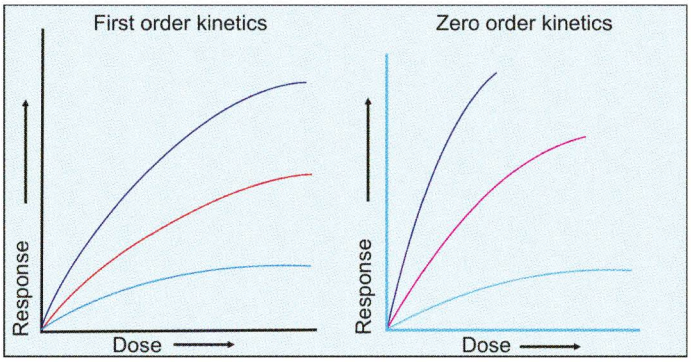



**Fig. 1.3:** *First order kinetics*: As the plasma concentration rises, metabolism and excretion proportionately increase; *Zero order kinetics*: In higher doses, the drug accumulates and the plasma concentration rises resulting in toxicity

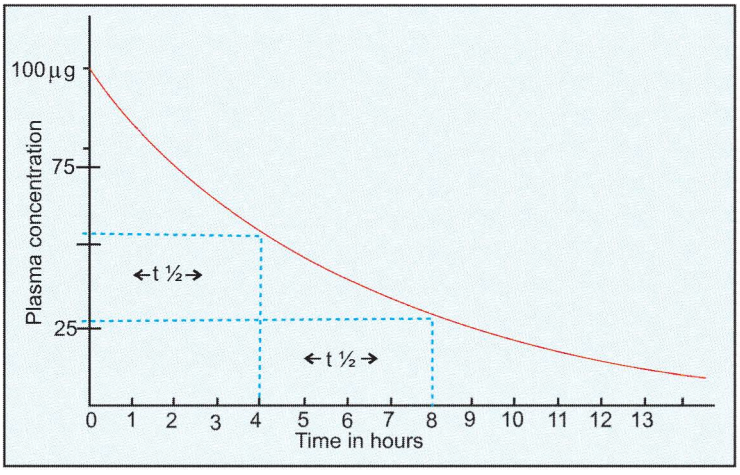



**Fig. 1.4:** Plasma concentration–time curve following intravenous administration of a drug. Plasma t½ of the drug = 4 hours

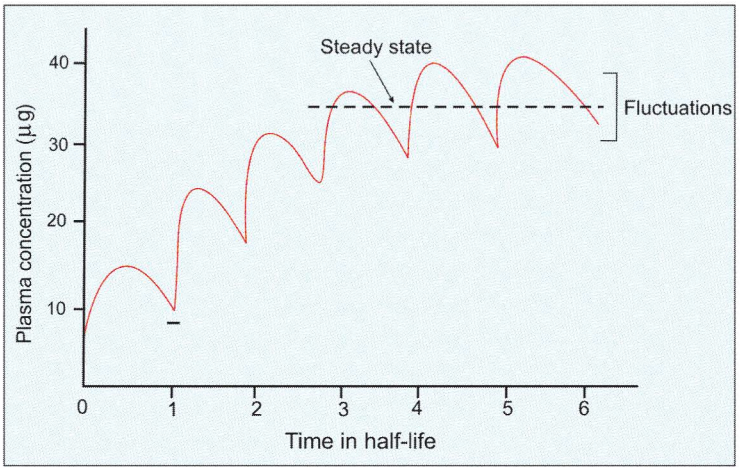
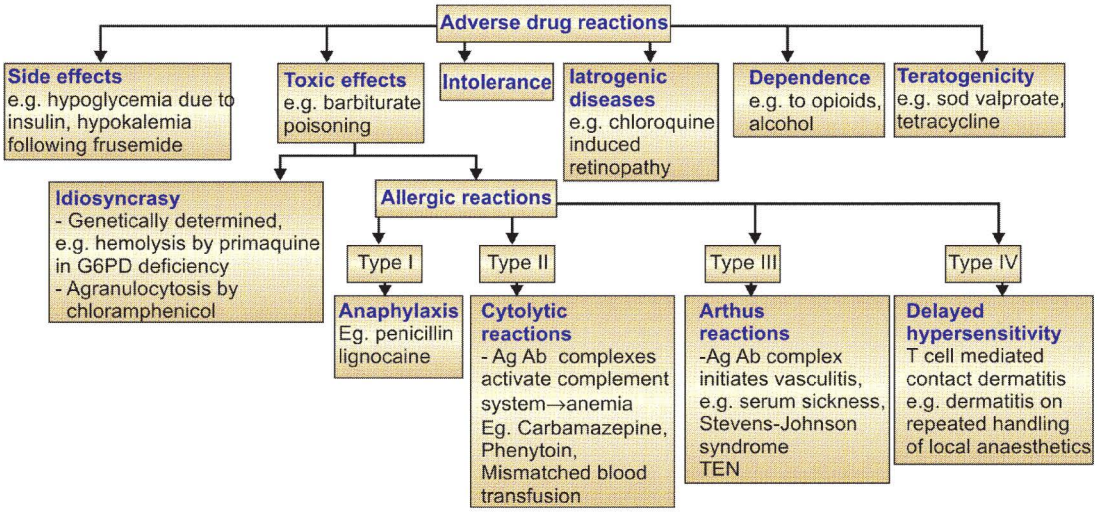



**Fig. 1.5:** Drug accumulation and attainment of steady state concentration. On oral administration, it takes 4–5 half lives to attain steady state concentration.




*Compilation of some useful examples*

**Drugs that are almost completely absorbed—on oral ingestion (100% bioavailability)**

- Diazepam
- Phenylbutazone
- Doxycycline
- Chlordiazepoxide
- Lithium
- Salicylic acid
- Digitoxin
- Minocycline
- Valproic acid
- Indomethacin
- Phenobarbitone
- Linezolid

**Drugs that undergo extensive first pass metabolism**

- Propranolol
- Lignocaine
- Verapamil
- Pentazocine
- Nitroglycerin
- Testosterone
- Hydrocortisone
- Metoprolol
- Chlorpromazine
- Morphine
- Pethidine
- Insulin
- Isoprenaline
- Levodopa

**Drugs that are highly bound to plasma proteins**

- Warfarin
- Diazepam
- Phenylbutazone
- Indomethacin
- Clofibrate
- Phenytoin
- Sulfonamides
- Salicylates
- Tolbutamide
- Frusemide

**Absorption increased by fatty food**

- Halofantrine
- Albendazole
- Atovaquone
- Griseofulvin
- Efavirenz
- Posaconazole

**Apparent volume of distribution ($V_d$)**

*Low $V_d$ drugs*

- Heparin
- Warfarin
- Aminoglycosides

*High $V_d$ drugs*

- Pethidine
- Digoxin
- Chloroquine
- Aspirin
- Furosemide
- Ampicillin
- Amoxicillin
- Nortriptyline
- Fluoxetine
- Haloperidol
- Amiodarone

**Some microsomal enzyme inducers**

- Phenobarbitone
- Rifampicin
- Tolbutamide
- Phenylbutazone
- DDT
- Carbamazepine
- Phenytoin
- Griseofulvin
- Metronidazole
- Cigarette smoke
- Alcohol

**Some microsomal enzyme inhibitors**

- Cimetidine
- Erythromycin
- Omeprazole
- Grape fruit juice
- Allopurinol
- Fluoxetine
- Quinidine
- Ketoconazole
- Chloramphenicol

**Some folate antagonists**

- Sulfonamides
- Trimethoprim
- Methotrexate
- Pemetrexed
- Pyrimethamine
- Proguanil
- Dapsone

**Prodrugs**

- Levodopa → Dopamine
- Prednisone → Prednisolone
- Enalapril → Enalaprilat
- Bacampicillin → Ampicillin
- Cortisone → Hydrocortisone
- Azathioprine → Mercaptopurine
- Cyclophosphamide → Aldophosphamide
- Zidovudine → Zidovudine triphosphate

*(contd.)*

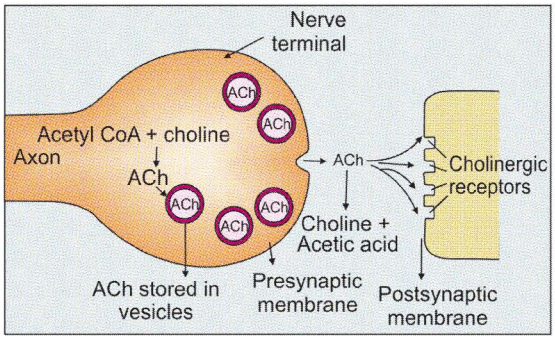



**Fig. 2.3:** Cholinergic transmission—schematic representation

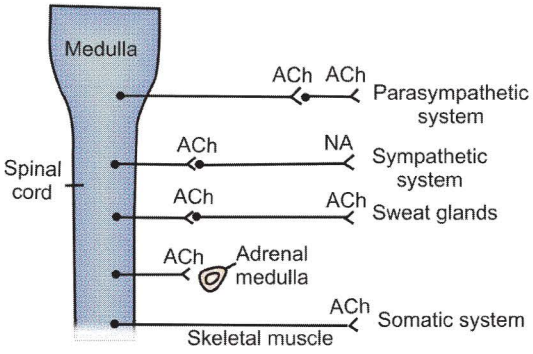



**Fig. 2.4:** Sites of release of neurotransmitters—acetylcholine and noradrenaline in the peripheral nervous system

*Notes*

## DRUGS USED IN ISCHAEMIC HEART DISEASES

### OVERVIEW

Ischaemic heart diseases may manifest as angina pectoris, unstable angina or myocardial infarction.

### CLASSIFICATION

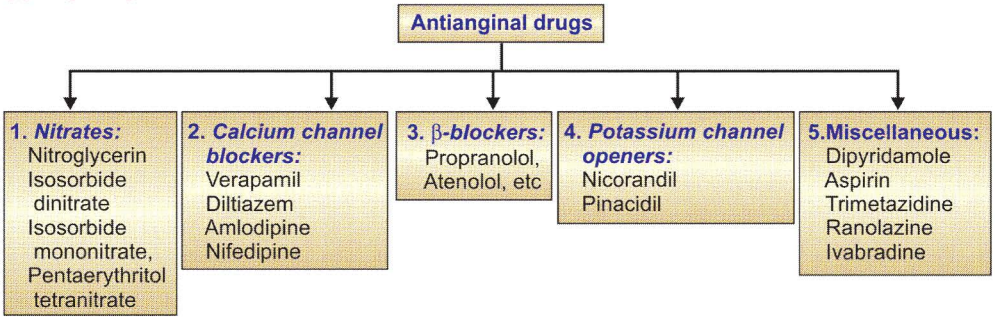



**Table 4.9:** *Salient features of drugs used in angina pectoris*

| *Drug and primary action* | *Mechanism of action* | *ADR* | *Current status in angina* |
|---|---|---|---|
| ***Nitrates***<br>Venular, arteriolar dilators—reduce preload, after load and coronary work load | Organic nitrates are denitrated to NO<br>↓<br>↑cGMP<br>↓<br>Smooth muscle relaxation<br>↓<br>Vasodilatation | Headache, flushing, sweating, palpitation, weakness, postural hypotension and rashes. Tolerance develops on long-term use | Sublingual nitroglycerin<br>• relieves pain in acute exertional angina and vasospastic angina<br>• acute prophylaxis<br>ISMN-for prophylaxis |
| ***Calcium channel blockers***<br>Arteriolar dilators | Bind L-type calcium channels<br>↓<br>Relax arterioles<br>↓<br>↓afterload and ↓PVR | Bradycardia, flushing, headache, dizziness, palpitation | • Prophylaxis of exertional angina<br>• Preferred over nitrates in vasospastic angina |
| ***Beta-blockers*** | Block cardiac beta-1 receptors<br>↓<br>Prevent increase in FOC, HR and BP<br>↓<br>↓Myocardial oxygen demand | Fatigue, dizziness, rebound hypertension. Contraindicated in asthma, heart block, heart failure. | • Long-term prophylaxis of classical angina<br>• Not useful in variant angina |
| ***Potassium channel openers***<br>Arterial and venous dilators | Opens ATP sensitive $K^+$ channels<br>↓<br>$K^+$ efflux<br>↓<br>Hyperpolarization<br>↓<br>Vascular smooth muscle relaxation | Flushing, headache, dizziness, palpitation | Used in angina when other drugs do not afford significant benefit |

(*contd.*)

# Contents