvent boiling point).
- Decomposition: sharp, abrupt loss $\geq$ 200 °C.

Step 1 — Calculate the expected mass loss for a monohydrate: MW of water = 18 g/mol; MW of drug = 340 g/mol.

$$\%\,\text{mass loss} = \frac{18}{340+18} \times 100 = \frac{18}{358} \times 100 \approx 5.03\,\%$$

The observed 5.0% loss at $\approx$100 °C matches dehydration of a monohydrate exactly.

Step 2 — Confirm temperature range: 100 °C is well within the dehydration range (50–150 °C) and far below typical decomposition temperatures (> 200 °C).

Why other options are wrong:

- Option A: Thermal decomposition occurs at > 200 °C, not at 100 °C.
- Option B: Loss of water of crystallisation; 5.0% loss at 100 °C matches monohydrate dehydration quantitatively. **Correct.**

- Option C: Sublimation occurs at much higher temperatures for most crystalline drugs.
- Option D: Residual organic solvents would give a smaller, often sharper peak at the solvent boiling point; 5.0% is too large for typical residual solvent levels ($\leq 0.5\%$, ICH Q3C).

Final Answer: 5.0% mass loss at 100 °C = monohydrate dehydration $\Rightarrow$ B

Answer: (B) Go Back to Q9

Q10.

Solution

Concept — Molecular Weight Averages and Measurement Techniques:

- M_n (number-average MW): each chain counted once; measured by colligative methods (osmometry, ebulliometry, cryoscopy).
- M_w (weight-average MW): each chain weighted by its mass; measured by static light scattering.
- M_z (Z-average MW): sensitive to highest MW chains; measured by sedimentation equilibrium ultracentrifugation.
- M_v (viscosity-average MW): determined by viscometry via Mark-Houwink equation.

Step 1 — Apply the van't Hoff equation: For ideal dilute solution: $\pi = cRT/M_n$. Rearranged: $\pi/c = RT/M_n$. In osmometry, each polymer chain (regardless of its MW) contributes one molecule of osmotic pressure. A long chain and a short chain each contribute equally to the osmotic pressure, hence the result is M_n (number-average).

Step 2 — Confirm the applicable MW range: Membrane osmometry is reliable for polymers of MW 10 000–1 000 000 Da; small molecules ($< 5\,000$ Da) diffuse through the membrane and give erroneous results.

Why other options are wrong:

- Option A: M_w is measured by static light scattering (scattered intensity $\propto M_w$), not by osmometry.
- Option B: M_z is measured by sedimentation equilibrium.
- Option C: Membrane osmometry gives M_n because osmotic pressure is a colligative (number-dependent) property. **Correct.**
- Option D: M_v is obtained from intrinsic viscosity via the Mark-Houwink equation; it is not measured by osmometry.

Final Answer: Osmometry is a colligative method $\Rightarrow$ measures M_n $\Rightarrow$ C

Answer: (C) Go Back to Q10

Q11.

Solution

Concept — ICH Q3D Elemental Impurity Classification: ICH Q3D classifies elemental impurities by their toxicity and natural occurrence in drug substances and excipients:

- **Class 1:** Highest toxicity; require control in all products. Members: As (PDE_{oral} 15 μg/day), Cd (5 μg/day), Hg (30 μg/day), Pb (5 μg/day).
- **Class 2A:** High probability of occurrence (Co, Ni, V).
- **Class 2B:** Low probability, but high toxicity if present (Pd, Pt, Ir, Os, Rh, Ru, Ag, Au, Se, Tl).
- **Class 3:** Low oral toxicity (Ba, Cr, Cu, Li, Mo, Sb, Sn).

Step 1 — Identify Class 1 elements with oral PDE of 5 μg/day: Both Cd (cadmium) and Pb (lead) have oral PDE = 5 μg/day. The question options include Pb (option D) but not Cd.

Step 2 — Eliminate distractors: As (option A): Class 1 but PDE = 15 μg/day (not 5). Hg (option B): Class 1 but PDE = 30 μg/day (not 5). Co (option C): Class 2A (not Class 1).

Why other options are wrong:

- Option A: Arsenic is Class 1 but PDE = 15 μg/day, not 5.
- Option B: Mercury is Class 1 but PDE = 30 μg/day, not 5.
- Option C: Cobalt is Class 2A (not Class 1).
- Option D: Lead (Pb), Class 1, oral PDE = 5 μg/day. **Correct.**

Final Answer: Pb (Lead) is Class 1 with oral PDE = 5 μg/day $\Rightarrow$ D

Answer: (D) Go Back to Q11

Q12.

Solution

Concept — USP ⟨2021⟩ TAMC and TYMC Test Conditions: USP ⟨2021⟩ (Microbial Examination of Non-Sterile Products) specifies the following incubation conditions:

- **TAMC** (Total Aerobic Microbial Count): **Casein soya bean digest agar (CSDA)**; incubation at **30–35 °C** for ≥ 5 **days**.
- **TYMC** (Total Yeasts and Moulds Count): Sabouraud dextrose agar (SDA) with antibiotics (chloramphenicol, gentamicin); incubation at **20–25 °C** for ≥ 5 **days**.

Step 1 — Match medium to count type: CSDA (also called TSA: Tryptic Soy Agar) supports growth of aerobic bacteria. SDA supports growth of yeasts and moulds (fungi).

Step 2 — Match temperature to count type: Aerobic bacteria: 30–35 °C (optimal for mesophilic bacteria). Fungi: 20–25 °C (optimal for most pharmaceutical-relevant moulds).

Why other options are wrong:

- Option A: CSDA at 30–35 °C for ≥5 days — TAMC conditions. **Correct.**
- Option B: SDA at 30–35 °C is incorrect; SDA is for TYMC and is incubated at 20–25 °C (not 30–35 °C).
- Option C: MacConkey agar at 37 °C is used for Enterobacteriaceae/E. coli detection (a specific pathogen test), not for the general TAMC.
- Option D: R2A agar at 20–25 °C for 7 days is specified for pharmaceutical water testing (USP ⟨1231⟩), not for product TAMC.

Final Answer: TAMC uses CSDA at 30–35 °C for ≥ 5 days $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q12

Q13.

Solution

Concept — Two-Point pH Meter Calibration: For accurate pH measurement, the two calibration buffers must *bracket* the expected measurement pH. The calibration establishes the slope (mV/pH, ideally 95–105% of the Nernst factor 59.16 mV/pH at 25 °C) and the zero-point offset.

Step 1 — Identify the measurement pH: Target measurement pH ≈ 5.5.

Step 2 — Select bracketing buffers:

- KHP pH 4.00: below 5.5 ✓
- Phosphate pH 6.86: above 5.5 ✓
- Measurement pH 5.5 lies *between* pH 4.00 and pH 6.86: optimal two-point calibration.

A pH 1.68 / pH 4.00 pair would both be below 5.5 (not bracketing). A pH 6.86 / pH 9.18 pair would both be above 5.5 (not bracketing). A pH 4.00 / pH 9.18 pair brackets 5.5 but the 5 pH-unit span reduces interpolation accuracy.

Why other options are wrong:

- Option A: Both pH 1.68 and pH 4.00 lie below the target pH 5.5; the measurement pH is not bracketed.
- Option B: pH 4.00 and pH 6.86 bracket pH 5.5. **Correct.**
- Option C: Both pH 6.86 and pH 9.18 lie above the target pH 5.5; the measurement pH is not bracketed.
- Option D: pH 4.00 and pH 9.18 do bracket pH 5.5 but the wide 5 pH-unit span is not optimal; accuracy is reduced compared to the narrower pH 4.00–6.86 bracket.

Final Answer: pH 4.00 and pH 6.86 bracket measurement pH 5.5 optimally $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q13

Q14.

Solution

Concept — Kinematic Viscosity by Ostwald (Ubbelohde) Viscometer: The Ostwald viscometer relies on Poiseuille's law: flow through a capillary is driven by the hydrostatic head of liquid. For a given viscometer, the kinematic viscosity is directly proportional to the efflux time:

$$\nu = C \times t$$

where C ($\text{mm}^2\,\text{s}^{-2}$) is the *instrument calibration constant* determined by measuring t_{water} and using the known $\nu_{\text{water}} = 0.8931\,\text{mm}^2/\text{s}$ at 25 °C: $C = \nu_{\text{water}}/t_{\text{water}}$. Dynamic viscosity $\eta = \nu \times \rho$ requires a separate density measurement.

Step 1 — Identify the correct formula: $\nu = C \times t$: kinematic viscosity obtained directly from efflux time and instrument constant. No density measurement is needed for ν.

Why other options are wrong:

- Option A: η/ρ gives ν from dynamic viscosity and density; this is a definition, not the Ostwald viscometer operating equation. Also, η would require a rotational rheometer.
- Option B: $\nu = \eta \times \rho \times t$ has no physical basis; multiplying by density gives a quantity with incorrect units.
- Option C: $\nu = C \times t$ is the correct Ostwald operating equation. **Correct.**
- Option D: $\nu = (t_{\text{sample}}/t_{\text{water}}) \times \nu_{\text{water}}$ is mathematically equivalent to option C (since $C = \nu_{\text{water}}/t_{\text{water}}$), but $C \times t$ is the standard stated formula in pharmacopoeia viscometry. Option D omits the instrument constant concept; the ratio shortcut is implicit in calibration, not the primary formula.

Final Answer: $\nu = C \times t$ (instrument constant $\times$ efflux time) $\Rightarrow$ C

Answer: (C) Go Back to Q14

Q15.

Solution

Concept — Dissolution Method Validation Characteristics (USP ⟨1092⟩ / ICH Q2(R1)):

- **Accuracy:** Closeness of measured value to true value. In dissolution: spike known drug amounts into medium at 80%, 100%, 120% of specification ⇒ measure by HPLC ⇒ % recovery should be 98–102%.
- **Precision (repeatability):** %RSD of replicate runs of same sample.
- **Linearity:** Calibration curve correlation coefficient r^2.
- **Robustness:** Effect of deliberate variation in method parameters.

Step 1 — Identify the accuracy test: Accuracy requires a "known amount added" experiment (standard addition or spiking). Adding accurately weighed drug (80%, 100%, 120% of specification) to dissolution medium and measuring recovery directly tests whether the overall method (dissolution conditions + HPLC quantitation) accurately recovers the expected amount.

Why other options are wrong:

- Option A: Replicate injections of the same standard measure *precision* (instrument repeatability), not accuracy.
- Option B: Calibration curve linearity test demonstrates *linearity*, not accuracy.
- Option C: Varying pH, paddle speed, temperature tests *robustness*, not accuracy.
- Option D: Spiking known drug amounts and measuring recovery tests accuracy of the dissolution method. **Correct.**

Final Answer: Accuracy assessed by spiking 80%, 100%, 120% drug and measuring recovery ⇒ $\boxed{\text{D}}$

Answer: (D) Go Back to Q15

Q16.

Solution

Concept — USP $\langle 905 \rangle$ Uniformity of Dosage Units: The Acceptance Value (AV) integrates both the mean deviation from target and the unit-to-unit variability:

$$\text{AV} = |M - \bar{X}| + ks$$

Stage 1: $n = 10$ units, $k = 2.4$. Stage 2: $n = 30$ units total (original 10 + 20 additional), $k = 2.0$. **Acceptance criteria for both stages:**

- AV $\leq L_1 = 15\%$: **pass** at Stage 1 or Stage 2 provided no individual unit is outside 75–125%.
- AV $> L_2 = 25\%$: **fail**; no further testing.
- $L_1 <$ AV $\leq L_2$: at Stage 1 $\Rightarrow$ proceed to Stage 2; at Stage 2 $\Rightarrow$ fail.

Step 1 — Identify the Stage 1 limit: At Stage 1 ($n = 10$), the batch passes content uniformity if AV $\leq L_1 = 15\%$.

Why other options are wrong:

- Option A: AV $\leq 15\%$ is the USP $\langle 905 \rangle$ Stage 1 acceptance limit. **Correct.**
- Option B: AV $> 25\%$ (L_2) is the outright *reject* criterion, not the Stage 1 pass criterion.
- Option C: 10% is not a USP $\langle 905 \rangle$ official limit; it may be an internal company specification.
- Option D: 5% is not defined as a USP $\langle 905 \rangle$ limit for any product category.

Final Answer: Stage 1 AV must not exceed $L_1 = 15\% \Rightarrow \boxed{\text{A}}$

Answer: (A) Go Back to Q16

Q17.

Solution

Concept — DLS Intensity Weighting and Rayleigh Scattering: In the Rayleigh scattering regime (particle diameter $d \ll \lambda$), the intensity of scattered light per particle is proportional to d^6:

$$I_{\text{scattered}} \propto d^6$$

This means a 100 nm particle scatters 10^6 times more light than a 10 nm particle (same number of particles). Consequently, even trace amounts of large particles (or aggregates) dominate the intensity-weighted distribution, shifting the reported

z-average diameter upward significantly.

Step 1 — Quantify the bias: Consider 1000 particles of 10 nm and 1 particle of 100 nm:

- Number-weighted mean ≈ 10 nm (1000 small : 1 large).
- Intensity contribution of 100 nm particle $= 1 \times 100^6 = 10^{12}$.
- Intensity contribution of 10 nm particles $= 1000 \times 10^6 = 10^9$.
- Intensity-weighted mean is dominated by the single large particle.

This d^6 dependence explains the systematic overestimation in intensity-weighted distributions.

Why other options are wrong:

- Option A: Particles in DLS do not sediment noticeably during the short measurement time (milliseconds); size is measured from Brownian motion, not sedimentation.
- Option B: $I \propto d^6$ (Rayleigh) causes intensity bias. **Correct.**
- Option C: The Stokes-Einstein equation relates diffusion coefficient to hydrodynamic diameter; it introduces spherical assumption error but does not explain the systematic overestimation direction.
- Option D: The cumulants analysis does assume near-monomodal distributions, but the systematic overestimation is caused by d^6 weighting, not the fitting algorithm per se.

Final Answer: Intensity $\propto d^6$ causes large particles to dominate the intensity distribution $\Rightarrow$ B

Answer: (B) Go Back to Q17

Q18.

Solution

Concept — Hollow Cathode Lamp in Atomic Absorption Spectroscopy: The HCL contains a cylindrical cathode made of the element being determined (e.g., copper for Cu, lead for Pb) inside a glass envelope filled with an inert gas (Ne or Ar) at low pressure. An electrical discharge causes the fill gas to sputter the cathode material; the sputtered atoms are excited and emit their characteristic resonance emission lines — extremely narrow spectral lines ($\Delta\lambda \approx 0.001$ nm).

These narrow lines exactly match the absorption wavelengths of the same element in the flame, enabling *element-selective* atomic absorption measurement according

to Beer-Lambert law.

Step 1 — Role of HCL: The HCL serves as a *primary radiation source* that emits the analyte element's own resonance wavelengths with extremely high spectral purity. This is fundamentally different from continuum sources used in UV-Vis, and it is what makes AAS inherently element-selective without needing an exceptionally high-resolution monochromator.

Why other options are wrong:

- Option A: Atomisation is performed by the flame or graphite furnace, not by the HCL. The HCL operates at low voltage (5–20 mA), not at plasma temperatures.
- Option B: Resonance ionisation amplification is not a mechanism in flame AAS; the HCL emits, not amplifies.
- Option C: The HCL emits narrow, element-specific resonance lines enabling selective atomic absorption. **Correct.**
- Option D: A continuum source would require a very high-resolution echelle spectrometer for AAS; the HCL provides a line source for single-element AAS without that requirement.

Final Answer: HCL emits element-specific narrow resonance lines for selective atomic absorption $\Rightarrow$ C

Answer: (C) Go Back to Q18

Q19.

Solution

Concept — Refractive Index and Brix Scale: The Brix scale (°Bx) is defined as % w/w sucrose in aqueous solution. The refractive index increases linearly with sucrose concentration near ambient temperatures:

$$\Delta n = n_{\text{solution}} - n_{\text{water}} \quad ; \quad {}^{\circ}\text{Bx} = \frac{\Delta n}{0.00143}$$

(approximately, at 20 °C; more precise tables exist in ICUMSA).

Step 1 — Calculate Δn:

$$\Delta n = 1.3620 - 1.3330 = 0.0290$$

Step 2 — Convert to Brix:

$$^{\circ}\text{Bx} = \frac{0.0290}{0.00143} \approx 20.3$$

Therefore the syrup contains approximately 20.3% w/w sucrose.

Step 3 — Check other options:

- 10 %: $n = 1.3330 + 10 \times 0.00143 = 1.3473$ — not 1.3620.
- 13.7 %: $n = 1.3330 + 13.7 \times 0.00143 = 1.3526$ — not 1.3620.
- 16.8 %: $n = 1.3330 + 16.8 \times 0.00143 = 1.3570$ — not 1.3620.
- 20.3 %: $n = 1.3330 + 20.3 \times 0.00143 = 1.3620$ — matches!

Why other options are wrong:

- Options A, B, C: Each corresponds to a refractive index lower than the measured 1.3620; they underestimate the sucrose concentration.
- Option D: $^{\circ}\text{Bx} = 0.0290/0.00143 \approx 20.3\%$. **Correct.**

Final Answer: $\Delta n = 0.0290$; $^{\circ}\text{Bx} \approx 20.3\%$ w/w sucrose $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q19

Q20.

Solution

Concept — Specific Optical Rotation Formula:

$$[\alpha]_D^T = \frac{100\,\alpha}{l \times c}$$

where α = observed rotation (degrees); l = path length (dm); c = concentration (g/100 mL). This formula normalises the rotation to a standard path length of 1 dm and concentration of 1 g/100 mL.

Step 1 — Substitute values: $\alpha = +5.2^{\circ}$; $l = 2$ dm; $c = 5.0$ g/100 mL.

$$[\alpha]_D^{25} = \frac{100 \times 5.2}{2 \times 5.0} = \frac{520}{10} = +52^{\circ}$$

Step 2 — Interpret the result: A specific rotation of $+52^{\circ}$ means the compound rotates plane-polarised light dextrarotatorily (clockwise), with this value being a characteristic physical constant used for identity and chiral purity assessment.

Why other options are wrong:

- Option A: $+52^\circ$ from $100 \times 5.2/(2 \times 5.0)$. **Correct.**
- Option B: $+26^\circ$ results from $\alpha/(l \times c) = 5.2/(2 \times 5.0)$ — omitting the factor of 100 in the numerator.
- Option C: $+104^\circ$ results from $100 \times 5.2 \times c/l$ — multiplying rather than dividing by concentration.
- Option D: $+5.2^\circ$ is the raw observed rotation α, not the specific rotation; no normalisation applied.

Final Answer: $[\alpha]_D^{25} = 100 \times 5.2/(2 \times 5.0) = +52^\circ \Rightarrow \boxed{\text{A}}$

Answer: (A) Go Back to Q20

Q21.

Solution

Concept — Cylinder-Plate Bioassay vs. HPLC for Antibiotic Potency: The cylinder-plate (agar diffusion) bioassay measures *biological potency* — the total ability of a sample to inhibit microbial growth. HPLC measures *chemical concentration* of a specific molecular species based on its chromatographic and spectroscopic properties.

Step 1 — Identify the fundamental difference: Bioassay: any chemical entity that inhibits the test organism contributes to the measured zone of inhibition. This includes:

- The parent antibiotic in all its active forms.
- Active metabolites with the same mechanism of action.
- Biosynthetically related congeners (e.g., aminoglycoside mixtures).
- Degradation products that retain partial antimicrobial activity.

HPLC: measures only species that (1) elute at the expected retention time and (2) absorb at the detection wavelength. Structurally different but biologically active species with different chromatographic behaviour will be missed or quantified under separate peaks.

Step 2 — Apply to quality control significance: If a portion of the antibiotic converts to a structurally different but equally active form during storage, HPLC would underestimate total potency while the bioassay would give the correct biological activity value. This is the pharmacopoeial rationale for retaining bioassay as the primary potency standard for certain antibiotics.

Why other options are wrong:

- Option A: Sensitivity is not the differentiating advantage; HPLC can be more sensitive analytically for specific chemical species.
- Option B: Bioassay responds to all biologically active species, including those invisible to HPLC. **Correct.**
- Option C: Organic HPLC mobile phases at standard concentrations do not chemically degrade antibiotics on the timescale of an analysis.
- Option D: HPLC sample preparation is routine for antibiotics and achieves recoveries $> 95\%$; this is not the main advantage of the bioassay.

Final Answer: Bioassay detects all biologically active species regardless of chemical structure or chromatographic character $\Rightarrow$ B

Answer: (B) Go Back to Q21

Q22.

Solution

Concept — TLC Retardation Factor R_f:

$$R_f = \frac{\text{distance of spot migration from origin}}{\text{distance of solvent front from origin}}$$

R_f ranges from 0 (spot at origin, unretained by mobile phase) to 1 (spot at solvent front, no retention on stationary phase). Optimal R_f for quantitative TLC: 0.3–0.7.

Step 1 — Substitute values: Spot travels 3.6 cm; solvent front travels 9.0 cm.

$$R_f = \frac{3.6}{9.0} = 0.40$$

Step 2 — Verify reasonableness: $R_f = 0.40$ lies within the optimal range (0.3–0.7); good separation from the origin and from the solvent front, suitable for identity confirmation and impurity quantitation.

Why other options are wrong:

- Option A: $R_f = 0.25 = 2.25/9.0$ — would require spot at 2.25 cm; not consistent with the given 3.6 cm.
- Option B: $R_f = 0.30 = 2.7/9.0$ — spot at 2.7 cm, not 3.6 cm.
- Option C: $R_f = 0.40 = 3.6/9.0$. **Correct.**
- Option D: $R_f = 0.60 = 5.4/9.0$ — spot at 5.4 cm, not 3.6 cm.

Final Answer: $R_f = 3.6/9.0 = 0.40 \Rightarrow$ C

Answer: (C) Go Back to Q22

Q23.

Solution

Concept — Why Fluorimetry is More Sensitive than UV-Vis Absorbance: In UV-Vis spectrophotometry, the detector measures a *small decrease* in a large transmitted beam ($I_0 - I$). Even with 99.9% light reaching the detector (absorbance = 0.0004), the signal is measured against a large I_0 background. Small fluctuations in I_0 (source flicker noise) limit the detection limit.

In fluorimetry, the emission detector is positioned at **90**° to the excitation beam. No excitation photons reach the emission detector directly. The fluorescence signal is measured against a near-zero dark background. Signal-to-noise ratio (SNR):

$$\text{SNR}_{\text{fluorimetry}} \approx \frac{\Phi\,\varepsilon\,c\,l\,I_0}{B} \gg \text{SNR}_{\text{UV-Vis}}$$

where B is the (very low) background at the emission detector. This dark-field measurement strategy gives fluorimetry 100–1000-fold higher sensitivity than UV-Vis for the same compound at the same concentration.

Why other options are wrong:

- Option A: Molar absorptivity ε of fluorescent compounds is not always higher; quinine ($\varepsilon \approx 10\,000$) has lower ε than many non-fluorescent compounds.
- Option B: Monochromator bandwidth affects selectivity, not the fundamental sensitivity advantage; both UV-Vis and fluorimeters can use narrow bandwidths.
- Option C: Fluorescence emission wavelength (Stokes shift) is longer than UV excitation but may still be in the UV or near-UV; PMT sensitivity is not the primary reason.
- Option D: 90° dark-field geometry measures signal against near-zero background ⇒ far superior SNR. **Correct.**

Final Answer: Emission detector at 90° measures against a near-zero background, giving vastly superior SNR ⇒ D

Answer: (D) Go Back to Q23

Q24.

Solution

Concept — USP Tailing Factor T_f:

$$T_f = \frac{W_{0.05h}}{2\,f}$$

$W_{0.05h}$ = total width at 5% of peak height (leading edge to trailing edge); f = distance from the *peak maximum* to the *leading edge* at 5% height.

- $T_f = 1.00$: perfect symmetry.
- $T_f > 1.0$: tailing (trailing edge wider than leading edge).
- $T_f < 1.0$: fronting (leading edge wider).
- USP system suitability: $T_f \leq 2.0$ (some methods: 0.8–2.0).

Step 1 — Calculate T_f:

$$T_f = \frac{W_{0.05h}}{2\,f} = \frac{0.44}{2 \times 0.18} = \frac{0.44}{0.36} = 1.22$$

Step 2 — Interpret: $T_f = 1.22 > 1.0$: slight tailing (trailing edge is slightly wider). $T_f = 1.22 \leq 2.0$: within USP system suitability acceptable range.

Why other options are wrong:

- Option A: $T_f = 0.44/(2\times0.18) = 1.22$; slight tailing, within acceptable range. **Correct.**
- Option B: $T_f = 0.82$ would require $f > W_{0.05h}/2$, indicating fronting; but $f = 0.18 < 0.22 = W_{0.05h}/2$, confirming tailing (not fronting).
- Option C: $T_f = 2.44 = 0.44/0.18$ — uses f in place of $2f$ in the denominator; forgetting the factor of 2 gives an inflated result.
- Option D: $T_f = 1.54$ has no basis in the given values with any correct formula.

Final Answer: $T_f = 0.44/(2 \times 0.18) = 1.22$; acceptable tailing $\Rightarrow$ A

Answer: (A) Go Back to Q24

Q25.

Solution

Concept — Isosbestic Point in UV-Vis Spectroscopy: An isosbestic point occurs at a wavelength λ_{iso} where two interconverting species A and B have *identical* molar absorptivities: $\varepsilon_A(\lambda_{\text{iso}}) = \varepsilon_B(\lambda_{\text{iso}})$. At this wavelength, the total absorbance:

$$A_{\text{total}} = (\varepsilon_A c_A + \varepsilon_B c_B)l = \varepsilon_{\text{iso}}(c_A + c_B)l = \varepsilon_{\text{iso}}\, c_{\text{total}}\, l$$

is *constant* regardless of the $c_A : c_B$ ratio (as long as total concentration is conserved). All spectra in a kinetic series pass through the same point only if **exactly two** absorbing species are present.

Step 1 — Significance for stability studies: A clean isosbestic point in spectra taken over time confirms:

(a) Mass balance is maintained (no loss to non-UV-absorbing products).
(b) The system is binary: parent drug $\rightarrow$ one absorbing product.
(c) No intermediate (third species) accumulates.

If a third absorbing species accumulates even transiently, the spectra will no longer pass through the same isosbestic point.

Why other options are wrong:

- Option A: An isosbestic point confirms the number of species (two), not the kinetic order; first-order kinetics would require additional analysis of concentration vs. time data.
- Option B: The isosbestic point is a property of the two-species mixture, not of the independence of ε from temperature or pH.
- Option C: If the degradation product were non-absorbing, total absorbance would *decrease monotonically*; no isosbestic point would be observed.
- Option D: A clean isosbestic confirms only two absorbing species with no intermediate accumulation. **Correct.**

Final Answer: Isosbestic point $\Rightarrow$ exactly two absorbing species, no intermediate $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q25

Answer Key

Q	Ans	Q	Ans	Q	Ans	Q	Ans	Q	Ans
1	B	2	C	3	D	4	A	5	B
6	C	7	D	8	A	9	B	10	C
11	D	12	A	13	B	14	C	15	D
16	A	17	B	18	C	19	D	20	A
21	B	22	C	23	D	24	A	25	D