

Anticoagulants.

Four Note

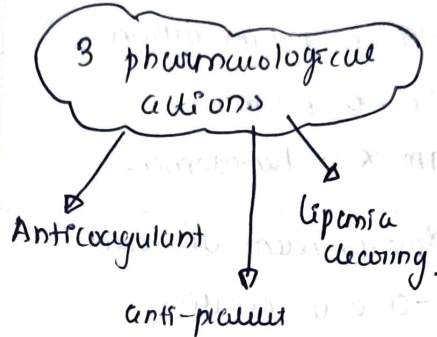
Heparin.

- Normally present in mast cells
- Rich source - Liver, Intestine, lung.
- Extracted - porcine intestinal mucosa.

- Strongest organic acid in human body
- highly electronegative at physiological pH
↓
not given orally.

- both in vivo & in vitro Anticoagulant.

Mechanism of Action



Anticoagulant.

MOA:

- powerful & rapid acting.
- effective both in vivo & in vitro.

At low dose.

heparin binds with Antithrombin III

Complex is formed

Increase its function by 1000 fold.

binds and (-) factor Xa & thrombin.

Inhibit conversion of fibrinogen → fibrin.

At higher con.

heparin bind to AT III

Complex is formed

binds to and inactivates factors

Xa, IIa, IXa, XIa, XIIa, XIIIa.

10a, 20, 9a, 11a, 12a, 13a.

Inhibit fibrinogen → fibrin

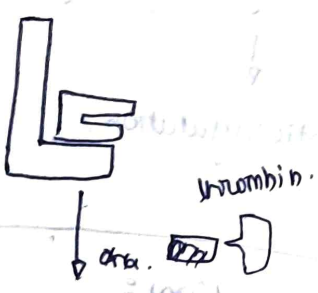
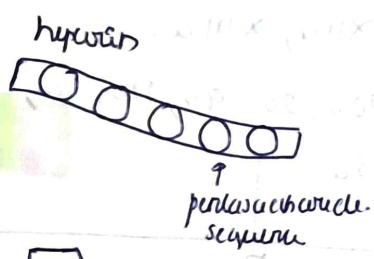
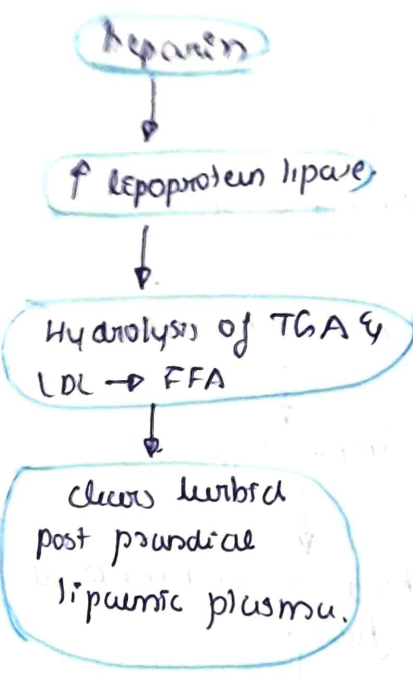
anticoagulation

other actions:

antiplatelet:

Heparin in higher doses (-) platelet aggregation & prolongs bleeding time.

Lipemia clearing.



pharmacokinetics

ABSORPTION

- large, highly ionized.
- ↓
- not given orally
- IV → instant action
- SC → 60 min.
- IM X → hematoma.

close dependent clearance.

- 0 order kinetics.

Distribution

- doesn't cross BBB/placenta.
- Doc → pregnancy.

metabolism - liver

Excretion - kidney.

T_{1/2} - 30-60 min.

longer - renal failure, cirrhotic

shock - pulmonary embolism.

INDICATIONS

- ① venous thromboembolic disease.
 - DVT.
 - Pulmonary embolism.
- ② arterial thromboembolic disease.
 - CAD
 - mural cardiac thrombi
- ③ DIC.

Dosing & monitoring

• 5000U IV/SC & Continuous - bolus dose. 750-1000U

• monitored by aPTT.

• antidote - protamine sulfate
1mg → 100U

Adverse effect

- Bleeding due to overdose
- Hypertension Induced Thrombocytopenia (HIT)
- alopecia
- hyperkalemia
- Osteoporosis → long term.
- Rare - hypersensitivity
- liver damage - ↑ AST

Contraindications

- * Bleeding disorders
- * History of HIT
- * Severe hypertension (bleeding through major vessels)
- threatened abortion.
- hemorrhoids.
- * • Ocular & Neurosurgery.
- lumbar puncture.
- * • Liver & renal failure
- Aspirin

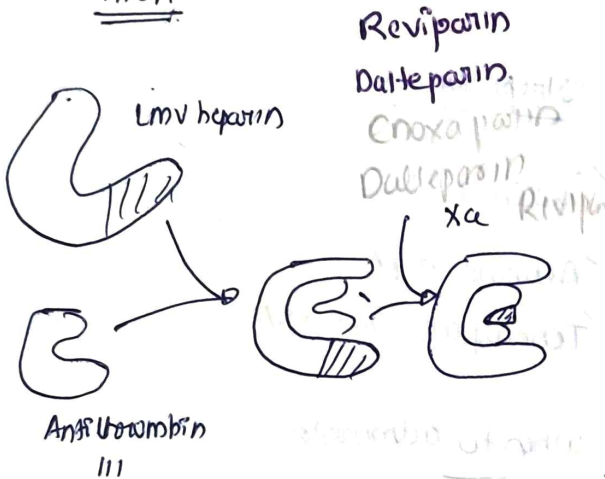
Limitation (SIT-N2)

- * Short duration
- * IV infusion is difficult
- * Toxicity → HIT, Bleeding
- * Need monitoring
- * Zero order kinetics

Low molecular weight Heparin

- Mean molecular weight is 5000Da.
- prepared from UFH by enzymatic / chemical depolymerization.

MOA



LMW heparin

binds to Antithrombin III.

Conformational change in ATIII. & exposes its interactive site.

Inhibition of factor Xa.

little effect on. ~~Factor Xa~~ IIa (Thrombin).

Inactivate Xa.

(-) Prothrombin - fibrin.

Anticoagulation.

Advantages over UFH.

- * higher SC bioavailability than UFH. (70-90% vs 20-30%) (SIT-NZ)
- * less HIT.
- * longer acting - once daily.
- * more predictable response.
 - ↓
 - first order kinetics at all doses.
- * lab monitoring not needed cause aPTT / clotting time is not prolonged.
- * dose calculation - Body weight basis.
- * lower risk of osteoporosis after long term use compared to UFH.

Disadvantages

- effects are not fully reversed by protamine.
- less effective in preventing catheter thrombosis.
 - ↓
 - not preferred during. Cardio-pulmonary bypass surgery.

Indications

- * Unstable angina & MI (replace UFH continuous)
- * established DVT
- * .

Fondaparinux - synthetic analogue.

- 100% SC
- antithrombin binding pentasaccharide sequence
- clearance is not dose dependent
- No HIT
- No HITX
- low bleeding/osteoporosis.

Protamin Sulfate

- Heparin - neutralize
- LMW - reversible
- Fondaparinux → cannot
- (1mg - 100u)

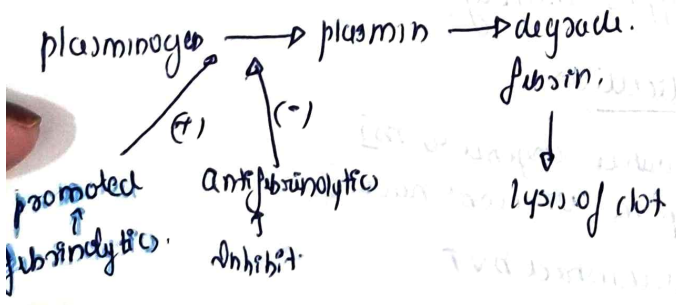
- strongly **basic** LMW protein
- from sperm of salmon fish.
- essential after cardiac & vascular surgery.
- act as weak anticoagulant in absence of heparin.
- HS never reported.

Anti

PPT

FIBRINOLYTIC DRUGS (Thrombolytic drug)

Fibrinolytic are drugs that lyse thrombi rapidly by promoting conversion of plasminogen → plasmin.



Drugs

- streptokinase
- urokinase
- alteplase
- reteplase
- Tenecteplase

Streptokinase

Urokinase

alteplase rPA

Tenecteplase. mut tPA

When to administer

- within 1hr - ideal time
- Max - 12 hrs

Use

- 1 acute MI
- 2 DVT
- 3 PE

Indication

Contraindication

Clopidogrel - PPT