

1. Basic Drug Structure & Functional Groups

Functional Groups & Their Properties:

- **Carboxyl (-COOH)** → Acidic, increases water solubility.
- **Amine (-NH₂, -NR₂)** → Basic, influences drug ionization.
- **Hydroxyl (-OH)** → Increases polarity and hydrogen bonding.
- **Ketone (-C=O) & Aldehyde (-CHO)** → Common in metabolic oxidation.
- **Ester (-COO-) & Amide (-CONH₂)** → Prone to **hydrolysis** (metabolism).
- **Sulfonamide (-SO₂NH₂)** → Found in antibacterial drugs.

Chirality & Stereochemistry:

- Many drugs exist as **enantiomers**.
 - **Example:** S-enantiomer of **thalidomide** causes teratogenicity.
 - **Example:** R-warfarin is less potent than S-warfarin.
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2. Drug Mechanism of Action (MOA)

- **Antibiotics:**
 - **β-Lactams (Penicillins, Cephalosporins):** Inhibit bacterial **cell wall** synthesis.
 - **Fluoroquinolones (Ciprofloxacin):** Inhibit **DNA gyrase** (Topoisomerase II).
 - **Macrolides (Azithromycin, Erythromycin):** Bind **50S ribosomal subunit**, blocking protein synthesis.
 - **Sulfonamides (Trimethoprim-Sulfamethoxazole):** Block **folic acid** synthesis.
- **Antifungals:**
 - **Azoles (Fluconazole, Ketoconazole):** Inhibit **ergosterol** synthesis in fungal membranes.
 - **Amphotericin B:** Binds **ergosterol**, creating pores.

- **Antivirals:**
 - **Acyclovir:** Inhibits **viral DNA polymerase**.
 - **Oseltamivir (Tamiflu):** Inhibits **neuraminidase** (flu virus replication).
 - **Pain & Inflammation:**
 - **NSAIDs (Ibuprofen, Diclofenac, Aspirin):** Inhibit **COX enzymes**, reducing prostaglandins.
 - **Acetaminophen (Paracetamol):** Acts centrally, weak **COX inhibitor**.
 - **Opioids (Morphine, Codeine):** Bind **μ-opioid receptors**.
 - **Cardiovascular Drugs:**
 - **ACE Inhibitors (Ramipril, Enalapril):** Inhibit **angiotensin-converting enzyme**, reducing BP.
 - **ARBs (Losartan, Valsartan):** Block **angiotensin II** receptors.
 - **Beta-Blockers (Atenolol, Metoprolol):** Block **β₁ adrenergic receptors**, reducing HR.
 - **Calcium Channel Blockers (Amlodipine, Verapamil):** Block **Ca²⁺ channels**, causing vasodilation.
 - **Diabetes Medications:**
 - **Metformin:** Decreases **hepatic glucose production**.
 - **Sulfonylureas (Gliclazide, Glibenclamide):** Stimulate **pancreatic insulin secretion**.
 - **Psychiatric Drugs:**
 - **SSRIs (Fluoxetine, Sertraline):** Block **serotonin reuptake**.
 - **Benzodiazepines (Diazepam, Lorazepam):** Enhance **GABA-A receptor** function.
 - **Lithium:** Affects **Na⁺ channels**, used for **bipolar disorder**.
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3. Drug Metabolism (Phase I & II)

- **Phase I: Functionalization (Chemical Modification)**
 - Oxidation, Reduction, Hydrolysis (via **CYP450 enzymes**).
 - **Example:** Codeine → Morphine (**CYP2D6**).
 - **Example:** Diazepam → Active metabolites via oxidation.
 - **Phase II: Conjugation (Makes Drugs More Hydrophilic)**
 - **Glucuronidation (Major pathway):** Paracetamol, Morphine.
 - **Sulfation:** Steroids, Paracetamol.
 - **Acetylation:** Isoniazid (**fast vs. slow acetylators**).
 - **Methylation:** Epinephrine, Dopamine.
 - **CYP450 Inhibitors vs. Inducers**
 - **Inhibitors (Increase Drug Effects/Toxicity)** → Erythromycin, Ciprofloxacin, Ketoconazole, Grapefruit juice.
 - **Inducers (Decrease Drug Effects)** → Rifampicin, Carbamazepine, Phenytoin, Smoking.
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4. Pharmacokinetics & Drug Properties

- **Absorption:**
 - Lipophilic drugs **cross membranes better** (e.g., CNS penetration).
 - Weak acids absorb better in the **stomach** (e.g., Aspirin).
 - Weak bases absorb better in the **intestine** (e.g., Morphine).
- **Distribution:**
 - **Volume of Distribution (Vd):** High Vd → Drug is widely distributed in tissues (e.g., Amiodarone).

- **Elimination:**
 - **Renal Clearance:** Hydrophilic drugs excreted by kidneys.
 - **Hepatic Clearance:** Lipophilic drugs metabolized by liver (e.g., Verapamil).
 - **First-Pass Metabolism:**
 - Drugs like **Propranolol**, **Nitroglycerin**, **Morphine** undergo high **first-pass effect**, reducing bioavailability.
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5. Important Medicinal Chemistry Reactions

- **Fischer Esterification:** Converts **carboxylic acids** to **esters** (lipophilicity change).
 - **Hydrolysis:** Common in prodrugs (e.g., **Aspirin** → **Salicylic Acid**).
 - **Reduction:** Nitro groups → Amines (e.g., **Chloramphenicol** metabolism).
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6. Special Topics

- **Drug Interactions:**
 - **Warfarin + NSAIDs** → **Increased Bleeding Risk**.
 - **MAO Inhibitors + Tyramine Foods** → **Hypertensive Crisis**.
- **Prodrugs & Bioactivation:**
 - **Examples:**
 - ◆ **Codeine** → **Morphine** (via **CYP2D6**).
 - ◆ **Enalapril** → **Enalaprilat** (ACE inhibitor activation).
- **Toxicology Highlights:**
 - **Acetaminophen Overdose:** **N-Acetylcysteine (NAC)** is antidote.
 - **Methanol Poisoning:** **Ethanol** or **Fomepizole** used as treatment.