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Compare and contrast the pharmacology of heparin and enoxaparin.

	Heparin	**Enoxaparin**
	Anionic mucopolysaccharide organic acid, containing sulphide residues. Variable molecular weight 5000-25000 Daltons	Low molecular weight heparin (~ 5000 Da). Consists of smaller fragments of heparin, and is produced by controlled enzymatic or chemical depolymerisation of unfractionated heparin.
Indications	• Prevention and treatment of VTE • Treatment of ACS • Priming of lines; haemodialysis and ECMO	
Pharmaceuticals	• Available as s/c or i.v. injection • Described in i.u. not mg due to variable potencies • Dosing: 5000i.u. BD s/c or 5000i.u. i.v. then infusion (rate initially based on weight, then titrated to APTT)	• Usually given s/c, but can be given i.v. • 20mg or 40mg BD s/c as prophylaxis, 1mg/kg BD s/c as therapeutic dose
Pharmacodynamics		
Mechanism	Binds reversibly to antithrombin III, causing a conformational change that makes ATIII more accessible to its target proteases. Heparin enhances ATIII effects of inhibiting proteases in the clotting cascade, particularly thrombin and Factor X.	Binds to ATIII, potentiating its effects of inhibiting proteases in the coagulation cascade. Most of the saccharide chains of LMWH are too short to bridge thrombin to ATIII, therefore targets Factor Xa inhibition much more than thrombin.
Side effects	• Can cause heparin-induced thrombocytopaenia and thrombosis • Osteoporosis	• Better side effect profile with significantly less thrombocytopaenia and osteoporosis • Requires dose adjustment in renal impairment, as is renally excreted
Monitoring	APTT is monitored during i.v. infusion, either 6 or 24-hourly, depending on the result	Usually not monitored as response is normally consistent. Can perform LMWH assay, for anti-Factor Xa activity.
Reversal	Can be reversed by protamine (1mg/100i.u. heparin)	Can be partially reversed by heparin in the first 8 hrs after administration (1mg/1mg LMWH), but max effect is < 60%
Pharmacokinetics		
Absorption	Bioavailability equally reduced for s/c and i.v. due to endothelial binding	Bioavailability 90% after s/c (greater than heparin)
Distribution	• $^1/_3$ bound in plasma to ATIII; the rest to albumin, fibrinogen and other proteases • V_D 40-100mL/kg	• Does not bind to heparin-binding proteins • V_D 4.3L
Metabolism	By heparinases in the liver, reticuloendothelial system and kidneys	Hepatic depolymerisation and desulfation to less active fragments
Elimination	• Excretion in urine → renal impairment has little effect • Variable half-life due to rapid binding to endothelial cells → low doses ~ 30 mins; high doses ~ 150 mins	• 40% of dose excreted in urine, with 10% of dose excreted as active fragments • Half-life 2-4x longer than heparin, independent of dose • Renal impairment requires dose adjustment