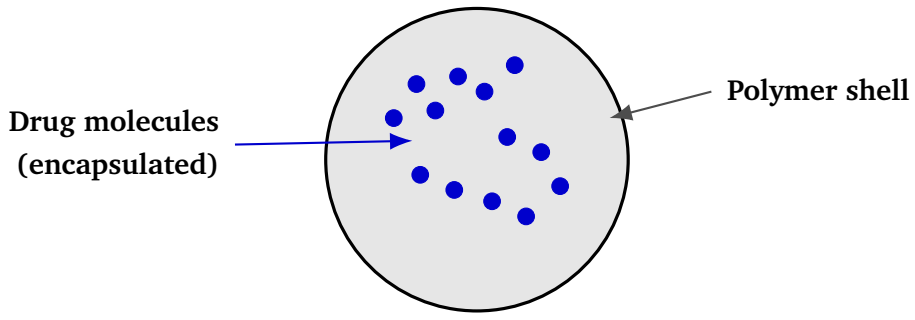
GPAT Pharmaceutics

Sample Paper – 3

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 — Novel Drug Delivery Systems, Transdermal Drug Delivery, Pulmonary Drug Delivery, Preformulation.**
- 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.



Schematic cross-section of a polymeric nanoparticle (PLGA)

Q1. The diagram shows a polymeric nanoparticle prepared from **PLGA** (poly-lactic-*co*-glycolic acid). Which preparation method involves dissolving PLGA and drug in a *water-miscible* organic solvent (e.g. acetone) and adding this solution dropwise into an aqueous phase, causing **spontaneous nanopar-**

ticle formation by rapid solvent diffusion—without the need for sonication or high-energy homogenisation?

(A) Emulsion-solvent evaporation

(B) Salting-out

(C) Nanoprecipitation (solvent displacement)

(D) Spray drying

Q2. PEGylated liposomes ("stealth" liposomes) show significantly prolonged blood-circulation half-lives compared with conventional (non-PEGylated) liposomes of similar size and lipid composition. Which mechanism **primarily** accounts for this extended circulation?

(A) PEG chains enhance drug encapsulation efficiency by forming hydrophobic interactions within the lipid bilayer

(B) PEG chains create a steric barrier that hinders adsorption of opsonins (IgG, complement proteins C3b), thereby reducing recognition and phagocytic clearance by reticuloendothelial system (RES) macrophages

(C) PEG increases the rigidity of the liposomal membrane, preventing mechanical rupture in the bloodstream

(D) PEG selectively binds folate receptors on tumour vasculature, preventing hepatic first-pass uptake

Q3. Which statement **correctly** differentiates a **microsphere** from a **microcapsule** in microparticulate drug-delivery systems?

(A) A microsphere has drug molecules uniformly dispersed throughout a polymer matrix (monolithic system), whereas a microcapsule has drug enclosed within a continuous polymer membrane shell (reservoir system)

(B) A microsphere is always smaller (below 1 μm) than a microcapsule (1–1000 μm) by definition

(C) Microcapsules are prepared exclusively by emulsion-solvent evaporation; microspheres require coacervation techniques

(D) Microspheres release drug solely by matrix erosion, while microcapsules release drug exclusively by membrane diffusion

Q4. PAMAM (polyamidoamine) dendrimers are synthesised divergently by stepwise addition of branching units. The number of surface terminal amine groups doubles with each generation. How many terminal $-NH_2$ groups does a **Generation 4 (G4)** PAMAM dendrimer possess?

(A) 16

(B) 32

(C) 48

(D) 64

Q5. Solid lipid nanoparticles (SLN) are prepared from lipids that remain **solid** at body temperature. Which of the following is a **key advantage** of SLNs over conventional oil-in-water nanoemulsions for sustained drug delivery?

(A) SLNs always achieve higher drug loading capacity than nanoemulsions because crystalline lipids accommodate more drug per unit volume

(B) SLNs are formulated entirely without surfactants, unlike nanoemulsions which require large amounts of emulsifiers

(C) The solid lipid matrix of SLNs provides controlled (extended) drug release and physically protects encapsulated drugs from chemical degradation—advantages absent in the fluid oil core of nanoemulsions

(D) SLNs exhibit lower cytotoxicity than nanoemulsions across all cell lines and species

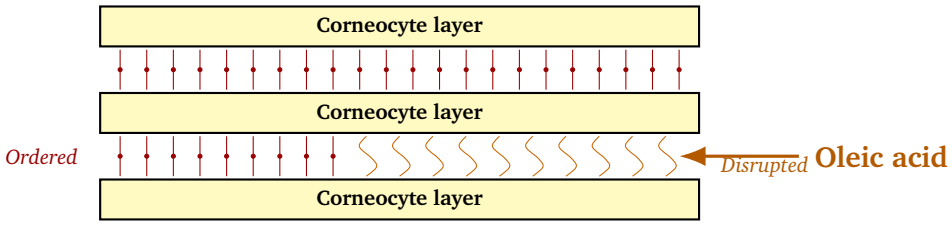
Q6. A reservoir-type transdermal drug-delivery system (TDDS) patch contains a drug reservoir sandwiched between an impermeable backing membrane and a skin-contact adhesive layer. Which component is **primarily responsible** for controlling the *rate* of drug delivery to the skin?

(A) Pressure-sensitive adhesive (PSA) layer

(B) Impermeable backing membrane

(C) Drug reservoir containing a saturated drug solution or suspension

(D) Rate-controlling polymeric membrane placed between the reservoir and the adhesive layer



Stratum corneum: oleic acid disrupts intercellular lipid bilayer order (right side of gap)

Q7. The diagram shows two zones of the stratum corneum intercellular space: ordered lipid bilayers (left) and a region disrupted by oleic acid (right). Which mechanism **best** explains why oleic acid (*cis*-18:1) is an effective transdermal penetration enhancer?

(A) Oleic acid forms a thick occlusive film on the skin surface that hydrates the stratum corneum, passively facilitating drug permeation

(B) Oleic acid intercalates into the intercellular lipid bilayers of the stratum corneum via its kinked *cis* double bond, creating disordered "liquid lake" domains that markedly increase lipid fluidity and drug diffusivity

(C) Oleic acid acts primarily as a co-solvent in the vehicle, raising the thermodynamic activity of the drug and improving its partitioning into the stratum corneum

(D) Oleic acid irreversibly extracts ceramides from the stratum corneum, creating permanent aqueous pores for drug transport

Q8. In transdermal **iontophoresis**, a low direct electric current drives ionised drug molecules across the skin. Under which electrode should a **cationic (positively charged)** drug be

placed for effective transdermal delivery?

(A) Anode (positive electrode), because like charges repel and push the cationic drug toward and across the skin

(B) Cathode (negative electrode), because opposite charges attract and draw the cationic drug into the skin

(C) Either electrode, since transdermal iontophoresis efficacy is entirely electrode-independent for all ionised drugs

(D) Neither electrode; cationic drugs are delivered exclusively by electroosmotic flow, which is independent of electrode placement

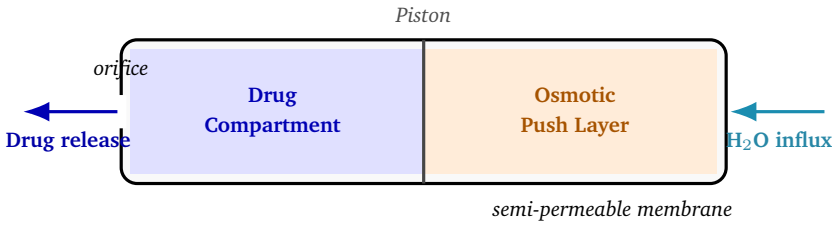
Q9. A scientist compares the *in vitro* drug-release profiles of a **matrix-type** transdermal patch with a **reservoir-type** patch of identical drug loading. Which statement **correctly** describes the expected difference in release kinetics?

(A) The matrix-type patch gives zero-order release; the reservoir-type patch gives first-order release

(B) Both matrix-type and reservoir-type patches give zero-order release throughout their designed use period

(C) The reservoir-type patch gives near zero-order (constant-rate) release controlled by the rate-controlling membrane; the matrix-type patch gives Higuchi (square-root-of-time) kinetics as drug depletes from the polymer matrix

(D) Matrix patches always exhibit a pronounced initial burst release, whereas reservoir patches show a steep lag time before any measurable drug is released



Cross-section of an OROS Push-Pull Osmotic Tablet

Q10.

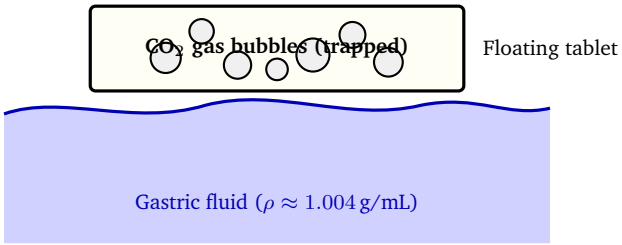
The diagram shows an OROS (Osmotic Release Oral System) tablet: water enters through the semi-permeable coat by osmosis, expanding the push layer and extruding drug through the precision orifice at a controlled rate. Which force is the **primary driver** of drug delivery in this system?

(A) Mechanical spring pressure compressed within the tablet core

(B) Osmotic pressure generated by water influx across the semi-permeable coat into the osmotic push layer

(C) Acid-base gas generation creating hydraulic pressure within the tablet

(D) Electrostatic repulsion between ionised drug molecules in the drug compartment



Floating tablet: trapped CO_2 reduces bulk density below gastric fluid density

Q11.

The diagram shows a floating tablet with CO_2 gas bubbles trapped in the polymer matrix, reducing bulk density below 1 g/mL and enabling floatation on gastric contents. Which

combination of excipients generates the carbon dioxide required for buoyancy when the tablet contacts gastric fluid?

(A) Magnesium stearate and talc

(B) Hydroxypropylmethylcellulose (HPMC) and ethyl cellulose

(C) Carbopol 934 and Eudragit® S100

(D) Sodium bicarbonate and citric acid

Q12. Mucoadhesive drug-delivery systems exploit polymer–mucus interactions to prolong formulation residence at absorptive sites. Which polymer generally exhibits the **highest mucoadhesive strength** among the following commonly used mucoadhesive excipients?

(A) Sodium carboxymethylcellulose (Na-CMC)

(B) Hydroxypropylmethylcellulose (HPMC)

(C) Carbopol 934 (cross-linked polyacrylic acid)

(D) Methylcellulose (MC)

Q13. Several theories have been proposed to explain the molecular basis of bioadhesion. Which theory proposes that **electron transfer between the mucous membrane surface and the bioadhesive polymer** creates an electrical double layer at the interface, with the resulting attractive Coulombic forces responsible for adhesion?

(A) Electronic theory

(B) Adsorption theory (secondary valence forces: van der Waals, hydrogen bonds)

(C) Wetting theory (contact angle / surface energy approach)

(D) Fracture theory (energy required to separate bonded surfaces)

Q14. Colon-targeted prodrug delivery exploits the unique enzymatic environment of the large intestine. Which enzyme is **specifically** responsible for activating azo-linked prodrugs (e.g. sulfasalazine) in the colon to release the active drug at the site of action?

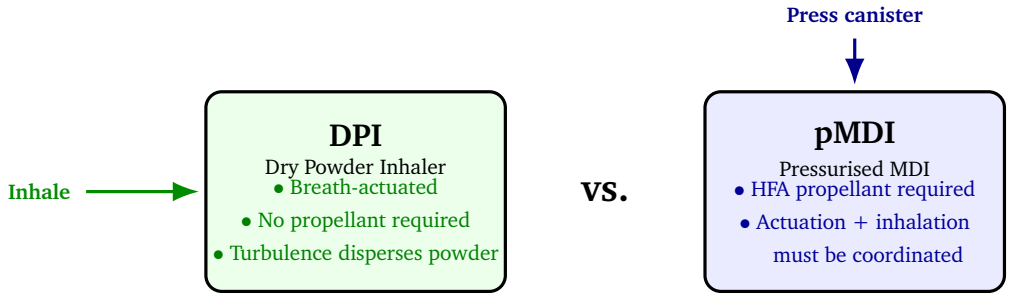
(A) Glucuronidase produced by colonic bacteria, which hydrolyses glucuronide-conjugated prodrugs

(B) Azoreductase produced by anaerobic colonic bacteria, which cleaves the azo (−N=N−) bond linking the drug to its carrier

(C) Pectinase secreted by colonic epithelial cells, which degrades pectin-based polymer coatings

(D) Alkaline phosphatase released under the alkaline pH conditions of the distal colon

Q15.



DPI (breath-actuated, propellant-free) vs. pMDI (propellant-driven, requires hand–breath coordination)

The diagram compares a DPI and a pMDI. Which statement **correctly** describes a key operational difference between these two inhaler types?

(A) DPIs use a pressurised propellant to disperse drug powder into the airways, while pMDIs are breath-actuated and propellant-free

(B) pMDIs consistently deliver particles with a larger mass median aerodynamic diameter (MMAD) than DPIs across all formulations

(C) DPIs require a spacer (valved holding chamber) for efficient lung deposition; pMDIs do not

(D) DPIs are breath-actuated and propellant-free, whereas pMDIs rely on a pressurised HFA propellant and require coordinated canister actuation with inhalation

Q16. The **mass median aerodynamic diameter** (MMAD) of aerosol particles delivered from an inhaler is a critical characterisation parameter for predicting respiratory-tract deposition site. Which instrument is the standard method for measuring MMAD of inhaled aerosols?

(A) Andersen Cascade Impactor (ACI) or Next Generation Impactor (NGI), which separate aerosol particles by inertial impaction across calibrated multi-stage size-cut plates

(B) Dynamic light scattering (DLS), which measures the hydrodynamic diameter of particles in liquid suspension

(C) Laser diffraction particle size analyser, which measures the geometric (physical) diameter of dispersed powder particles by light scattering patterns

(D) Scanning electron microscopy (SEM), which provides high-resolution images of particle morphology and size

Q17. Following the Montreal Protocol (1987), chlorofluorocarbon (CFC) propellants were phased out from pressurised metered-dose inhalers due to their ozone-depleting potential. Which class of propellants replaced CFC-11 and CFC-12 in pMDIs?

(A) Nitrogen (N_2) compressed-gas propellants

(B) Dimethyl ether (DME)-based propellants

(C) Hydrofluoroalkanes (HFAs), specifically HFA-134a and HFA-227ea, which contain no chlorine

(D) Hydrochlorofluorocarbons (HCFCs), which retain a small but non-zero ozone-depleting potential

Q18. During preformulation stability assessment, the **critical relative humidity (CRH)** of a new drug substance is determined. Which statement **most accurately** defines CRH and describes what occurs when the environmental relative hu-

midity exceeds this value?

(A) CRH is the relative humidity at which the drug begins to undergo significant hydrolytic degradation by atmospheric water molecules

(B) CRH is the minimum relative humidity above which a crystalline solid absorbs sufficient atmospheric moisture to dissolve (deliquesce) from its surface, losing its dry solid character

(C) CRH is the optimal relative humidity required for successful wet granulation of a hygroscopic drug substance

(D) CRH is the maximum allowable relative humidity in a packaging facility for moisture-sensitive drugs as specified in ICH Q1A(R2)

Q19. Differential Scanning Calorimetry (DSC) is routinely used in preformulation to characterise the solid-state properties of drug substances. What does a **sharp endothermic peak** in a DSC thermogram most likely represent for a pure crystalline drug substance?

(A) Melting (fusion) of the crystalline drug at its characteristic melting point (T_m)

(B) Exothermic crystallisation from an amorphous state upon heating (cold crystallisation)

(C) Exothermic thermal decomposition of the drug at elevated temperature

(D) Glass transition (T_g) of the amorphous form of the drug substance

Q20. The angle of repose (θ) is a simple measure of powder flowability. A batch of granules is characterised and classified as having **very poor flowability**, indicating that granulation optimisation or glidant addition is required before tableting. Which angle of repose range corresponds to **very poor flowability**?

(A) Less than 25°

(B) 25°–30°

(C) 30°–35°

(D) Greater than 40°

Q21. Oral delivery of therapeutic peptides is limited by enzymatic degradation and poor intestinal membrane permeability. Which approach improves oral peptide absorption specifically by **modulating tight junctions** to increase paracellular permeability of the intestinal epithelium?

(A) Coating the peptide with enteric polymers (e.g. Eudragit® L100) to protect it from gastric acid degradation

(B) Co-administration of protease inhibitors (e.g. aprotinin, soybean trypsin inhibitor) to reduce enzymatic degradation in the gastrointestinal lumen

(C) Use of tight-junction modulators such as SNAC (sodium *N*-[8-(2-hydroxybenzoyl)amino]caprylate) that transiently

and reversibly open paracellular channels

(D) Formulating the peptide in a self-emulsifying drug-delivery system (SEDDS) to promote lymphatic absorption via intestinal chylomicrons

Q22. PLGA is widely used for biodegradable implantable drug-delivery systems. Which statement about PLGA **biodegradation** in an implant is **correct**?

(A) PLGA degrades by surface erosion only, releasing drug sequentially from the outer shell inwards, similar to polyanhydrides

(B) PLGA undergoes bulk hydrolysis throughout the entire matrix to yield lactic and glycolic acids; a 50:50 lactide:glycolide ratio degrades significantly faster than an 85:15 ratio

(C) Higher molecular weight PLGA always degrades faster than lower molecular weight PLGA, regardless of the lactide:glycolide ratio

(D) PLGA implants require tissue-derived esterase enzymes for hydrolysis; they do not degrade spontaneously in aqueous media

Q23. Conventional ophthalmic eye drops achieve very low bioavailability (typically below 5%) at target ocular tissues. Which is the **major barrier** responsible for this poor bioavailability?

(A) Precorneal drainage via the nasolacrimal duct, which rapidly removes the instilled dose from the conjunctival sac within

1–2 minutes of instillation

(B) The hydrophobic corneal stroma, which acts as an impenetrable barrier to most drug molecules

(C) Tight junctions of the conjunctival epithelium, which block all passive drug transport into the eye

(D) Extensive protein binding in the tear film that sequesters all free drug and prevents corneal penetration

Q24. Bioadhesive polymers are incorporated into vaginal drug-delivery systems to prolong drug residence time in the vaginal cavity. Which polymer is **most widely used** in bioadhesive vaginal gels due to its strong adhesion to vaginal mucosa?

(A) Hydroxyethylcellulose (HEC)

(B) Sodium alginate

(C) Xanthan gum

(D) Polycarbophil (cross-linked polyacrylic acid, e.g. Noveon® AA-1)

Q25. A pharmaceutical company files an **Abbreviated New Drug Application (ANDA)** with the USFDA for approval of a generic drug product. What is the **primary regulatory requirement** that the ANDA applicant must fulfil to obtain approval?

(A) Conduct and submit data from Phase III randomised controlled clinical trials demonstrating the efficacy and safety of the proposed generic product

(B) Submit a complete New Drug Application (NDA) with full preclinical toxicology, pharmacology, and clinical study data for the drug substance

(C) Demonstrate **bioequivalence** to the Reference Listed Drug (RLD) through pharmacokinetic studies in which the 90% confidence interval for AUC and $C_{\max}$ ratios falls within 80.00–125.00%

(D) Obtain a new independent patent for the generic formulation technology before the ANDA can be filed with the FDA

Detailed Solutions

Q1.

Solution

Concept — Nanoparticle Preparation Methods: Polymeric nanoparticles from PLGA can be prepared by several methods depending on the solvent used and the energy input required. Nanoprecipitation exploits the Marangoni effect: rapid interfacial solvent diffusion triggers spontaneous polymer precipitation without any mechanical energy input.

Step 1 — Identify the solvent requirement: The question specifies a *water-miscible* organic solvent (e.g. acetone). Emulsion-solvent evaporation uses a water-*immiscible* solvent (e.g. dichloromethane) to form an o/w emulsion requiring sonication or homogenisation. Nanoprecipitation uniquely uses a water-miscible solvent to produce spontaneous nanoparticle formation upon addition to water.

Step 2 — Confirm mechanism: When the acetone/PLGA solution contacts the aqueous phase, rapid solvent diffusion creates local supersaturation at the interface, causing polymer chains to coalesce into nanoparticles spontaneously—no high-energy processing needed.

Why other options are wrong:

- Option A: Emulsion-solvent evaporation uses a water-immiscible solvent and requires sonication or high-pressure homogenisation to form an emulsion.
- Option B: Salting-out adds a high-concentration electrolyte or polymer to a water-miscible organic phase to salt out the polymer; it is not driven by simple solvent diffusion into water.
- Option C: Nanoprecipitation (solvent displacement) uses a water-miscible solvent and requires no sonication. **Correct.**
- Option D: Spray drying atomises a drug-polymer solution into a hot drying gas; nanoparticle formation is by moisture evaporation, not solvent diffusion into water.

Final Answer: Spontaneous nanoparticle formation by rapid solvent diffusion from a water-miscible solvent $\Rightarrow$ C

Answer: (C) Go Back to Q1

Q2.

Solution

Concept — PEGylation and Reticuloendothelial System (RES) Evasion: Conventional liposomes are rapidly opsonised (coated with IgG, C3b) and phagocytosed by Kupffer cells and splenic macrophages (RES), with half-lives of minutes to hours. PEGylation extends circulation to tens of hours by a purely steric mechanism.

Step 1 — Mechanism of PEG coating: The flexible, hydrophilic PEG chains form a dense polymer brush on the liposome surface. This brush creates a steric cloud that physically repels incoming plasma proteins, preventing the adsorption of opsonins (IgG, complement C3b) that would otherwise mark the liposome for macrophage uptake.

Step 2 — Consequence for circulation: Without opsonin coating, Fc and complement receptors on RES macrophages cannot recognise the liposome, dramatically reducing hepatic and splenic clearance and prolonging the circulation half-life from 2–4 h to 20–40 h.

Why other options are wrong:

- Option A: PEG is a hydrophilic polymer; it does not form hydrophobic interactions within the lipid bilayer and does not primarily affect encapsulation efficiency.
- Option B: Steric hindrance of opsonin adsorption by the PEG brush, reducing RES recognition. **Correct.**
- Option C: PEG does not rigidify the lipid membrane; it forms a flexible hydrophilic layer external to the bilayer and has no significant effect on membrane mechanical properties.
- Option D: Folate-receptor targeting is a property of folate-conjugated liposomes, not plain PEGylated liposomes; PEG does not bind folate receptors.

Final Answer: PEG chains sterically block opsonin adsorption, reducing RES clearance $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q2

Q3.

Solution

Concept — Monolithic vs Reservoir Microparticulate Systems: Microparticles are classified by their internal architecture: *matrix* systems (microspheres) have drug homogeneously dispersed throughout the polymer, while *reservoir* systems (microcapsules) have a discrete drug core enclosed by a polymer membrane shell.

Step 1 — Microsphere (matrix) architecture: In a microsphere, drug molecules are uniformly dissolved or dispersed within a continuous polymer matrix (monolithic structure). Release is governed by drug diffusion through the matrix and/or matrix erosion.

Step 2 — Microcapsule (reservoir) architecture: In a microcapsule, the drug occupies a central core (liquid, solid, or semi-solid) completely surrounded by a continuous polymer membrane shell (reservoir structure). The membrane controls release by diffusion, and the release rate depends on membrane thickness and permeability.

Why other options are wrong:

- Option A: Microsphere = monolithic drug-polymer matrix; microcapsule = drug core within a polymer shell (reservoir). **Correct.**
- Option B: The distinction is structural (matrix vs reservoir), not based on absolute particle size; both types overlap in the 1–1000 μm range and submicron particles also exist in both categories.
- Option C: Both microspheres and microcapsules can be prepared by multiple methods including emulsion-solvent evaporation, coacervation, and spray drying; neither technique is exclusive to one type.
- Option D: Microspheres can release drug by both diffusion and erosion; microcapsules can also release by osmotic rupture or swelling in addition to membrane diffusion.

Final Answer: Microsphere = drug dispersed in polymer matrix; microcapsule = drug enclosed in polymer membrane shell $\Rightarrow$ A

Answer: (A) Go Back to Q3

Q4.

Solution

Concept — Dendrimer Generation and Terminal Group Count: PAMAM dendrimers are synthesised divergently from an ethylenediamine core. Each generation doubles the number of surface terminal amine groups. Starting from a G0 core with 4 terminal $-NH_2$ groups, successive generations follow the pattern $N = 4 \times 2^G$.

Step 1 — Apply the formula for each generation:

$$G0 : 4{\times}2^0 = 4 \quad G1 : 4{\times}2^1 = 8 \quad G2 : 4{\times}2^2 = 16 \quad G3 : 4{\times}2^3 = 32 \quad G4 : 4{\times}2^4 = 64$$

Step 2 — Identify G4: At Generation 4, the number of surface $-NH_2$ groups $= 4 \times 2^4 = 4 \times 16 = 64$. This large number of surface amines allows extensive functionalisation for drug conjugation, targeting ligand attachment, and charge-based interactions.

Why other options are wrong:

- Option A: 16 corresponds to G2 ($4 \times 2^2 = 16$), not G4.
- Option B: 32 corresponds to G3 ($4 \times 2^3 = 32$), not G4.
- Option C: 48 does not correspond to any valid PAMAM generation; it is not a power-of-two multiple of 4.
- Option D: $64 = 4 \times 2^4$, which is the correct terminal group count for G4. **Correct.**

Final Answer: G4 PAMAM has $4 \times 2^4 = 64$ terminal $-NH_2$ groups $\Rightarrow$ D

Answer: (D) Go Back to Q4

Q5.

Solution

Concept — Solid Lipid Nanoparticles vs Nanoemulsions: SLNs replace the liquid oil core of nanoemulsions with a solid lipid matrix that is crystalline or semi-crystalline at body temperature (37 °C). This physicochemical difference underpins their key advantage for sustained delivery.

Step 1 — Role of the solid lipid matrix: The crystalline lipid lattice creates physical diffusion barriers: drug molecules must diffuse through a rigid matrix, slowing release compared to the fluid oil core of nanoemulsions where drug diffusion is rapid. The solid matrix also physically shields encapsulated drug from hydrolysis,

oxidation, and light.

Step 2 — Why nanoemulsions lack this advantage: In a nanoemulsion, the oil core is liquid at body temperature, offering no diffusion barrier beyond simple partitioning. Drug release is rapid and burst-prone, with poor protection from chemical degradation.

Why other options are wrong:

- Option A: SLNs often have *lower* drug loading than nanoemulsions because the crystalline lipid lattice expels drug molecules during crystallisation (polymorphic transition problem), not higher.
- Option B: SLNs still require surfactants/emulsifiers (e.g. poloxamer 188, lecithin, Tween 80) for colloidal stability; the claim that they are formulated entirely without surfactants is false.
- Option C: The solid lipid matrix provides extended release and chemical protection not available from a fluid nanoemulsion oil core. **Correct.**
- Option D: Cytotoxicity of SLNs depends on lipid type, surfactant concentration, and cell line; it is not universally lower than nanoemulsions across all conditions.

Final Answer: Solid lipid matrix provides controlled drug release and chemical protection absent in nanoemulsions $\Rightarrow$ C

Answer: (C) Go Back to Q5

Q6.

Solution

Concept — Reservoir-Type TDDS Patch Architecture: A reservoir transdermal patch has four functional layers: (i) impermeable backing membrane, (ii) drug reservoir, (iii) rate-controlling polymeric membrane, and (iv) pressure-sensitive adhesive. Each layer has a specific role; only one controls the *rate* of drug delivery.

Step 1 — Function of each component: The *backing membrane* provides mechanical support and prevents drug loss from the back of the patch. The *reservoir* stores a saturated drug solution or suspension and provides a constant thermodynamic activity. The *PSA* adheres the patch to skin. The *rate-controlling membrane* (e.g. ethylene-vinyl acetate copolymer) is the only component that limits the flux of drug to the skin.

Step 2 — Why rate-controlling membrane governs release: At steady state, the flux $J = D_m K_m \Delta C / h_m$, where D_m, K_m, and h_m are the membrane's diffusivity,

partition coefficient, and thickness. By designing this membrane, the pharmaceutical scientist controls the maximum delivery rate independently of reservoir composition.

Why other options are wrong:

- Option A: The PSA layer controls adhesion to the skin surface, not the drug-delivery rate; it must be permeable enough not to be the rate-limiting barrier.
- Option B: The impermeable backing membrane prevents drug loss from the top of the patch; it does not govern the rate to the skin.
- Option C: The drug reservoir maintains a constant concentration gradient (thermodynamic driving force) but does not limit the rate; the rate-controlling membrane does.
- Option D: The rate-controlling polymeric membrane placed between reservoir and adhesive governs drug flux to the skin. **Correct.**

Final Answer: Rate-controlling polymeric membrane between reservoir and adhesive governs delivery rate $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q6

Q7.

Solution

Concept — Oleic Acid as a Transdermal Penetration Enhancer: The stratum corneum (SC) barrier arises from the highly ordered lamellar lipid bilayers in the intercellular spaces between corneocytes. Penetration enhancers reduce this barrier by disrupting lipid packing order.

Step 1 — Structural basis for oleic acid's activity: Oleic acid (*cis*-18:1 fatty acid) has a 30° kink at its C9 double bond. When oleic acid intercalates between the ordered, predominantly saturated lipid chains (ceramides, free fatty acids) in the SC, this geometric kink disrupts the tight packing of acyl chains. The result is localised fluid "liquid lake" domains of markedly higher lipid fluidity.

Step 2 — Effect on drug diffusivity: In these disordered domains, the diffusion coefficient D of co-administered drug molecules increases by orders of magnitude relative to the rigid gel-phase bilayers, dramatically increasing transdermal flux according to Fick's first law: $J = D \cdot K \cdot \Delta C/h$.

Why other options are wrong:

- Option A: Occlusion (surface film) can increase skin hydration but is not

the primary mechanism of oleic acid's penetration-enhancing activity; many fatty acids form films without significant enhancement.

- Option B: Oleic acid intercalates into SC intercellular lipid bilayers via its *cis* double bond, creating disordered "liquid lake" domains that increase drug diffusivity. **Correct.**
- Option C: Co-solvent action (raising thermodynamic activity) is a property of the vehicle formulation, not a specific action of oleic acid on SC lipid structure; it is not the dominant mechanism of enhancement.
- Option D: Ceramide extraction by oleic acid is not irreversible; oleic acid reversibly disrupts lipid organisation rather than permanently removing ceramides, which distinguishes it from detergents and chemical extractants.

Final Answer: Oleic acid's *cis* double bond creates disordered lipid "liquid lake" domains, increasing drug diffusivity $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q7

Q8.

Solution

Concept — Iontophoresis: Electrode Polarity and Drug Ion Charge: Iontophoresis uses a small direct current (typically $\leq 0.5\,\text{mA/cm}^2$) to drive ionic drugs across the skin. The principle governing electrode placement is simple electrostatics: like charges repel, unlike charges attract.

Step 1 — Anode for cationic drugs: The anode (positive electrode) repels positively charged (cationic) drug ions, driving them away from the electrode and *into* the skin toward the negatively charged cathode placed elsewhere on the body. This electrophoretic repulsion is the primary driving force.

Step 2 — Electroosmotic contribution: In addition to direct electrophoresis, electroosmotic flow (bulk water flow from anode to cathode through skin appendages) also assists cationic drug transport from the anode side, further supporting anode placement for cationic drugs.

Why other options are wrong:

- Option A: Placing a cationic drug at the anode causes electrophoretic repulsion that drives the drug into the skin—the correct choice. **Correct.**
- Option B: Placing a cationic drug at the cathode would attract the drug *toward* the electrode (back toward the device), opposing transdermal delivery.
- Option C: Electrode polarity critically determines which ionic species is driven through the skin; the statement that efficacy is electrode-independent

is false.

- Option D: Electroosmotic flow assists cationic drug delivery from the anode but is not independent of electrode placement; furthermore, electrophoresis (which depends on electrode placement) is typically the dominant mechanism for small ionic drugs.

Final Answer: Cationic drug placed at the anode; like-charge repulsion drives it into the skin $\Rightarrow$ A

Answer: (A) Go Back to Q8

Q9.

Solution

Concept — Release Kinetics of Matrix vs Reservoir Transdermal Patches: The internal architecture of a transdermal patch determines its drug-release kinetics. A reservoir patch has a rate-controlling membrane; a matrix patch releases drug as it diffuses out of the polymer matrix.

Step 1 — Reservoir patch kinetics: The rate-controlling membrane maintains a constant concentration gradient and thus a constant flux ($J = P \cdot \Delta C$, where P is the membrane permeability). This produces near zero-order (constant-rate) release, which is independent of the remaining drug amount in the reservoir as long as the reservoir is not depleted.

Step 2 — Matrix patch kinetics (Higuchi model): In a matrix patch, drug is dispersed homogeneously in the polymer. As drug near the surface is depleted, the diffusion path length increases over time. The Higuchi equation describes cumulative release: $Q = \sqrt{D(2A - C_s)C_s \cdot t}$, giving a $\sqrt{t}$ (square-root-of-time) relationship, i.e. decreasing release rate over time.

Why other options are wrong:

- Option A: This is exactly reversed; the *reservoir* patch gives near zero-order kinetics, and the *matrix* patch gives Higuchi ($\sqrt{t}$) kinetics, not the other way around.
- Option B: Matrix patches do NOT give zero-order release; Higuchi kinetics are inherently square-root-of-time (declining rate), not constant rate.
- Option C: Reservoir = near zero-order (rate-controlling membrane); matrix = Higuchi square-root-of-time kinetics. **Correct.**
- Option D: While matrix patches can show initial burst and reservoir patches may have a lag time, these are secondary phenomena; the fundamental and

consistently described kinetic difference is zero-order (reservoir) vs. Higuchi (matrix).

Final Answer: Reservoir patch → zero-order; matrix patch → Higuchi $\sqrt{t}$ kinetics ⇒ C

Answer: (C) Go Back to Q9

Q10.

Solution

Concept — OROS Osmotic Tablet Mechanism: The OROS (Osmotic Release Oral System) tablet uses the thermodynamic principle of osmosis to drive drug delivery at a controlled rate, independent of pH or GI motility.

Step 1 — Water influx via osmosis: The tablet is coated with a semi-permeable membrane (cellulose acetate). Water from the GI lumen enters the osmotic push layer (containing a highly osmotic agent such as sodium chloride or polyethylene oxide) by osmosis, driven by the osmotic pressure gradient $\Delta\pi = i \cdot M \cdot R \cdot T$.

Step 2 — Drug extrusion through the orifice: Expansion of the push layer displaces the piston and extrudes drug solution or suspension through the laser-drilled orifice at a rate controlled by the osmotic pressure gradient and membrane permeability. This gives near-constant (zero-order) drug release as long as the osmotic pressure driving force remains constant.

Why other options are wrong:

- Option A: OROS tablets contain no mechanical spring; the driving force is osmotic pressure generated by water influx across the semi-permeable coat.
- Option B: Osmotic pressure generated by water influx across the semi-permeable membrane into the push layer is the primary driver. **Correct.**
- Option C: Acid-base gas generation (as in floating tablets) is a different technology; OROS tablets do not use gas-generation chemistry for delivery.
- Option D: Electrostatic repulsion between ionised drug molecules is not a mechanistic driver of drug extrusion in OROS tablets; the system works for neutral, cationic, or anionic drugs equally.

Final Answer: Osmotic pressure generated by water influx across the semi-permeable coat is the primary driving force ⇒ B

Answer: (B) Go Back to Q10

Q11.

Solution

Concept — Gas-Generating Floating Tablets (Effervescent Mechanism): Gastroretentive floating tablets reduce bulk density below that of gastric contents ($\rho \approx 1.004$ g/mL) by trapping CO_2 gas within the hydrated polymer matrix. The gas must be generated in situ upon contact with gastric acid.

Step 1 — Effervescent reaction: When the tablet contacts acidic gastric fluid, sodium bicarbonate reacts with citric acid (or tartaric acid) in a neutralisation reaction:

$$NaHCO_3 + H^+ \longrightarrow Na^+ + H_2O + CO_2 \uparrow$$

The CO_2 gas is trapped within the swelling HPMC polymer matrix, reducing the bulk density of the tablet below 1 g/mL and causing it to float.

Step 2 — Role of the two components: Sodium bicarbonate is the carbonate source; citric acid lowers local pH and accelerates CO_2 liberation. Their combination produces a reproducible, sustained gas-generation profile within the gastric environment.

Why other options are wrong:

- Option A: Magnesium stearate (lubricant) and talc (glidant) are tableting excipients with no gas-generating capability; they cannot produce CO_2.
- Option B: HPMC (matrix-forming polymer) and ethyl cellulose (film-forming polymer) control drug release but do not generate CO_2; they are often used as the matrix in floating tablets but are not the gas source.
- Option C: Carbopol 934 (bioadhesive) and Eudragit® S100 (enteric coating polymer) are functional excipients for bioadhesion and pH-triggered release respectively; neither generates CO_2.
- Option D: Sodium bicarbonate (CO_2 precursor) and citric acid (acidulant) react in gastric fluid to liberate CO_2 for buoyancy. **Correct.**

Final Answer: $NaHCO_3$ + citric acid $\rightarrow$ CO_2 in gastric fluid, enabling floatation $\Rightarrow$ $\boxed{D}$

Answer: (D) Go Back to Q11

Q12.

Solution

Concept — Mucoadhesive Strength and Polymer Structure: Mucoadhesion depends on the ability of the polymer to form strong non-covalent interactions (hydrogen bonds, ionic interactions, chain entanglement) with mucin glycoproteins. Polymers rich in carboxylic acid groups at physiological pH are particularly effective due to ionic and hydrogen-bonding interactions with mucin.

Step 1 — Carbopol 934 structure: Carbopol 934 is a cross-linked poly(acrylic acid) with an extremely high density of carboxylic acid ($-$COOH) groups. Above its pK_a ($\sim$6), these groups ionise to carboxylate anions ($-COO^-$) that form strong electrostatic interactions with the cationic amino groups of mucin glycoproteins, producing very high mucoadhesive force. Cross-linking also promotes physical entanglement with mucin chains.

Step 2 — Comparison with other polymers: Na-CMC and HPMC are cellulose derivatives with fewer and weaker mucoadhesive groups; methylcellulose (MC) is non-ionic and relies only on weak van der Waals forces. All three have significantly lower mucoadhesive strength than Carbopol.

Why other options are wrong:

- Option A: Na-CMC has carboxymethyl groups that offer moderate mucoadhesion but far less than Carbopol 934 because it is not as densely functionalised and not cross-linked.
- Option B: HPMC is a non-ionic polymer with limited mucoadhesion (primarily van der Waals and weak hydrogen bonding); its mucoadhesive strength is modest.
- Option C: Carbopol 934 possesses the highest mucoadhesive strength due to its dense ionisable carboxylic acid groups and cross-linked architecture. **Correct.**
- Option D: Methylcellulose is a non-ionic cellulose ether with the weakest mucoadhesive interactions among those listed; it is rarely used as a primary mucoadhesive agent.

Final Answer: Carbopol 934 has the highest mucoadhesive strength due to dense ionisable $-$COOH groups $\Rightarrow$ C

Answer: (C) Go Back to Q12

Q13.

Solution

Concept — Theories of Bioadhesion: Multiple theories have been proposed to explain the molecular mechanisms of bioadhesion between polymer and mucosal surfaces. Each theory emphasises a different physical or chemical phenomenon.

Step 1 — Electronic theory defined: The electronic theory proposes that the bioadhesive polymer and the mucous membrane surface have different electronic structures (different Fermi energy levels). Upon contact, electrons transfer across the interface to equilibrate electronic chemical potentials, generating an electrical double layer at the interface. The resulting Coulombic (electrostatic) attractive forces between the oppositely charged layers are responsible for the adhesive bond.

Step 2 — Distinguish from other theories: The adsorption theory attributes adhesion to secondary valence forces (van der Waals, hydrogen bonds, electrostatic) at the molecular level after intimate contact. The wetting theory uses contact angle and surface energy (thermodynamic work of adhesion) to predict spreading. The fracture theory quantifies adhesion by the energy needed to separate two bonded surfaces.

Why other options are wrong:

- Option A: Electronic theory involves electron transfer between the polymer and mucosa creating an electrical double layer with Coulombic attractive forces. **Correct.**
- Option B: Adsorption theory invokes secondary valence forces (van der Waals, hydrogen bonds, ionic) between polymer functional groups and mucin, not electron transfer or electrical double layers.
- Option C: Wetting theory applies thermodynamic surface energy concepts and contact angle to predict whether a polymer will spread over and adhere to a mucosal surface.
- Option D: Fracture theory considers the stress required to separate two adhered surfaces and relates adhesive strength to energy of fracture, not electron transfer.

Final Answer: Electron transfer creates an electrical double layer $\rightarrow$ Coulombic adhesion forces = Electronic theory $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q13

Q14.

Solution

Concept — Colon-Targeted Prodrug Activation by Microbial Enzymes: The large intestine has a distinct enzymatic environment dominated by anaerobic microbial flora. These bacteria produce specific reductive and hydrolytic enzymes absent (or present at negligible levels) in the upper GI tract, enabling site-specific prodrug activation.

Step 1 — Azo bond chemistry: Sulfasalazine is a classic azo prodrug: 5-aminosalicylic acid (5-ASA, the active moiety) is linked to sulfapyridine (carrier) via an azo (−N=N−) bond. This bond is stable in the stomach and small intestine (where reductive conditions are absent or limited) but is cleaved reductively in the colon.

Step 2 — Azoreductase specificity: Azoreductase (azo-reductase) is produced by anaerobic colonic bacteria (*Bacteroides*, *Clostridium*, *Bifidobacterium* spp.) and specifically catalyses the 4-electron reductive cleavage of azo bonds, releasing the two amine-containing drug fragments at the colon—the intended site of action for inflammatory bowel disease.

Why other options are wrong:

- Option A: Glucuronidase from colonic bacteria activates glucuronide-conjugated prodrugs (e.g. glucuronide-linked NSAIDs), not azo-linked prodrugs; it is a hydrolytic, not reductive, enzyme.
- Option B: Azoreductase produced by anaerobic colonic bacteria cleaves the azo bond of sulfasalazine and related prodrugs. **Correct.**
- Option C: Pectinase is relevant to pectin-coated colon delivery systems; it degrades the pectin polymer coating to release drug but does not activate azo prodrugs.
- Option D: Alkaline phosphatase is found in the intestinal brush border and cleaves phosphate ester bonds; it is not responsible for azo bond cleavage, and the distal colon is not particularly alkaline.

Final Answer: Azoreductase from anaerobic colonic bacteria cleaves the azo bond to release active drug ⇒ B

Answer: (B) Go Back to Q14

Q15.

Solution

Concept — DPI vs pMDI Operational Differences: Dry Powder Inhalers (DPIs) and pressurised Metered Dose Inhalers (pMDIs) differ fundamentally in the energy source used to aerosolise and deliver the drug, which has critical implications for patient technique and propellant requirements.

Step 1 — DPI mechanism: DPIs are breath-actuated: the patient's inspiratory airflow (typically requiring $> 60\,\text{L/min}$) passes through the device, generating turbulence that de-aggregates the powder blend (drug + carrier lactose) into respirable particles. No propellant or external energy source is required. Drug release is automatically synchronised with inhalation because the breath itself is the actuating force.

Step 2 — pMDI mechanism: pMDIs use a pressurised liquefied HFA propellant (HFA-134a or HFA-227ea) stored in a canister. Pressing the canister releases a metered dose of propellant-drug mixture through the valve at high velocity. The patient must coordinate pressing the canister with beginning inhalation—a hand-breath coordination requirement absent in DPIs.

Why other options are wrong:

- Option A: This is completely reversed; DPIs do NOT use a pressurised propellant—they are breath-actuated and propellant-free; pMDIs are the propellant-driven devices.
- Option B: MMAD comparison between DPIs and pMDIs is formulation-dependent; as a general rule pMDIs typically produce finer particles (MMAD 2–4 μm) but this is not a consistent, universal difference across all DPI and pMDI products.
- Option C: It is pMDIs that may benefit from a spacer (valved holding chamber) to improve lung deposition and reduce oropharyngeal deposition; DPIs should never be used with a spacer as spacers impede the turbulent airflow needed for powder de-aggregation.
- Option D: DPIs are breath-actuated and propellant-free; pMDIs use HFA propellant and require coordinated canister actuation with inhalation. **Correct.**

Final Answer: DPI = breath-actuated, propellant-free; pMDI = HFA propellant + hand–breath coordination $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q15

Q16.

Solution

Concept — MMAD Measurement: Cascade Impaction: Mass Median Aerodynamic Diameter (MMAD) is defined by aerodynamic behaviour, not geometric size. A particle's aerodynamic diameter depends on its geometric size, density, and shape. The standard method must separate particles by their aerodynamic properties.

Step 1 — Principle of cascade impaction: The Andersen Cascade Impactor (ACI) and Next Generation Impactor (NGI) are the pharmacopoeial standard instruments (USP $\langle 601 \rangle$, Ph. Eur. 2.9.18). Each multi-stage impactor has a series of plates with progressively smaller jets and decreasing size-cut diameters. At each stage, particles with sufficient inertia (i.e. above the stage's cut-off aerodynamic diameter d_{50}) impact on the collection plate; smaller particles pass to the next stage. Plotting cumulative mass collected vs. aerodynamic diameter gives the MMAD (50th percentile of the mass distribution).

Step 2 — Why MMAD matters for inhalation: Particles with MMAD 1–5 μm deposit in the lower airways and alveoli (therapeutic target); those $>5\,\mu$m impact in the throat; those $<1\,\mu$m may be exhaled. MMAD from cascade impaction directly predicts in vivo regional lung deposition.

Why other options are wrong:

- Option A: ACI or NGI separate aerosol particles by inertial impaction across calibrated size-cut plates, directly measuring the aerodynamic size distribution and MMAD. **Correct.**
- Option B: DLS measures the hydrodynamic diameter of particles in liquid dispersion (Brownian motion); it cannot measure aerodynamic diameter of dry aerosol particles and is not applicable to inhaler characterisation.
- Option C: Laser diffraction measures geometric (optical) diameter of dispersed powder from light scattering patterns; it does not account for particle density or shape and therefore cannot measure aerodynamic diameter.
- Option D: SEM provides high-resolution morphological images and geometric size measurements of individual particles but is not a method for measuring the MMAD of the aerosol cloud produced by an inhaler.

Final Answer: ACI or NGI—inertial impaction across calibrated stages—is the standard method for MMAD determination $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q16

Q17.

Solution

Concept — CFC Phase-Out and HFA Propellants in pMDIs: CFC-11 (trichlorofluoromethane) and CFC-12 (dichlorodifluoromethane) were widely used pMDI propellants until it was established that their chlorine content catalysed stratospheric ozone destruction. The Montreal Protocol (1987) mandated their phase-out.

Step 1 — Chemistry of HFA propellants: Hydrofluoroalkanes (HFAs) contain only hydrogen, fluorine, and carbon—no chlorine. The absence of chlorine eliminates ozone-depleting potential (ODP = 0). The two HFAs approved for pMDI use are HFA-134a (1,1,1,2-tetrafluoroethane, CH_2FCF_3) and HFA-227ea (1,1,1,2,3,3,3-heptafluoropropane, CF_3CHFCF_3). Their vapour pressures, boiling points, and toxicity profiles were validated for human inhalation.

Step 2 — Regulatory and formulation implications: The switch to HFA required complete reformulation of existing pMDI products (new co-solvents such as ethanol, new surfactants) because CFC-based formulations were not directly compatible with HFA propellants. Many reformulations (e.g. HFA salbutamol Ventolin®) were developed during the 1990s–2000s.

Why other options are wrong:

- Option A: Compressed nitrogen gas propellants exist for some dry powder dispensers (e.g. Spinhaler adaptations) but were not the mainstream replacement for CFC propellants in pressurised MDIs; nitrogen lacks the vapour pressure profile needed for consistent metered dosing.
- Option B: Dimethyl ether (DME) is a propellant used in some consumer aerosols but has not been approved for inhalation use in pMDIs due to flammability and safety concerns.
- Option C: HFA-134a and HFA-227ea (chlorine-free) replaced CFC-11 and CFC-12 in pMDIs. **Correct.**
- Option D: HCFCs (e.g. HCFC-22) still contain chlorine and retain non-zero ozone-depleting potential; they were used as transitional refrigerants but were not adopted as pMDI propellant replacements due to residual environmental concerns.

Final Answer: HFA-134a and HFA-227ea (chlorine-free hydrofluoroalkanes) replaced CFCs in pMDIs $\Rightarrow$ C

Answer: (C) Go Back to Q17

Q18.

Solution

Concept — Critical Relative Humidity (CRH) in Preformulation: CRH is a fundamental physical property of crystalline solids, defining the threshold of atmospheric moisture above which the solid spontaneously absorbs water and begins to dissolve at its surface (deliquescence). It is essential for packaging and storage condition selection.

Step 1 — Definition of CRH: CRH is the minimum relative humidity at which a crystalline solid (drug or excipient) will absorb sufficient water from the atmosphere to dissolve in that absorbed water, forming a concentrated solution at the surface (deliquescence). Below the CRH, the solid may absorb some moisture without dissolving; above CRH, continuous moisture absorption and surface dissolution occur.

Step 2 — Practical significance: A drug with a low CRH (e.g. 45–60% RH) must be stored and processed below that humidity level to prevent deliquescence, caking, and chemical degradation. CRH is measured gravimetrically (dynamic vapour sorption, DVS) or by the saturated salt solution equilibrium method.

Why other options are wrong:

- Option A: Hydrolytic degradation rate is a stability phenomenon related to water activity but is not the definition of CRH; CRH specifically refers to the physical process of deliquescence (dissolution), not chemical degradation.
- Option B: CRH is the minimum RH above which a crystalline solid absorbs enough moisture to begin dissolving (deliquesce) at its surface. **Correct.**
- Option C: Wet granulation RH requirements are process-specific; CRH is an intrinsic physicochemical property of the drug substance, not a process condition for granulation.
- Option D: ICH Q1A(R2) specifies storage conditions for stability studies (25°C/60% RH for long-term; 40°C/75% RH for accelerated) but does not define CRH as a packaging facility limit; CRH is a drug-substance property, not a guideline specification.

Final Answer: CRH = minimum RH above which a crystalline solid absorbs moisture and begins to dissolve (deliquesce) $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q18

Q19.

Solution

Concept — DSC Thermogram Interpretation: Differential Scanning Calorimetry measures the heat flow to or from a sample relative to a reference as a function of temperature. The direction (endothermic vs exothermic) and shape (sharp peak vs broad step change) of thermal events reveal the solid-state nature of the material.

Step 1 — Endothermic vs exothermic events: *Endothermic* events require energy input (heat flows into the sample): melting, dehydration/desolvation of solvates, and solid–solid polymorphic transitions (in one direction). *Exothermic* events release energy: crystallisation, chemical decomposition (often), and some polymorphic transitions.

Step 2 — Sharp endothermic peak = melting: A sharp, narrow endothermic peak at a well-defined temperature is the hallmark of *melting* (fusion) of a crystalline substance. The sharpness reflects the uniformity of crystalline lattice energy; a pure, well-crystallised drug gives a very sharp peak. The peak temperature is the melting point T_m. Broad endotherms suggest less crystalline material or desolvation.

Why other options are wrong:

- Option A: A sharp endothermic peak in a pure crystalline drug corresponds to melting (fusion) at T_m. **Correct.**
- Option B: Cold crystallisation (exothermic recrystallisation from amorphous form on heating) is an *exothermic* event, appearing as a downward peak on a heat-flow-up DSC trace—opposite in direction to the endothermic melting peak.
- Option C: Thermal decomposition may be exothermic or endothermic but is typically broad, occurs at temperatures above T_m, and is often irreversible; it does not produce a sharp, reproducible endothermic peak.
- Option D: The glass transition (T_g) of an amorphous drug appears as a step change (shift in baseline heat capacity), not a sharp peak; it is an endothermic step in the thermogram, distinct from a sharp peak associated with crystalline melting.

Final Answer: Sharp endothermic peak = melting (fusion) of crystalline drug at its melting point $T_m \Rightarrow \boxed{\text{A}}$

Answer: (A) Go Back to Q19

Q20.

Solution

Concept — Powder Flowability Classification by Angle of Repose: The angle of repose (θ) is formed by a powder cone when material is allowed to flow freely onto a flat surface. It reflects inter-particle friction, cohesion, and electrostatic forces. Lower θ indicates better flow.

Step 1 — Standard flowability classification: The widely used classification scale (USP $\langle 1174 \rangle$ and literature) is:

$< 25^\circ$	Excellent flow
25°–30°	Good flow
30°–35°	Fair (passable) flow
35°–40°	Poor flow
$> 40^\circ$	Very poor (non-flowing)

Step 2 — Apply to the question: The question identifies the batch as having *very poor flowability*, requiring corrective action (granulation or glidant addition) before tableting. From the classification table, this corresponds to $\theta > 40^\circ$.

Why other options are wrong:

- Option A: $\theta < 25^\circ$ indicates *excellent* flow—no corrective action needed; this is the desirable range for direct compression.
- Option B: 25°–30° indicates *good* flow—still acceptable for many tableting processes without intervention.
- Option C: 30°–35° indicates *fair* (passable) flow—may be borderline but is not classified as "very poor."
- Option D: $\theta > 40^\circ$ corresponds to very poor (non-flowing) powder; such material requires granulation, particle size modification, or glidant (e.g. colloidal SiO_2) addition before tableting. **Correct.**

Final Answer: Angle of repose $> 40^\circ$ corresponds to very poor flowability $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q20

Q21.

Solution

Concept — Paracellular Transport and Tight Junction Modulation: Oral peptide bioavailability is limited by two barriers: enzymatic degradation in the GI lumen and poor membrane permeability. The paracellular route (between cells) is normally restricted by tight junctions (zonula occludens). Transient modulation of tight junctions opens paracellular channels to permit peptide absorption.

Step 1 — SNAC mechanism: SNAC (sodium *N*-[8-(2-hydroxybenzoyl)amino]caprylate) is a medium-chain fatty acid derivative approved as an absorption enhancer in semaglutide oral tablets (Rybelsus®). SNAC transiently and reversibly modulates tight junction proteins (claudins, occludin, ZO-1) in the gastric epithelium, increasing paracellular permeability without causing permanent cellular damage.

Step 2 — Specificity of tight junction modulation: SNAC acts locally at the site of drug co-administration. Its effect is pH-dependent and self-limiting. The paracellular channel is large enough to permit peptide molecules (MW typically <10 kDa) to pass through alongside free water, bypassing transcellular permeation barriers.

Why other options are wrong:

- Option A: Enteric coating with Eudragit® L100 protects the peptide from gastric acid by preventing dissolution at low pH; it addresses enzymatic/acid degradation but does not modulate tight junctions or increase paracellular permeability.
- Option B: Protease inhibitors (aprotinin, soybean trypsin inhibitor) reduce luminal enzymatic degradation; they improve peptide stability but do not open paracellular pathways.
- Option C: SNAC transiently and reversibly opens tight junction paracellular channels, specifically increasing paracellular permeability. **Correct.**
- Option D: SEDDS (self-emulsifying drug-delivery systems) promote lymphatic absorption via chylomicron-mediated transport through M cells and lymphatics; this is a transcellular/lymphatic mechanism, not tight junction modulation.

Final Answer: SNAC transiently opens tight junctions to increase paracellular permeability for oral peptide absorption $\Rightarrow$ C

Answer: (C) Go Back to Q21

Q22.

Solution

Concept — PLGA Biodegradation: Bulk Hydrolysis and Composition Effects: PLGA undergoes hydrolytic degradation of its ester bonds in aqueous environments. Unlike polyanhydrides (surface erosion), PLGA degrades predominantly by bulk hydrolysis—water penetrates throughout the entire matrix and ester bonds hydrolyse throughout the volume.

Step 1 — Bulk hydrolysis mechanism: Water diffuses rapidly into the PLGA matrix (because PLGA is relatively hydrophilic compared to polyanhydrides). Ester bonds throughout the matrix cleave to give lactic acid and glycolic acid. Autocatalysis occurs as acid degradation products accumulate inside the matrix, accelerating internal hydrolysis (hollow core formation is observed in thick PLGA implants).

Step 2 — Effect of lactide:glycolide (L:G) ratio: Glycolide units are more hydrophilic than lactide units because glycolic acid lacks the methyl group of lactic acid. A higher glycolide content (lower lactide fraction) increases water uptake and hydrolysis rate. Therefore, 50:50 PLGA degrades significantly faster ($t_{1/2} \approx$ 6–12 weeks) than 85:15 PLGA ($t_{1/2} \approx$ 5–6 months).

Why other options are wrong:

- Option A: PLGA undergoes *bulk* hydrolysis, not surface erosion; surface erosion is characteristic of polyanhydrides (e.g. PCPP-SA), which are specifically designed with highly hydrophobic backbones that limit water penetration to the surface.
- Option B: PLGA undergoes bulk hydrolysis; 50:50 L:G degrades faster than 85:15 L:G because glycolide units are more hydrophilic and promote faster water uptake and ester hydrolysis. **Correct.**
- Option C: Higher molecular weight PLGA degrades *more slowly* (not faster) because it has fewer chain ends (end groups are slightly more hydrophilic) and the longer chains take more time to hydrolyse to oligomers; lower MW PLGA has more end groups and degrades faster.
- Option D: PLGA undergoes spontaneous chemical hydrolysis in aqueous media at physiological temperature; it does not require tissue esterase enzymes. This is why PLGA degrades in buffered solution and in cell-free aqueous environments.

Final Answer: PLGA bulk hydrolysis throughout matrix; 50:50 L:G ratio degrades faster than 85:15 L:G $\Rightarrow$ B

Answer: (B) Go Back to Q22

Q23.

Solution

Concept — Precorneal Drainage and Ophthalmic Bioavailability: Conventional eye drops (30–50 μL) are instilled into a conjunctival sac that has a physiological capacity of only 7–10 μL (the lacrimal fluid volume). The excess volume, combined with reflex lacrimation, is rapidly drained via the nasolacrimal duct.

Step 1 — Precorneal drainage kinetics: The normal lacrimal fluid turnover rate is $\approx 1\,\mu$L/min. After eye drop instillation, the conjunctival sac rapidly returns to its resting volume. Most of the instilled dose (70–90%) is drained into the nasolacrimal duct and absorbed systemically (nasal mucosa) or swallowed within 1–2 minutes, contributing to systemic side effects rather than ocular efficacy.

Step 2 — Consequence for bioavailability: Because less than 5–10% of the instilled dose remains in the conjunctival sac long enough to penetrate the cornea, ocular bioavailability is typically $<$5%. Precorneal drainage is the *single most important barrier* limiting conventional eye drop efficacy, which is why mucoadhesive, viscosity-enhancing, and in-situ gelling formulations are developed to prolong pre-corneal residence.

Why other options are wrong:

- Option A: Precorneal drainage via the nasolacrimal duct removes most of the instilled dose within 1–2 minutes, representing the primary barrier to ocular bioavailability. **Correct.**
- Option B: The corneal stroma is hydrophilic and is actually a barrier for highly lipophilic molecules; however, it is not the *major* barrier for most drugs. The corneal epithelium (lipophilic) is the primary transcorneal diffusion barrier once the drug reaches the cornea—but even this is secondary to the loss of drug via drainage before corneal contact occurs.
- Option C: Conjunctival tight junctions restrict paracellular transport but are not the primary barrier to overall ocular bioavailability; drainage removes most drug before these junctions even become relevant.
- Option D: Protein binding in the tear film (lactoferrin, albumin, lysozyme) may reduce the free drug fraction but is not the predominant cause of the very low ($<$5%) ocular bioavailability; precorneal drainage is overwhelmingly the major loss mechanism.

Final Answer: Precorneal drainage via the nasolacrimal duct removes $>$70% of the instilled dose within 1–2 min $\Rightarrow$ A

Answer: (A) Go Back to Q23

Q24.

Solution

Concept — Bioadhesive Polymers for Vaginal Drug Delivery: Vaginal bioadhesive formulations (gels, tablets, rings) require a polymer that adheres strongly to the vaginal mucosa, tolerates the mildly acidic vaginal pH (3.8–4.5), and provides prolonged drug contact time at this absorptive surface.

Step 1 — Polycarbophil properties: Polycarbophil (cross-linked polyacrylic acid; commercial grade: Noveon® AA-1) is structurally similar to Carbopol but is slightly less cross-linked and optimised for mucosal adhesion at low pH. Its dense array of ionisable carboxylic acid groups forms strong hydrogen bonds and electrostatic interactions with mucin glycoproteins. Unlike Carbopol, polycarbophil is specifically characterised and approved for vaginal use.

Step 2 — Clinical relevance: Polycarbophil is the active bioadhesive agent in Replens® vaginal moisturiser and several vaginal drug-delivery research products. Its superior mucoadhesion to vaginal mucosa, combined with pH-buffering capacity in the acidic vaginal environment, makes it the most widely used bioadhesive polymer for this route.

Why other options are wrong:

- Option A: Hydroxyethylcellulose (HEC) is a thickening/viscosity-modifying polymer used in vaginal lubricants and some gel bases; it has limited bioadhesive properties and is not primarily a bioadhesive agent.
- Option B: Sodium alginate forms a gel in the presence of calcium ions; it has moderate mucoadhesion but is not as widely used or as strongly adhesive as polycarbophil in vaginal systems.
- Option C: Xanthan gum is a microbial polysaccharide used as a viscosity enhancer; its mucoadhesion is limited compared to polyacrylates.
- Option D: Polycarbophil (cross-linked polyacrylic acid, e.g. Noveon® AA-1) is the most widely used bioadhesive polymer in vaginal gels due to strong adhesion to vaginal mucosa. **Correct.**

Final Answer: Polycarbophil (Noveon® AA-1) is the most widely used bioadhesive polymer for vaginal delivery $\Rightarrow$ D

Answer: (D) Go Back to Q24

Q25.

Solution

Concept — ANDA Regulatory Requirements for Generic Drug Approval: An Abbreviated New Drug Application (ANDA) is the regulatory pathway for approving generic drug products in the United States. It is "abbreviated" because the applicant relies on the safety and efficacy data established by the innovator (RLD) and does not repeat full clinical development.

Step 1 — Bioequivalence as the primary requirement: The FDA requires ANDA applicants to demonstrate that the generic product is *bioequivalent* to the Reference Listed Drug (RLD). Bioequivalence is established by pharmacokinetic studies (in healthy volunteers) showing that the 90% confidence intervals for the AUC_{0-t}, $AUC_{0-\infty}$, and C_{max} ratios (generic:RLD) fall within the acceptance criteria of 80.00–125.00%.

Step 2 — Regulatory basis: Bioequivalent products are presumed therapeutically equivalent (substitutable for the RLD) under the FDA's pharmaceutical equivalence and bioequivalence standards outlined in the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 320. No Phase III efficacy and safety trials are required because the innovator's approved NDA already established these for the same active ingredient.

Why other options are wrong:

- Option A: Phase III randomised clinical trials are required for a New Drug Application (NDA), not an ANDA; the ANDA pathway was specifically created to avoid the need for redundant clinical trials for well-characterised drugs.
- Option B: Submitting a complete NDA with full preclinical and clinical data is the requirement for a brand-new (innovator) drug, not for a generic product following the ANDA pathway.
- Option C: Demonstrating bioequivalence to the RLD (90% CI for AUC and C_{max} within 80.00–125.00%) is the primary ANDA requirement. **Correct.**
- Option D: Generic manufacturers do not need to obtain a new patent for their formulation technology; they file a Paragraph IV certification (or appropriate patent certification) regarding existing innovator patents, but no new patent is required for ANDA filing.

Final Answer: Bioequivalence to the RLD (90% CI 80.00–125.00% for AUC and C_{max}) is the primary ANDA requirement $\Rightarrow$ C

Answer: (C) Go Back to Q25

Answer Key

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