GPAT Pharmaceutical Chemistry

Sample Paper – 1

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

Instructions

- This paper contains **25** Multiple Choice Questions (Single Correct Answer), modelled on the Pharmaceutical Chemistry 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 2025 — QSAR/SAR principles, Analgesics & NSAIDs, UV-Vis Spectrophotometry.**
- 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. The Hammett substituent constant (σ) is a quantitative measure used in QSAR. Which of the following statements correctly defines σ and the property it measures?

(A) σ is defined as the logarithm of the octanol–water partition coefficient of the substituted compound relative to the unsubstituted parent.

(B) σ is defined as $\log(K_{a,X}/K_{a,H})$, where $K_{a,X}$ and $K_{a,H}$ are the ionisation constants of substituted and unsubstituted benzoic acid, respectively; it measures the electronic (polar) effect of substituent X.

(C) σ represents the steric bulk of a substituent, derived from Taft's E_s parameter.

(D) σ is the lipophilicity fragment constant (π) for aromatic ring substituents introduced by Hansch and Leo.

Q2. The Hansch equation for correlating biological activity with physico-chemical parameters is given by:

$$\log\left(\frac{1}{C}\right) = a \log P - b(\log P)^2 + c\sigma + d$$

In this equation, the terms $\log P$ and $(\log P)^2$ together account primarily for:

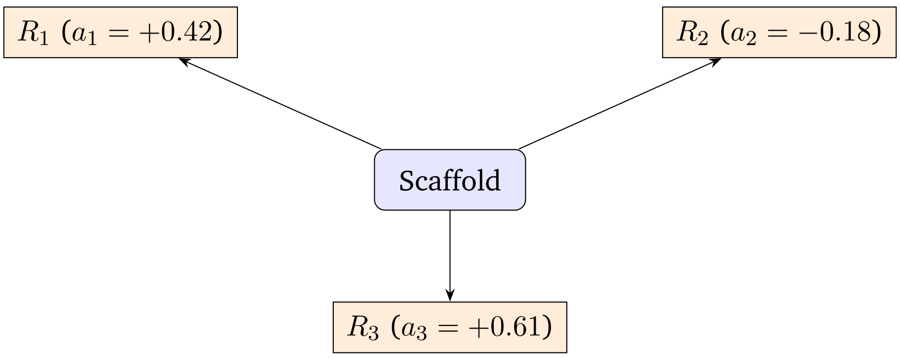
(A) Drug lipophilicity governing membrane partitioning and transport to the site of action, with the parabolic term reflecting an optimal hydrophobicity for activity.

(B) The electronic effect of the drug on its receptor, analogous to the Hammett σ constant.

(C) The steric volume of the drug molecule at the receptor binding cleft.

(D) The ionisation state of the drug at physiological pH.

Q3. The Free–Wilson model of QSAR proposes that biological activity is the sum of additive, independent contributions from each substituent. The general equation is $\log(1/C) = \mu + \sum a_i$, where μ is the overall average activity and a_i is the contribution of substituent i. Which statement about this model is correct?



$$\log(1/C) = \mu + \sum a_i$$

(A) The model requires non-linear regression because substituent effects interact multiplicatively at the receptor.

(B) Activity is predicted solely from the electronic contribution (σ) of each substituent without considering lipophilicity.

(C) Each substituent contributes a fixed, independent additive increment (a_i) to biological activity, allowing prediction for any untested combination of substituents.

(D) The model is equivalent to the Hansch equation when $\log P$ is set to zero.

Q4. In medicinal chemistry, bioisosteres are groups that have similar physicochemical properties and can mimic each other at a receptor. Which of the following is the most widely employed **classical bioisostere** for a carboxylic acid ($-\mathrm{COOH}$) group that retains acidic character and similar spatial geometry?

(A) Ester ($-\mathrm{COOR}$), because it contains the same carbonyl group as the carboxylic acid.

(B) Primary amide ($-\mathrm{CONH_2}$), because it can form hydrogen bonds like the carboxylate.

(C) Hydroxamic acid ($-\mathrm{CONHOH}$), because it has both hydroxyl and carbonyl groups.

(D) Tetrazole ring, because it has a $\mathrm{p}K_\mathrm{a}$ (≈ 4.9) close to that of carboxylic acids, is lipophilically similar, and is metabolically more stable.

Q5. A prodrug is a pharmacologically inactive compound that is biotransformed *in vivo* to the active drug. Enalapril is a classic example of a prodrug activated by which specific mechanism?

(A) Hepatic CYP3A4-mediated oxidative demethylation to release the active renin inhibitor.

(B) Ester hydrolysis by hepatic esterases *in vivo* to release enalaprilat, the active diacid ACE inhibitor.

(C) Colonic bacterial reduction of an azo bond to release the active sulfide metabolite.

(D) Intracellular phosphorylation by kinases to yield the active nucleoside triphosphate.

Q6. Loteprednol etabonate is used as a topical ophthalmic corticosteroid. In drug design terminology, it is classified as a **soft drug**. Which statement best explains this classification?

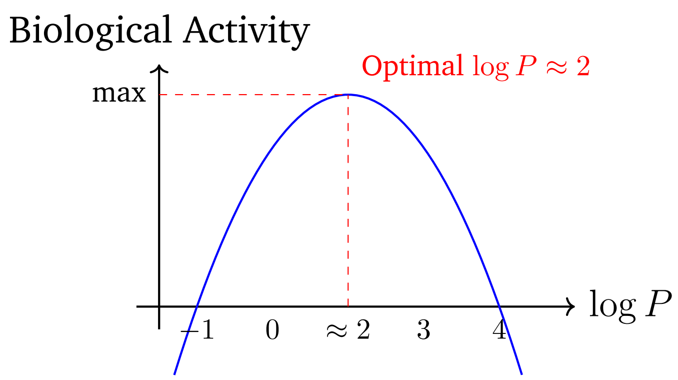
(A) It is designed so that after exerting its local anti-inflammatory effect in ocular tissue, it undergoes predictable, site-specific metabolic inactivation to non-toxic, pharmacologically inactive metabolites, minimising systemic side-effects.

(B) It is a prodrug that requires ester hydrolysis at the corneal surface to release the active steroidal moiety before receptor binding.

(C) Its high molecular weight (> 600 Da) prevents trans-corneal absorption, confining it to the tear film.

(D) It partitions preferentially into the vitreous humor through selective lipid binding, avoiding systemic circulation entirely.

Q7. Lipinski's "Rule of Five" (Ro5) predicts oral bioavailability of drug candidates. The parabolic relationship between biological activity and lipophilicity ($\log P$) is shown below. Which of the following physicochemical parameters is **NOT** one of the four original Ro5 criteria?



(A) Molecular weight ≤ 500 Da.

(B) $\log P$ (calculated octanol–water partition coefficient, clog P) ≤ 5.

(C) Polar surface area (PSA) $\leq 140\,\text{Å}^2$.

(D) Number of hydrogen-bond donors ≤ 5.

Q8. A weakly acidic drug has a $\mathrm{p}K_\mathrm{a}$ of 4.2. At blood plasma pH of 7.4, what percentage of the drug exists in the **ionised** (conjugate base, A^-) form? Use the Henderson–Hasselbalch equation: $\mathrm{pH} = \mathrm{p}K_\mathrm{a} + \log\left(\frac{[\mathrm{A}^-]}{[\mathrm{HA}]}\right)$.

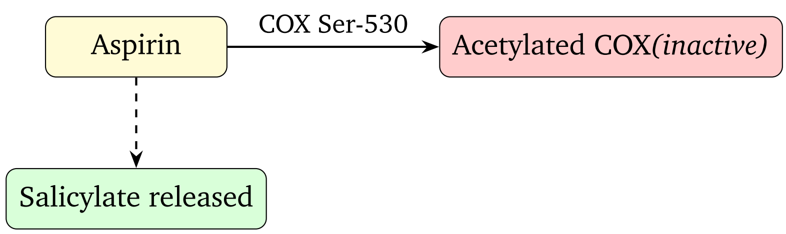
(A) Approximately 20%, because weak acids are predominantly unionised in the blood.

(B) Exactly 50%, since the pH equals the $\mathrm{p}K_\mathrm{a}$ of the drug.

(C) Approximately 1%, because the pH is far below the $\mathrm{p}K_\mathrm{a}$.

(D) Approximately 99.94% (essentially fully ionised), because $\mathrm{pH} - \mathrm{p}K_\mathrm{a} = +3.2$, giving $[\mathrm{A}^-]/[\mathrm{HA}] \approx 1585$.

Q9. Aspirin (acetylsalicylic acid) is classified as an irreversible COX inhibitor. Its mechanism of action is best depicted by the scheme below. Which statement correctly describes this mechanism?



(A) Aspirin competitively and reversibly occupies the arachidonic acid binding site of COX-1 and COX-2.

(B) Aspirin irreversibly acetylates the hydroxyl group of Serine-530 (Ser-530) in the COX-1 channel, preventing arachidonic acid access and permanently inactivating the enzyme.

(C) Aspirin allosterically inhibits the peroxidase domain of COX, preventing conversion of PGG_2 to PGH_2.

(D) Aspirin acts as a prodrug; salicylate (the active metabolite) non-covalently inhibits both COX-1 and COX-2 with equal potency.

Q10. Ibuprofen is a widely used NSAID. Which of the following correctly identifies its chemical class and the pharmacologically active enantiomer?

(A) Propionic acid class; the $S(+)$-enantiomer is the active COX inhibitor (the $R(-)$-enantiomer is chiral-inverted to the $S(+)$ form *in vivo*).

(B) Acetic acid class; the $R(-)$-enantiomer is the exclusive COX inhibitor.

(C) Anthranilic acid (fenamate) class; only the racemic mixture exhibits full COX inhibition.

(D) Enolic acid (oxicam) class; the $S(+)$-enantiomer is pharmacologically inactive but serves as a depot prodrug.

Q11. Hepatotoxicity from paracetamol (acetaminophen) overdose is a major clinical concern. Which of the following correctly describes the mechanism of hepatocellular damage?

(A) The parent drug directly inhibits mitochondrial complex I, leading to ATP depletion and hepatocyte death at therapeutic doses.

(B) Excessive glucuronide conjugate accumulates and undergoes hydrolysis to a reactive intermediate that alkylates hepatic proteins.

(C) CYP2E1 (and CYP3A4) oxidises paracetamol to N-acetyl-p-benzoquinone imine (NAPQI); NAPQI depletes glutathione and covalently binds hepatic macromolecules, causing necrosis; treated with N-acetylcysteine.

(D) Sulfate conjugate saturation at overdose levels leads to accumulation of the parent drug, which is directly nephrotoxic and secondarily hepatotoxic.

Q12. Mefenamic acid is a member of the fenamate class of NSAIDs. Which statement best distinguishes it pharmacologically from most other NSAIDs?

(A) It is a selective COX-2 inhibitor, with no measurable inhibitory activity against COX-1 at therapeutic plasma concentrations.

(B) Its analgesic effect is mediated exclusively through inhibition of thromboxane A_2 synthesis in platelets.

(C) It is a prodrug requiring ester hydrolysis in intestinal mucosa to release the active anthranilic acid form.

(D) In addition to inhibiting both COX-1 and COX-2 enzymes, mefenamic acid also directly antagonises prostaglandin E_1 and E_2 receptors, producing a dual anti-prostaglandin effect.

Q13. Piroxicam is an NSAID of the oxicam chemical class. Which of the following pharmacokinetic or pharmacological statements about piroxicam is most accurate?

(A) It has a short plasma half-life of approximately 2 hours, necessitating dosing four times daily for adequate anti-inflammatory coverage.

(B) It has a long plasma half-life of approximately 45 hours, allowing once-daily dosing and making it suitable for chronic inflammatory conditions such as rheumatoid arthritis.

(C) It is a selective COX-2 inhibitor specifically developed to reduce the cardiovascular thromboembolic risk associated with earlier coxibs.

(D) It is a prodrug that undergoes N-demethylation *in vivo* to yield meloxicam, the pharmacologically active species.

Q14. Indomethacin is used for acute gout, pericarditis, and patent ductus arteriosus closure. Which of the following correctly states its chemical class and pharmacological distinction?

(A) Indole acetic acid class; indomethacin is among the most potent non-selective COX inhibitors available, with inhibitory potency superior to aspirin and ibuprofen.

(B) Propionic acid class; indomethacin selectively inhibits COX-2 at therapeutic doses while sparing COX-1.

(C) Pyrazolone class; its primary mechanism involves inhibition of COX-3 in the CNS, explaining its prominent antipyretic effect.

(D) Anthranilic acid class; indomethacin acts primarily as a prostaglandin receptor antagonist rather than a COX enzyme inhibitor.

Q15. Celecoxib (a diaryl pyrazole) is a selective COX-2 inhibitor. Which structural feature is primarily responsible for its COX-2 selectivity over COX-1?

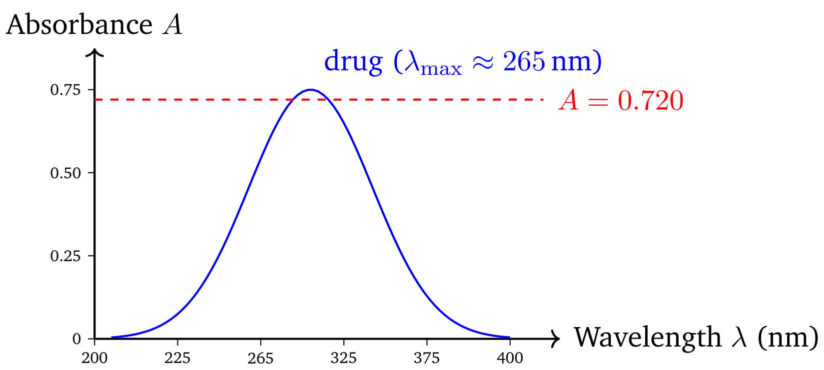
(A) An indole acetic acid side-chain that preferentially fits the elongated hydrophobic channel of COX-2 near isoleucine-523.

(B) A γ-butyrolactone (furanone) ring that forms selective hydrogen bonds with the arginine-120 residue unique to the COX-2 active site.

(C) A para-sulfonamide ($-SO_2NH_2$) group on the diaryl pyrazole scaffold that penetrates the secondary (side) pocket of COX-2 created by the Val-523 (vs. Ile-523 in COX-1) substitution, an access point absent in COX-1.

(D) A vinyl sulfone moiety that forms a covalent Michael adduct with Ser-530 of COX-2 but not COX-1.

Q16. A drug solution is analysed in a UV-Vis spectrophotometer using a $1\,\mathrm{cm}$ path-length cell. The measured absorbance is $A = 0.720$ and the molar absorptivity is $\varepsilon = 1800\,\mathrm{L\,mol^{-1}\,cm^{-1}}$. Using Beer–Lambert law ($A = \varepsilon c l$), calculate the molar concentration of the solution. The absorption profile is shown below:



(A) $1.25 \times 10^{-3}\,\mathrm{mol\,L^{-1}}$

(B) $2.50 \times 10^{-3}\,\mathrm{mol\,L^{-1}}$

(C) $1.30 \times 10^{-3}\,\mathrm{mol\,L^{-1}}$

(D) $4.00 \times 10^{-4}\,\mathrm{mol\,L^{-1}}$

Q17. In the Beer–Lambert law, the molar absorptivity ε links absorbance to concentration and path length. What are the correct SI-derived units of ε, and what does a higher ε value signify?

(A) $\mathrm{mol\,L^{-1}\,cm^{-1}}$; a higher ε indicates greater solubility of the compound.

(B) $\mathrm{L\,mol^{-1}\,cm^{-1}}$; a higher ε indicates a more intense (stronger) absorption at that wavelength.

(C) $\mathrm{cm^{-1}\,g^{-1}}$; higher ε corresponds to a lower molecular weight chromophore.

(D) $\mathrm{mol^{-1}\,cm^2}$; ε is dimensionless at concentrations below $10^{-3}\,\mathrm{M}$.

Q18. In UV-Vis spectroscopy, chromophores and auxochromes play distinct roles in light absorption. Which of the following statements about auxochromes is correct?

(A) An auxochrome (e.g., $-\mathrm{OH}$, $-\mathrm{NH_2}$, $-\mathrm{OR}$) cannot absorb UV-Vis radiation by itself, but when conjugated to a chromophore, it intensifies the absorption (hyperchromic effect) and causes a bathochromic (red) shift of λ_{max} by donating electrons into the π-system.

(B) An auxochrome is any unsaturated functional group (e.g., $\mathrm{C=O}$, $\mathrm{C=C}$) that is solely responsible for absorbing electromagnetic radiation in the UV region.

(C) A chromophore cannot produce measurable UV-Vis absorption unless it is covalently linked to an auxochrome group.

(D) The nitro group ($-\mathrm{NO_2}$) is classified as an auxochrome rather than a chromophore because it only modifies the existing absorption.

Q19. Woodward's rules allow prediction of λ_{max} for α,β-unsaturated carbonyl compounds (enones) in UV absorption. What is the **base value** for an acyclic α,β-unsaturated ketone (enone in s-$trans$ conformation), and how are increments applied?

(A) The base value is $250\,\mathrm{nm}$ for cyclic six-membered ring enones and $215\,\mathrm{nm}$ for acyclic systems, with no further increments needed for substitution.

(B) The base value is $217\,\mathrm{nm}$ (identical to the homoannular diene), and β-methyl substituents decrease λ_{max} by $5\,\mathrm{nm}$ each.

(C) The base value is $215\,\mathrm{nm}$ for acyclic enones; increments are added for α-substituents ($+10\,\mathrm{nm}$), β-substituents ($+12\,\mathrm{nm}$), ring residues, and exocyclic double bonds to calculate predicted $\lambda_{\max}$.

(D) The base value is $230\,\mathrm{nm}$ for all conjugated ketones regardless of substitution pattern or ring size.

Q20. A **bathochromic shift** (red shift) in UV-Vis spectroscopy refers to a shift of $\lambda_{\max}$ to a longer wavelength. Which of the following correctly causes a bathochromic shift?

(A) Introduction of a strong electron-withdrawing group that reduces π-electron density and increases the HOMO–LUMO energy gap.

(B) Extension of conjugation by addition of another double bond or aromatic ring, or attachment of electron-donating groups ($-\mathrm{OH}$, $-\mathrm{NR}_2$) that lower the HOMO–LUMO energy gap.

(C) Increasing solvent polarity, which always blue-shifts all UV-Vis bands due to stronger solvation of the ground state.

(D) Using a shorter optical path length (l) in the spectrophotometric cell to prevent inner-filter effect.

Q21. Sandell sensitivity is a figure of merit used to compare the sensitivity of colorimetric methods. Which of the following is the correct definition of Sandell sensitivity?

(A) The minimum concentration (in $\mu\mathrm{g\,mL^{-1}}$) detectable in a $1\,\mathrm{cm}$ cell when the absorbance equals unity.

(B) The ratio of molar absorptivity (ε) to the molecular weight of the analyte, expressed in $\mathrm{L\,g^{-1}\,cm^{-1}}$.

(C) The absorbance produced by $1\,\mu\mathrm{g\,mL^{-1}}$ of the analyte measured in a $1\,\mathrm{cm}$ path-length cell.

(D) The mass of analyte (in $\mu\mathrm{g}$) per unit cross-sectional area (cm^2) of the light beam that produces an absorbance of 0.001; numerically equal to $M/(\varepsilon \times 10^3)$.

Q22. Stray light in a UV-Vis spectrophotometer consists of radiation reaching the detector at wavelengths other than the selected analytical wavelength. What is the primary consequence of stray light on Beer–Lambert law compliance?

(A) It causes a **negative** (downward) deviation from Beer–Lambert law at high analyte concentrations: the apparent absorbance is lower than expected, resulting in a flattening of the calibration curve at higher concentrations.

(B) It causes a positive (upward) deviation at all analyte concentrations, making the calibration curve steeper than predicted.

(C) It introduces random noise only at very low concentrations where signal-to-noise ratio is limiting, with no effect at higher concentrations.

(D) It shifts the measured $\lambda_{\max}$ to shorter wavelengths (hypsochromic shift) without affecting the linearity of Beer–Lambert law.

Q23. A double-beam UV-Vis spectrophotometer uses a beam splitter to direct the source radiation through both the sample and the reference cells simultaneously (or in rapid alternation). What is the principal analytical advantage of this design over a single-beam instrument?

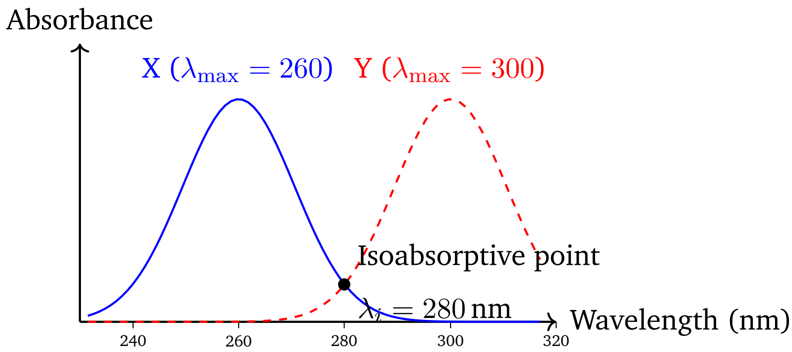
(A) The double-beam design doubles the source light intensity reaching the detector, halving the detection limit and improving sensitivity by a factor of two.

(B) It eliminates the need for a monochromator by using two broadband light sources filtered by interference filters to cover the full UV-Vis range.

(C) It continuously and automatically corrects for fluctuations in source intensity, detector sensitivity, and solvent/cell absorption by measuring the sample and reference simultaneously, yielding more stable baselines and accurate spectra.

(D) It can measure two different analytical wavelengths simultaneously without resetting the monochromator, enabling rapid multi-analyte determination.

Q24. An isoabsorptive (isobestic) point is observed in the UV spectra of a two-component mixture as the ratio of components changes. The figure below shows the spectra of components X and Y:



(A) The isoabsorptive point is the wavelength at which the sample shows maximum absorbance regardless of composition or total concentration.

(B) At the isoabsorptive point, the molar absorptivities of components X and Y are equal ($\varepsilon_X = \varepsilon_Y$); measuring total absorbance at this wavelength gives the total concentration of both components without prior separation.

(C) The isoabsorptive point is the wavelength where the first derivative of the absorption spectrum of the mixture equals zero.

(D) It is a wavelength chosen for baseline correction in derivative spectroscopy to eliminate interference from the solvent.

Q25. First-derivative spectroscopy involves plotting $\mathrm{d}A/\mathrm{d}\lambda$ versus wavelength instead of A versus λ. Which of the following statements about first-derivative UV-Vis spectroscopy is correct?

(A) The first derivative spectrum shows peaks of doubled intensity at all λ_{max} values of the parent (zero-order) spectrum.

(B) Overlapping peaks cannot be resolved by first-derivative spectroscopy because differentiation amplifies high-frequency noise and broad peaks equally.

(C) The first derivative is zero at all points on a flat (constant) baseline, making it *less* useful than zero-order spectra for resolving overlapping peaks from a rising background.

(D) A constant background absorbance (baseline) differentiates to zero, effectively eliminating it; crossing of the derivative baseline (zero-crossing) pinpoints the true $\lambda_{\max}$ of each component, enabling resolution of overlapping peaks that are unresolvable in the zero-order spectrum.

Detailed Solutions

Q1.

Solution

Concept — QSAR: Hammett Substituent Constant (σ): The Hammett σ value quantifies the electronic (polar) effect of a ring substituent on a reaction centre. It was derived empirically from the ionisation equilibria of para- and meta-substituted benzoic acids in water at 25 °C.

Step 1 — Definition: $\sigma_X = \log(K_{a,X}/K_{a,H})$, where $K_{a,X}$ is the ionisation constant of the substituted benzoic acid and $K_{a,H}$ is that of benzoic acid itself. Electron-withdrawing groups give positive σ; electron-donating groups give negative σ.

Step 2 — Application: The Hammett equation $\log(k/k_0) = \rho\sigma$ or $\log(K/K_0) = \rho\sigma$ uses σ to predict rate or equilibrium constants for reactions sensitive to substituent electronic effects, and by extension, biological activities in QSAR.

Why other options are wrong:

- Option A: Describes the Hansch lipophilicity fragment constant π ($\log P_{sub}/P_{parent}$), not σ.
- Option C: Describes Taft's steric parameter E_s, which measures steric effects, not electronic effects.
- Option D: Describes the lipophilicity fragment constant π introduced separately by Hansch and Leo.

Final Answer: σ is the log ratio of ionisation constants of substituted to unsubstituted benzoic acid, measuring electronic effects. $\Rightarrow$ B

Answer: (B) **Go Back to Q1**

Q2.

Solution

Concept — QSAR: Hansch Equation and Partition Coefficient: The Hansch equation is a multiparameter linear free-energy relationship (LFER) that correlates biological activity ($\log 1/C$) with lipophilicity ($\log P$), electronic (σ), and steric (E_s) parameters.

Step 1 — Role of $\log P$: The terms $a \log P - b(\log P)^2$ describe a parabolic (non-linear) dependence of activity on lipophilicity. At low $\log P$ the drug is too hydrophilic to cross membranes; at high $\log P$ it is sequestered in lipid phases. An optimal $\log P_{\text{opt}} = a/(2b)$ exists.

Step 2 — Identification: Because $\log P$ governs membrane partitioning and transport to the biophase (site of action), the combined $\log P$ and $(\log P)^2$ terms account for the hydrophobic component of drug distribution, not electronics or sterics.

Why other options are wrong:

- Option B: The σ term ($c\sigma$) accounts for electronic effects; $\log P$ terms address lipophilicity, not electronics.
- Option C: Steric effects are captured by Taft's E_s, a separate term not shown in the basic Hansch equation.
- Option D: Molecular weight is not directly encoded in $\log P$; absorption is related to $\log P$ but $\log P$ itself is a partition coefficient.

Final Answer: The $\log P$ and $(\log P)^2$ terms capture drug lipophilicity and optimal partitioning for membrane transport. $\Rightarrow \boxed{\text{A}}$

Answer: (A) **Go Back to Q2**

Q3.

Solution

Concept — QSAR: Free–Wilson Additive Model: The Free–Wilson (de novo) model assumes that the biological activity of a compound equals the sum of a constant baseline (μ, the average activity) and independent additive contributions (a_i) from each substituent at defined positions.

Step 1 — Mathematical form: $\log(1/C) = \mu + \sum_i a_i$. Each a_i is determined by regression from a training set of analogues. The model does not require knowledge of physical properties such as $\log P$ or σ.

Step 2 — Practical implication: Once a_i values are established for substituents at each position, the activity of any untested combination can be predicted by simple addition, provided the substituents act independently (no synergism or antagonism).

Why other options are wrong:

- Option A: The model is solved by *linear* multiple regression; substituents contribute additively, not multiplicatively; no non-linear regression is required.

- Option B: The Free–Wilson model does not explicitly use Hammett σ; it is a de novo approach based on substituent identity, not on physicochemical parameters.
- Option D: The Free–Wilson and Hansch equations are complementary but distinct; setting $\log P = 0$ in Hansch does not convert it to the Free–Wilson model.

Final Answer: Each substituent contributes a fixed, independent additive increment a_i to biological activity in the Free–Wilson model. $\Rightarrow \boxed{\text{C}}$

Answer: (C) **Go Back to Q3**

Q4.

Solution

Concept — Drug Design: Classical Bioisosterism: Classical bioisosteres are atoms or groups that have similar size, shape, and electronic configuration, often producing comparable biological activity. Replacing a labile or problematic group with a bioisostere can improve metabolic stability or pharmacokinetics.

Step 1 — Properties of carboxylic acid: $-\mathrm{COOH}$ is a Brønsted acid (p$K_\mathrm{a} \approx 4$–5), planar, capable of hydrogen bonding (donor and acceptor), and ionised at physiological pH.

Step 2 — Why tetrazole: The $1H$-tetrazole ring has a p$K_\mathrm{a} \approx 4.9$, similar acidity to carboxylic acids, is planar, and is ionised at pH 7.4. Crucially, tetrazole is *more* lipophilic (better membrane permeability) and *resistant* to metabolic hydrolysis compared to $-\mathrm{COOH}$. Losartan ($\mathrm{AT_1}$ antagonist) uses a tetrazole bioisostere in place of $-\mathrm{COOH}$.

Why other options are wrong:

- Option A: Esters ($-\mathrm{COOR}$) are not acidic and are hydrolysed *in vivo*; they are often used as prodrugs, not as bioisosteres of carboxylic acids.
- Option B: Primary amides ($-\mathrm{CONH_2}$) are weakly acidic (p$K_\mathrm{a} > 15$) and behave very differently from $-\mathrm{COOH}$ at physiological pH.
- Option C: Hydroxamic acids ($-\mathrm{CONHOH}$, p$K_\mathrm{a} \approx 9$) are much weaker acids and are generally classified as bioisosteres of hydroxyl or amide groups, not carboxylic acids.

Final Answer: Tetrazole is the best classical bioisostere for $-\mathrm{COOH}$ due to similar pK_a and improved metabolic stability. $\Rightarrow \boxed{\text{D}}$

Answer: (D) **Go Back to Q4**

Q5.

Solution

Concept — Drug Design: Prodrug Activation by Ester Hydrolysis: A prodrug is a pharmacologically inactive (or less active) compound designed to be converted *in vivo* into the active drug. Esterification of an active drug's carboxylic acid to an ethyl ester is a common strategy to improve oral absorption.

Step 1 — Enalapril structure: Enalaprilat (the active ACE inhibitor) contains two carboxylic acid groups that reduce its oral bioavailability due to poor membrane permeability. Esterification of the more lipophilic carboxyl gives enalapril (the ethyl ester prodrug).

Step 2 — Activation: After oral absorption, enalapril undergoes rapid hepatic esterase-catalysed hydrolysis of the ethyl ester to release enalaprilat, which then inhibits ACE and lowers blood pressure. Oral bioavailability of enalapril is $\approx 60\%$ vs $< 10\%$ for enalaprilat.

Why other options are wrong:

- Option A: CYP3A4 oxidation and demethylation are phase I oxidative reactions, not the activation mechanism of enalapril; renin inhibitors (e.g., aliskiren) are a different drug class.
- Option C: Azo bond reduction by gut flora applies to sulfasalazine (prodrug of mesalazine and sulfapyridine), not to enalapril.
- Option D: Intracellular phosphorylation is the activation mechanism of nucleoside analogue antivirals (e.g., acyclovir), not of enalapril.

Final Answer: Enalapril is activated by *in vivo* ester hydrolysis to release enalaprilat, the active ACE inhibitor. $\Rightarrow \boxed{B}$

Answer: (B) **Go Back to Q5**

Q6.

Solution

Concept — Drug Design: Soft Drug Strategy: A soft drug is an *active* drug (not a prodrug) that is designed to undergo a *predictable, controlled* metabolic inactivation after exerting its pharmacological effect at the target site, converting to non-toxic, inactive metabolites. This minimises systemic toxicity.

Step 1 — Loteprednol design: Loteprednol etabonate is a corticosteroid designed with a C-20 ester and C-17 carbonate (etabonate) that is metabolised by corneal and conjunctival esterases (and hepatic esterases) to the inactive Δ^1-cortienic acid etabonate. This local inactivation prevents systemic corticosteroid side-effects (HPA axis suppression, cataract, raised IOP).

Step 2 — Contrast with prodrug: Unlike a prodrug (inactive $\rightarrow$ active), loteprednol is already active at the receptor *as administered*; it is a soft drug (active $\rightarrow$ inactive metabolite at or near site of action).

Why other options are wrong:

- Option B: Loteprednol is already active; requiring corneal hydrolysis *before* receptor binding would make it a prodrug, not a soft drug.
- Option C: Loteprednol MW is ≈ 467 Da; high MW can reduce absorption but is not the basis of its "soft drug" classification.
- Option D: Preferential vitreous partitioning is not the defining mechanism; the key is *metabolic* (enzymatic) inactivation, not physical sequestration.

Final Answer: Loteprednol is a soft drug that undergoes predictable, site-specific metabolic inactivation near the site of action, minimising systemic effects. $\Rightarrow \boxed{A}$

Answer: (A) **Go Back to Q6**

Q7.

Solution

Concept — Drug Design: Lipinski Rule of Five (Ro5): Lipinski's Ro5 provides a simple, empirical filter predicting whether a compound is likely to have poor oral absorption/permeability (drug-likeness). Poor permeability is predicted when **more than one** of these four criteria is violated.

Step 1 — The four original Ro5 rules:

(a) Molecular weight (MW) ≤ 500 Da
(b) Calculated $\log P$ (clog P) ≤ 5
(c) Number of hydrogen-bond donors (HBD, OH + NH) ≤ 5
(d) Number of hydrogen-bond acceptors (HBA, N + O) ≤ 10

Step 2 — Polar surface area (PSA): PSA ($\leq 140\,\text{Å}^2$) is an important descriptor for predicting intestinal absorption and blood–brain barrier penetration, but it was *not* one of Lipinski's original four rules. PSA was added later by Ertl and colleagues as a complementary filter.

Why other options are wrong:

- Option A: MW $\leq 500\,\text{Da}$ is rule 1 of the original Ro5.
- Option B: $\log P \leq 5$ is rule 2 of the original Ro5.
- Option D: HBD ≤ 5 is rule 3 of the original Ro5.

Final Answer: Polar surface area (PSA) is not part of Lipinski's original Rule of Five. $\Rightarrow \boxed{\text{C}}$

Answer: (C) **Go Back to Q7**

Q8.

Solution

Concept — Henderson–Hasselbalch Equation for Weak Acids: For a weak acid HA $\rightleftharpoons$ H^+ + A^-, the Henderson–Hasselbalch equation is $\text{pH} = \text{p}K_\text{a} + \log([\text{A}^-]/[\text{HA}])$. At pH $>$ pK_a, the ionised form predominates.

Step 1 — Calculate the ratio:

$$\text{pH} - \text{p}K_\text{a} = 7.4 - 4.2 = 3.2$$

$$\log\left(\frac{[\text{A}^-]}{[\text{HA}]}\right) = 3.2 \implies \frac{[\text{A}^-]}{[\text{HA}]} = 10^{3.2} \approx 1585$$

Step 2 — Calculate % ionised:

$$\%\,\text{ionised} = \frac{[\text{A}^-]}{[\text{A}^-] + [\text{HA}]} \times 100 = \frac{1585}{1585 + 1} \times 100 \approx 99.94\%$$

The drug is essentially completely ionised at blood plasma pH.

Why other options are wrong:

- Option A: 20% ionised would correspond to pH only slightly above pK_a; at $\Delta\text{pH} = +3.2$, ionisation is near-complete.
- Option B: 50% ionised occurs *only* when pH = pK_a exactly; here pH $\gg$ pK_a.
- Option C: 1% ionised would require pH $\ll$ pK_a; the drug would be *mostly un-ionised*, the opposite of the correct answer.

Final Answer: Approximately 99.94% of the weak acid is ionised at blood plasma pH 7.4 (pK_a 4.2). $\Rightarrow \boxed{\text{D}}$

Answer: (D) **Go Back to Q8**

Q9.

Solution

Concept — NSAIDs: Aspirin's Irreversible COX Inhibition: Aspirin is unique among common NSAIDs because it inhibits COX enzymes covalently and irreversibly. This property underlies its use in antiplatelet therapy at low doses.

Step 1 — Mechanism: The acetyl group of aspirin is transferred to the hydroxyl side chain of **Serine-530** (Ser-530) in the COX-1 active-site channel via an ester bond (acetylation). This sterically blocks arachidonic acid from reaching the catalytic Tyr-385, permanently inactivating the enzyme. Simultaneously, acetylsalicylate releases salicylate.

Step 2 — Selectivity: At low doses (≤ 100 mg/day), aspirin preferentially acetylates platelet COX-1 (platelets lack nuclei and cannot synthesise new COX). COX-2 has a larger active-site channel; aspirin can also acetylate Ser-516 of COX-2 but with lower potency. Low-dose aspirin gives sustained platelet inhibition without equivalent COX-2 suppression.

Why other options are wrong:

- Option A: Aspirin's inhibition is *irreversible* (covalent acetylation), not competitive and reversible.
- Option C: Aspirin acts on the cyclooxygenase domain of COX, not the peroxidase domain. The peroxidase converts PGG_2 to PGH_2; aspirin blocks formation of PGG_2 itself.
- Option D: Salicylate has weak, reversible COX inhibition at high concentrations; the therapeutic effect of aspirin at low doses is primarily due to the parent drug acetylating COX-1, not to salicylate.

Final Answer: Aspirin irreversibly acetylates Ser-530 of COX-1, permanently blocking arachidonic acid binding and PG synthesis. $\Rightarrow \boxed{B}$

Answer: (B) **Go Back to Q9**

Q10.

Solution

Concept — NSAIDs: Ibuprofen Chemical Class and Stereochemistry: Ibuprofen (2-(4-isobutylphenyl)propionic acid) belongs to the **propionic acid** (arylpropionic acid) class of NSAIDs. Its propionic acid side chain contains a chiral centre.

Step 1 — Active enantiomer: The $S(+)$-enantiomer is the pharmacologically active form that inhibits COX-1 and COX-2. The $R(-)$-enantiomer is largely inactive but is enzymatically *inverted* to the $S(+)$ form by α-methylacyl-CoA racemase (AMACR) in vivo, so commercially available racemic ibuprofen is therapeutically effective.

Step 2 — Class members: Other propionic acid NSAIDs include naproxen, ketoprofen, flurbiprofen, and fenoprofen. Naproxen is marketed as the pure $S(-)$-enantiomer.

Why other options are wrong:

- Option B: Ibuprofen belongs to the propionic acid class, not the acetic acid class (which includes indomethacin, diclofenac). The $R(-)$ form is inactive, not active.
- Option C: Anthranilic acid (fenamate) class includes mefenamic acid and flufenamic acid; ibuprofen has no anthranilic acid structural feature.
- Option D: Enolic acid (oxicam) class includes piroxicam and meloxicam; ibuprofen is not an oxicam.

Final Answer: Ibuprofen is a propionic acid class NSAID; the $S(+)$-enantiomer is the active COX inhibitor. $\Rightarrow$ $\boxed{A}$

Answer: (A) **Go Back to Q10**

Q11.

Solution

Concept — NSAIDs: Paracetamol Hepatotoxicity Mechanism: At therapeutic doses, paracetamol (acetaminophen) is safely conjugated with glucuronic acid ($\sim$ 55%) and sulfate ($\sim$ 30%) and excreted renally. A small fraction ($\sim$ 5–10%) is oxidised by CYP enzymes.

Step 1 — NAPQI formation: CYP2E1 (and CYP3A4) oxidises paracetamol to ***N*-acetyl-*p*-benzoquinone imine (NAPQI)**, a highly reactive electrophilic metabolite. At therapeutic doses, NAPQI is rapidly scavenged by hepatic glutathione

(GSH) to form a non-toxic mercapturic acid conjugate.

Step 2 — Overdose toxicity: In overdose, glucuronide and sulfate pathways are saturated, increasing NAPQI formation. Hepatic GSH is depleted faster than it can be replenished. Unscavenged NAPQI covalently binds (arylates) hepatic proteins and mitochondria, causing oxidative stress and centrizonal hepatic necrosis. **Treatment:** N-acetylcysteine (NAC) replenishes GSH.

Why other options are wrong:

- Option A: The parent drug does not directly inhibit mitochondrial complex I at pharmacological doses; mitochondrial injury is secondary to NAPQI arylation.
- Option B: Glucuronide conjugates of paracetamol are pharmacologically and toxicologically inert; they are not reactive intermediates.
- Option D: Sulfate conjugate saturation shifts metabolism toward CYP-mediated oxidation (increasing NAPQI), but the sulfate conjugate itself is non-toxic and excreted harmlessly.

Final Answer: Paracetamol hepatotoxicity results from CYP2E1-generated NAPQI depleting GSH and arylating hepatic macromolecules; treated with N-acetylcysteine. $\Rightarrow$ $\boxed{\text{C}}$

Answer: (C) **Go Back to Q11**

Q12.

Solution

Concept — NSAIDs: Mefenamic Acid (Fenamate Class) Dual Action: Fenamates are derived from anthranilic acid (N-arylanthranilic acid) and represent one of the earlier NSAID classes. Mefenamic acid is notable for a pharmacological action that distinguishes it from most other NSAIDs.

Step 1 — COX inhibition: Like other NSAIDs, mefenamic acid inhibits both COX-1 and COX-2 non-selectively, reducing prostaglandin biosynthesis from arachidonic acid.

Step 2 — Prostaglandin receptor antagonism: In addition to COX inhibition, mefenamic acid also **directly antagonises prostaglandin** E_1 **and** E_2 **receptors** at smooth muscle and other target tissues. This dual mechanism produces a synergistic anti-inflammatory and analgesic effect and is a unique pharmacological feature among the classical NSAIDs.

Why other options are wrong:

- Option A: Mefenamic acid inhibits both COX-1 and COX-2; it is not COX-2 selective. Selective COX-2 inhibitors are coxibs (e.g., celecoxib).
- Option B: Thromboxane A_2 synthesis inhibition is not the primary or exclusive mechanism; mefenamic acid's main action is COX inhibition and PG receptor antagonism.
- Option C: Mefenamic acid is not a prodrug; it is active as administered. Ester hydrolysis activation is characteristic of prodrugs like enalapril or aspirin (partial).

Final Answer: Mefenamic acid is unique in both inhibiting COX enzymes and antagonising prostaglandin E_1/E_2 receptors directly. $\Rightarrow \boxed{D}$

Answer: (D) **Go Back to Q12**

Q13.

Solution

Concept — NSAIDs: Piroxicam (Oxicam Class) Pharmacokinetics: Piroxicam is a member of the enolic acid (oxicam) subclass of NSAIDs. Its distinguishing pharmacokinetic feature is an exceptionally long elimination half-life.

Step 1 — Half-life: Piroxicam has a plasma half-life of approximately **45 hours** (range: 30–86 hours depending on patient factors). This long $t_{1/2}$ is due to extensive enterohepatic recycling and high plasma protein binding ($\approx 99\%$).

Step 2 — Clinical significance: The long $t_{1/2}$ permits **once-daily dosing**, improving patient adherence for chronic inflammatory conditions such as rheumatoid arthritis and osteoarthritis. However, it also means that adverse effects (GI ulceration) persist longer if they occur.

Why other options are wrong:

- Option A: A 2-hour half-life is characteristic of short-acting NSAIDs like aspirin or ibuprofen, not piroxicam.
- Option C: Piroxicam is a *non-selective* COX-1/COX-2 inhibitor; it has no COX-2 selectivity and is not designed to reduce cardiovascular risk. Selective COX-2 inhibitors are celecoxib and etoricoxib.
- Option D: Piroxicam is not a prodrug; meloxicam is a structurally related but distinct oxicam NSAID with some COX-2 preference.

Final Answer: Piroxicam (oxicam class) has a plasma half-life of ≈ 45 hours, enabling once-daily dosing. ⇒ B

Answer: (B) **Go Back to Q13**

Q14.

Solution

Concept — NSAIDs: Indomethacin Chemical Class and Potency: Indomethacin was introduced in 1963 as one of the first potent synthetic NSAIDs. Its high efficacy makes it a reference compound in COX inhibition studies.

Step 1 — Chemical class: Indomethacin is a **substituted indole acetic acid** (1-p-chlorobenzoyl-5-methoxy-2-methyl-1H-indole-3-acetic acid). The indole ring system provides rigid planarity and lipophilicity required for deep insertion into the COX active-site channel.

Step 2 — Pharmacological potency: Among classic NSAIDs, indomethacin exhibits among the highest *in vitro* and *in vivo* COX inhibition potency (IC_{50} for COX-1 ≈ 0.01–$0.1\ \mu$M), exceeding aspirin and ibuprofen. Its strong COX inhibition underlies both its efficacy and its high incidence of GI adverse effects. It is used for acute gout, ankylosing spondylitis, and ductal closure in neonates.

Why other options are wrong:

- Option B: Propionic acid class drugs include ibuprofen, naproxen; indomethacin is not in this class. Indomethacin is non-selective for COX-1/COX-2.
- Option C: Pyrazolone class includes phenylbutazone; COX-3 inhibition is associated with paracetamol (though its relevance is debated), not with indomethacin.
- Option D: Anthranilic acid class is the fenamate class (mefenamic acid); indomethacin is not a prostaglandin receptor antagonist.

Final Answer: Indomethacin belongs to the indole acetic acid class and is among the most potent non-selective COX inhibitors among classic NSAIDs. ⇒ A

Answer: (A) **Go Back to Q14**

Q15.

Solution

Concept — NSAIDs: Structural Basis of Celecoxib's COX-2 Selectivity: Celecoxib is a diarylheterocyclic compound (4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide) that exploits a structural difference between COX-1 and COX-2.

Step 1 — The secondary pocket: COX-2 contains a secondary hydrophilic side pocket adjacent to the main arachidonic acid channel, formed because residue 523 is **valine** (Val-523) in COX-2, compared to the bulkier **isoleucine** (Ile-523) in COX-1. This valine substitution creates an accessible pocket in COX-2.

Step 2 — Sulfonamide interaction: The p**-sulfonamide (**$-SO_2NH_2$**)** group on the phenyl ring of celecoxib inserts into this secondary pocket and forms hydrogen bonds with Arg-513 and His-90 of COX-2. The larger Ile-523 in COX-1 sterically prevents the sulfonamide from accessing this pocket, conferring COX-2 selectivity ($SI = IC_{50,COX-1}/IC_{50,COX-2} \approx 375$).

Why other options are wrong:

- Option A: An indole acetic acid side-chain is the structural feature of indomethacin, not celecoxib.
- Option B: The furanone (butenolide) ring is the structural feature of rofecoxib (Vioxx), another COX-2 selective inhibitor; celecoxib has a pyrazole ring.
- Option D: Celecoxib does not form a covalent bond with Ser-530 (that is aspirin's mechanism); celecoxib is a *non-covalent*, reversible inhibitor.

Final Answer: Celecoxib's p-sulfonamide group accesses the Val-523 secondary pocket unique to COX-2, conferring selectivity. $\Rightarrow \boxed{C}$

Answer: (C) **Go Back to Q15**

Q16.

Solution

Concept — UV-Vis: Beer–Lambert Law ($A = \varepsilon cl$): Beer–Lambert law states that absorbance (A) is directly proportional to both the molar concentration (c) and the path length (l) of the absorbing solution, with ε as the proportionality constant (molar absorptivity).

Step 1 — Rearrange for concentration:

$$c = \frac{A}{\varepsilon \cdot l} = \frac{0.720}{1800\,\mathrm{L\,mol^{-1}\,cm^{-1}} \times 1\,\mathrm{cm}}$$

Step 2 — Calculate:

$$c = \frac{0.720}{1800} = 4.00 \times 10^{-4}\,\mathrm{mol\,L^{-1}}$$

Units check: $[\mathrm{L\,mol^{-1}\,cm^{-1}} \cdot \mathrm{cm}]^{-1} = \mathrm{mol\,L^{-1}}$ ✓

Why other options are wrong:

- Option A: $1.25 \times 10^{-3}\,\mathrm{mol\,L^{-1}}$ would arise from $c = A \times \varepsilon$ (incorrect rearrangement; should divide, not multiply).
- Option B: $2.50 \times 10^{-3}\,\mathrm{mol\,L^{-1}}$ corresponds to $c = A \times \varepsilon/(A^2)$, an erroneous calculation.
- Option C: $1.30 \times 10^{-3}\,\mathrm{mol\,L^{-1}}$ does not correspond to any correct manipulation of the given data.

Final Answer: Using $c = A/(\varepsilon l) = 0.720/(1800 \times 1) = 4.00 \times 10^{-4}\,\mathrm{mol\,L^{-1}}$. $\Rightarrow \boxed{\mathrm{D}}$

Answer: (D) **Go Back to Q16**

Q17.

Solution

Concept — UV-Vis: Molar Absorptivity (ε) Units and Meaning: From Beer–Lambert law $A = \varepsilon cl$, dimensional analysis gives $\varepsilon = A/(c \cdot l)$. Since A is dimensionless, c is in $\mathrm{mol\,L^{-1}}$, and l is in cm:

Step 1 — Derive units:

$$[\varepsilon] = \frac{[\text{dimensionless}]}{[\mathrm{mol\,L^{-1}}][\mathrm{cm}]} = \mathrm{L\,mol^{-1}\,cm^{-1}}$$

Step 2 — Physical significance: A higher ε means that for the same concentration and path length, the compound absorbs more light (greater probability of photon absorption per molecule per unit concentration). This is related to the transition dipole moment; strongly allowed electronic transitions (e.g., $\pi \to \pi^*$ in extended conjugated systems) have ε of 10^4–$10^5\,\mathrm{L\,mol^{-1}\,cm^{-1}}$, while weakly allowed ($n \to \pi^*$) transitions have $\varepsilon \approx 10$–$100\,\mathrm{L\,mol^{-1}\,cm^{-1}}$.

Why other options are wrong:

- Option A: $\text{mol}\,\text{L}^{-1}\,\text{cm}^{-1}$ are the units of c/l, not of ε; the units are inverted.
- Option C: $\text{cm}^{-1}\,\text{g}^{-1}$ are units of the specific absorptivity (a) in the mass-based form ($A = a \cdot \rho \cdot l$), not molar absorptivity.
- Option D: $\text{mol}^{-1}\,\text{cm}^2$ (or equivalently $\text{L}\,\text{mol}^{-1}\,\text{cm}^{-1}$ expressed differently) is close but the "dimensionless" claim for dilute solutions is incorrect; ε always carries units.

Final Answer: ε has units $\text{L}\,\text{mol}^{-1}\,\text{cm}^{-1}$; higher ε means more intense UV-Vis absorption. $\Rightarrow \boxed{\text{B}}$

Answer: (B) **Go Back to Q17**

Q18.

Solution

Concept — UV-Vis: Role of Auxochromes and Chromophores: A **chromophore** is a group that absorbs UV-Vis radiation due to $\pi \to \pi^*$ or $n \to \pi^*$ electronic transitions (e.g., $\text{C}=\text{O}$, $\text{C}=\text{C}$, NO_2, aromatic rings). An **auxochrome** modifies chromophore absorption without absorbing UV-Vis radiation on its own.

Step 1 — Auxochrome properties: Auxochromes (e.g., $-\text{OH}$, $-\text{NH}_2$, $-\text{OR}$, $-\text{NR}_2$, $-\text{Cl}$) bear lone pairs of electrons. When attached to a chromophore, they donate lone pair electrons into the chromophore's π-system (mesomeric/resonance donation), raising the HOMO energy and lowering the HOMO–LUMO gap. This results in:

- **Bathochromic shift** (red shift): λ_{max} moves to longer wavelength.
- **Hyperchromic effect**: ε increases (absorption intensifies).

Step 2 — Alone they do not absorb: Pure methanol ($-\text{OH}$) or aniline ($-\text{NH}_2$ on benzene is a chromophore, but the amino group alone is not) in the UV-Vis region: alkyl amines and alcohols do not absorb above 200 nm in the absence of a π-system.

Why other options are wrong:

- Option B: This describes a chromophore (e.g., $\text{C}=\text{O}$, $\text{C}=\text{C}$), not an auxochrome.
- Option C: Many chromophores ($\text{C}=\text{O}$, extended polyenes) absorb strongly in UV-Vis without any auxochrome attached.

- Option D: $-NO_2$ is classified as a *chromophore* (absorbs at ≈ 270 nm, $n \rightarrow \pi^*$), not an auxochrome; it is an electron-withdrawing group.

Final Answer: Auxochromes cannot absorb UV-Vis alone but intensify and red-shift chromophore absorption via lone-pair donation into the π-system. $\Rightarrow$ A

Answer: (A) **Go Back to Q18**

Q19.

Solution

Concept — UV-Vis: Woodward Rules for α, β-Unsaturated Ketones (Enones): Woodward's empirical rules allow prediction of λ_{max} for enone chromophores ($\pi \rightarrow \pi^*$ band) by adding standard increments to a base value.

Step 1 — Base value and increments:

- **Base value: 215 nm** (acyclic enone or 6-membered ring enone, s-trans)
- α-substituent (alkyl, ring residue): $+10$ nm each
- β-substituent: $+12$ nm each
- Double-bond exocyclic to a ring: $+5$ nm
- Homodiene component (additional conjugated $C = C$): $+30$ nm

Step 2 — Example: For methyl vinyl ketone (CH_3-CO-CH $= CH_2$): base 215 nm; α-methyl (+10 nm) = 225 nm. Experimental $\lambda_{max} \approx$ 213–219 nm confirms the utility.

Why other options are wrong:

- Option A: The base value for cyclic 5-membered ring enones is 202 nm; for 6-membered and acyclic, it is 215 nm. Increments must always be applied for substitution.
- Option B: 217 nm is the Woodward base value for a *homodiene* (s-trans diene), not for an enone; β-alkyl groups increase, not decrease, λ_{max}.
- Option D: 230 nm is not the universal base value; substitution always modifies the base value upward.

Final Answer: Woodward base value for acyclic enones is 215 nm; increments for α- (+10 nm) and β- (+12 nm) substituents and ring residues are added. $\Rightarrow$ C

Answer: (C) **Go Back to Q19**

Q20.

Solution

Concept — UV-Vis: Bathochromic (Red) Shift Mechanisms: A bathochromic shift is a shift of λ_{max} to a longer wavelength, resulting from a decrease in the HOMO–LUMO energy gap of the chromophore system.

Step 1 — Extension of conjugation: Adding additional double bonds or aromatic rings to a π-system extends the conjugation, narrows the HOMO–LUMO gap (particle-in-a-box analogy: longer box $\to$ lower ΔE), and shifts absorption to longer λ. Example: ethylene (165 nm) $\to$ butadiene (217 nm) $\to$ hexatriene (258 nm).

Step 2 — Electron-donating groups: Auxochromes such as $-\text{OH}$ and $-\text{NR}_2$ donate electrons into the π-system, raising HOMO energy and decreasing ΔE, causing a red shift. Example: benzene (254 nm) $\to$ aniline (280 nm).

Why other options are wrong:

- Option A: Electron-withdrawing groups (EWG) can cause bathochromic shifts for some transitions ($n \to \pi^*$ bands may red-shift) but for $\pi \to \pi^*$ transitions, EWGs generally lower LUMO energy while raising HOMO, giving a net red shift only in push-pull systems; the statement as written ("reduces π-electron density and increases HOMO-LUMO gap") would cause a blue shift.
- Option C: Increasing solvent polarity causes a blue shift (hypsochromic) for $n \to \pi^*$ transitions (stabilises ground state n orbital more than excited π^*) but a red shift for $\pi \to \pi^*$ transitions; the statement "always blue-shifts all bands" is incorrect.
- Option D: Path length (l) affects absorbance magnitude (Beer–Lambert law) but has no effect on λ_{max}; it does not cause any spectral shift.

Final Answer: Extended conjugation or electron-donating groups lower the HOMO–LUMO gap, causing a bathochromic (red) shift of λ_{max}. $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) **Go Back to Q20**

Q21.

Solution

Concept — UV-Vis: Sandell Sensitivity Definition: Sandell sensitivity (S) is a figure of merit used to compare analytical methods in colorimetry and spectrophotometry. It is preferred over molar absorptivity alone because it is independent of the molecular weight of the analyte.

Step 1 — Definition: Sandell sensitivity is defined as the **mass of analyte per unit cross-sectional area (cm^2) of the light path that produces an absorbance of exactly 0.001** (i.e., 0.1% transmittance change):

$$S = \frac{M_r}{\varepsilon \times 10^3} \ [\mu\text{g cm}^{-2}]$$

where M_r is the relative molecular mass and ε is in $\text{L mol}^{-1}\text{ cm}^{-1}$.

Step 2 — Physical meaning: A smaller S value indicates higher sensitivity (less analyte needed per cm^2 to produce the detection threshold absorbance).

Why other options are wrong:

- Option A: This describes the limit of detection concept (minimum detectable concentration), not Sandell sensitivity; furthermore the absorbance threshold is 0.001, not unity.
- Option B: ε/M_r gives sensitivity in $\text{L g}^{-1}\text{ cm}^{-1}$ and is the specific molar absorptivity, not Sandell sensitivity; Sandell sensitivity uses M_r/ε.
- Option C: Absorbance produced by $1\ \mu\text{g mL}^{-1}$ in 1 cm cell is the specific absorbance ($A_1^{1\%}$ concept for 0.1%), not Sandell sensitivity; Sandell uses mass per area, not concentration.

Final Answer: Sandell sensitivity $= \mu$g of analyte per cm^2 of beam cross-section giving $A = 0.001$; numerically $S = M_r/(\varepsilon \times 10^3)$. $\Rightarrow$ $\boxed{D}$

Answer: (D) **Go Back to Q21**

Q22.

Solution

Concept — UV-Vis: Stray Light and Negative Deviation from Beer–Lambert Law: Stray light (I_s) comprises photons at wavelengths other than λ selected by the monochromator that reach the detector. These photons are typically unabsorbed (or weakly absorbed) by the analyte.

Step 1 — Mathematical effect: True Beer–Lambert law assumes monochromatic radiation. With stray light (I_s not absorbed by the analyte):

$$A_{\text{apparent}} = \log \frac{I_0 + I_s}{I_t + I_s}$$

At *high* concentration, $I_t \to 0$ (analyte absorbs nearly all primary radiation), but I_s passes through unattenuated, so $A_{\text{apparent}} \to \log \frac{I_0 + I_s}{I_s}$, which is a *finite* value less than the true absorbance. The calibration curve flattens (negative deviation).

Step 2 — Practical consequence: At low concentrations stray light has negligible effect ($I_s \ll I_t$); at high concentrations (high absorbance) stray light causes the apparent absorbance to be lower than expected, leading to underestimation of concentration and non-linear calibration curves.

Why other options are wrong:

- Option B: Stray light causes a *negative* (downward) deviation, not a positive one.
- Option C: Stray light is *most problematic* at high concentrations (high absorbance), not at low concentrations; random noise limiting detection is a different issue (detector/electronic noise).
- Option D: Stray light does not shift λ_{max}; monochromator calibration or bandpass errors cause peak shifts.

Final Answer: Stray light causes a negative deviation from Beer–Lambert law at high analyte concentrations, flattening the calibration curve. $\Rightarrow \boxed{A}$

Answer: (A) **Go Back to Q22**

Q23.

Solution

Concept — UV-Vis: Double-Beam vs Single-Beam Spectrophotometer: In a single-beam instrument, the reference is measured first (to blank the instrument), then the sample is inserted. Source fluctuations between the two measurements introduce error. A double-beam design eliminates this limitation.

Step 1 — Double-beam operation: A beam splitter (rotating mirror or half-mirror) divides the monochromatic radiation into two beams: one passes through the **sample cell**, the other through the **reference cell** (blank). The detector (or two matched detectors) alternately (or simultaneously) measures I_t (sample) and I_0 (reference). Absorbance is computed as $A = \log(I_0/I_t)$ in real-time.

Step 2 — Advantage: Any drift in source intensity, detector sensitivity, or cell/solvent absorption is automatically compensated because both beams are affected equally. This produces highly stable baselines and accurate spectra, especially during wavelength scans where source intensity varies with λ.

Why other options are wrong:

- Option A: Splitting the beam *halves* the light intensity in each path; sensitivity is not doubled. The advantage is stability/accuracy, not higher intensity.
- Option B: Both single- and double-beam instruments use monochromators; the double-beam design does not eliminate the need for monochromatic radiation.
- Option D: Standard double-beam spectrophotometers measure one wavelength at a time (scanning); simultaneous multi-wavelength measurement at two λ values requires diode-array (PDA) detectors, not a standard double-beam design.

Final Answer: The double-beam spectrophotometer simultaneously measures sample and reference, automatically correcting for source fluctuations and solvent absorption. $\Rightarrow \boxed{C}$

Answer: (C) **Go Back to Q23**

Q24.

Solution

Concept — UV-Vis: Isoabsorptive (Isobestic) Point: When two components X and Y that interconvert or are mixed in varying ratios have equal molar absorptivities at a specific wavelength, that wavelength is called the isoabsorptive (or isobestic) point.

Step 1 — Definition: At λ_i (isoabsorptive point), $\varepsilon_X(\lambda_i) = \varepsilon_Y(\lambda_i)$. Therefore:

$$A(\lambda_i) = \varepsilon_X(\lambda_i) \cdot c_X \cdot l + \varepsilon_Y(\lambda_i) \cdot c_Y \cdot l = \varepsilon_i \cdot l \cdot (c_X + c_Y)$$

Since ε_i is fixed, measuring A at λ_i directly gives the *total concentration* $(c_X + c_Y)$ regardless of the ratio of X to Y.

Step 2 — Application: Isoabsorptive points are used: (1) to verify that only two species are interconverting (multiple spectra passing through one point confirm a two-component system); (2) to determine total concentration of X + Y in mixtures without prior separation (e.g., simultaneous analysis of acid and base forms of an ionisable drug).

Why other options are wrong:

- Option A: The isoabsorptive point is not the $\lambda_{\max}$ of any single component; it is the crossover point where both components happen to have equal absorptivity.
- Option C: The zero-crossing of the first derivative occurs at $\lambda_{\max}$ of the zero-order spectrum, not at the isoabsorptive point; these are different concepts.
- Option D: Baseline correction in derivative spectroscopy uses a different principle (differentiation of a flat baseline yields zero); the isoabsorptive point is not a baseline correction tool.

Final Answer: At the isoabsorptive point, $\varepsilon_X = \varepsilon_Y$, so total absorbance gives total concentration $(c_X + c_Y)$ without prior separation. $\Rightarrow \boxed{\text{B}}$

Answer: (B) **Go Back to Q24**

Q25.

Solution

Concept — UV-Vis: First-Derivative Spectroscopy ($dA/d\lambda$): Derivative spectroscopy involves mathematically differentiating the absorbance spectrum. The first derivative ($n = 1$) of the Beer–Lambert spectrum has useful analytical properties.

Step 1 — Elimination of constant background: If the background (matrix, solvent) contributes a constant (wavelength-independent) absorbance A_0, then:

$$\frac{d}{d\lambda}(A_{\text{analyte}} + A_0) = \frac{dA_{\text{analyte}}}{d\lambda} + 0$$

The constant background term differentiates to **zero**, eliminating it entirely. Similarly, a linearly sloping background (first-order interference) is eliminated by the *second* derivative.

Step 2 — Zero-crossing for λ_{max} identification: At λ_{max} of the zero-order spectrum, the slope $dA/d\lambda = 0$ (maximum of a smooth curve). Thus the first derivative **crosses zero** at each true λ_{max}. For overlapping peaks that appear as a single broad envelope in the zero-order spectrum, the derivative reveals the underlying components as separate zero-crossings, enabling resolution.

Why other options are wrong:

- Option A: The derivative spectrum shows zero (not doubled peaks) at λ_{max}; the first derivative has positive and negative peaks flanking each λ_{max}, not peaks at the same positions.
- Option B: While differentiation amplifies high-frequency noise (a practical limitation requiring smoothing), broad overlapping peaks with different λ_{max} values *are* resolved by derivative methods; the statement is incorrect.
- Option C: The first derivative is indeed zero at a *flat* baseline, which is *advantageous* (not disadvantageous); derivative spectroscopy is more useful than zero-order for resolving overlapping peaks from rising backgrounds.

Final Answer: First-derivative spectroscopy eliminates constant background and identifies λ_{max} by zero-crossings, resolving overlapping peaks. $\Rightarrow \boxed{D}$

Answer: (D) **Go Back to Q25**

Answer Key

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