CHAPTER 1

General Pharmacology

OVERVIEW

Pharmacology is the study of drugs. In general pharmacology section, important definitions, salient features of routes of drug administration, pharmacokinetics and pharmacodynamics are highlighted.

DEFINITIONS

Pharmacology: The science that deals with the study of drugs and their interaction with the living systems.

Drug (*Drogue*—a dry herb in French) is a substance used in the diagnosis, prevention or treatment of a disease. WHO definition: "A drug is any substance or product that is used or intended to be used to modify or explore physiological systems or pathological states for the benefit of the recipient."

Pharmacokinetics is the study of absorption, distribution, metabolism and excretion of drugs, i.e. what the body does to the drug (in Greek, *Kinesis* = movement).

Pharmacodynamics is the study of **effects of drugs** on the body and their **mechanisms of action**, i.e. what the drug does to the body.

Pharmacoeconomics deals with the cost, i.e. economic aspects of drugs used therapeutically.

Pharmacogenetics is the science that deals with the study of genetic basis for variation in drug responses.

Pharmacoepidemiology is the study of both useful and adverse effects of drugs on **large numbers** of people.

Toxicology deals with the **adverse effects** of drugs and also the study of **poisons**, i.e. detection, prevention and treatment of poisonings.

Adverse drug reaction—"is any response to a drug that is noxious and unintended and that occurs at doses used in man for prophylaxis, diagnosis or therapy of disease or for the modification of physiological function."

Pharmacovigilance is related to the detection, assessment, understanding and prevention of adverse effects of drugs.

Materiovigilance is monitoring the use of medical devices. It is a coordinated system for identifying, collecting, reporting and analysing adverse events or incidents associated with the use of medical devices.

Haemovigilance is monitoring adverse reaction asssociated with transfusion of blood and blood products. It is reported through the software 'haemovigil'.

Teratogenicity is the ability of a drug to cause **fetal abnormalities** when administered to a pregnant woman.

Chemotherapy is the use of drugs and chemicals for the treatment of infections. It also includes the use of chemical compounds to treat malignancies.

Pharmacopoeia (in Greek, *Pharmacon* = drug; *poeia* = to make) is the official publication containing a list of drugs and medicinal preparations approved for use, their formulae and other information needed to prepare a drug. Pharmacopoeia also has information on the sources of drugs, their physical properties, doses and tests for identity, purity and potency.

Chronopharmacology involves the correlation of drug effects to *circadian rhythm* to obtain optimum therapeutic effects and minimise the adverse effects. For example, bronchospasm usually occurs at night.

- Blood pressure rises at dawn and dusk and is the lowest at midnight.
- Acute myocardial infarction is more common in the morning hours.

Chronotherapy is the administration of drugs to match the circadian rhythm.

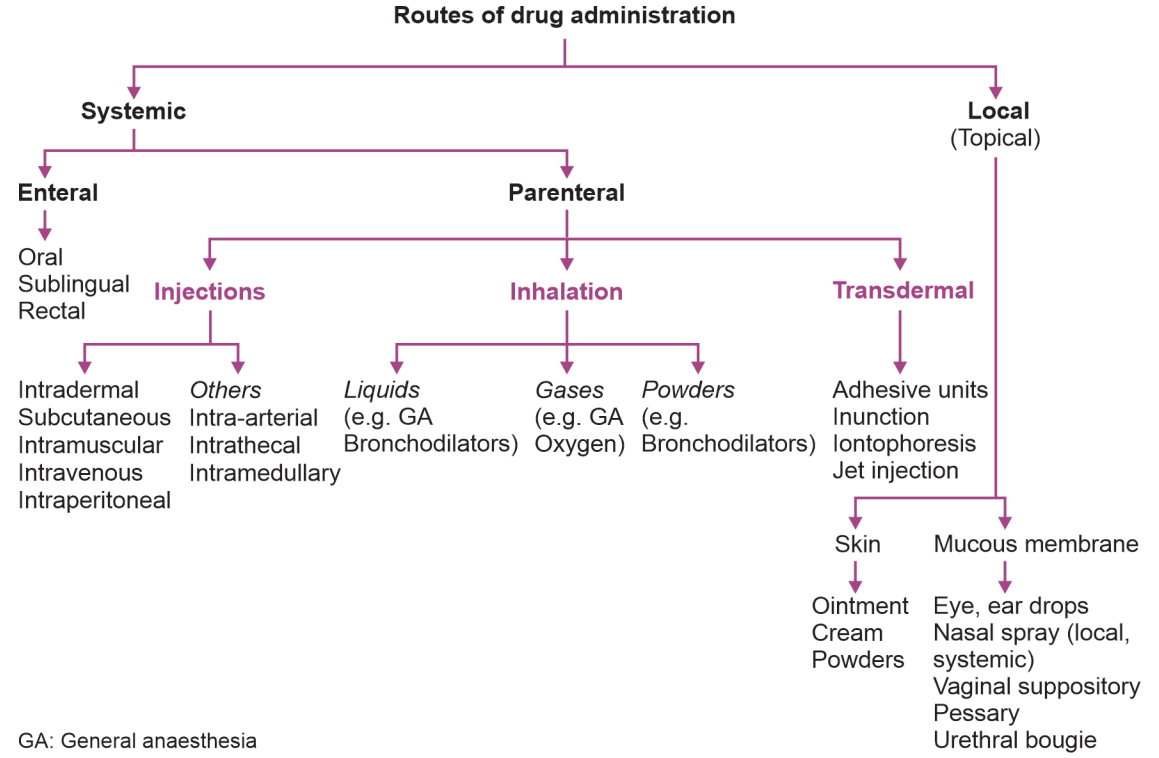
Chronobiotics are drugs that can be used to modify or reset the circadian rhythm and may be useful in sleep disorders and jet lag.

Absorption is the passage of the drug from the site of administration into the circulation.

Bioavailability is the fraction of the drug that reaches the systemic circulation following administration by any route.

Bioequivalence: Comparison of bioavailability of different formulations of the same drug is the study of bioequivalence **(Fig. 1.1)**.

ROUTES OF DRUG ADMINISTRATION



GA: General anaesthesia

Table 1.1: Salient features of important routes of drug administration

Route	Advantages	Disadvantages	Other important features
Enteral route	• Safest route – Most convenient – Most economical – Drugs can be self-administered • Non-invasive route	• Onset of action is slower • Irritant and unpalatable drugs cannot be administered. • Some drugs may not be absorbed, e.g. streptomycin. • Irritation to the GIT may lead to vomiting. • Absorption may be irregular. • Drugs may be destroyed by gastric juices, e.g. insulin. • Cannot be given to unconscious and uncooperative patients. • May undergo extensive first pass metabolism.	Sometimes drugs are coated with substances, like synthetic resins, gums, sugar, colouring and flavouring agents making them more acceptable.
Enteric coated tablets	• Frequency of administration may be reduced. • Therapeutic concentration may be maintained for longer periods.	• Failure may result in the release of the entire amount of drug in a short time, leading to toxicity. • More expensive	
Sublingual	• Absorption is rapid. • First pass metabolism is avoided. • After the desired effect is obtained, the drug can be spat out to avoid the unwanted effects.	Buccal ulceration can occur. Drugs which cannot be given by this route are: – Lipid-insoluble drugs – Drugs of higher molecular weight – Irritants – Unpalatable drugs	E.g. nitroglycerin
Rectal	• Gastric irritation avoided. • Can be administered by unskilled persons. • Useful in geriatric patients, patients with vomiting, those unable to swallow and after gastrointestinal surgery. • Useful in unconscious and uncooperative patients.	• Irritation of the rectum can occur. • Absorption may be irregular and unpredictable.	• Drug absorbed from the upper part of gut—carried by superior haemorrhoidal vein to portal circulation. • From lower part of gut—middle and inferior haemorrhoidal veins to systemic circulation.
Parenteral route	• Action is more rapid and predictable. • Can be employed in an unconscious or uncooperative patient. • Gastric irritants can be given parenterally. • Can be used in patients with vomiting or those unable to swallow. • Digestion by the gastric and intestinal juices and the first pass metabolism are avoided.	• Asepsis must be maintained. • Injections may be painful • More expensive • Less safe and inconvenient • Injury to nerves and other tissues possible	Drugs are directly delivered into tissues

Table 1.1: Salient features of important routes of drug administration (*Contd...*)

Route	Advantages	Disadvantages	Other important features
Subcutaneous route	• Absorption slow and uniform • Reliable • Duration of action prolonged • Can be trained for self-injection	• Irritant drugs cannot be injected because they can cause severe pain. • In shock, absorption is not dependable because of vasoconstriction. • Repeated injections at the same site can cause lipo-atrophy resulting in erratic absorption.	E.g. insulin, heparin
Intra-muscular	• Reliable route • Absorption is rapid. • Soluble substances, mild irritants, depot preparations, suspensions and colloids can be injected	• IM injection may be painful or may result in an abscess. • Nerve injury should be avoided; irritant solutions can damage the nerve, if injected near a nerve. • Local infection and tissue necrosis are possible	• Aqueous drug solution injected into a large muscle, like deltoid, gluteus • Absorption by simple diffusion • Maximum 10 ml • Oily solution absorbed slowly • Infants → use rectus femoris as gluteus not developed
Intravenous	• Most useful route in emergencies • Provides predictable blood concentrations – 100% bioavailability • Large volumes of solutions can be given. • Irritants can be given. • Rapid dose adjustments are possible.	• Once injected, the drug cannot be withdrawn. • Thrombophlebitis possible • Extravasation may cause irritation and sloughing. • Only aqueous solutions can be given IV; but not suspensions, oily solutions and depot preparations. • Self-medication is difficult.	• May be given as bolus, slow injection or infusion. • Generally 1 litre in 3–4 hrs.
Inhalation	• Almost instantaneous drug absorption • In pulmonary diseases, it serves as a local route. • Smaller dose needed. • First pass metabolism avoided. • Blood levels of volatile anaesthetics can be conveniently controlled.	• Irritant gases may enhance pulmonary secretions, should be avoided. • Drug particles may induce cough, e.g. cromolyn sodium.	Volatile liquids and gases can be inhaled

Table 1.2: Salient features of pharmacokinetic processes

Definition	Salient features
Absorption *Definition*: Absorption is the passage of the drug from the site of administration into the circulation. • Involves processes like diffusion, filtration and specialised transport. • Lipid-soluble, unionised drugs are well-absorbed. • Acidic drugs absorbed from the stomach and basic drugs absorbed from the intestines.	*Factors influencing absorption*: • Disintegration and dissolution time • Particle size • Lipid solubility • pH and ionisation • Presence of food • Area and vascularity of absorbing surface • Formulation • Gastrointestinal motility • Diseases • Metabolism
Distribution • After a drug reaches systemic circulation, it gets distributed to other tissues. • Involves processes, like filtration, diffusion and specialised transport. • Unionised lipid-soluble drugs widely distributed.	*Factors influencing distribution*: • Lipid solubility, ionisation • Blood flow • Binding to plasma proteins and cellular proteins (**Table 1.3**, **Fig. 1.2**)
Redistribution: Highly lipid-soluble drugs given IV/ inhalation (e.g. Thiopentone sodium) are rapidly distributed into highly perfused tissues, like brain and heart, but soon get redistributed into less vascular tissues, like muscle and fat → termination of drug action.	Some drugs bind to specific tissues due to special affinity—serve as drug reservoir, delay elimination and prolong action.
Metabolism/biotransformation (**Fig. 1.6** and **Table 1.4**) Biotransformation is the process of biochemical alteration of the drug in the body. • It converts the drugs into more polar, water-soluble compounds for easy excretion through kidneys. • Some drugs like furosemide, excreted unchanged. Drugs largely metabolised in liver and to a small extent by the kidney, lungs, gut, mucosa, blood and skin. • Some metabolites may also be active and action gets prolonged. • Active metabolite may be toxic.	*Factors influencing metabolism*: • Genetic variation, e.g. atypical pseudocholinesterase. • Environmental pollutants: Like cigarette smoke, cause enzyme induction. • Age: Extremes of age enzyme activity is low. • Diseases of the liver: Reduced metabolism: • Biotransformation reactions include phase I and phase II reactions **(Table 1.4)**
Excretion Drugs are converted to water-soluble metabolites and some are directly excreted. Excretion through kidneys, intestines, biliary system, lungs, sweat, saliva and milk. Ionised drugs of low mol wt (<10,000) easily filtered by glomerular membrane. Large water-soluble conjugates excreted in bile.	Cells of proximal tubules actively secrete acids and bases. Acids—penicillin, salicylic acid, probenecid Base—amphetamine Drugs may compete for same transport system. Some drugs reabsorbed from the gut and carried back to liver called **'enterohepatic circulation',** e.g. Tetracyclines.

Table 1.3: Some important concepts in pharmacokinetics

Definition	Examples	Salient features
Prodrug: Inactive form of a drug which gets metabolised to the active derivative in the body.	Levodopa, enalapril	• ↑ drug availability at the site, e.g. Levodopa • Prolong duration of action, e.g. bacampicillin • Improve tolerability, e.g. cyclophosphamide • Drug targeting, e.g. selective toxicity to infected cells, e.g. zidovudine • Improve stability, e.g. aspirin more stable at gastric pH
First pass metabolism: Metabolism of a drug during its passage from the site of absorption to systemic circulation.	Nitroglycerine, propranolol, salbutamol, insulin	• Partial → give higher dose • Complete → change route of administration
Bioavailability (Fig. 1.1): Fraction of the drug that reaches the systemic circulation following administration by any route.	Chlortetracycline → 30%, Carbamazepine → 70%, Diazepam → 100%	• Transdermal → 80–100% bioavailability • IM/SC inj → >75% • Large bioavailability variations → toxicity or therapeutic failure, e.g. halofantrine • Comparison of bioavailability of different formulations of a drug is study of **bio-equivalence**.
Plasma protein binding: On reaching circulation, most drugs bind plasma proteins. Acidic drugs bind albumin; basic drugs bind alpha acid glycoprotein.	Warfarin → 99%, Morphine → 35%, Ethosuximide and Lithium → 0%	• Only free fraction available for action • Serves as a reservoir and prolongs action. • Competition for binding sites → displacement interactions, e.g. warfarin and indomethacin. • Highly protein-bound drugs use carefully in chronic liver/kidney disease.
Volume of distribution: Volume necessary to accommodate entire amount of drug administered, if the drug is homogeneously distributed.	***Small V_d***— aspirin, aminoglycosides; ***Large V_d***— pethidine, chloroquine	• Drug retained mostly in plasma → small V_d • Drugs widely distributed → large V_d • Knowledge of V_d useful for treatment of poisoning; small V_d drugs easily removed by haemodialysis. • Tissue permeability, protein binding influence V_d
Enzyme induction: Synthesis of microsomal enzymes ↑ed by drugs—called enzyme inducers; Cytochrome P450 enzymes are induced	Phenobarbitone, rifampicin, alcohol, cigarette smoke, DDT, griseofulvin	Enzyme induction may result in: • **Therapeutic failure**, e.g. failure of oral contraceptives in patients taking rifampicin. • **Toxicity:** High amounts of toxic intermediate metabolites, e.g. paracetamol • **Tolerance** to drugs → autoinduction, e.g. carbamazepine • **Result in disease** → antiepileptics ↑ vit D breakdown → osteomalacia • **Variable response** → in chronic smokers, alcoholics • **Therapeutic application** → phenobarbitone in neonatal jaundice
Enzyme inhibition: Inhibition of CYP 450 and other enzymes by drugs	Chloramphenicol, erythromycin, ciprofloxacin	• Irreversible binding of enzymes → suicide inhibitors, e.g. selegiline, ticlopidine • Non-microsomal enzyme inhibitors → e.g. allopurinol inhibits XO, NSAIDs inhibit COX, theophylline inhibits PDE

(*Contd…*)

Table 1.3: Some important concepts in pharmacokinetics (*Contd...*)

Definition	Examples	Salient features
First order kinetics (Fig. 1.2): A constant **fraction** of the drug is metabolised/eliminated per unit time.	Most drugs	• First order kinetics applies also for absorption. • Relatively safe
Zero order kinetics: A constant **amount** of drug present in the body is metabolised/eliminated per unit time.	Alcohol, aspirin, phenytoin, heparin	• Enzyme gets saturated and high toxicity in over dose • Mixed order kinetics: Initially first order, higher dose → zero order, e.g. phenytoin, warfarin
Plasma half-life (Fig. 1.3): Time taken for plasma concentration of a drug to be reduced to half of its value. **Biological t½**—time required for total amount of drug in the body to be reduced to half. **Biological effect t½**—time required for biological effect of drug to be halved.	Esmolol → 10 min, Aspirin → 4 hours, Suramin → 90 days, Mefloquine → 16–24 days	• Indicates duration of action, frequency of administration, time needed for steady state and helps to calculate loading and maintenance dose. • Plasma protein binding, enterohepatic circulation, metabolism and tissue storage influence t½
Therapeutic drug monitoring: Treatment monitored by measuring plasma drug concentrations.	Theophylline, lithium, digoxin, aminoglycosides	**Needed for:** • Drugs with low safety margin to avoid therapeutic failure, e.g. digoxin, lithium. • To reduce risk of toxicity, e.g. aminoglycosides. • When there are no reliable methods to assess benefit, e.g. antidepressants. • To treat poisoning. • Unexplainable therapeutic failure to check patient compliance. **Not required for:** • Drugs whose response can be easily measured chemically, e.g. blood pressure for antihypertensives. • 'Hit and run' drugs, whose effect persist for a long time even after the drug is eliminated, e.g. proton pump inhibitors like pantoprazole. • Drugs to which significant tolerance develops. • When estimation of plasma levels is too expensive, TDM should be restricted.

Steady-state Concentration (SSC)

If a drug is administered repeatedly at short intervals before complete elimination, the drug accumulates in the body and reaches a 'state' at which the rate of elimination equals the rate of administration called 'steady-state' or plateau level **(Fig. 1.4)**. Steady-state plasma concentration (C_{pss}) formula:

$$C_{pss} = \frac{\text{Dose rate}}{\text{Clearance}}$$

After attaining this, the plasma concentration fluctuates around an average steady level. It takes 4–5 half-lives for the plasma concentration to reach the plateau level. A drug with t½ >24 hr, if given daily, accumulates on prolonged use and could lead to toxicity. Hence for such drugs, once the SSC is attained, the dose given should be equal to the dose eliminated everyday.

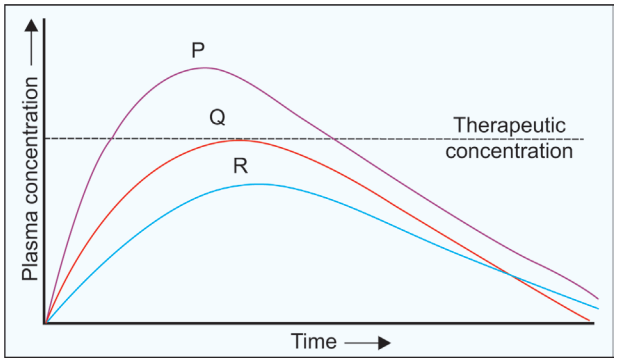


Fig. 1.1: Study of bioavailability and bioequivalence—three different oral formulations—P, Q and R of the same drug yield different bioavailability values. The area under each curve gives the bioavailability of the respective formulation

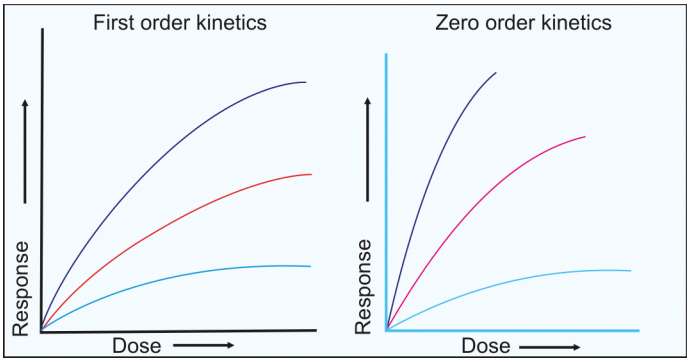


Fig. 1.2: First order kinetics: As the plasma concentration rises, metabolism and excretion proportionately increase; Zero order kinetics: In higher doses, the drug accumulates and the plasma concentration rises resulting in toxicity

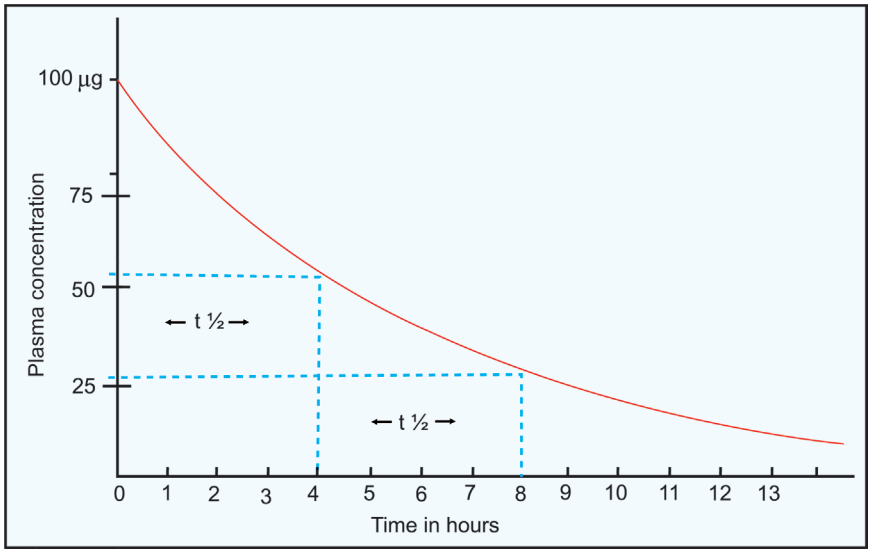


Fig. 1.3: Plasma concentration–time curve following intravenous administration of a drug. Plasma t½ of the drug = 4 hours

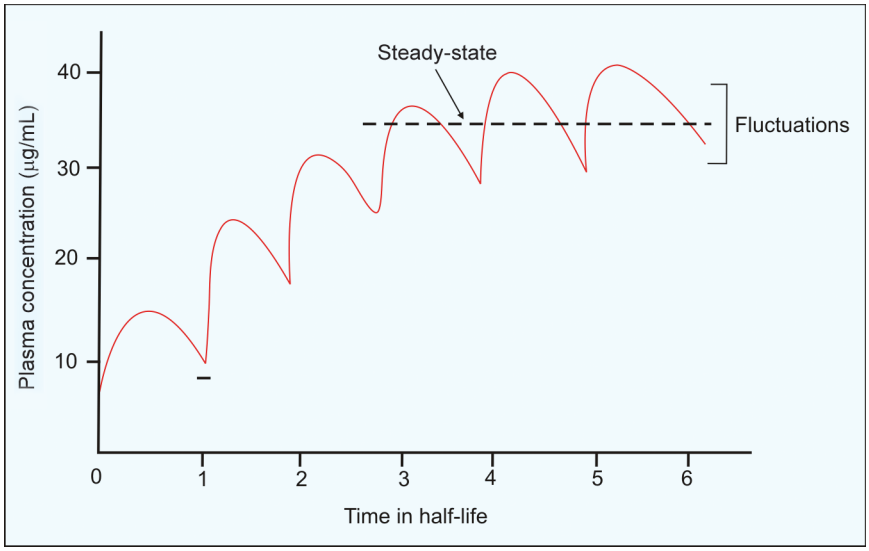


Fig. 1.4: Drug accumulation and attainment of steady-state concentration. On oral administration, it takes 4–5 half lives to attain steady-state concentration

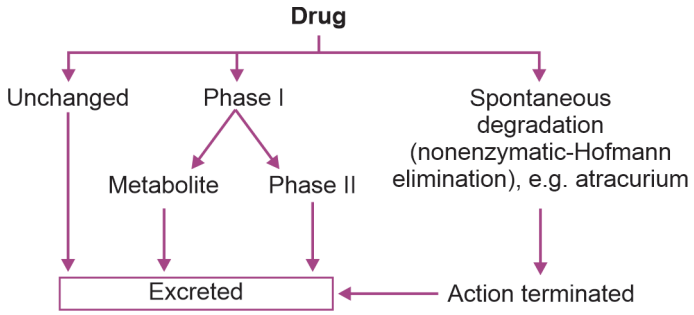


Fig. 1.5: Phases in metabolism of drugs. A drug may be excreted as phase I metabolite or as phase II metabolite. Some drugs may be excreted as such

Table 1.4: Important drug biotransformation reactions

Reactions	Example of drugs
	Phase I reactions
Oxidation	Phenytoin, diazepam, ibuprofen, amphetamine, chlorpromazine, dapsone
Reduction	Chloramphenicol, halothane
Hydrolysis	Pethidine, procaine, enalapril
	Phase II reactions
Conjugation reactions	
Glucuronide conjugation	Chloramphenicol, morphine, diazepam, aspirin
Acetylation	Sulphonamides, isoniazid
Methylation	Adrenaline, noradrenaline, dopamine, histamine
Glutathione conjugation	Paracetamol
Sulfate conjugation	Paracetamol, steroids
Amino acid conjugation	Salicylic acid, benzoic acid

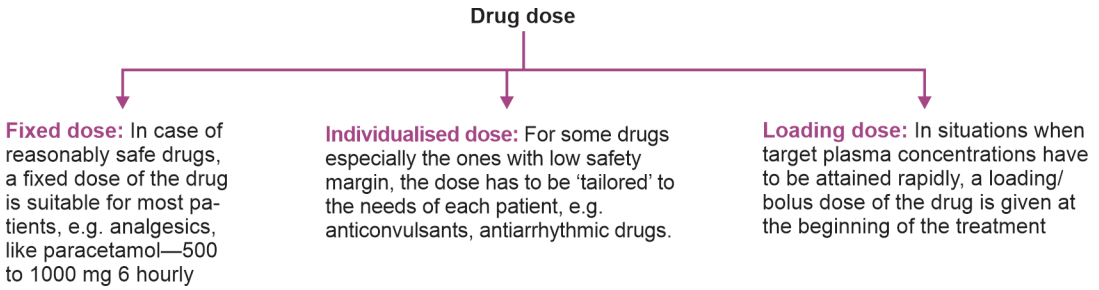


Table 1.5: Methods of prolonging duration of action of drugs

Processes	Methods	Examples
	Pharmaceutical modification	
1. Oral	Sustained release preparations, controlled release preparation, coating with resins, etc.	Iron, deriphylline, diclofenac
2. Parenteral	1. Reducing solubility—oily suspension	Procaine + penicillin, benzathine penicillin
	2. Altering particle size	Depot progestins
		Insulin zinc suspension as large crystals that are slowly absorbed
	3. Pellet implantation—sialistic capsules	DocA
		Testosterone
	4. Combining with protein	Protamine + zinc + insulin
	5. Chemical alteration—esterification	Estrogen, testosterone
3. Topical	Transdermal adhesive patches, ointments	Scopolamine, nitroglycerin
	Ocuserts (transmucosal)—used in eye	Pilocarpine
	Pharmacokinetic intervention	
1. Absorption	Reducing vascularity of absorbing surface	Adrenaline + lignocaine (vasoconstrictor)
2. Distribution	Choosing more protein bound member of the group	Sulfonamides like sulfamethoxypyridazine
3. Metabolism	• Inhibiting the metabolising enzyme cholinesterase	Physostigmine—prolongs action of acetylcholine
	• Inhibiting the enzyme peptidase in renal tubular cells	Cilastatin—prolongs action of imipenem
4. Excretion	Competition for same transport system—for renal tubular secretion	Probenecid—prolongs the action of penicillin and ampicillin

Notes

Receptor

Definition: Receptor is a macromolecular site on the cell to which an agonist binds and brings about a response, e.g. adrenergic receptor, opioid receptor

Agonist: Binds to the receptor and produces a response→ has both affinity and intrinsic activity, e.g. adrenaline (α, β receptor; morphine mu (μ) receptor).

Partial agonist: Binds to the receptor but has low intrinsic activity, e.g. pentazocin at μ receptor, pindolol at β receptor

Antagonist: Binds to the receptor and prevents the action of the agonist on the receptor; has affinity but no intrinsic activity, e.g. tubocurarine is antagonist at nicotinic receptors.

Inverse agonist: Binds to the receptor and produces effect opposite to that of pure agonist, e.g. β carbolenes on $GABA_A$ receptor.

Receptor types

1. **Ion channel receptor** (ionotropic receptor) e.g. nicotinic receptor
2. **G-protein coupled receptors** (metabotropic receptor), e.g. adrenergic and muscarinic receptors

Effector pathways
– Adenylyl cyclase pathway
– Phospholipase C/IP3 – DAG
– Ion channel regulation

3. **Enzymatic receptors** (kinase linked receptor), e.g. Insulin receptor→JAK-STAT kinase binding
4. **Non-enzymatic receptor,** e.g. growth hormone, interferons
5. **Nuclear receptors** (transcription factors or receptors that regulate gene transcription), e.g. steroid, thyroid, vitamin D receptor

Factors Modifying Drug Actions

- **Body weight:** For obese and underweight—calculate the dose.
- **Age**—newborn, infants and elderly more prone to ADRs.
- **Sex, species and race**—blacks tolerant to atropine.
- **Diet and environment**—pollutants like DDT cause enzyme induction.
- **Route and time of drug administration:** Magnesium sulphate—different actions by different routes.
- **Genetic factors:** Production of drug-metabolising enzymes is genetically controlled and could vary.
- **Dose**, e.g. tetracyclines chelate calcium in food and interfere with absorption.
- **Diseases**, e.g. cardiac, renal, liver and endocrine dysfunction.
- **Repeated dosing**—cumulation, tolerance.
- **Psychological factor**—doctor's personality can influence; placebo.
- **Presence of other drugs**—drug interactions.

Drug interactions: Alteration in the duration or magnitude of the pharmacological effects of one drug by another drug. It could result from pharmacokinetic and pharmacodynamic mechanisms.

Orphan drugs: Drugs used for the prevention and treatment of rare or orphan diseases, e.g. acetylcysteine for paracetamol poisoning.

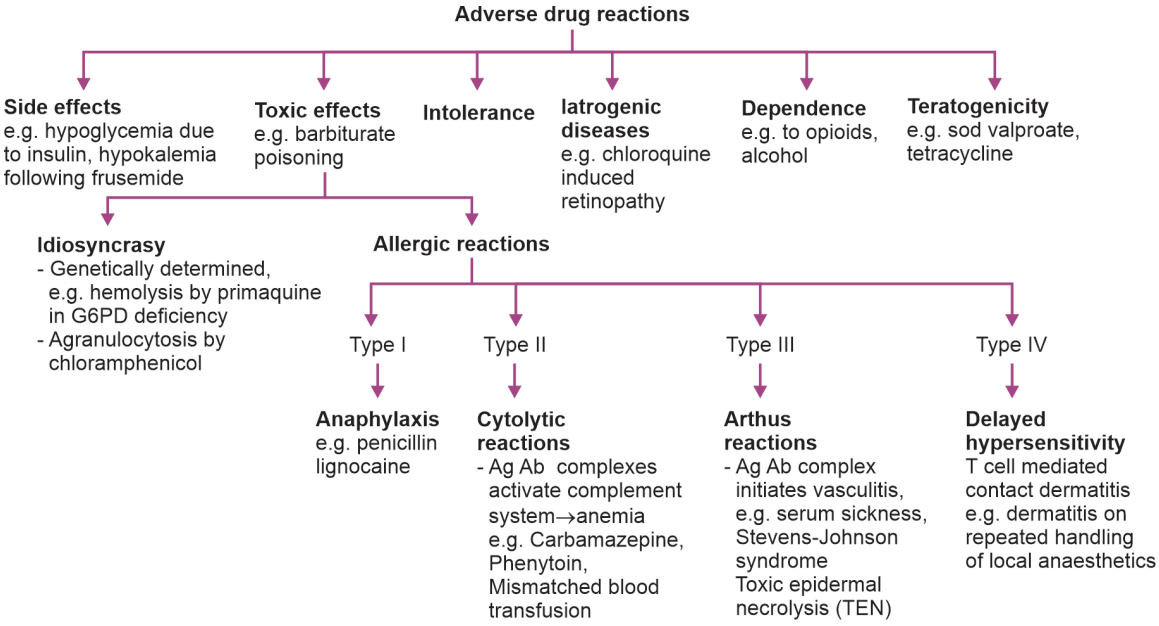
Orphan diseases are diseases that affect only small number of patients (as per WHO <6.5–10 per 10,000 persons). For example, Gaucher's disease, Kyasanur Forest disease, acromegaly.

Table 1.6: Some important concepts in pharmacodynamics

	Definition	Examples	Other salient features
Receptor	A site on the cell with which an agonist binds to bring about a change.	Muscarinic receptor, opioid receptor, adrenergic receptor	**Functions:** • Recognises the ligand • Propagates the message. **Families:** GPCRs, ion channels, enzymatic receptors, nuclear receptors.
Therapeutic index (TI)	TI indicates the safety margin of the drug. It is the ratio of LD50 to ED50.	TI of penicillin and diazepam: High Lithium: Low	• TI varies from species to species • May vary for each action • Higher the TI, safer is the drug
Additive effect	Effect of two or more drugs get added up and the total effect is equal to the sum of their individual effects.	Ephedrine + theophylline, Nitrous oxide + ether	
Synergism	Action of one drug is enhanced or facilitated by another drug and the combination is synergistic.	Acetylcholine + physostigmine Levodopa + carbidopa	Synergistic combinations are generally preferred
Antagonism	One drug opposing or inhibiting the action of another.	**Chemical antagonism** Chelating agents+ antacids **Physiological antagonism** Adrenaline + histamine Insulin + glucagon **Pharmacological antagonism** ***Reversible antagonism:*** Acetylcholine plus atropine ***Irreversible antagonism:*** Adrenaline plus phenoxybenzamine. **Non-competitive antagonism** Verapamil blocks cardiac calcium channels	
Tolerance	Requirement of higher doses of a drug to produce a given response.	Morphine, barbiturates, opioids **Natural tolerance**—some species less sensitive to the drug. **Acquired tolerance** develops on repeated administration.	Mechanisms: Pharmacokinetic—changes in ADME of drug Pharmacodynamic—target tissue less responsive to the drugs, like downregulation of receptors.
Tachyphylaxis (acute tolerance)	Some drugs given repeatedly at short intervals → tolerance develops rapidly.	Ephedrine, amphetamine, tyramine, 5HT	Displacing NA from sympathetic nerve endings → depletion of NA stores
Placebo (dummy medication)	Inert dosage form with no specific biological activity, but resembles the actual preparation in appearance.	Distilled water inj, vitamins, minerals, lactose	Used in clinical trials as a comparator To please a patient psychologically Placebo reactors: People more likely to respond to placebo.

Table 1.7: Phases of clinical trials

Phases	Number of subjects	Objectives	Conducted by
Phase I	20–50 normal volunteers	To establish safety, to know biological effects, pharmacokinetic profile and to design a safe dose	Clinical pharmacologist
Phase II	100–300 patients	To establish efficacy, detect adverse effects and pharmacokinetics	Clinical pharmacologists and clinical investigators
Phase III	250 to >1000 selected patients	To establish efficacy, safety, to identify latent side effects, tolerance; design ideal dose range and to compare with existing drugs	Clinical investigators
Phase IV (post-marketing surveillance)	2,000 to >10,000 patients	Long-term safety and efficacy; to identify other possible therapeutic uses	Medical practitioners



Compilation of some useful examples

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

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

Drugs that undergo extensive first pass metabolism

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

Drugs that are highly bound to plasma proteins

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

Absorption increased by fatty food

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

Apparent volume of distribution (V_d)

Low V_d drugs	*High V_d drugs*
• Heparin	• Pethidine
• Warfarin	• Digoxin
• Aminoglycosides	• Chloroquine
• Aspirin	• Nortriptyline
• Furosemide	• Fluoxetine
• Ampicillin	• Haloperidol
• Amoxicillin	• Amiodarone

Some microsomal enzyme inducers

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

Some microsomal enzyme inhibitors

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

Some folate antagonists

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

Prodrugs

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

Hit and run drugs

- Reserpine
- Omeprazole

Drugs metabolised by zero-order kinetics

- Alcohol
- Phenytoin
- Salicylates
- Heparin
- Phenylbutazone

Drugs that undergo enterohepatic recycling

- Tetracyclines
- Amphetamine
- Doxorubicin
- Metronidazole
- Mefloquine
- Morphine
- Indomethacin
- Phenytoin
- Estradiol

Drugs available as transdermal patches

- Nitroglycerin
- Hyoscine
- Fentanyl
- Estrogen
- Testosterone

Drugs to which tolerance develops easily	
• Nitrates	• Hydralazine
• Barbiturates	• Opioids
Agents which exhibit tachyphylaxis	
• Ephedrine	• Amphetamine
• 5-HT	• Tyramine
Drugs which need tapering (after long-term use)	
• β blockers	• Glucocorticoids
• Antiepileptics	• Clonidine
• Sedatives	• Antidepressants
• Antipsychotics	
Drugs with very short t½ (2–10 min)	
• Dobutamine	• Sodium nitroprusside
• Dopamine	• Alteplase
• Esmolol	• 5-Fluorouracil
• Adenosine	
Drugs with long t½	
Drug	*t½ in days*
• Chloroquine	10–24
• Etanercept	3–4
• Phenylbutazone	3–4
• Mefloquine	16–24
• Gold salts	7
• Suramin	90
Some haemodialysable drugs	
• Isoniazid	• Ethanol and methanol
• Barbiturates	• Amphetamines
• Methaqualone	• Lithium
• Phenytoin	• Salicylates
• Theophylline	
Histamine liberators	
• Morphine	• Tubocurarine
• Pentamidine	• Vancomycin
• Hydralazine	• Amphetamine
Drugs that colour urine	
• Rifampicin (orange red)	• Vitamin B complex (yellow)
• Phenazopyridine (orange red)	• Nitazoxanide (green)
• Daunorubicin (red)	

Nitric oxide donors	
• Sodium nitroprusside	• Nitrites
• Nitrates	
Drugs with low therapeutic index	
• Digoxin	• Lithium
• Theophylline	• Quinidine
Drugs which need plasma concentration monitoring or therapeutic drug monitoring	
• Lithium	• Carbamazepine
• Digoxin	• Theophylline
• Aminoglycosides	
Some teratogenic drugs	
• Thalidomide	• Tetracyclines
• Sodium valproate	• Phenytoin
• Carbamazepine	• Phenobarbitone
• Lithium	• Glucocorticoids
• Androgens	• Oestrogens
• Progestins	• Antithyroid drugs
• Anticancer drugs	
Drugs to be used with caution in renal failure	
• Aminoglycosides	• Amphotericin
• Cyclosporine	• Acyclovir
• Foscarnet	• Pentamidine
• Ifosphamide	• NSAIDs
• ACE inhibitors	• Sulphonamides
• Anticancer drugs like Cisplatin, Methotrexate	• Penicillamine
Drugs that can produce gingival hyperplasia	
• Phenytoin	• Cyclosporine
• Calcium channel blockers	
Drugs that can induce haemolysis in G6PD deficient patients	
• Sulfonamides	• Primaquine
• Nitrofurans	• NSAIDs
• Vitamin K analogs	• Dapsone
• Some vegetables	
Drugs excreted in saliva	
• Clarithromycin	• Metronidazole
• Phenytoin	• Disulfiram
• Metoclopramide	