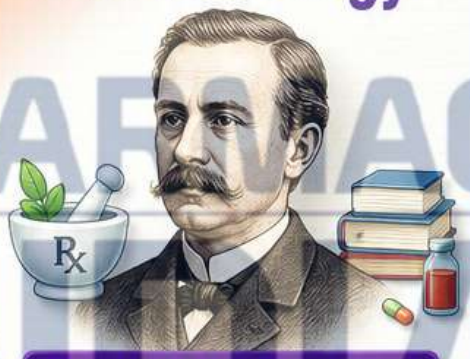
Pharmacology Classification + Specific Mechanism of Action (MOA) – 200 High-Yield One-Liners

Pharmacy Legend

Father of Pharmacology*



Oswald Schmiedeberg

(1838 – 1921)

Pioneer of Experimental Pharmacology

1. DEFINITION

- Oswald Schmiedeberg is known as the "Father of Pharmacology".
- He established pharmacology as an experimental science.

2. CLASSIFICATION

- Not a drug.
- Not a class.
- A pioneer/ personality in Pharmacology.

3. MECHANISM OF ACTION

- Established experimental methods to study drug effects scientifically.
- Introduced quantitative approach in pharmacology.

4. PHARMACOLOGICAL EFFECTS

- Laid foundation for understanding drug actions.
- Promoted concept of receptor theory.

5. THERAPEUTIC USES

- His work helps in rational use of drugs.
- Basis for development of safe and effective therapies.

6. ADVERSE EFFECTS

- No direct adverse effects (he is not a drug).
- His work reduced irrational drug use and toxicity.

7. CONTRAINDICATIONS

- Not applicable (Not a drug).
- Historical figure – no clinical use.

8. DRUG INTERACTIONS

- Not applicable (Not a drug).
- His principles help understand interactions.

9. IMPORTANT EXAMPLES

- He studied effects of:
  - ✓ Nicotine
  - ✓ Atropine
  - ✓ Curare
  - ✓ Pilocarpine

10. MNEMONICS

"SCHMIEDE" reminds his key contributions:

- **S** – Scientist
- **C** – Chemist
- **H** – Human experimenter
- **M** – Mechanism explorer
- **I** – Investigator
- **E** – Experimentalist
- **D** – Discoverer
- **E** – Eminent pioneer

11. EXAM POINTS

- Most important pioneer in Pharmacology
- Established experimental pharmacology
- Discovered / studied many drugs
- Promoted receptor theory

12. IMPORTANT QUESTIONS

Q1. Who is the Father of Pharmacology?
A. Oswald Schmiedeberg

Q2. What is his major contribution?
A. Established experimental pharmacology

Q3. Which theory did he support?
A. Receptor theory

QUICK FACT

He bridged chemistry and medicine and made pharmacology a scientific discipline.

Pharmacology Classification + Specific Mechanism of Action (MOA) – 200 High-Yield One-Liners

DEFINITION

Paul Ehrlich is known as the "Father of Chemotherapy" for his pioneering work on selective toxicity and chemotherapeutic agents, especially Salvarsan (Arsphenamine).

CLASSIFICATION (Contributions)

- By Contribution → Founder of Chemotherapy
- By Field → Immunology, Pharmacology, Microbiology
- By Era → Late 19th – Early 20th Century Pioneer

MECHANISM OF ACTION (Contribution Mechanism)

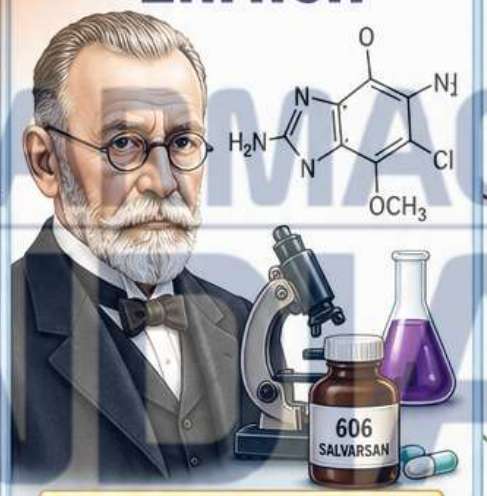
- Introduced the concept of "Magic Bullet" – selective toxicity.
- Developed Salvarsan (Arsphenamine) which selectively targets Treponema pallidum.
- Binds to sulfhydryl groups of bacterial enzymes → disrupts metabolism → kills bacteria.
- Paved the way for synthetic chemotherapeutic agents.

PHARMACOLOGICAL EFFECTS (Contributions)

- Established the principle of selective toxicity.
- Demonstrated that chemicals can selectively kill pathogens without harming host cells.
- Laid foundation for rational drug design.
- Introduced systematic testing of drugs.

FATHER OF CHEMOTHERAPY*

Paul Ehrlich



"He laid the foundation of modern Chemotherapy."

THERAPEUTIC USES (Impact)

- Treatment of syphilis with Salvarsan (first effective chemotherapeutic agent).
- Foundation for chemotherapy in infectious diseases.
- Inspired development of anticancer and antimicrobial drugs.

ADVERSE EFFECTS (Not Direct)

- Arsphenamine (Salvarsan) may cause nausea, vomiting, rash, fever.
- Can cause liver and kidney toxicity.
- Injection site reactions possible.

CONTRAINDICATIONS (Not Applicable)

- Hypersensitivity to arsenical compounds.
- Severe hepatic or renal impairment.
- Pregnancy (relative contraindication).

DRUG INTERACTIONS (Conceptual Impact)

- Arsphenamine interacts with heavy metals (e.g., Hg, Pb) forming complexes.
- Interaction with other arsenical compounds increases toxicity.
- Incompatible with strong oxidizing agents.

IMPORTANT EXAMPLES (Related Contributions)

- Salvarsan (Arsphenamine) – first synthetic antimicrobial.
- Neo-Salvarsan (Tryparsamide) – improved derivative.
- Introduced concept for future sulfa drugs, antibiotics, anticancer drugs.

MNEMONICS

"EHRLICH"

- **E** – Early pioneer
- **H** – He discovered Salvarsan
- **R** – Rational drug design
- **L** – Laid foundation
- **I** – Immunology expert
- **C** – Chemotherapy founder
- **H** – Haematology contributor

EXAM POINTS

- Paul Ehrlich → Father of Chemotherapy.
- Introduced "Magic Bullet" concept.
- Salvarsan (1909) → first successful chemotherapy.
- Nobel Prize in Physiology or Medicine (1908).
- Major contribution to immunology & haematology.

IMPORTANT QUESTIONS

1. Who is known as the Father of Chemotherapy?
   → Paul Ehrlich
2. Which was the first successful chemotherapeutic drug introduced by Paul Ehrlich?
   → Salvarsan (Arsphenamine)
3. What is the "Magic Bullet" concept?
   → Selective action of a drug on pathogens without harming host cells.
4. For which disease was Salvarsan first used?
   → Syphilis
5. In which year did Paul Ehrlich receive the Nobel Prize?
   → 1908

QUICK RECALL SUMMARY

Paul Ehrlich Pioneer of Chemotherapy → Magic Bullet Concept (Selective Toxicity) → Discovery of Salvarsan (1909) → Effective against Syphilis (Treponema pallidum) → Foundation for Modern Chemotherapy

REMEMBER! Paul Ehrlich's work transformed treatment of infectious diseases and inspired modern drug discovery.

Pharmacology Classification + Specific Mechanism of Action (MOA) – 200 High-Yield One-Liners

1. DEFINITION

- Bioavailability = fraction of unchanged drug reaching systemic circulation.
- IV route = 100% bioavailability.

2. CLASSIFICATION

- Absolute bioavailability
- Relative bioavailability
- IV is the reference standard.

3. MECHANISM OF ACTION

- Drug enters directly into bloodstream.
- No absorption barrier.
- No first-pass metabolism.

4. PHARMACOLOGICAL EFFECTS

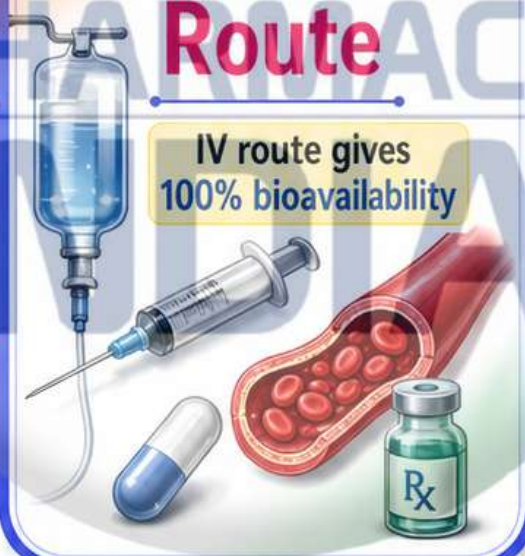
- Fastest onset of action.
- Predictable plasma level.
- Complete systemic availability.

5. THERAPEUTIC USES

- Emergencies
- Shock / critical care
- Fluids, antibiotics, anesthetics

Drug Bioavailability is Highest by → Intravenous Route

IV route gives 100% bioavailability



6. ADVERSE EFFECTS

- Infection risk
- Thrombophlebitis
- Extravasation
- Rapid toxicity if overdosed

7. CONTRAINDICATIONS

- Poor venous access
- Non-sterile conditions
- Unsuitable oily / insoluble preparations

8. DRUG INTERACTIONS

- Incompatibility in IV fluids
- Mixing drugs may cause precipitation.
- Monitor infusion combinations.

9. IMPORTANT EXAMPLES

- IV glucose
- IV ceftriaxone
- IV mannitol
- IV diazepam / anesthetic agents

10. MNEMONICS

"IV = Instant & Intact Availability"

11. EXAM POINTS

- Highest bioavailability → IV route
- Bioavailability of IV route = 1 or 100%
- Bypasses first-pass effect
- Used as standard for comparison

12. IMPORTANT QUESTIONS

Q. Which route has highest bioavailability?
Ans. Intravenous route

Q. Why is IV bioavailability 100%?
Ans. Direct entry into circulation

Q. Does IV route undergo first-pass metabolism?
Ans. No

QUICK FACT / EXAM BOOSTER

All other extravascular routes have bioavailability less than 100% due to incomplete absorption and/or first-pass metabolism.

Pharmacology Classification + Specific Mechanism of Action (MOA) – 200 High-Yield One-Liners

1 DEFINITION

- First-pass metabolism is the presystemic metabolism of a drug before it reaches systemic circulation.
- It occurs mainly after oral administration.
- The liver is the principal site; the intestinal wall also contributes.

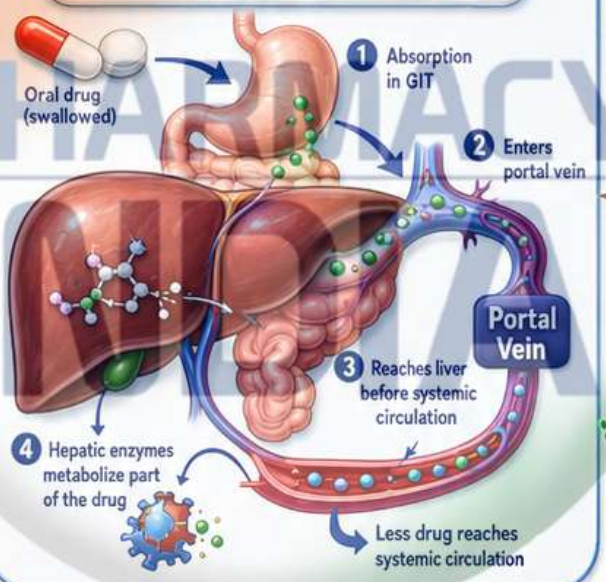
2 CLASSIFICATION

- Hepatic first-pass metabolism
- Intestinal first-pass metabolism
- Extensive first-pass effect
- Moderate / low first-pass effect

3 MECHANISM OF ACTION

- Oral drug is absorbed from GIT.
- Drug enters portal circulation.
- It reaches the liver before systemic circulation.
- Hepatic enzymes metabolize part of the drug.
- Bioavailability decreases.

FIRST-PASS METABOLISM OCCURS MAINLY IN* LIVER



PHARMACOLOGICAL EFFECTS

- Reduces amount of active drug reaching blood.
- Lowers oral bioavailability.
- May require higher oral dose.
- Can reduce or delay therapeutic response.

THERAPEUTIC USES / CLINICAL RELEVANCE

- Important in dose selection for oral drugs.
- Helps choose route of administration.
- Explains why some drugs work better sublingually or parenterally.
- Important in rational pharmacotherapy.

ADVERSE EFFECTS / CLINICAL IMPACT

- Variable response after oral dosing.
- Risk of treatment failure if bioavailability is too low.
- Possibility of active or toxic metabolites being formed.

CONTRAINDICATIONS / WHEN TO AVOID ORAL ROUTE

- Severe liver disease may alter first-pass metabolism.
- Drugs with extensive first-pass effect may be unsuitable orally.
- Consider alternative routes in emergency situations.

DRUG INTERACTIONS

- Enzyme inducers may increase first-pass metabolism.
- Enzyme inhibitors may decrease first-pass metabolism.
- Food and other drugs can alter hepatic enzyme activity.
- Examples: CYP-related interactions.

IMPORTANT EXAMPLES

- **Nitroglycerin:** extensive first-pass effect
- **Lidocaine:** not effective orally due to first-pass metabolism
- **Propranolol:** significant first-pass metabolism
- **Morphine:** considerable first-pass effect
- **Verapamil:** reduced oral bioavailability

10 MNEMONICS

"FIRST PASS = LIVER FIRST"

- **F** = From gut to portal vein
- **I** = Into liver first
- **R** = Reduced bioavailability
- **S** = Systemic blood receives less drug
- **T** = Think oral route

EXAM POINTS

- First-pass metabolism occurs mainly in → Liver
- Important after oral administration
- Decreases bioavailability
- Portal circulation carries drug to liver first
- Sublingual and parenteral routes bypass first-pass effect

IMPORTANT QUESTIONS

1. What is first-pass metabolism?
2. It occurs mainly in which organ?
3. Which route is most affected?
4. Which routes bypass first-pass metabolism?
5. Give two examples of drugs showing extensive first-pass effect.

REMEMBER: Oral drug → Portal vein → Liver → Less bioavailability

QUICK RECALL SUMMARY

1. **Oral route** — Drug taken by mouth
2. **Portal circulation** — Drug absorbed → portal vein
3. **Liver metabolism** — Hepatic enzymes metabolize part of drug
4. **Reduced bioavailability** — Less active drug reaches systemic circulation
5. **Alternative routes bypass it** — Sublingual, parenteral, transdermal, etc.

Pharmacology Classification + Specific Mechanism of Action (MOA) – 200 High-Yield One-Liners

1. DEFINITION

- Absorption = movement of drug from site of administration into systemic circulation.
- Maximum absorption occurs in the **small intestine.**

2. CLASSIFICATION

- Main parts: duodenum, jejunum, ileum.
- **Jejunum/upper small intestine** is the major site for most drugs.

3. MECHANISM OF ACTION

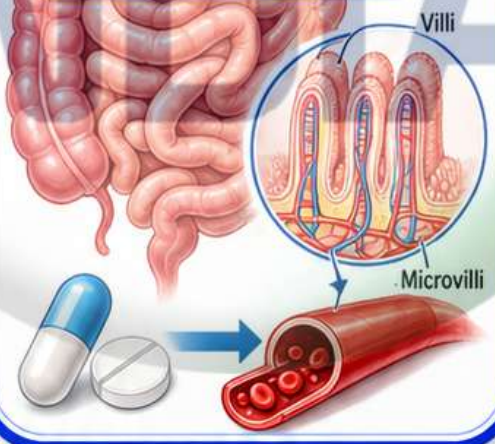
- Very large surface area due to **folds, villi, and microvilli.**
- **Rich blood supply** maintains concentration gradient.
- **Thin epithelial membrane** favors diffusion.
- **Longer transit time** improves absorption.

4. PHARMACOLOGICAL EFFECTS

- Increases oral drug uptake.
- Improves systemic availability of many drugs.
- Supports predictable therapeutic response.

Drug Absorption is Maximum in → Small Intestine

Large surface area + rich blood supply + long contact time



5. THERAPEUTIC USES

- Basis for most oral dosage forms.
- Important in tablets, capsules, syrups, and solutions.
- Helps explain effective oral therapy.

6. ADVERSE EFFECTS

- Reduced absorption in diarrhea or malabsorption.
- GI disease may lower drug absorption.
- Food or pH changes may alter uptake.

7. CONTRAINDICATIONS

- Not a direct contraindication topic.
- Severe intestinal disease can reduce absorption reliability.
- Vomiting/rapid transit may affect oral route.

8. DRUG INTERACTIONS

- Chelation with calcium/iron may reduce absorption.
- Antacids may change pH-dependent absorption.
- Food and other drugs can delay or decrease uptake.

9. IMPORTANT EXAMPLES

- Paracetamol
- Aspirin
- Amoxicillin
- Metformin
- Most orally administered drugs

10. MNEMONICS

"Small Intestine = Small but Super Absorption"

Villi + Blood + Time = Best absorption site

11. EXAM POINTS

- Drug absorption is maximum in **small intestine.**
- Stomach has **less absorption** despite acidity.
- Colon has **lower surface area** than small intestine.
- **IV route** bypasses absorption.

12. IMPORTANT QUESTIONS

Q. Drug absorption is maximum in?
Ans. **Small intestine.**

Q. Why is small intestine the main site?
Ans. **Large surface area and rich blood supply.**

Q. Which structures increase absorptive area?
Ans. **Villi and microvilli.**

EXAM BOOSTER

Most orally administered drugs are absorbed mainly from the **small intestine** because of its **enormous surface area, rich blood flow,** and **favorable membrane.**

Pharmacology Classification + Specific Mechanism of Action (MOA) – 200 High-Yield One-Liners

1 DEFINITION

- Albumin is the major plasma protein responsible for binding many drugs in blood.
- It binds mainly acidic drugs and some neutral drugs.
- Protein-bound drug remains in circulation; only free drug is pharmacologically active.

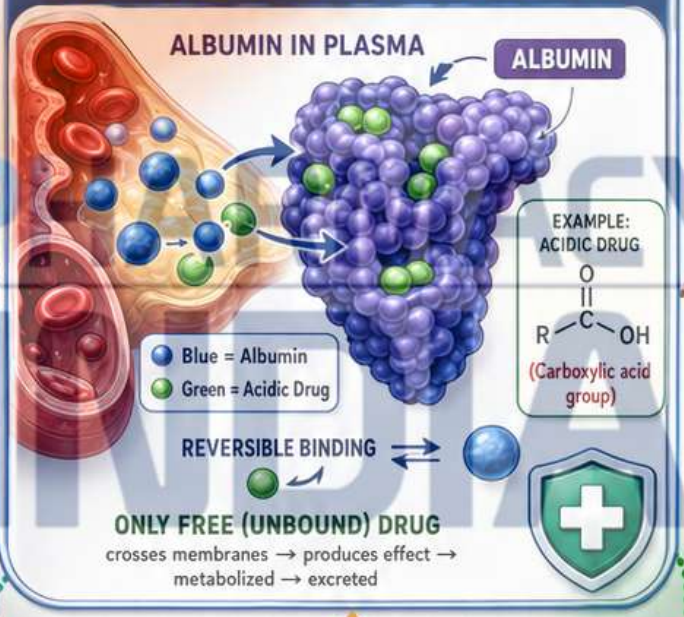
2 CLASSIFICATION

- Albumin → mainly acidic drugs.
- Alpha-1 acid glycoprotein → mainly basic drugs.
- Lipoproteins / globulins → highly lipophilic or special drugs.
- Degree of binding may be low, moderate, or high.

3 MECHANISM OF ACTION

- Acidic drugs interact with albumin binding sites in plasma.
- Binding is reversible.
- Bound drug acts as a reservoir.
- Only unbound drug crosses membranes, produces effect, is metabolized, and is excreted.
- Increased binding lowers free drug concentration initially.

ALBUMIN BINDS MAINLY* → ACIDIC DRUGS



PHARMACOLOGICAL EFFECTS

- Reduces free fraction of drug.
- Decreases immediate tissue distribution.
- Often lowers volume of distribution.
- Can prolong duration / half-life by reservoir effect.
- Modifies onset and intensity of action.

THERAPEUTIC USES / CLINICAL RELEVANCE

- Helps predict drug distribution and dosing.
- Important in therapeutic drug monitoring.
- Important in drugs with narrow therapeutic index.
- Helps explain altered response in liver disease, renal disease, burns, malnutrition, and pregnancy.

ADVERSE EFFECTS / CLINICAL IMPACT

- Hypoalbuminemia increases free drug level.
- Toxicity risk rises when highly protein-bound drugs are displaced.
- Small change in binding can cause large clinical effect for narrow-therapeutic-index drugs.

CONTRAINDICATIONS / EXCEPTIONS

- Basic drugs usually do NOT bind mainly to albumin; they bind alpha-1 acid glycoprotein.
- In severe liver disease or nephrotic syndrome, albumin level falls.
- In renal failure, binding may be altered by uremic substances.
- Neonates and elderly may show altered protein binding.

DRUG INTERACTIONS

- Drug displacement may transiently increase free drug concentration.
- Classic concern: warfarin displacement can increase bleeding risk.
- Aspirin / NSAIDs, sulfonamides, valproate, and phenytoin may show displacement-related issues.
- Enzyme inhibition or hypoalbuminemia can further magnify toxicity.

IMPORTANT EXAMPLES

- Warfarin
- Phenytoin
- Salicylates (Aspirin)
- Valproic acid
- Sulfonamides
- Furosemide

These are mainly acidic or highly albumin-bound examples.

10 MNEMONICS

"A for Albumin, A for Acidic"

- A = Albumin
- A = Acidic drugs
- F = Free drug = Active drug
- B = Bound drug = Bank / reservoir

Memory Trick: *"Albumin hugs acids in plasma."*

EXAM POINTS

- Albumin binds mainly acidic drugs.
- Alpha-1 acid glycoprotein binds mainly basic drugs.
- Only free drug is active.
- Hypoalbuminemia ↑ free drug and toxicity.
- Highly protein-bound drugs show important displacement interactions.
- Asked commonly in biopharmaceutics and pharmacology exams.

REMEMBER:
Albumin mainly binds acidic drugs; free drug is the active drug.

IMPORTANT QUESTIONS

Q1. Which plasma protein mainly binds acidic drugs? → Albumin

Q2. Which protein mainly binds basic drugs? → Alpha-1 acid glycoprotein

Q3. Which form of drug is pharmacologically active? → Free / unbound form

Q4. Name one highly albumin-bound acidic drug. → Warfarin

Q5. What happens in hypoalbuminemia? → Free drug concentration increases

QUICK RECALL SUMMARY

Pharmacology Classification + Specific Mechanism of Action (MOA) – 200 High-Yield One-Liners

Definition:

- α1-Acid glycoprotein (AGP) is a plasma protein.
- It is also called orosomucoid.
- It binds mainly **basic** (cationic) drugs.

Classification:

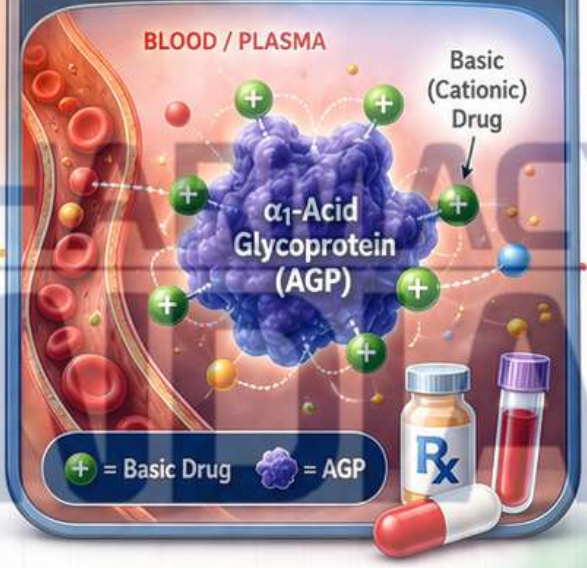
- Major plasma binding proteins:
- Albumin → **acidic drugs**
- AGP → **basic drugs**
- Lipoproteins → lipophilic drugs

Mechanism of Action:

- AGP is an acidic glycoprotein.
- It attracts positively charged basic drugs.
- Binding lowers the **free** (active) drug fraction.
- Only unbound drug can diffuse and act.

α_1-Acid Glycoprotein Binds Mainly → Basic Drugs

AGP / Orosomucoid = plasma protein for basic drugs



Pharmacological Effects:

- Decreases **free drug** concentration.
- Limits distribution of basic drugs.
- May reduce immediate drug effect.
- Can increase plasma retention.

Therapeutic Uses:

- Important in dose interpretation.
- Useful in therapeutic drug monitoring.
- Helps explain altered response in illness.

Adverse Effects:

- High AGP → less **free** drug, weaker effect.
- Low AGP → more **free** drug, toxicity risk.
- Binding changes can alter response.

Contraindications:

- No direct contraindication.
- Use caution in neonates and liver disease.
- Critical illness may change binding.

Drug Interactions:

- Basic drugs may compete for AGP sites.
- Displacement may raise **free drug** briefly.
- Monitor highly bound basic drugs.

Important Examples:

- Lidocaine
- Propranolol
- Quinidine
- Imipramine

Mnemonics:

- "AAG Grabs Alkaline Agents"
- "AGP = Acid protein for **Basic drugs**"

Exam Points:

- Albumin binds **acidic drugs.**
- AGP binds **basic drugs.**
- AGP rises in stress and inflammation.
- Increased AGP lowers **free basic drug.**

Important Questions:

Q. Which plasma protein binds basic drugs?
Ans. α1-Acid glycoprotein.

Q. What is another name for AGP?
Ans. Orosomucoid.

Q. What happens if AGP increases?
Ans. Free basic drug decreases.

EXAM BOOSTER!

Remember: Albumin → **acidic drugs,** - α1-Acid glycoprotein → **basic drugs.**

PHARMACOLOGY CLASSIFICATION + SPECIRIC MECHANISM OF ACTION (MOA) – 200 HIGH-YIELD ONE-LINERS

12 IMPORTANT QUESTIONS

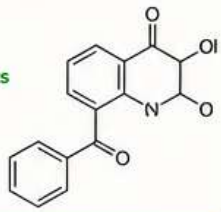
- Q. Why is PT/INR monitored in warfarin therapy?
- Q. Why does warfarin have a delayed onset of action?
- Q. Why is vitamin K given in warfarin overdose?
- Q. Why is warfarin highly protein bound?

1 DEFINITION

- Warfarin is an oral anticoagulant that prevents formation of functional clot by inhibiting vitamin K dependent synthesis of clotting factors.

2 CLASSIFICATION

- Anticoagulants
  - ▶ Vitamin K Antagonists
    - – Warfarin
    - – Acenocoumarol



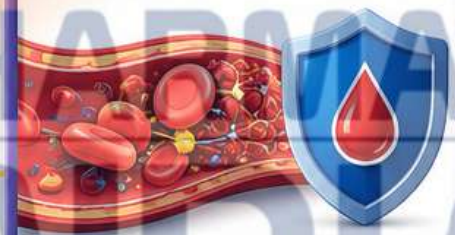
11 EXAM POINTS

- ★ Highly protein bound (>99%)
- ★ Narrow therapeutic index
- ★ Monitored by PT/INR
- ★ Delayed onset (2–5 days)
- ★ Long duration of action
- ★ Antidote: Vitamin K_1 (Phytonadione)
- ★ Teratogenic – Category X

WARFARIN

ANTICOAGULANT

VITAMIN K ANTAGONIST



Warfarin is highly bound to* → Plasma proteins.

3 MECHANISM OF ACTION

- Inhibits vitamin K epoxide reductase complex (VKORC1)
- ↓
- Prevents regeneration of reduced vitamin K
- ↓
- Decreases γ-carboxylation of glutamate residues
- ↓
- Reduces synthesis of active clotting factors II, VII, IX, X and proteins C & S.

10 MNEMONICS

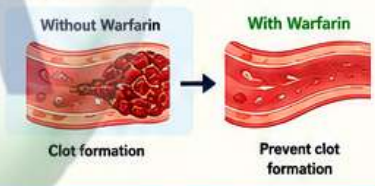
For Warfarin (Vitamin K Antagonist)

W A R F A R I N

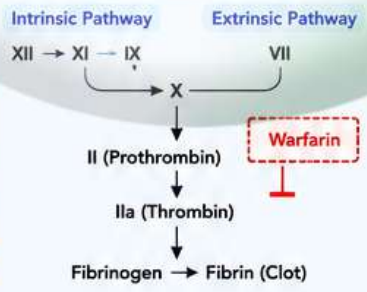
- W – Vitamin K antagonist
- A – Anticoagulant
- R – Reduces clotting factors
- F – Factor II, VII, IX, X
- A – Antidote: Vitamin K
- R – Requires INR monitoring
- I – Interaction with many drugs
- N – Not for pregnancy

4 PHARMACOLOGICAL EFFECTS

- Anticoagulant
- Prevents thrombus formation
- Does not dissolve existing clots



CLOTTING CASCADE (Affected by Warfarin)



Factors Affected: II, VII, IX, X

9 IMPORTANT EXAMPLES

- Warfarin
- Acenocoumarol
- Phenindione

5 THERAPEUTIC USES

- Prevention & treatment of DVT
- Pulmonary embolism
- Prevention of systemic embolism in atrial fibrillation
- Mechanical heart valves
- Post myocardial infarction
- Prevent recurrent strokes

8 DRUG INTERACTIONS

↑ Effect (↑ Bleeding)

- Aspirin, NSAIDs
- Amiodarone
- Metronidazole
- Sulfonamides
- Azole antifungals

↓ Effect (↓ Anticoagulation)

- Rifampicin
- Carbamazepine
- Phenytoin
- St. John's wort

7 CONTRAINDICATIONS

- Active bleeding
- Pregnancy (teratogenic)
- Severe liver disease
- Peptic ulcer
- Thrombocytopenia
- Uncontrolled hypertension
- Recent surgery / trauma

6 ADVERSE EFFECTS

- Bleeding (major)
- Hemorrhage
- Purple toe syndrome
- Skin necrosis
- Teratogenicity (Category X)
- Alopecia (rare)

ROUTE	ONSET	DURATION	MONITORING	ANTIDOTE
Oral	2–5 Days	2–5 Days	PT/INR	Vitamin K_1 (Phytonadione)

HIGH-YIELD PEARL

Warfarin prevents new clot formation, but does NOT dissolve old clots.

Pharmacology Classification + Specific Mechanism of Action (MOA) – 200 High-Yield One-Liners

1 DEFINITION

- Phase I reactions are functionalization reactions in drug metabolism.
- Oxidation is the most common Phase I reaction.
- It usually introduces or exposes a polar functional group.
- Common site: mainly liver microsomal enzymes.

2 CLASSIFICATION

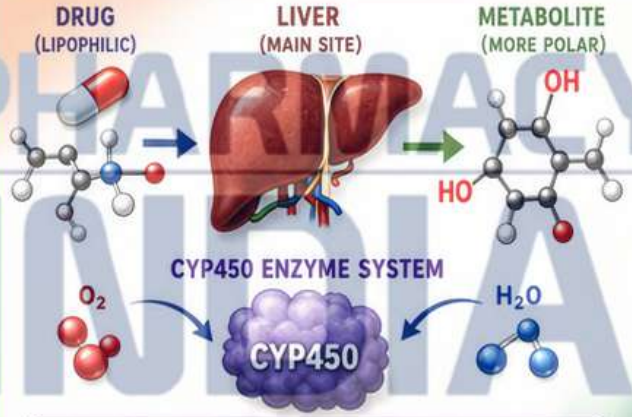
- Phase I reactions include oxidation, reduction, and hydrolysis.
- Among these, oxidation is the most frequent.
- Oxidation may be microsomal or non-microsomal.
- Major microsomal system: cytochrome P450 (CYP450).

3 MECHANISM OF ACTION

- Drug reaches metabolizing enzymes, mainly CYP450.
- Enzyme adds oxygen or removes hydrogen from the drug.
- Product becomes more polar and often more water-soluble.
- Metabolite may become inactive, active, or sometimes toxic.
- Phase II conjugation may follow.

MOST COMMON PHASE I REACTION* → OXIDATION

* MOST FREQUENT PHASE I REACTION IN DRUG METABOLISM



OXIDATION = ADD OXYGEN OR REMOVE HYDROGEN

Drug (Lipophilic) Less Polar → Oxidation (CYP450) → Metabolite More Polar → Easier Excretion (Water-Soluble)

PHARMACOLOGICAL EFFECTS

- Increases polarity of many drugs.
- Facilitates renal or biliary excretion.
- Usually reduces lipid solubility.
- Can terminate drug action.
- Sometimes activates prodrugs.

THERAPEUTIC USES / CLINICAL RELEVANCE

- Helps in detoxification and elimination of drugs.
- Important for dose selection and dosing interval.
- Explains variability in drug response.
- Important in understanding prodrug activation.
- Crucial in pharmacokinetics and rational therapeutics.

ADVERSE EFFECTS / CLINICAL IMPACT

- Rapid oxidation may reduce efficacy of some drugs.
- Slow oxidation may increase toxicity.
- Some oxidative metabolites can be reactive or harmful.
- Liver disease can alter oxidation capacity.

CONTRAINDICATIONS / CAUTION

- Use caution in hepatic impairment.
- Elderly and neonates may have altered metabolism.
- Genetic polymorphism may affect CYP activity.
- Enzyme induction or inhibition can change drug levels.

DRUG INTERACTIONS

- CYP inducers increase oxidation of substrate drugs.
- CYP inhibitors decrease oxidation and may raise toxicity.
- Food and herbs may alter CYP enzymes.
- Important examples: rifampicin induces; cimetidine and erythromycin inhibit.

IMPORTANT EXAMPLES

- ✓ Phenytoin – oxidized in liver.
- ✓ Diazepam – oxidative metabolism.
- ✓ Propranolol – Phase I oxidation.
- ✓ Codeine – oxidative activation pathway involved.
- ✓ Paracetamol – oxidation can form toxic NAPQI metabolite.

10 MNEMONICS

OXIDATION = MOST COMMON

Memory trick: "OXY adds Oxygen, opens way for Output."

- O = Oxygen addition
- X = Xenobiotic metabolism
- I = Increases polarity
- D = Drug becomes metabolite
- A = Activates or inactivates
- T = Through CYP450
- I = In liver mainly
- O = Output by excretion
- N = Next may be Phase II

EXAM POINTS

- ✓ Most common Phase I reaction → Oxidation.
- ✓ Major enzyme system → CYP450.
- ✓ Major organ → Liver.
- ✓ Purpose → increase polarity and facilitate excretion.
- ✓ Phase I includes oxidation, reduction, hydtolysis.
- ✓ Toxic metabolite example → NAPQI from paracetamol.

IMPORTANT QUESTIONS

1. What is the most common Phase I reaction?
2. Which enzyme system mainly carries out oxidation?
3. In which organ does most drug oxidation occur?
4. Name other Phase I reactions besides oxidation.
5. Give one example where oxidation forms a toxic metabolite.

REMEMBER

Oxidation is the commonest Phase I reaction and is mainly mediated by hepatic CYP450 enzymes.

QUICK RECALL SUMMARY

Drug (Lipophilic) → Liver / CYP450 (Metabolizing Site) → Oxidation (Add O_2 / Remove H) → ↑ Polarity (More Water-Soluble) → Excretion (Renal / Biliary) → Sometimes Activation or Toxicity

PHARMACOLOGY CLASSIFICATION + SPECIFIC MECHANISM OF ACTION (MOA) – 200 HIGH-YIELD ONE-LINERS

12 IMPORTANT QUESTIONS

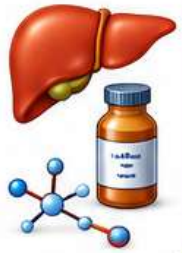
- Q. What are Phase II drug metabolism reactions?
- Q. What is the main purpose of Phase II reactions?
- Q. Which enzyme families are involved in Phase II reactions?
- Q. What is the product of Phase II reactions?

1 DEFINITION

Phase II reactions (Conjugation reactions) are drug metabolism reactions in which an endogenous polar molecule is attached to the drug or its metabolite to **increase water solubility** and facilitate excretion.

2 CLASSIFICATION

- Major Types of Conjugation
  1. Glucuronidation
  2. Sulfation
  3. Acetylation
  4. Methylation
  5. Glutathione Conjugation
  6. Amino Acid Conjugation
  7. Conjugation with other endogenous molecules



11 EXAM POINTS

- ★ Phase II = Conjugation
- ★ Increases water solubility
- ★ Decreases activity
- ★ Facilitates excretion
- ★ Occurs mainly in liver
- ★ Catalyzed by transferases
- ★ Examples: Glucuronidation, Sulfation, Acetylation

PHASE II REACTIONS INVOLVE* CONJUGATION

Phase II reactions involve* → Conjugation.

3 MECHANISM OF ACTION

- Drug (or active metabolite) + Endogenous polar molecule
- ↓
- Catalyzed by specific transferase enzymes in liver
- ↓
- Formation of conjugated, more polar compound
- ↓
- Increased water solubility
- ↓
- Enhanced excretion via bile or urine

10 MNEMONICS

CONJU-GATE

- **C** – Conjugation increases solubility
- **O** – Occurs in liver
- **N** – Needs endogenous substrate
- **J** – Join (drug + substrate)
- **U** – Useful for excretion
- **G** – Glucuronidation is major
- **A** – Adds polarity
- **T** – Transferase enzymes
- **E** – Easy elimination

4 PHARMACOLOGICAL EFFECTS

- Generally ↓ pharmacological activity
- ↑ Water solubility
- ↑ Excretion (biliary or renal)
- Detoxification of lipophilic drugs and metabolites

More soluble ⟶ Easy excretion

TYPES OF CONJUGATION – QUICK VIEW

Glucuronidation	+ Glucuronic acid (UGT enzymes)
Sulfation	SO_3 + Sulfate (SULT enzymes)
Acetylation	+ Acetyl group (NAT enzymes)
Methylation	CH_3 + Methyl group (MT enzymes)
Glutathione Conjugation	GSH + Glutathione (GST enzymes)
Amino Acid Conjugation	+ Amino acids (Glycine, Taurine, etc.)
Others	••• With N-acetylcysteine, Ethylamine, etc.

9 IMPORTANT EXAMPLES

- Paracetamol (Glucuronidation, Sulfation)
- Morphine (Glucuronidation)
- Chloramphenicol (Glucuronidation)
- Lamotrigine (Glucuronidation)
- Isoniazid (Acetylation)

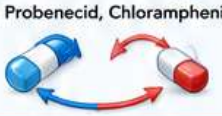
5 THERAPEUTIC RELEVANCE

- Conjugation makes drugs inactive or less active
- Prevents accumulation and toxicity
- Important for detoxification of xenobiotics

8 DRUG INTERACTIONS

Enzyme Inducers ↑ Conjugation
(e.g., Rifampicin, Phenobarbital, Carbamazepine)

Enzyme Inhibitors ↓ Conjugation
(e.g., Probenecid, Chloramphenicol)



6 ADVERSE EFFECTS

- Accumulation of toxic substances if conjugation is impaired
- Hepatotoxicity (in severe liver disease)
- Drug toxicity (e.g., acetaminophen overdose → ↓ glucuronidation)
- May lead to adverse drug reactions

7 CONTRAINDICATIONS

- Severe hepatic impairment
- Genetic enzyme deficiencies (e.g., UGT deficiency)
- Neonates (immature conjugation system)
- Caution in patients with liver dysfunction

EXAM BOOSTER

- ✓ Purpose → Detoxification
- ✓ Outcome → Polar, inactive, easily excreted
- ✓ Site → Liver (mainly)
- ✓ Key Enzymes → Transferases
- ✓ Result → ↑ Excretion via bile/urine

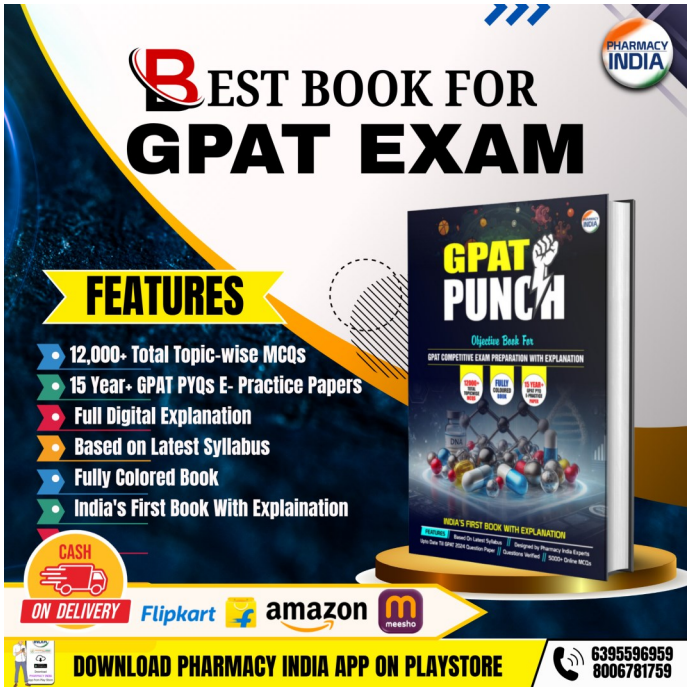
HIGH-YIELD PEARL

Phase II reactions involve* → CONJUGATION.

ONELINER

"Conjugation makes it soluble, excretable and safe."

Available on Flipkart and Amazon



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