1. a. With regard to drugs, what is “potency”?

   Potency refers to the affinity or attraction between an agonist and its receptor.

   A good measure of drug potency is the EC$_{50}$—the concentration that produces 50% of the maximal response.

   b. How is this different to Efficacy?

   Efficacy is the maximal response that a drug (agonist) can produce ($E_{\text{max}}$) when all receptors are occupied, irrespective of the concentration required to produce that response.

   c. Draw a concentration-response curve showing 2 drugs with the same potency but different efficacy.

   ![Concentration-response curve](image)
2. a. Describe the mechanism of action of glyceryl trinitrate.

- Taken up by **vascular smooth muscle**
- Interacts with tissue sulfhydryl groups
- Releases free radical **nitric oxide**
- Activates cGMP
- Dephosphorylates myosin light chains
- **Reduces intracellular Ca levels**
- Smooth muscle relaxation & **vasodilation**

- Low doses – venodilation ⇒ ↓ preload & stroke volume
- Higher doses – arterial dilation ⇒ ↓ **blood pressure**
⇒ ↓ cardiac output & ↓ **myocardial oxygen demand**
+ dilation of coronary arteries/redistribution of perfusion
⇒ improved oxygen delivery to myocardium & resolution of ischaemic pain

[Prompt if needed “What other clinical effects may be seen?”]
- Adverse effects: postural hypotension, tachycardia, dizziness, headache, flushing, blurred vision, dry mouth, rash

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<tbody>
<tr>
<td>vascular smooth muscle</td>
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<tr>
<td>nitric oxide</td>
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<tr>
<td>vasodilation</td>
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b. What are the clinical effects of nitrates

- Must state
- **↓ BP**
- **↓ myocardial oxygen demand**
- 2 listed other effects

3. a. What is pancuronium?

**Non-depolarising NM blocker**
Quaternary ammonium compound
Potent competitive antagonist of ACh at nicotinic receptors
skeletal muscle motor end-plate
Interruption of transmission requires > 70% occupancy; blockade requires > 95% occupancy

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<tr>
<th>Nondepolarising NM blocker</th>
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<tr>
<th>Question</th>
<th>Description</th>
<th>Adverse Effects</th>
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<tbody>
<tr>
<td>b. Describe the pharmacokinetics of pancuronium?</td>
<td>Poorly absorbed after oral admin Rapidly and widely distributed after iv Rapid elimination ($T_{1/2}$ 30min) by urinary excretion unchanged drug (highly water soluble), and hepatic metabolism with biliary excretion&lt;br&gt;[Prompt: Describe its distribution and elimination]</td>
<td>Uncommon Minor tachycardia, hypertension, sl ↑ CO can occur Life-threatening anaphylaxis &lt; 1:10,000</td>
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<tr>
<td>c. What are the adverse effects of pancuronium?</td>
<td></td>
<td>A cardiac and allergy effect</td>
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<tr>
<td>4. a. Describe the pharmacokinetics of lithium</td>
<td>Rapidly absorbed (except SR preparations) with peak plasma concs in 1-3hrs. High bioavailability. Not metabolised Renally excreted unchanged with partial reabsorption from PT. Long $T_{1/2}$ of 24hrs in adults Steady state plasma concs not reached for 5-7 days&lt;br&gt;[PROMPT – How long does it take to reach steady state plasma conc?]</td>
<td>Long $T_{1/2}$ so steady state plasma concs not reached for days. Renally excreted unchanged.</td>
</tr>
<tr>
<td>b. What are the adverse effects of Lithium at therapeutic levels?</td>
<td>Tremor, nausea, polydypsia /polyuria, diarrhoea, weight gain. Long-term: Acne / psoriasis, hypothyroidism, nephrogenic diabetes insipidus (inhibits the effect of ADH on the DT cells -&gt; polyuria).</td>
<td>Polyuria &amp; Polydipsia OR NDI.</td>
</tr>
<tr>
<td>c. What are the signs/symptoms of lithium toxicity?</td>
<td>GIT: Vomiting. Neuro: Tremors, confusion, slurred speech, ataxia, drowsiness, blurred vision, seizures.</td>
<td>CNS effects with at least 3 symptoms</td>
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5. 

| a. List the advantages of eye ointments over eye drops. | More stable  
Less absorption into lacrimal ducts  
Longer retention time on conjunctival surface  
Safer with potent drugs  
Ointment bases provide protection and comfort at night | 2 to pass |
|---|---|---|
| b. List by action the types of drugs used topically in the eye | Mydriatics  
Miotics  
Cycloplegics  
Decongestants  
Antibiotics  
Antivirals  
Antiseptics  
Corticosteroids  
Local anaesthetics  
Stains eg. Fluoroscein | 4 to pass |
| c. List the ideal properties of an ocular local anaesthetic | Quick onset of action (10-20 secs.)  
Useful duration of action (10-20 mins.)  
No obvious effects on function or healing  
No interactions with drugs used concurrently | Quick onset and useful duration of action |
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</table>
| 1. a. What routes of drug administration are there?                     | Enteral: Sublingual, buccal, oral, rectal  
Parenteral: SC, IM, IV, intrathecal, epidural  
Inhalational  
Topical | Enteral/oral + 3 non-entaloral  
Must mention drug factors and gut factors |
| 1. b. What factors affect the rate of drug absorption from the small intestine? | Ionisation status of drug: alkaline  
Intestinal pH (7-8) favours absorption of un-ionised basic drugs  
Intestinal motility; increased motility lead to reduced transit time and drug absorption  
Gut surface area, blood flow, solubility of drug, formulation of drug |                                                                                                       |
| 1. c. What are potential disadvantages of rectal drug administration?   | Erratic absorption because of rectal contents  
Local drug irritation  
Uncertainty of drug retention                                                                 | 1/3                                                                                                    |
| 2. a. Describe the mechanism of action of ACE inhibitors               | • competitive **block conversion of angiotensin I to II** ⇒  
  o **decreased vascular tone** from prevention of vasoconstrictor effects of Ang II (main effect)  
  o **inhibition of aldosterone secretion** caused by Ang II leading to reduced Na & H₂O resorption ⇒ decreased BP | 3 in **bold** to pass                                                                                  |
| 2. b. What are the adverse effects of ACE inhibitors                    | • **dizziness, hypotension**  
• headaches, weakness  
• loss of taste, nausea, diarrhoea  
• rash, fever, joint pain  
• **cough**  
• mild hyperkalemia due to decrease in aldosterone secretion  
• acute renal failure | **hypotension or dizziness**  
**cough**  
**plus 2 others** }
<table>
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<th>Question</th>
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| c. What are some drug interactions that occur with ACE inhibitors | • Diuretics ⇒ hypotension  
• General anaesthetics ⇒ hypotension  
• Lithium ⇒ lithium toxicity  
• NSAIDS ⇒ hyperkalaemia & reduced effects of ACE inhibitor  
• Potassium sparing diuretics / potassium supplements ⇒ hyperkalaemia |
| 3. a. What is the mechanism of action of erythromycin? | **Inhibits** RNA-dependent **protein synthesis** by binding to the 50S ribosomal subunit.  
**Bacteriostatic** (at high conc with selected organisms can be bactericidal)  
**Inhibits hepatic CYP3A4.** Usually inhibits metabolism of other drugs metabolism causing increased activity.  
Examples: benzodiazepines, carbamazepine, cisapride (cardiotoxicity), digoxin, warfarin, theophylline, cyclosporine, tacrolimus |
| b. What is the mechanism for the drug interactions associated with erythromycin & give some examples? | Protein synthesis inhibitor  
Bacteriostatic  
Inhibit hepatic metabolism  
One example |
| c. What are the adverse effects of erythromycin? | Common: **GIT**: abdo cramp, diarrhoea, N&V, candida (oral,vag)  
Rare: hypersensitivity, hearing loss, pancreatitis, hepatotoxicity  
Rapid iv may cause ventric arrhythmias. |
| 4. a. Describe the pharmacokinetics of phenytoin. | Oral absorption slow and variable: Time to peak levels 1.5-3hrs.  
Saturable hepatic metabolism leading to non-linear PK and variable T ½ of 7-42hrs.  
Metabolites excreted in the bile & urine. |
| | Saturable metabolism/non-linear pharmacokinetics |
| b. What are the adverse effects of phenytoin? | Idiosyncratic: hirsuitism. gingival hyperplasia & overgrowth with bleeding, acne & facial coarsening.  
Dose related neurotoxic effects: drowsiness, dizziness, blurred vision, hallucinations, slurred speech, clumsiness, dizziness and confusion.  
Rapid IV administration associated with CV collapse. | Dose-related CNS effects  
Cardiac with IV administration & 1 other. |
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<td>PROMPT: Are there any specific problems with IV administration.</td>
<td></td>
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</table>

| 5.  
a. What are the indications for benzodiazepine use? | Anxiety Disorders  
Preoperative Medication  
Insomnia  
Sleep Disturbances  
Seizure Disorders  
Panic Disorder  
Alcohol Withdrawal  
Muscle Spasm  
Induce amnesia during cardioversion/endoscopic procedures | Seizures and 2 others |
| b. Explain the rationale for use of benzodiazepines in alcohol withdrawal | Down-regulation of neuro-inhibitory GABA receptors in alcohol dependent individual leads to symptoms of GABA deficiency in withdrawal.  
BZD act at a modulatory site on the the GABA$_A$ receptor to facilitate GABA binding to the GABA$_A$ receptors, enhance chloride channel opening, and overcome neuroexcitatory symptoms of GABA deficiency. | Facilitate GABA binding to the GABA$_A$ receptors  
Control neuroexcitatory symptoms of alcohol withdrawal. |
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<tr>
<td>1. a. What is meant by Total Body Clearance” of a drug</td>
<td><em>Describes the ability of the body to eliminate a drug.</em> It refers to the theoretical volume of plasma emptied of drug per unit time (usually L/h). Total body clearance reflects the sum of all clearance process including renal, hepatic and other.</td>
<td>Definition</td>
</tr>
<tr>
<td>b. Name 2 drugs that have a high hepatic clearance and explain why this is important.</td>
<td>Lignocaine, Morphine, Propranolol, Pethidine. Drugs with high hepatic elimination may only be suitable for parenteral administration or have significant dosing variations depending on the route of administration.</td>
<td>2 drugs</td>
</tr>
<tr>
<td>c. What factors determine drug half-life</td>
<td>Volume of Distribution and Clearance ($t_{1/2} = 0.693 \times \text{Vd} / \text{Cl}$ ) Vd and clearance change with disease states - cardiac, hepatic and renal failure</td>
<td>Vd and clearance</td>
</tr>
</tbody>
</table>
| 2. a. What are the pharmacokinetic properties of frusemide? | • Rapid absorption after oral admin  
• Oral bioavailability 50% (range 10 –100%)  
• Highly protein-bound (>95%)  
• 50% conjugated in kidney & 50% excreted in urine unchanged (tubular secretion)  
• Elimination $t_{1/2} 1.5 – 2$ hours  
• Peak effect 30 minutes IV / 1 hour oral | Must list 3 properties |
| b. What are the site and mechanism of action of frusemide? | • Actively secreted into lumen of nephron from proximal tubule cells via organic-base pump  
• Inhibits Na$^+$.K$^+$.2Cl$^-$ transporter in **thick ascending limb of loop of Henle** thus preventing resorption of Na$^+$ & Cl$^-$  
• Abolishes counter-current concentrating mechanism leading to a dilute urine | Must mention thick ascending limb of loop of Henle and reduced resorption of Na and Cl. |
C. What are the adverse effects of the frusemide?

- Electrolyte disturbances – **hypokalemia, hyponatraemia**, hypomagnesaemia, hyperuricaemia
- Postural **hypotension** & dizziness
- Increased LDL & triglycerides, decreased HDL
- Ototoxicity (high dose IV)
- Drug interactions

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<tbody>
<tr>
<td>- Hypokalemia</td>
</tr>
<tr>
<td>- Hyponatremia</td>
</tr>
<tr>
<td>- Hypotension or dizziness</td>
</tr>
<tr>
<td>- 1 other</td>
</tr>
</tbody>
</table>

### 3. a. What is the mechanism of action of cephalosporins

**Inhibit bacterial cell wall synthesis**, cell division and growth (similar to penicillins)

**Bactericidal**
Most effective in rapidly dividing cells.

**Gram negative** as for 3rd generation e.g. E Coli, H Influenza, Klebsiella

**Some gm positive** (S Pneumonia) but less than 1st generation

**More resistant to B Lactamases** than earlier generations

5-15% possibility of cross-reaction with penicillin allergy.

| Bolded material |

| Aware of cross-reactivity |

### 4. a. Describe the general pharmacokinetic characteristics of antipsychotic drugs

Most are readily but incompletely absorbed.
Many undergo significant first pass metabolism
Most are lipid soluble (lipophilic)
Most have high PPB (92-99%)
Most are completely metabolised by hepatic enzymes (oxidation; demethylation)
These are catalysed by liver enzymes.

**PROMPT: Use chlorpromazine as an example**

| Lipid soluble. Hepatic metabolism + 1 other |
### Define the term “atypical” antipsychotic and provide an example.

Newer antipsychotic agents with less propensity to cause extrapyramidal side-effects. Better at treating negative features of schizophrenia. They share a greater ability to alter $SHT_{2A}$ receptor activity than to interfere with $D_2$-receptor action.

Examples: olanzapine; clozapine; quetiapine; risperidone; loxapine

### c. Describe the adverse drug reactions to olanzapine.

- Weight gain
- Sedation (but less than typical antipsychotics)
- Minor orthostatic hypotension
- Minor anticholinergic effects (dry mouth, urine retention etc)
- (Extrapyramidal effects less prominent)

### 5. a. What is the mechanism of action of flumazenil?

Antagonist at the BZD binding site on the GABA$_A$ receptor (ligand-gated chloride channel).

Decreases the binding of GABA.

Blocks GABA-induced increase in Cl$^-$ permeability and influx of Cl$^-$ into the cell causing hyperpolarisation and decreased excitability of the neuron.

### b. What are the indications for flumazenil use

- Avoid intubation or ICU admission in BZD overdose.
- Reverse BZD sedation after procedures
- Diagnostic role

### c. What potential problems should be anticipated when using flumazenil?

- Precipitate seizures in mixed overdoses with BZD and proconvulsants
- Precipitate seizures in pts taking BZD to control epilepsy
- Precipitate withdrawal symptoms and seizures in BZD-dependent
- Duration of action is only 1-3hrs thus repeated administration may be necessary
- Reversal of BZD-induced respiratory depression has not been demonstrated, so resp and cardiovasc support may be required
- Adverse Effects: headache, visual disturbance, increased anxiety, nausea, light-headedness

### Specific BZD receptor antagonist at GABA receptor

- Specific BZD receptor antagonist at GABA receptor

### Reverse the sedative effects of BZD

- Precipitate fits
- Need for repeated doses