NEET PG Pharmacology Sample Paper-3

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 new competitive antagonist for the μ-opioid receptor is under investigation. In an in vitro tissue assay, the addition of a fixed concentration of this antagonist shifts the agonist log concentration-response curve to the right without changing the maximal response (E_{max}). Which of the following parameters is mathematically quantified by the Schild regression analysis using this relationship?

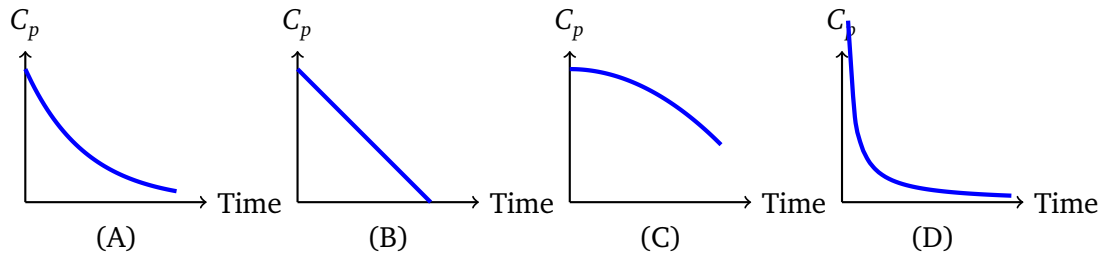
(A) The efficacy (α) of the agonist

(B) The dissociation constant (K_d) of the agonist

(C) The equilibrium dissociation constant (K_i or K_B) of the antagonist

(D) The therapeutic index (TI) of the antagonist

Q2. An 45-year-old chronic alcoholic patient requires therapy with an anti-epileptic drug that undergoes significant zero-order elimination at therapeutic concentrations. Which of the following graphical representations best represents the plasma concentration vs time profile of such a drug following a single high-dose administration, where the clearance is inversely proportional to the plasma concentration?



(A) Graph A

(B) Graph B

(C) Graph C

(D) Graph D

Q3. A 62-year-old male with chronic kidney disease (creatinine clearance = 22 mL/min) requires maintenance dosing of an antimicrobial agent. The drug has a normal half-life of 6 hours, is 80% eliminated unchanged via renal filtration, and has a volume of distribution of 40 L. If the standard maintenance dose is 500 mg every 12 hours for a patient with normal renal function (Cl = 100 mL/min), what is the adjusted maintenance dose for this patient if the dosing interval is kept at 12 hours?

(A) 188 mg

(B) 100 mg

(C) 250 mg

(D) 376 mg

Q4. A candidate drug molecule 'X' is discovered to be a weak base with a pK_a of 8.4. During an overdose scenario, a clinician intends to manipulate the urinary pH to accelerate the renal clearance of this drug through ion trapping. Which of the following therapeutic actions should be taken, and what will be the predominant ionization state of drug 'X' in the modified urine?

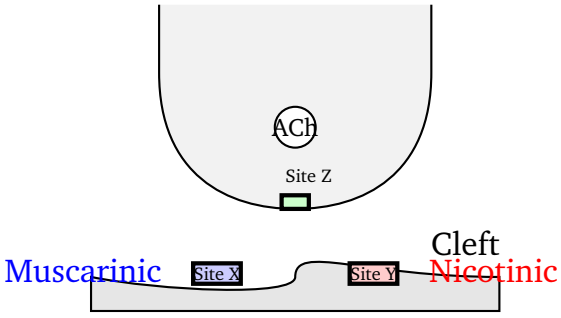
(A) Administer Sodium bicarbonate; Un-ionized form predominates

(B) Administer Ammonium chloride; Ionized form predominates

(C) Administer Sodium bicarbonate; Ionized form predominates

(D) Administer Ammonium chloride; Un-ionized form predominates

Q5. A 35-year-old patient presenting with severe organophosphate poisoning is treated with atropine and pralidoxime. Pralidoxime works by reactivating phosphorylated acetylcholinesterase. At which of the following sites shown in the synaptic junction diagram below does pralidoxime fail to reverse the neuromuscular/autonomic paralysis induced by organophosphates?



(A) Atropine sensitive receptors localized at Site X

(B) Receptors localized at Site Z which control the vesicle storage

(C) All postganglionic parasympathetic terminals regardless of structural modifications

(D) Receptors localized at Site Y once the enzyme has undergone "aging"

Q6. An experimental drug is administered intravenously to an anesthetized animal. It produces a transient rise in blood pressure followed by a prolonged fall, along with marked bradycardia. When hexamethonium is pre-administered, the blood pressure response to this experimental drug is completely abolished. The experimental drug is most likely acting as an agonist at which of the following receptors?

(A) Nicotinic neuronal (N_N) receptors

(B) α_1-adrenergic receptors

(C) β_2-adrenergic receptors

(D) Muscarinic M_2 receptors

Q7. A 29-year-old pregnant woman at 32 weeks of gestation presents with preterm labor contractions. The obstetrician decides to administer a selective β_2-adrenergic agonist to achieve tocolysis. Which of the following biochemical

cascades is triggered directly by this drug inside the uterine smooth muscle cell to bring about relaxation?

(A) Activation of G_q protein → Increased IP_3/DAG → Intracellular calcium release

(B) Activation of G_i protein → Decreased cAMP → Opening of voltage-gated calcium channels

(C) Direct opening of ATP-sensitive potassium channels (K_{ATP}) inducing hyperpolarization

(D) Activation of G_s protein → Increased cAMP → Phosphorylation and inactivation of myosin light chain kinase (MLCK)

Q8. A 58-year-old male with open-angle glaucoma is prescribed a topical ophthalmic medication. He subsequently develops severe bronchospasm and symptomatic bradycardia. Which of the following pairs correctly identifies the medication prescribed and the anatomical site responsible for these adverse systemic manifestations?

(A) Brimonidine; α_2 receptors in the bronchial tree

(B) Pilocarpine; M_3 receptors in the cardiac pacemaker cells

(C) Timolol; β_2 receptors in bronchi and β_1 receptors in the SA node

(D) Latanoprost; Prostaglandin FP receptors in the ciliary body

Q9. A 34-year-old woman diagnosed with schizophrenia has been treated with haloperidol for the past 14 months. She is brought to the emergency department with altered mental status, severe generalized "lead-pipe" muscle rigidity, hyperthermia (104.2°F), autonomic instability, and an elevated serum creatine kinase level. What is the immediate drug of choice to reverse this condition, and what is its specific molecular mechanism of action?

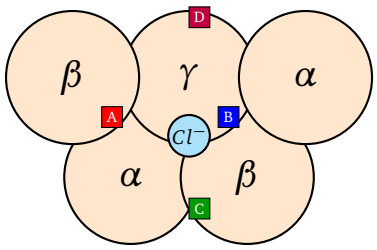
(A) Bromocriptine; Centrally acting D_2 receptor agonist

(B) Dantrolene; Ryanodine receptor ($RyR1$) antagonist inhibiting calcium release from sarcoplasmic reticulum

(C) Benztropine; Central muscarinic antagonist restoring dopamine-acetylcholine balance

(D) Physostigmine; Reversible acetylcholinesterase inhibitor that crosses the blood-brain barrier

Q10. The following diagram maps the structural components of the $GABA_A$ receptor complex channel pore. A patient presenting with an acute overdose of a sedative-hypnotic agent exhibits marked respiratory depression. The clinician administers Flumazenil, which completely reverses the sedation. At which lettered allosteric/binding site on this receptor complex does Flumazenil act as a competitive antagonist?



(A) Site A (Interface between α and β subunits)

(B) Site B (Interface between α and γ subunits)

(C) Site C (Deep inside the channel pore matrix)

(D) Site D (Outer surface of the β subunit exclusively)

Q11. A 24-year-old graduate student presents with generalized tonic-clonic seizures. The neurologist decides to initiate monotherapy with an antiepileptic drug that acts primarily by prolonging the inactivated state of voltage-gated sodium channels, preventing high-frequency repetitive firing without altering low-frequency physiological firing. Which of the following drugs shares this specific mechanism?

(A) Ethosuximide

(B) Vigabatrin

(C) Tiagabine

(D) Phenytoin

Q12. A Parkinson's disease patient on long-term Levodopa-Carbidopa therapy begins experiencing unpredictable, rapid switches between mobility and severe rigidity throughout the day (the "on-off" phenomenon). Which of the following therapeutic strategies would be most appropriate to add to their regimen to minimize these fluctuations by extending the half-life of dopamine in the central nervous system without increasing peripheral conversion?

(A) Entacapone

(B) Tolcapone

(C) Selegiline

(D) Amantadine

Q13. A 28-year-old male treated for pulmonary tuberculosis develops tingling, numbness, and burning sensations in his bilateral lower extremities. A peripheral neuropathy secondary to isoniazid therapy is suspected. Which of the following statements correctly details the structural biochemical basis for this drug-induced adverse effect?

(A) Isoniazid forms a hydrazone complex with pyridoxal phosphate (B_6), leading to its depletion and impaired myelin synthesis.

(B) Isoniazid directly competes with thiamine (B_1) for active transport absorption mechanisms in the gut.

(C) Isoniazid causes safe accumulation of cyanocobalamin (B_{12}) within the hepatic storage pools, inducing systemic deficiency.

(D) Isoniazid inhibits dihydrofolate reductase, blocking the formation of active tetrahydrofolic acid within schwann cells.

Q14. A 33-year-old HIV-positive patient with a CD4 count of 85/μL is treated empirically for an opportunistic infection. During therapy, the patient exhibits a sudden elevation in serum creatinine, oliguria, and crystals shaped like "sheaves of wheat" in the urine sediment. Which antimicrobial agent is most likely responsible for causing this presentation of crystal nephropathy?

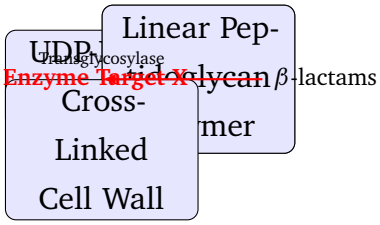
(A) Amphotericin B

(B) Sulfadiazine

(C) Ganciclovir

(D) Clindamycin

Q15. The graphic illustration below outlines the bacterial cell wall synthesis pathway and the enzymatic steps targeted by different classes of β-lactam antibiotics and related agents. A strain of MRSA displays resistance to Cephems by altering the target structural element labeled as 'Enzyme Target X'. Which of the following drugs is specifically designed to overcome this resistance mechanism by retaining high binding affinity to this altered structure?



(A) Ceftriaxone

(B) Cefepime

(C) Ceftaroline

(D) Piperacillin

Q16. A 42-year-old female presents with severe pelvic inflammatory disease caused by *Bacteroides fragilis* along with aerobic Gram-negative bacilli. The clinician intends to utilize an antibiotic that inhibits bacterial protein synthesis by binding to the 50S ribosomal subunit, specifically blocking transpeptidation. Which of the following options represents the optimal choice matching this mechanism and spectrum?

(A) Azithromycin

(B) Linezolid

(C) Clindamycin

(D) Gentamicin

Q17. A patient undergoing chemotherapy for acute myeloid leukemia develops a life-threatening systemic fungal infection due to *Aspergillus fumigatus*. The clinician prescribes an antifungal agent that disrupts fungal cell wall synthesis by non-competitively inhibiting β-(1,3)-D-glucan synthase. Which antifungal belongs to this drug category?

(A) Amphotericin B

(B) Caspofungin

(C) Voriconazole

(D) Flucytosine

Q18. A 67-year-old male with chronic heart failure and atrial fibrillation is receiving Digoxin. He presents to the clinic complaining of nausea, abdominal pain, and dynamic visual disturbances ("yellow-green halos"). His ECG demonstrates paroxysmal atrial tachycardia with variable AV block. What cellular event, directly downstream from Digoxin's primary mechanism of action, is responsible for triggering these arrhythmic developments?

(A) Increased intracellular K^+ concentration due to activation of the Na^+/K^+ ATPase pump

(B) Accumulation of intracellular Na^+, which slows down or reverses the Na^+/Ca^{2+} exchanger (NCX), leading to increased intracellular Ca^{2+}

(C) Direct opening of L-type calcium channels causing an exaggerated calcium influx during phase 2 of the action potential

(D) Intracellular magnesium depletion leading to spontaneous depolarization of the Purkinje fibers

Q19. A 49-year-old postmenopausal female presenting with estrogen-receptor-positive (ER^+) breast cancer is started on hormonal therapy. The drug prescribed functions as a competitive antagonist at estrogen receptors in breast tissue but acts as a partial agonist in endometrial tissue and bone. Which of the following drugs matches this profile, and what is its most concerning long-term adverse consequence?

(A) Tamoxifen; Increased risk of endometrial carcinoma

(B) Anastrazole; Severe accelerated osteoporosis

(C) Letrozole; Deep vein thrombosis and pulmonary embolism

(D) Raloxifene; Increased risk of invasive ductal breast cancer

Q20. A 54-year-old male with type 2 diabetes mellitus is started on a modern oral antidiabetic medication. Within 3 months, he demonstrates significant weight loss, a modest drop in blood pressure, and a lower HbA1c. However, he returns to the clinic with an acute genitourinary tract infection. The drug prescribed works by inhibiting which specific physiological transporter in the nephron?

(A) Sodium-Hydrogen Exchanger 3 ($NHE3$) in the proximal convoluted tubule

(B) Sodium-Glucose Cotransporter 2 ($SGLT2$) in the early segment of the proximal convoluted tubule

(C) Sodium-Potassium-2Chloride Cotransporter ($NKCC2$) in the thick ascending limb of loop of Henle

(D) Sodium-Chloride Cotransporter (NCC) in the distal convoluted tubule

Detailed Solutions

Q1.

Solution

Concept: Schild regression analysis evaluates the mathematical relationship between a competitive antagonist concentration and the parallel rightward shift it induces in the agonist concentration-response curve.

Solution:

(a) A competitive antagonist binds reversibly to the same receptor active site as the agonist molecule. By occupying these binding sites, it prevents agonist attachment unless higher concentrations of the agonist are introduced.

(b) This specific pharmacology causes a parallel rightward shift of the log concentration-response curve, meaning that the half-maximal effective concentration increases while the maximal response remains completely unchanged.

(c) The degree of this rightward shift can be quantified using the dose ratio, which is the ratio of the agonist concentration needed to produce a specific response in the presence of the antagonist to that needed in its absence.

(d) The Schild equation relates this dose ratio to the antagonist concentration through a linear regression model.

(e) By plotting the log of the dose ratio minus one against the log concentration of the competitive antagonist, a straight line with a characteristic slope of one is obtained.

(f) The x-intercept of this linear regression plot yields the logarithm of the equilibrium dissociation constant of the antagonist, denoted as K_B or K_i, reflecting its receptor binding affinity.

Final Answer: The equilibrium dissociation constant (K_i or K_B) of the antagonist

Answer: (C)

Go Back to Question 1

Q2.

Solution

Concept: Zero-order elimination kinetics occur when the metabolic pathways of a drug become completely saturated, causing the elimination rate to remain constant regardless of the total plasma concentration.

Solution:

(a) When an anti-epileptic drug like phenytoin or a high dose of ethanol is administered, the hepatic metabolic enzymes can become completely saturated at therapeutic or toxic levels.

(b) Under these specific conditions, the clearance mechanisms operate at their absolute maximum capacity, meaning that a constant amount of the drug is eliminated per unit of time rather than a constant fraction.

(c) Because the elimination rate is independent of the amount of drug remaining in the systemic circulation, the clearance value becomes inversely proportional to the total plasma concentration.

(d) This kinetic behavior alters the mathematical relationship between the remaining plasma concentration and elapsed time following a single high-dose administration.

(e) A constant elimination rate means that the drop in plasma concentration over time forms a straight, downward-sloping linear profile.

(f) Reviewing the provided graphical illustrations, Graph B depicts a steady linear decline with a constant negative slope over time, which accurately represents the signature profile of zero-order elimination kinetics.

Final Answer: Graph B

Answer: (B)

Go Back to Question 2

Q3.

Solution

Concept: Adjusting drug maintenance dosing for renal impairment requires calculating the remaining fraction of overall drug clearance based on the patient's specific creatinine clearance.

Solution:

(a) The antimicrobial agent exhibits a dual elimination pathway, where 80% of the drug is cleared unchanged through renal filtration while the remaining 20% undergoes non-renal elimination.

(b) The patient has a significantly reduced renal function, with a measured creatinine clearance of 22 mL/min compared to a normal baseline clearance value of 100 mL/min.

(c) We can determine the patient's remaining renal function fraction by taking the ratio of the impaired clearance to the normal clearance, which yields exactly 0.22.

(d) To compute the overall remaining drug clearance factor, we multiply the renal elimination portion by this function fraction and add the unaffected non-renal portion.

(e) This mathematical calculation is expressed as the fraction formula: $(0.80 \times 0.22) + 0.20 = 0.176 + 0.20 = 0.376$.

(f) Because the standard dosing interval of 12 hours remains unchanged, the adjusted maintenance dose is found by multiplying the normal dose of 500 mg by this overall fraction factor, giving $500 \times 0.376 = 188$ mg.

Final Answer: 188 mg

Answer: (A)

Go Back to Question 3

Q4.

Solution

Concept: Ion trapping exploits the pH-dependent ionization of weak acids or bases across biological membranes, where adjusting the urine pH converts the drug into an impermeable charged state to accelerate excretion.

Solution:

(a) Drug X is described as a weak molecular base, meaning it exists in an equilibrium between its un-ionized neutral form and its protonated, positively charged ionized form.

(b) According to the Henderson-Hasselbalch principle, a weak base becomes increasingly protonated and ionized when it enters an environment with a lower pH value.

(c) The ionized, charged form of a drug molecule possesses high water solubility but very low lipid permeability, making it unable to cross the lipid bilayer membranes of the renal tubular cells.

(d) To prevent the renal reabsorption of a weak base back into the systemic bloodstream, a clinician must maximize the proportion of the drug that exists in this trapped, ionized state within the urinary filtrate.

(e) To shift the chemical equilibrium toward the protonated ionized form, the urinary environment must be acidified relative to the drug's dissociation constant.

(f) Administering ammonium chloride safely acidifies the urine, which drives the weak base into its highly ionized form, trapping it in the renal tubules and accelerating its clearance.

Final Answer: Administer Ammonium chloride; Ionized form predominates

Answer: (B)

Go Back to Question 4

Q5.

Solution

Concept: Chemical aging of the phosphorylated acetylcholinesterase enzyme breaks an alkyl group bond, stabilizing the complex and rendering oxime reactivators completely ineffective at reversing paralysis.

Solution:

(a) Organophosphate compounds are toxic agents that bind covalently to the active esteratic site of the acetylcholinesterase enzyme, causing a persistent accumulation of acetylcholine within the synaptic cleft.

(b) Pralidoxime is an oxime reactivator designed to break this covalent bond by binding to the peripheral anionic site, removing the phosphate group and restoring normal enzyme function.

(c) However, if the phosphorylated enzyme complex is allowed to remain bound over time, it undergoes a chemical dealkylation process known as aging.

(d) The loss of this alkyl group creates a highly stable, negatively charged monophosphorylated enzyme complex that resists nucleophilic attack by pralidoxime.

(e) Once the enzyme complex undergoes aging, pralidoxime can no longer reactivate the acetylcholinesterase enzyme at the post-synaptic neuromuscular junction membrane labeled as Site Y.

(f) Because the nicotinic receptors at Site Y remain overstimulated by excess acetylcholine, the resulting neuromuscular paralysis and respiratory failure cannot be reversed by oxime therapy.

Final Answer: Receptors localized at Site Y once the enzyme has undergone "aging"

Answer: (D)

Go Back to Question 5

Q6.

Solution

Concept: Nicotinic neuronal receptor agonists stimulate autonomic ganglionic pathways, triggering complex biphasic blood pressure changes that can be completely blocked by ganglionic blockers like hexamethonium.

Solution:

(a) The experimental drug produces a complex systemic response consisting of an initial temporary rise in blood pressure, a subsequent prolonged drop, and a significant slowing of the heart rate.

(b) Nicotinic neuronal receptors are located within both the sympathetic and parasympathetic autonomic ganglia, as well as the adrenal medulla.

(c) Activating these ganglionic receptors simultaneously stimulates both arms of the autonomic nervous system, resulting in competing cardiovascular signaling profiles.

(d) The initial transient rise in blood pressure is driven by sympathetic ganglionic activation and epinephrine release from the adrenal medulla, which causes vasoconstriction.

(e) This surge in blood pressure triggers a robust baroreceptor reflex, which activates parasympathetic pathways to slow the heart rate and lower systemic blood pressure.

(f) Pre-treating the animal with hexamethonium—a selective antagonist for nicotinic neuronal receptors—completely prevents ganglionic transmission, abolishing the entire biphasic response and confirming that the drug acts as an agonist at these receptors.

Final Answer: Nicotinic neuronal (N_N) receptors

Answer: (A)

Go Back to Question 6

Q7.

Solution

Concept: Activating smooth muscle beta-2 adrenergic receptors triggers a cyclic adenosine monophosphate signaling pathway that phosphorylates myosin light chain kinase, inhibiting its function and inducing relaxation.

Solution:

(a) Selective beta-2 adrenergic receptor agonists are utilized clinically as tocolytic agents to suppress premature uterine contractions and delay preterm labor.

(b) The beta-2 adrenergic receptor belongs to the family of transmembrane G-protein coupled receptors, specifically interacting with the stimulatory G-protein subunit.

(c) Binding of the agonist to the receptor stimulates the intramembrane enzyme adenylyl cyclase, which accelerates the conversion of cellular ATP into cyclic adenosine monophosphate.

(d) The resulting accumulation of intracellular cyclic AMP activates protein kinase A, a downstream regulatory enzyme.

(e) Active protein kinase A phosphorylates myosin light chain kinase, the key enzyme responsible for phosphorylating myosin heads to initiate cross-bridge cycling and smooth muscle contraction.

(f) This phosphorylation inactivates myosin light chain kinase, reducing its affinity for the calcium-calmodulin complex and preventing smooth muscle contraction to cause uterine relaxation.

Final Answer: Activation of G_s protein → Increased cAMP → Phosphorylation and inactivation of myosin light chain kinase (MLCK)

Answer: (D)

Go Back to Question 7

Q8.

Solution

Concept: Topical ophthalmic beta-blockers can undergo systemic absorption through the nasolacrimal duct, leading to systemic beta-receptor antagonism that can cause bronchospasm and severe bradycardia.

Solution:

(a) Timolol is a non-selective beta-adrenergic receptor antagonist frequently prescribed as eye drops to manage elevated intraocular pressure in open-angle glaucoma.

(b) When administered topically to the eye, a significant portion of the medication drains through the nasolacrimal duct directly into the nasal mucosa.

(c) The highly vascularized nasal mucosa allows the drug to enter the systemic venous circulation, completely bypassing first-pass hepatic metabolism.

(d) Once in the systemic circulation, the non-selective beta-blocker reaches the respiratory and cardiovascular systems, where it binds to beta-adrenergic receptors.

(e) In the respiratory tract, blockading beta-2 adrenergic receptors prevents smooth muscle relaxation, triggering bronchospasm in susceptible individuals.

(f) Simultaneously, blocking beta-1 adrenergic receptors in the cardiac sinoatrial node pacemaker cells slows the heart rate, causing symptomatic bradycardia.

Final Answer: Timolol; $\beta_2 receptors in bronchi and \beta_1 receptors in the SA node$

Answer: (C)

Go Back to Question 8

Q9.

Solution

Concept: Neuroleptic malignant syndrome is a severe drug-induced reaction characterized by intense muscle rigidity and hyperthermia, treated primarily with skeletal muscle relaxants that block intracellular calcium release.

Solution:

(a) The patient exhibits the classic triad of neuroleptic malignant syndrome: severe lead-pipe muscle rigidity, extreme hyperthermia, altered mental status, and autonomic instability, induced by chronic haloperidol therapy.

(b) Haloperidol is a potent central dopamine D2 receptor antagonist, and its blockade within the striatal pathways triggers excessive, uncoordinated skeletal muscle contractions.

(c) This continuous, severe muscular rigidity generates an immense amount of metabolic heat, leading to life-threatening hyperthermia and an elevated serum creatine kinase level from muscle breakdown.

(d) To halt this dangerous hypermetabolic state, the primary therapeutic goal is to rapidly relax the rigid skeletal muscle fibers.

(e) Dantrolene is the immediate drug of choice, functioning as a direct-acting skeletal muscle relaxant.

(f) It binds selectively to ryanodine receptor channels located on the sarcoplasmic reticulum membrane, blocking the release of stored calcium into the intracellular cytoplasm to terminate muscle contraction and resolve hyperthermia.

Final Answer: Dantrolene; Ryanodine receptor ($RyR1$) antagonist inhibiting calcium release from sarcoplasmic reticulum

Answer: (B)

Go Back to Question 9

Q10.

Solution

Concept: The benzodiazepine allosteric binding site is located at the specific subunit interface between the alpha and gamma components of the pentameric GABA-A receptor channel complex.

Solution:

(a) The GABA-A receptor is a ligand-gated ion channel complex with a pentameric structure, typically composed of two alpha, two beta, and one gamma subunit surrounding a central chloride pore.

(b) Endogenous gamma-aminobutyric acid binds directly to its primary ligand binding sites located at the interfaces between the alpha and beta subunits to trigger chloride influx.

(c) Sedative-hypnotic agents like benzodiazepines do not bind to the primary GABA site; instead, they attach to a distinct allosteric modulatory site on the receptor complex.

(d) Structural mapping reveals that this specific allosteric benzodiazepine binding site is located at the interface between the alpha and gamma subunits, marked as Site B.

(e) Flumazenil is a selective, competitive antagonist designed to bind with high affinity to this exact alpha-gamma subunit interface.

(f) By occupying Site B, flumazenil competitively displaces sedative-hypnotic benzodiazepines, reversing their modulatory effects on chloride conductance and rapidly clearing respiratory depression.

Final Answer: Site B (Interface between $\alpha and \gamma subunits$)

Answer: (B)

Go Back to Question 10

Q11.

Solution

Concept: Antiepileptic medications often target specific configurations of voltage-gated ion channels, selectively reducing high-frequency repetitive firing by shifting the channels into an inactive state.

Solution:

(a) Voltage-gated sodium channels alternate between open, inactivated, and closed resting conformations during the propagation of neuronal action potentials.

(b) During abnormal high-frequency epileptic discharges, these channels rapidly cycle through the open and inactivated states.

(c) Phenytoin acts preferentially by binding to the transmembrane segments of sodium channels when they are in their inactive state.

(d) This binding stabilizes the inactive conformation, preventing the channels from resetting back to their resting state.

(e) By delaying this channel recovery, the drug increases the refractory period of the neuron, blocking sustained high-frequency repetitive action potential firing.

(f) Normal, low-frequency physiological firing remains largely unaffected because the intervals between normal action potentials provide sufficient time for drug dissociation.

Final Answer: Phenytoin

Answer: (D)

Go Back to Question 11

Q12.

Solution

Concept: Extending the half-life of dopamine within the central nervous system without altering its peripheral conversion minimizes clinical motor fluctuations in advanced Parkinson's disease.

Solution:

(a) The "on-off" phenomenon represents rapid, unpredictable fluctuations between mobility and profound rigidity due to variations in plasma levodopa concentrations.

(b) Entacapone is a selective, reversible catechol-O-methyltransferase inhibitor that acts exclusively within the peripheral circulation to prevent levodopa breakdown.

(c) Tolcapone inhibits the same metabolic pathway but possesses a distinct chemical structure that allows it to cross the blood-brain barrier.

(d) By entering the central nervous system, tolcapone prevents the local methylation of active dopamine into its inactive metabolite, 3-methoxytyramine.

(e) This dual central and peripheral enzyme inhibition increases the half-life of central dopamine, smoothing out the clinical response.

(f) While entacapone works purely in the periphery, tolcapone satisfies the requirement for central metabolic stabilization of dopamine.

Final Answer: Tolcapone

Answer: (B)

Go Back to Question 12

Q13.

Solution

Concept: Drug-induced peripheral neuropathy can result from chemical interactions that deplete essential vitamin cofactors required for axonal myelin maintenance and synthesis.

Solution:

(a) Isoniazid is a core antimicrobial agent used in antitubercular regimens that can cause dose-dependent neurotoxicity.

(b) Structurally, isoniazid contains a hydrazine group that undergoes a chemical reaction with pyridoxal molecules inside human tissues.

(c) This reaction forms an inactive hydrazone complex, which accelerates the renal excretion of pyridoxine (vitamin B6).

(d) Pyridoxal phosphate serves as an essential enzymatic cofactor for the synthesis of neurotransmitters and structural myelin lipids.

(e) The resulting intracellular depletion of vitamin B6 disrupts metabolic pathways within peripheral Schwann cells and neurons.

(f) This structural breakdown manifests clinically as distal, symmetric sensory abnormalities like tingling, numbness, and burning sensations.

Final Answer: Isoniazid forms a hydrazone complex with pyridoxal phosphate (B_6), leading to its depletion and impaired myelin synthesis.

Answer: (A)

Go Back to Question 13

Q14.

Solution

Concept: Crystal-induced nephropathy occurs when an antimicrobial drug or its metabolite concentrates within the renal tubules beyond its solubility limit, precipitating into distinctive crystalline aggregates.

Solution:

(a) Sulfadiazine is a sulfonamide antibiotic frequently utilized in immunodeficient individuals to treat or prevent opportunistic infections.

(b) The drug undergoes hepatic metabolism via acetylation, converting it into metabolites that exhibit limited solubility in acidic environments.

(c) As the glomerular filtrate moves through the nephron, water reabsorption concentrates these compounds within the collecting ducts.

(d) In acidic urine conditions, the accumulated sulfadiazine precipitates out of solution, forming solid microscopic structures.

(e) These crystals possess a characteristic morphology under light microscopy described as "sheaves of wheat."

(f) The mechanical obstruction of the renal tubules triggers an acute drop in glomerular filtration, leading to oliguria and elevated creatinine.

Final Answer: Sulfadiazine

Answer: (B)

Go Back to Question 14

Q15.

Solution

Concept: Overcoming bacterial resistance driven by altered target enzymes requires developing advanced antibiotics with structures tailored to fit the modified binding domains.

Solution:

(a) Methicillin-resistant *Staphylococcus aureus* (MRSA) develops resistance to beta-lactam antibiotics by acquiring the mecA gene.

(b) This gene encodes a modified transpeptidase enzyme known as Penicillin-Binding Protein 2a (PBP2a), labeled as Enzyme Target X.

(c) Standard cephalosporins and penicillins cannot bind to this altered transpeptidase due to structural changes in its active site.

(d) Ceftaroline is an advanced, fifth-generation cephalosporin designed with a distinct side-chain structure.

(e) This side-chain induces a conformational change in PBP2a, opening the active site and allowing the drug to bind tightly.

(f) By successfully binding to and inhibiting PBP2a, ceftaroline blocks cell wall cross-linking, overcoming MRSA resistance.

Final Answer: Ceftaroline

Answer: (C)

Go Back to Question 15

Q16.

Solution

Concept: Managing mixed aerobic and anaerobic pelvic infections requires selecting an antibiotic that provides coverage against anaerobic bacilli by targeting bacterial protein translation.

Solution:

(a) Pelvic inflammatory disease involving *Bacteroides fragilis* requires potent antimicrobial activity against Gram-negative obligate anaerobes.

(b) Clindamycin is a lincosamide antibiotic that binds selectively to the 23S ribosomal RNA subunit of the 50S bacterial ribosome.

(c) This binding physically obstructs the peptidyltransferase center, preventing peptide bond formation and halting transpeptidation.

(d) Inhibiting this step prevents the elongation of the nascent polypeptide chain, shutting down bacterial protein synthesis.

(e) Clindamycin maintains strong activity against anaerobic pathogens, making it effective for mixed pelvic infections.

(f) While macrolides like azithromycin share a similar binding site, they lack sufficient efficacy against *Bacteroides fragilis*.

Final Answer: Clindamycin

Answer: (C)

Go Back to Question 16

Q17.

Solution

Concept: Echinocandin antifungals target the fungal cell wall rather than the cell membrane by non-competitively inhibiting the synthesis of core structural glucan polymers.

Solution:

(a) Severe invasive aspergillosis in immunocompromised individuals requires target-specific antifungal therapies.

(b) Unlike polyenes or azoles that target ergosterol in the fungal cell membrane, echinocandins act on the cell wall.

(c) Caspofungin is an echinocandin that non-competitively inhibits the transmembrane enzyme complex beta-(1,3)-D-glucan synthase.

(d) This enzyme is responsible for synthesizing beta-glucan polymers, which provide structural integrity to the fungal cell wall.

(e) Blocking this pathway depletes these essential structural elements, weakening the mechanical stability of the wall.

(f) This compromise makes the fungal cell vulnerable to osmotic pressure, leading to lysis and cell death.

Final Answer: Caspofungin

Answer: (B)

Go Back to Question 17

Q18.

Solution

Concept: Inhibiting the sodium-potassium ATPase pump alters secondary active transport mechanisms, causing intracellular calcium overload that can trigger delayed afterdepolarizations.

Solution:

(a) Digoxin binds reversibly to the extracellular domain of the Na+/K+ ATPase pump, inhibiting its enzymatic activity.

(b) This blockade prevents the active transport of sodium out of the cell, leading to a accumulation of intracellular sodium.

(c) The resulting reduction in the transmembrane sodium gradient slows the activity of the secondary Na+/Ca2+ exchanger (NCX).

(d) Because the exchanger relies on the sodium gradient to pump calcium out, calcium begins to accumulate within the cytoplasm.

(e) This excess intracellular calcium is pumped into the sarcoplasmic reticulum, increasing stored calcium levels.

(f) Spontaneous calcium release from these stores can trigger transient inward currents, producing delayed afterdepolarizations that manifest as arrhythmias.

Final Answer: Accumulation of intracellular Na^+, which slows down or reverses the Na^+/Ca^{2+} exchanger (NCX), leading to increased intracellular Ca^{2+}

Answer: (B)

Go Back to Question 18

Q19.

Solution

Concept: Selective estrogen receptor modulators exert tissue-specific effects, acting as antagonists in breast tissue but as agonists in endometrial tissue, which can promote cell proliferation.
Solution:

(a) Tamoxifen is a selective estrogen receptor modulator (SERM) utilized as adjuvant hormonal therapy for estrogen-receptor-positive breast cancers.

(b) The drug's therapeutic profile stems from its ability to function as a competitive antagonist at estrogen receptors within breast tissue.

(c) However, its active metabolites act as partial agonists at estrogen receptors in other tissues, including bone and the endometrium.

(d) While its agonist activity in bone helps maintain mineral density, its agonist activity in the uterus stimulates endometrial proliferation.

(e) This chronic, unopposed estrogenic stimulation can induce endometrial hyperplasia, increasing the risk of malignant transformation.

(f) Consequently, endometrial carcinoma represents the most significant long-term adverse effect associated with tamoxifen therapy.

Final Answer: Tamoxifen; Increased risk of endometrial carcinoma

Answer: (A)

Go Back to Question 19

Q20.

Solution

Concept: Blocking glucose reabsorption in the proximal convoluted tubule lowers blood glucose levels but increases urinary glucose concentrations, predisposing patients to genitourinary infections.

Solution:

(a) SGLT2 inhibitors are oral antidiabetic medications that target glucose handling pathways within the kidneys.

(b) Under normal physiological conditions, the Sodium-Glucose Cotransporter 2 (SGLT2) reabsorbs roughly 90% of filtered glucose.

(c) This low-affinity, high-capacity transporter is localized to the early S1 segment of the proximal convoluted tubule.

(d) By inhibiting SGLT2, the drug blocks this reabsorption pathway, promoting glucose excretion in the urine (glucosuria).

(e) This loss of glucose lowers plasma glucose and HbA1c levels, while the associated osmotic diuresis reduces blood pressure and weight.

(f) However, the high glucose concentration in the urinary tract provides a favorable environment for microbial growth, increasing the risk of genitourinary infections.

Final Answer: Sodium-Glucose Cotransporter 2 ($SGLT2$) in the early segment of the proximal convoluted tubule

Answer: (B)

Go Back to Question 20

Answer Key

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