SNS COLLEGE OF ALLIED HEALTH SCIENCE

SNS Kalvi Nagar, Coimbatore - 35

Affiliated to Dr MGR Medical University, Chennai

DEPARTMENT OF OPERATION THEATRE AND ANAESTHESIA TECHNOLOGY - II YEAR

COURSE NAME: PHARMACOLOGY

TOPIC - ANTICOAGULANTS

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Lecturer

DEFINITION

Anticoagulants, commonly known as blood thinners, are chemical substances that prevent or reduce blood coagulation, prolonging clotting time.

CLASSIFICATION

- **Parenteral Anticoagulants (Injected):**
- Unfractionated Heparin (UFH): IV or subcutaneous.
- Low Molecular Weight Heparin (LMWH): e.g., Enoxaparin – subcutaneous.
- Synthetic Pentasaccharides: e.g., Fondaparinux – subcutaneous.
- **Oral Anticoagulants:**
- Vitamin K Antagonists (VKAs): e.g., Warfarin.
- Direct Oral Anticoagulants (DOACs):
  - Direct Thrombin Inhibitors: e.g., Dabigatran.
  - Factor Xa Inhibitors: e.g., Rivaroxaban, Apixaban, Edoxaban.

HEPARINS

•**Class:** Heparins (UFH and LMWH).

•**Pharmacodynamics (Mechanism):** Indirect inhibitors; bind to antithrombin (AT) via pentasaccharide sequence, accelerating inactivation of factors XIIa, IXa, XIa, Xa, and thrombin (IIa). UFH has balanced anti-Xa/anti-IIa activity; LMWH has greater anti-Xa activity.

Aspect	Unfractionated Heparin (UFH)	Low Molecular Weight Heparins (LMWH, e.g., Enoxaparin)
Onset	Immediate (IV); 20-60 min (SC)	3-5 hours (peak anti-Xa activity, SC)
Duration	0.5-2 hours (dose-dependent half-life)	17-21 hours (longer half-life)
Dosage	VTE treatment: 80 U/kg IV bolus + 18 U/kg/h infusion (adjust to aPTT 1.5-2.5x control). Prophylaxis: 5,000 U SC q8-12h.	Enoxaparin VTE treatment: 1 mg/kg SC q12h or 1.5 mg/kg q24h. Prophylaxis: 40 mg SC daily. Adjust for CrCl <30 mL/min.

HEPARINS

•**Metabolism:** Not enzymatically degraded; depolymerized by endothelial cells/macrophages.

•**Excretion:** Renal

•**Interactions:**

Increases bleeding risk with aspirin, NSAIDs, fibrinolytics, glycoprotein IIb/IIIa inhibitors; herbs like garlic/ginger.

•**Adverse Effects:**

Bleeding (0-7%), heparin-induced thrombocytopenia (HIT, 1-5%), osteoporosis (long-term >1 month, ~2%), hyperkalemia.

VITAMIN K ANTAGONISTS (WARFARIN)

Mechanism: Inhibits vitamin K epoxide reductase, depleting vitamin K and preventing γ-carboxylation of factors II, VII, IX, X, and proteins C/S. Initial procoagulant effect due to faster depletion of protein C.

- **Metabolism:** Hepatic.
- **Excretion:** Urine.

Aspect	Details
Onset	24 hours (initial effect); peak 72-96 hours.
Duration	2-5 days (half-life 20-60 hours, mean 40 hours).
Dosage	Initial: 2-5 mg oral daily; maintenance: Adjust to INR 2-3 (e.g., VTE: 2-3; mechanical valves: 2.5-3.5). Forms: Tablets 1-10 mg.

•**Interactions:**
•Potentiated by CYP inhibitors (e.g., amiodarone)
•vitamin K-rich foods reduce efficacy
• herbs (St. John's Wort decreases effect).
•**Adverse Effects:**
•Bleeding (major risk)
•skin necrosis
•Calciphylaxis
• teratogenic (fetal warfarin syndrome)
• nephropathy.

DIRECT THROMBIN INHIBITORS

Examples: Dabigatran (oral), Argatroban/Bivalirudin (parenteral).

Mechanism: Directly bind thrombin's active site, inhibiting fibrinogen to fibrin conversion; AT-independent. Dabigatran: Prodrug converted to active form.

Drug	Onset	Duration	Dosage
Dabigatran	1-2 hours (peak)	Half-life 12-17 hours	VTE: 150 mg oral BID (after 5-10 days parenteral); prophylaxis: 110-150 mg BID.
Argatroban	Immediate (IV)	Half-life 40-50 min	HIT: 2 mcg/kg/min IV infusion (adjust for hepatic impairment).
Bivalirudin	Immediate (IV)	Half-life 25 min	PCI: 0.75 mg/kg IV bolus + 1.75 mg/kg/h infusion.

DIRECT THROMBIN INHIBITORS

Pharmacokinetics

•renal excretion

•Hepatic metabolism

Interactions:

•P-gp inhibitors (e.g., ketoconazole) increase dabigatran levels

•avoid with other anticoagulants.

Adverse Effects:

• Bleeding (GI for dabigatran)

•thrombocytopenia (less than heparins)

•dyspepsia (dabigatran).

FACTOR XA INHIBITORS

•**Examples:** Rivaroxaban, Apixaban, Edoxaban (oral DOACs); Fondaparinux (covered earlier).
•**Mechanism:** Directly inhibit Factor Xa, preventing prothrombin to thrombin conversion; rapid, direct action.

Drug	Onset	Duration	Dosage
Rivaroxaban	2-4 hours	Half-life 5-9 hours	VTE: 15 mg BID (21 days) then 20 mg daily; AF: 20 mg daily.
Apixaban	3-4 hours	Half-life 12 hours	VTE: 10 mg BID (7 days) then 5 mg BID; prophylaxis: 2.5 mg BID.
Edoxaban	1-2 hours	Half-life 10-14 hours	VTE/AF: 60 mg daily (after parenteral).

FACTOR XA INHIBITORS

Pharmacokinetics:

•hepatic metabolism

•renal excretion

Interactions:

• CYP3A4/P-gp inducers (e.g., rifampin) reduce efficacy

• inhibitors (e.g., ketoconazole) increase bleeding risk.

Adverse Effects:

• Bleeding (lower GI/ICH risk vs. warfarin)

• fatigue

•Nausea

• reversible with andexanet alfa.

THANK YOU