

# NEET PG Pharmacology Sample Paper-5

Duration: 15 Minutes

Maximum Marks: 80

## Instructions

- This paper contains **20** Multiple Choice Questions.
- Each correct answer carries **+4** mark. Incorrect answer: **-1** marks. Only **one** correct option.
- Unattempted questions carry **0** marks.
- Use of mobile phones, smartwatches, or any electronic gadgets is strictly prohibited.

**Q1.** A 45-year-old male with a history of chronic kidney disease is prescribed a newly approved drug for hypertension. The drug is primarily cleared by the kidneys via glomerular filtration. If the patient's creatinine clearance is reduced by 50%, which of the following parameters will double, assuming a single-compartment model with first-order elimination?

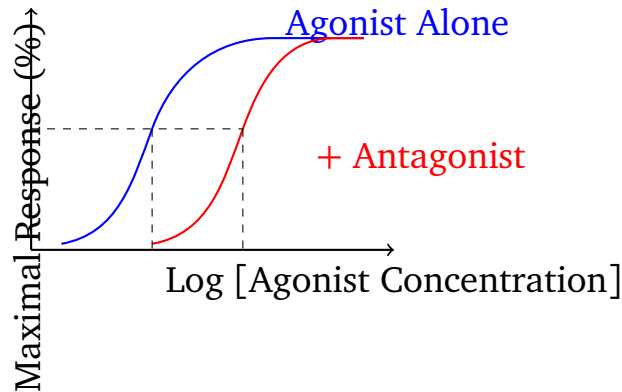
- (A) Volume of distribution ( $V_d$ )
- (B) Loading dose
- (C) Elimination half-life ( $t_{1/2}$ )
- (D) Bioavailability ( $F$ )

**Q2.** A 34-year-old pregnant female at 32 weeks of gestation presents with severe hypertension (170/110 mmHg). Which of the following antihypertensive agents acting via central  $\alpha_2$ -adrenergic receptors is considered first-line management in this scenario?

- (A) Clonidine
- (B) Reserpine
- (C) Guanfacine
- (D) Methyldopa



- Q3.** An experimental drug 'X' is tested on a prepared tissue isolated with ligand-gated ion channels. The following dose-response relationship curve is obtained in the presence of a fixed concentration of a known competitive antagonist:



Based on the shift observed in the diagram, which of the following parameters is altered by the competitive antagonist?

- (A) Efficacy decreases  
 (B) Potency decreases ( $EC_{50}$  increases)  
 (C) Potency increases ( $EC_{50}$  decreases)  
 (D) Efficacy increases
- Q4.** A 28-year-old female presents to the emergency department with acute lower abdominal pain, vaginal discharge, and fever, leading to a diagnosis of Pelvic Inflammatory Disease (PID). To cover both atypical organisms like *Chlamydia trachomatis* and Gram-negative anaerobes, a combination treatment protocol is initiated. Which of the following protein synthesis inhibitors acting on the 50S ribosomal subunit is highly effective against anaerobes in this scenario?
- (A) Clindamycin  
 (B) Azithromycin  
 (C) Doxycycline  
 (D) Linezolid
- Q5.** A 62-year-old male with long-standing heart failure with reduced ejection fraction (HFrEF) is currently taking an ACE inhibitor, a beta-blocker, and a



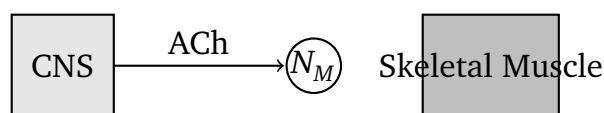
loop diuretic. Despite compliance, he remains symptomatic (NYHA Class III). The physician decides to add an aldosterone receptor antagonist. Which of the following adverse effects should be closely monitored via serum biochemistry in this patient?

- (A) Hypokalemia
- (B) Hypercalcemia
- (C) Hyperkalemia
- (D) Hyponatremia

**Q6.** A patient presents with signs of severe organophosphate poisoning after accidental pesticide exposure. He is treated with atropine to reverse the muscarinic symptoms. Which of the following clinical signs will NOT be reversed by atropine because it is mediated via nicotinic receptors at the neuromuscular junction?

- (A) Muscle fasciculations
- (B) Bradycardia
- (C) Bronchoconstriction
- (D) Excessive salivation

**Q7.** The autonomic nervous system pathways can be classified by their neurotransmitters and anatomical receptors. Examine the schematic diagram below representing a specific peripheral pathway:



Which of the following neuromuscular blocking drugs acts as a depolarizing agent directly at the receptor site indicated in the diagram?

- (A) Vecuronium
- (B) Succinylcholine
- (C) Pancuronium



(D) Atracurium

**Q8.** A 23-year-old male is brought to the psychiatry clinic with a 6-month history of auditory hallucinations, persecutory delusions, and social withdrawal. He is started on an atypical antipsychotic agent. Which of the following receptor profiles best explains the reduced incidence of extrapyramidal side effects (EPS) associated with atypical antipsychotics compared to typical options?

(A) Potent  $D_2$  receptor antagonism alone

(B) Selective  $\alpha_1$ -adrenergic receptor antagonism

(C) Pure  $H_1$  histamine receptor antagonism

(D) Combined 5-HT<sub>2A</sub> and weaker  $D_2$  receptor antagonism

**Q9.** A 54-year-old male tracking treatment for pulmonary tuberculosis develops numbness and a 'pins-and-needles' sensation in both feet. This condition is caused by a drug-induced depletion of pyridoxine (Vitamin B6). Which of the following first-line antitubercular drugs is responsible for this presentation?

(A) Rifampicin

(B) Isoniazid

(C) Ethambutol

(D) Pyrazinamide

**Q10.** A 35-year-old female presents with tremors, heat intolerance, weight loss, and an elevated free  $T_4$  level. She is diagnosed with Graves' disease and is prescribed propylthiouracil (PTU). Aside from inhibiting thyroid peroxidase in the thyroid gland, what unique peripheral mechanism of action does PTU possess over methimazole?

(A) Blockade of  $T_4$  to  $T_3$  peripheral conversion

(B) Inhibition of the sodium-iodide symporter (NIS)

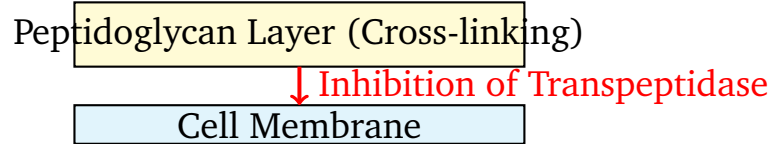
(C) Destruction of thyroid follicular cells via beta radiation

(D) Direct inhibition of thyroid hormone release into circulation



- Q11.** A clinical trial evaluates the steady-state plasma concentrations of a continuous intravenous infusion of an analgesic drug. If the drug follows first-order elimination kinetics, how many elimination half-lives are required for the drug to reach approximately 93.75% of its final steady-state concentration?
- (A) 2 half-lives  
(B) 3 half-lives  
(C) 4 half-lives  
(D) 5 half-lives
- Q12.** A 58-year-old female with a history of narrow-angle glaucoma requires a medication for overactive bladder. Which of the following antimuscarinic agents must be avoided or used with extreme caution due to the risk of precipitating acute angle-closure glaucoma?
- (A) Mirabegron  
(B) Oxybutynin  
(C) Bethanechol  
(D) Pilocarpine
- Q13.** A 72-year-old female with Parkinson's disease has been successfully treated with a combination of Levodopa and Carbidopa for 5 years. Recently, she reports that her symptoms return before her next scheduled dose. To manage this 'wearing-off' phenomenon, the neurologist decides to add Entacapone. What is the mechanism of action of Entacapone?
- (A) Inhibits central monoamine oxidase B (MAO-B)  
(B) Inhibits peripheral catechol-O-methyltransferase (COMT)  
(C) Acts as a direct dopamine receptor agonist  
(D) Enhances the release of endogenous dopamine storage vesicles
- Q14.** The bacterial cell wall synthesis pathway involves several sequentially regulated enzymatic steps. The diagram below illustrates the site of action of a major antibiotic class:





Which of the following antibiotics exerts its bactericidal mechanism of action at the specific cross-linking stage shown above?

- (A) Vancomycin
- (B) Ceftriaxone
- (C) Fosfomycin
- (D) Bacitracin

**Q15.** A 48-year-old female diagnosed with breast cancer is scheduled to receive a chemotherapy regimen containing Doxorubicin. To prevent the development of drug-induced dilated cardiomyopathy, which of the following cytoprotective iron-chelating agents can be co-administered?

- (A) Dexrazoxane
- (B) Amifostine
- (C) Leucovorin
- (D) Mesna

**Q16.** An emergency room patient who took an unknown overdose shows symptoms of respiratory depression and severe metabolic acidosis. The toxicology screen confirms toxic levels of an acidic drug with a  $pK_a$  of 3.5. Intravenous sodium bicarbonate administration is initiated. What is the pharmacological basis of this treatment?

- (A) Decreased ionization of the drug in the renal tubules, favoring reabsorption
- (B) Increased ionization of the drug in urine, promoting renal trapping and excretion
- (C) Direct chemical neutralization of the drug inside the plasma space



(D) Competition for the organic anion transport systems in the proximal tubule

**Q17.** A 65-year-old male with benign prostatic hyperplasia (BPH) and comorbid systemic hypertension is prescribed a medication that provides therapeutic benefit for both conditions by blocking vascular smooth muscle and prostatic smooth muscle receptors. Which drug was likely prescribed?

- (A) Prazosin
- (B) Tamsulosin
- (C) Propranolol
- (D) Atenolol

**Q18.** A 19-year-old college student with generalized tonic-clonic epilepsy is managed with Phenytoin. She requires strict therapeutic drug monitoring because Phenytoin shifts from first-order elimination to zero-order elimination at therapeutic plasma concentrations. This pharmacokinetic shift is due to which of the following?

- (A) Saturation of hepatic metabolic enzymes (*CYP2C9*)
- (B) Rapid renal clearance saturation
- (C) High plasma protein binding displacement
- (D) Auto-induction of microsomal enzymes

**Q19.** A 29-year-old male who recently traveled to an endemic area presents with high-grade fever, chills, and profuse sweating. Microscopic evaluation of a peripheral blood smear confirms infection with chloroquine-resistant *Plasmodium falciparum*. He is started on Oral Artemether-Lumefantrine therapy. What is the mechanism of action of artemisinin derivatives?

- (A) Production of free radicals via reaction with intraparasitic heme iron
- (B) Inhibition of dihydrofolate reductase
- (C) Blockade of parasitic protein translation via 30S ribosomal subunit binding



(D) Intercalation between parasitic DNA base pairs preventing replication

**Q20.** A 33-year-old HIV-positive patient with a  $CD_4$  count of  $120/\mu\text{L}$  presents to the clinic. The physician prescribes prophylactic trimethoprim-sulfamethoxazole (TMP-SMX) to prevent opportunistic infections. What is the synergy mechanism behind the combination of these two antimicrobial agents?

(A) Dual inhibition of cell wall transpeptidases

(B) Sequential blockade of successive steps in microbial folate synthesis

(C) Simultaneous disruption of mRNA translation and cell membrane integrity

(D) Competitive inhibition of identical bacterial target proteins



## Detailed Solutions

Q1.

## Solution

**Concept:**

Clearance defines the volume of plasma cleared of a drug per unit time, while half-life describes the time required to reduce the plasma concentration by half. In a single-compartment model following first-order kinetics, elimination parameters dictate that the half-life is inversely proportional to clearance and directly proportional to the volume of distribution.

**Solution:**

- (a) The relationship between elimination half-life ( $t_{1/2}$ ), volume of distribution ( $V_d$ ), and clearance ( $CL$ ) is mathematically expressed by the fundamental pharmacokinetic equation:  $t_{1/2} = \frac{0.693 \times V_d}{CL}$ .
- (b) When a drug is primarily eliminated by the kidneys through glomerular filtration, its total body clearance is directly dependent on renal function, which is clinically estimated using the patient's creatinine clearance.
- (c) In this clinical scenario, the patient's creatinine clearance is reduced by 50%, which directly translates to a 50% decrease (or a halving) of the drug's systemic clearance ( $CL$ ).
- (d) Substituting a clearance value of  $0.5 \times CL$  into the denominator of our core half-life equation mathematically doubles the resulting elimination half-life value ( $t_{1/2}$ ).
- (e) The volume of distribution and bioavailability are independent physiological parameters determined by drug chemistry and tissue binding, meaning they remain unchanged by renal impairment. Consequently, the loading dose, which depends strictly on target concentration and  $V_d$ , also remains constant.

**Final Answer:** The parameter that will double is elimination half-life.

**Answer:** (C)

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Q2.

**Solution****Concept:**

Hypertensive crises or severe chronic hypertension during pregnancy must be treated with specific, safe antihypertensive agents to prevent maternal complications like stroke while maintaining stable uteroplacental blood flow. Centrally acting alpha-2 adrenergic receptor agonists reduce sympathetic outflow from the brainstem vasomotor center.

**Solution:**

- (a) Methyldopa is a prodrug that is actively transported across the blood-brain barrier and metabolized centrally into alpha-methylnorepinephrine, which acts as a potent agonist at central alpha-2 adrenergic receptors.
- (b) Activation of these central alpha-2 receptors decreases efferent sympathetic tone from the central nervous system to the peripheral vasculature, leading to a reduction in systemic vascular resistance and blood pressure.

**Final Answer:** The antihypertensive agent is Methyldopa.

Answer: (D)

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Q3.

**Solution****Concept:**

Receptor antagonism describes the mechanism by which a molecule binds to a receptor and prevents agonist activation. Competitive antagonists bind reversibly to the exact same active site as the endogenous agonist, initiating a predictable and classic parallel shift in the graded dose-response curve.

**Solution:**

- (a) A competitive antagonist competes directly with the agonist for receptor binding sites, but this inhibitory effect can be completely overcome by increasing the concentration of the agonist molecule.
- (b) Because the maximal response (Efficacy or  $E_{max}$ ) can still be achieved at higher agonist concentrations, the peak of the dose-response curve remains entirely unaltered in the presence of the competitive antagonist.

**Final Answer:** The parameter altered is potency decreases.

Answer: (B)

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Q4.

**Solution****Concept:**

Pelvic Inflammatory Disease requires empirical broad-spectrum antimicrobial coverage targeting polymicrobial pathogens, including atypical organisms and obligate anaerobes. Antibiotics inhibiting protein synthesis bind to specific ribosomal subunits to disrupt bacterial translation.

**Solution:**

- (a) Clindamycin is a lincosamide antibiotic that binds reversibly to the 50S ribosomal subunit, suppressing bacterial protein synthesis by inhibiting the peptide bond formation steps.
- (b) It exhibits potent, targeted bactericidal or bacteriostatic activity against Gram-positive organisms and deep-tissue obligate anaerobes, making it a mainstay for anaerobic pelvic cover.

**Final Answer:** The protein synthesis inhibitor is Clindamycin.

**Answer: (A)**

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Q5.

**Solution****Concept:**

Mineralocorticoid receptor antagonists provide mortality benefits in heart failure with reduced ejection fraction by blocking aldosterone-mediated cardiac remodeling and fibrotic changes. However, blocking aldosterone in the distal nephron alters normal electrolyte excretion patterns.

**Solution:**

- (a) Aldosterone normally acts on the principal cells of the renal collecting duct to promote sodium and water reabsorption while enhancing potassium and hydrogen ion excretion into the lumen.
- (b) Antagonizing this receptor prevents potassium wasting, which poses a significant risk of severe potassium retention, especially when combined with an ACE inhibitor.

**Final Answer:** The adverse effect to monitor is Hyperkalemia.

**Answer: (C)**

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Q6.

**Solution****Concept:**

Organophosphate toxicity triggers an acute cholinergic crisis due to the irreversible inhibition of acetylcholinesterase, leading to massive acetylcholine accumulation at both muscarinic and nicotinic receptor sites throughout the peripheral nervous system.

**Solution:**

- (a) Atropine is a highly selective competitive antagonist at muscarinic acetylcholine receptors, effectively reversing toxic parasympathetic signs such as severe bradycardia, bronchoconstriction, and excessive salivation.
- (b) Skeletal muscle fasciculations, cramping, and subsequent flaccid paralysis are caused by excessive acetylcholine overstimulating nicotinic receptors located at the neuromuscular junction, which are completely unresponsive to atropine blockade.

**Final Answer:** The clinical sign not reversed is Muscle fasciculations.

**Answer: (A)**

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Q7.

**Solution****Concept:**

The somatic nervous system features a single motor neuron that extends directly from the central nervous system to terminate at the neuromuscular junction of skeletal muscle fibers, utilizing acetylcholine acting on nicotinic receptors.

**Solution:**

- (a) Succinylcholine is a depolarizing neuromuscular blocker composed of two joined acetylcholine molecules that binds directly to nicotinic receptors at the motor endplate, triggering prolonged membrane depolarization.
- (b) Non-depolarizing agents like vecuronium, pancuronium, and atracurium act instead as competitive antagonists, blocking acetylcholine without causing initial receptor activation or motor endplate depolarization.

**Final Answer:** The depolarizing agent is Succinylcholine.

**Answer: (B)**

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Q8.

**Solution****Concept:**

Antipsychotic drugs are utilized to manage schizophrenia by modulating dopamine pathways. The clinical distinction between typical and atypical antipsychotics lies in their specific receptor affinity profiles and resulting neurological side effects.

**Solution:**

- (a) Typical antipsychotics primarily cause extrapyramidal symptoms due to their potent, high-affinity blockade of dopamine D2 receptors located within the nigrostriatal pathway.
- (b) Atypical antipsychotics combine transient, low-affinity D2 receptor antagonism with potent serotonin 5-HT<sub>2A</sub> receptor blockade, which enhances dopamine release in the striatum to dramatically lower extrapyramidal side effects.

**Final Answer:** The receptor profile is Combined 5-HT<sub>2A</sub> and weaker D2 receptor antagonism.

**Answer: (D)**

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Q9.

**Solution****Concept:**

Standard antitubercular therapy relies on a combination regimen of first-line agents, each possessing unique mechanism profiles and specific toxicological footprints that require close clinical surveillance.

**Solution:**

- (a) Isoniazid functions by inhibiting the synthesis of mycolic acids essential for the mycobacterial cell wall. It chemically interacts with pyridoxal phosphate, accelerating its renal clearance and creating a nutritional deficiency.
- (b) This absolute depletion of active Vitamin B<sub>6</sub> impairs myelin synthesis, manifesting clinically as a symmetric peripheral neuropathy characterized by numbness, tingling, and paresthesias in the extremities.

**Final Answer:** The first-line antitubercular drug is Isoniazid.

**Answer: (B)**

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Q10.

**Solution****Concept:**

Thionamides are antithyroid agents utilized to manage hyperthyroidism by interrupting the synthesis of thyroid hormones within follicular cells, but individual agents possess distinct peripheral activities.

**Solution:**

- (a) Both propylthiouracil and methimazole act within the thyroid gland to inhibit the thyroid peroxidase enzyme, blocking the vital iodination and coupling steps of hormone synthesis.
- (b) Propylthiouracil uniquely exerts an additional peripheral mechanism by inhibiting the type 1 deiodinase enzyme, which prevents the peripheral conversion of low-activity thyroxine (T4) into the highly metabolic triiodothyronine (T3).

**Final Answer:** The unique peripheral mechanism is Blockade of T4 to T3 peripheral conversion.

**Answer: (A)**

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Q11.

**Solution****Concept:**

Steady state kinetics describe the equilibrium where the rate of drug administration equals the rate of drug elimination. For drugs following first order elimination kinetics during a continuous intravenous infusion, accumulation toward steady state concentration is a predictable, time dependent function determined solely by the elimination half-life of the molecule.

**Solution:**

- (a) When a drug is infused at a constant rate, the plasma concentration increases asymptotically. The percentage of the ultimate plateau or steady state concentration achieved at the completion of any given number of half-lives can be computed using the mathematical fraction formula:  $1 - (0.5)^n$ , where  $n$  represents the total number of elapsed elimination half-lives.
- (b) After the passage of one half-life, the plasma concentration reaches exactly 50% of steady state. After two half-lives, it achieves 75%, and at the end of three half-lives, the accumulation stands at 87.5%.
- (c) Following the completion of four full elimination half-lives, the equation yields  $1 - (0.5)^4 = 1 - 0.0625$ , which equals 0.9375 or precisely 93.75% of the final steady state concentration.
- (d) A complete clinical steady state is traditionally considered achieved after four to five half-lives, at which point concentration fluctuations become clinically negligible. Because 93.75% falls precisely at the four half-life milestone, this value represents the exact kinematic threshold requested.

**Final Answer:** The number of half-lives required is 4 half-lives.

**Answer: (C)**

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Q12.

**Solution****Concept:**

Overactive bladder therapy frequently relies on blocking muscarinic receptors to reduce detrusor muscle hyperactivity. However, systemic antimuscarinic administration blocks parasympathetic tone globally, which can dangerously exacerbate conditions reliant on normal aqueous humor drainage pathways.

**Solution:**

- (a) Oxybutynin is a non-selective muscarinic receptor antagonist that blocks M3 receptors on the detrusor muscle to alleviate urinary urgency. However, it also blocks M3 receptors located on the pupillary sphincter muscle and the ciliary body within the eye.
- (b) This blockade prevents parasympathetic induced miosis and accommodation, causing mydriasis. In patients with anatomically narrow anterior chamber angles, mydriasis causes the iris tissue to fold into and mechanically occlude the trabecular meshwork.
- (c) This mechanical obstruction dramatically impedes the drainage of aqueous humor out of the anterior chamber, rapidly elevating intraocular pressure and precipitating a medical emergency known as acute angle closure glaucoma.
- (d) Mirabegron is a beta-3 adrenergic receptor agonist that relaxes the detrusor muscle without exerting antimuscarinic effects, making it safe for glaucoma patients. Bethanechol and pilocarpine are cholinergic agonists that induce miosis and lower intraocular pressure.

**Final Answer:** The antimuscarinic agent to avoid is Oxybutynin.

**Answer: (B)**

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Q13.

**Solution****Concept:**

Long term levodopa therapy in Parkinson's disease is frequently complicated by motor fluctuations, such as the wearing off phenomenon, as progressive nigrostriatal neurodegeneration reduces the brain's capacity to store and smoothly release dopamine synthesized from exogenous levodopa.

**Solution:**

- (a) Levodopa is combined with carbidopa to inhibit peripheral aromatic L-amino acid decarboxylase, allowing more levodopa to cross the blood brain barrier. However, remaining peripheral levodopa is still broken down via an alternative metabolic pathway controlled by the enzyme catechol-O-methyltransferase.
- (b) Entacapone is a selective and reversible inhibitor of peripheral catechol-O-methyltransferase that directly prevents the methylation of levodopa into its inactive metabolite, 3-O-methyldopa.
- (c) By blocking this peripheral enzymatic degradation pathway, entacapone significantly extends the plasma half-life of levodopa, increases its systemic bioavailability, and ensures a more continuous and sustained delivery of dopamine precursors into the central nervous system.
- (d) This mechanistic action smooths out the peaks and troughs of levodopa concentrations, effectively minimizing the wearing off periods and expanding total daily on time for the patient without inducing central monoamine oxidase inhibition.

**Final Answer:** The mechanism of action is Inhibits peripheral catechol-O-methyltransferase (COMT).

**Answer: (B)**

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Q14.

**Solution****Concept:**

Bacterial cell wall synthesis is an intricate, multi-stage process that serves as a highly vulnerable target for several distinct classes of bactericidal and bacteriostatic antimicrobial agents. Understanding the exact biochemical step inhibited by each class is crucial for clinical selection.

**Solution:**

- (a) The final stage of peptidoglycan synthesis involves cross-linking linear glycan strands via peptide side chains to provide structural integrity to the cell wall. This critical cross-linking reaction is catalyzed by transpeptidase enzymes, also known as penicillin-binding proteins.
- (b) Ceftriaxone is a third-generation cephalosporin belonging to the beta-lactam class. It acts as a structural analogue of the natural D-alanyl-D-alanine substrate, binding irreversibly to the active site of transpeptidases and completely inhibiting their cross-linking activity.
- (c) This direct inhibition weakens the structural framework of the bacterial peptidoglycan layer, rendering the cell highly susceptible to osmotic pressure differences and ultimately leading to bacterial autolysis and cell death.
- (d) Vancomycin also prevents cross-linking but acts by binding directly to the D-alanyl-D-alanine terminus of the peptide precursor rather than the transpeptidase enzyme itself. Fosfomycin acts much earlier in the cytoplasm by inhibiting MurA, while bacitracin blocks lipid carrier dephosphorylation.

**Final Answer:** The antibiotic acting at this stage is Ceftriaxone.

**Answer: (B)**

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Q15.

**Solution****Concept:**

Anthracycline antineoplastic agents like doxorubicin are highly effective chemotherapy tools, but their clinical utility is strictly limited by cumulative, dose-dependent cardiotoxicity that culminates in irreversible dilated cardiomyopathy and congestive heart failure.

**Solution:**

- (a) The primary mechanism underlying doxorubicin-induced cardiotoxicity involves the generation of iron-dependent reactive oxygen species and free radicals within myocardial tissue, paired with the direct inhibition of topoisomerase II beta, which triggers severe cardiomyocyte apoptosis.
- (b) Dexrazoxane is a specialized cardioprotective agent that diffuses into cardiac cells and undergoes intracellular hydrolysis to form a strong chelating metabolite structurally resembling EDTA.
- (c) This active metabolite binds tightly to intracellular iron, preventing the formation of the toxic doxorubicin-iron complex and significantly reducing the generation of destructive hydroxyl free radicals within mammalian myocardium.
- (d) Additionally, dexrazoxane alters the conformation of topoisomerase II beta, protecting cardiac cells from anthracycline-mediated DNA damage without interfering with the therapeutic, topoisomerase II alpha-mediated antitumor efficacy of doxorubicin in breast tissue.
- (e) Amifostine is used as a cytoprotectant to minimize cisplatin nephrotoxicity; leucovorin rescues healthy cells from methotrexate toxicity; and mesna inactivates acrolein to prevent cyclophosphamide-induced hemorrhagic cystitis.

**Final Answer:** The cytoprotective agent is Dexrazoxane.

**Answer: (A)**

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Q16.

**Solution****Concept:**

Manipulating urinary pH to alter the ionization state of weak acids or weak bases is an established therapeutic strategy in clinical toxicology designed to accelerate the clearance of specific renally eliminated toxins.

**Solution:**

- (a) According to the Henderson-Hasselbalch principle, weak acids exist in an equilibrium between their non-ionized, lipid-soluble form and their ionized, water-soluble conjugate base. The relative proportion of these forms depends on the local pH.
- (b) Administering intravenous sodium bicarbonate alkalinizes the blood and the renal tubular fluid, raising the urine pH significantly above the toxic drug's dissociation constant ( $pK_a = 3.5$ ).
- (c) In this alkaline environment, the weak acid sheds hydrogen ions, shifting the chemical equilibrium heavily toward the ionized, negatively charged form of the drug molecule.
- (d) Because the renal tubular membrane is a lipid bilayer, it is highly impermeable to charged species. The ionized drug molecules become trapped within the tubular lumen, preventing passive reabsorption back into systemic circulation.
- (e) This process, termed ion trapping, dramatically enhances the absolute clearance and net renal excretion of the toxin, helping reverse severe systemic toxicity.

**Final Answer:** The pharmacological basis is Increased ionization of the drug in urine, promoting renal trapping and excretion.

**Answer: (B)**

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Q17.

**Solution****Concept:**

Sympathetic tone regulates vascular smooth muscle contraction and prostatic urethral resistance via specific adrenergic receptor subtypes. Antagonizing these targets allows for simultaneous management of systemic vascular resistance and urinary outflow obstruction.

**Solution:**

- (a) Prazosin is a selective, competitive antagonist at alpha-1 adrenergic receptors located on both vascular smooth muscle cells and the smooth muscle structures of the bladder neck and prostate gland.
- (b) Blockade of alpha-1 receptors on peripheral blood vessels prevents endogenous catecholamine binding, inducing vasodilation, reducing systemic vascular resistance, and lowering systemic arterial blood pressure.
- (c) Concurrently, blocking alpha-1 receptors in the stromal prostate tissue and bladder neck relaxes prostatic smooth muscle, reducing mechanical resistance to urinary flow and relieving symptoms of benign prostatic hyperplasia.
- (d) Tamsulosin is a highly selective antagonist targeting the alpha-1A receptor subtype predominant in the prostate, which minimizes systemic vascular side effects and makes it ineffective as a primary treatment for systemic hypertension. Propranolol and atenolol are beta-blockers that do not improve bladder outflow dynamics.

**Final Answer:** The prescribed medication is Prazosin.

**Answer:** (A)

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Q18.

**Solution****Concept:**

The rate of drug elimination can display different kinetics depending on plasma concentration relative to metabolic capacity. First order elimination features a constant fraction of drug cleared per unit time, whereas zero order elimination features a constant absolute amount cleared.

**Solution:**

- (a) At low plasma concentrations, the abundance of active hepatic metabolic enzymes vastly exceeds the number of circulating drug molecules, resulting in first order clearance kinetics where elimination matches plasma availability.
- (b) Phenytoin is metabolized primarily by the hepatic microsomal cytochrome P450 enzyme system, specifically the CYP2C9 isoenzyme pathway.
- (c) As phenytoin doses are adjusted upward into the therapeutic window, the concentration of the drug approaches and eventually surpasses the Michaelis-Menten constant ( $K_m$ ) of these specific metabolic enzymes.
- (d) This induces complete saturation of the CYP2C9 enzymes. Once saturated, the clearance mechanism can no longer increase its processing speed in response to higher concentrations, causing the elimination profile to flatten into zero order kinetics.
- (e) Because elimination is fixed at a maximum capacity, even small dosage increases can lead to sudden, disproportionate elevations in plasma concentrations, inducing acute toxicity and necessitating strict therapeutic drug monitoring.

**Final Answer:** The kinetic shift is due to Saturation of hepatic metabolic enzymes (CYP2C9).

**Answer: (A)**

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Q19.

**Solution****Concept:**

Artemisinin derivatives represent the frontline therapeutic standard for managing severe or multidrug-resistant falciparum malaria. Their rapid, potent schizonticidal activity relies on exploiting the unique intraerythrocytic metabolic environment of the parasite.

**Solution:**

- (a) Malaria parasites reside inside host erythrocytes and digest hemoglobin, releasing large quantities of free, potentially toxic heme iron into their specialized digestive vacuoles.
- (b) Artemether contains a unique, chemically reactive endoperoxide bridge structure. Upon entry into the parasite, this endoperoxide bridge undergoes a chemical cleavage reaction catalyzed directly by the intraparasitic heme iron.
- (c) This cleavage triggers the generation of highly reactive carbon-centered free radical intermediates within the organism.
- (d) These free radicals alkylate and damage essential parasitic proteins, including the PfATP6 calcium pump and various structural lipids, rapidly disrupting membrane integrity and causing widespread intracellular damage.
- (e) This targeted destructive cascade ensures swift clearance of the parasitemia. Lume-fantrine, co-administered for its longer half-life, prevents re-emergence by clearing any remaining residual parasites through distinct, independent mechanisms.

**Final Answer:** The mechanism of action is Production of free radicals via reaction with intraparasitic heme iron.

**Answer: (A)**

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Q20.

**Solution****Concept:**

Antimicrobial synergy can be achieved by combining two distinct agents that target different enzymatic steps within the same essential metabolic pathway, significantly enhancing net antimicrobial efficacy compared to either drug used in isolation.

**Solution:**

- (a) Bacteria must synthesize tetrahydrofolate de novo to produce critical nucleic acids and proteins, a pathway requiring several sequential enzymatic transformations.
- (b) Sulfamethoxazole acts as a structural analogue to para-aminobenzoic acid (PABA) and competitively inhibits the enzyme dihydropteroate synthase, blocking the initial step of folate synthesis.
- (c) Trimethoprim acts further downstream in the exact same metabolic pathway, binding to and inhibiting the enzyme dihydrofolate reductase, preventing the reduction of dihydrofolate into its active form, tetrahydrofolate.
- (d) This dual, sequential blockade of successive metabolic steps exerts a highly synergistic bactericidal effect, as it severely depletes bacterial folate pools and minimizes the likelihood of the organism developing resistance.
- (e) In immunocompromised patients, such as HIV-positive individuals with low CD4 counts, this combination provides vital, broad-spectrum prophylaxis against opportunistic pathogens like *Pneumocystis jirovecii*.

**Final Answer:** The synergy mechanism is Sequential blockade of successive steps in microbial folate synthesis.

**Answer: (B)**

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## Answer Key

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

