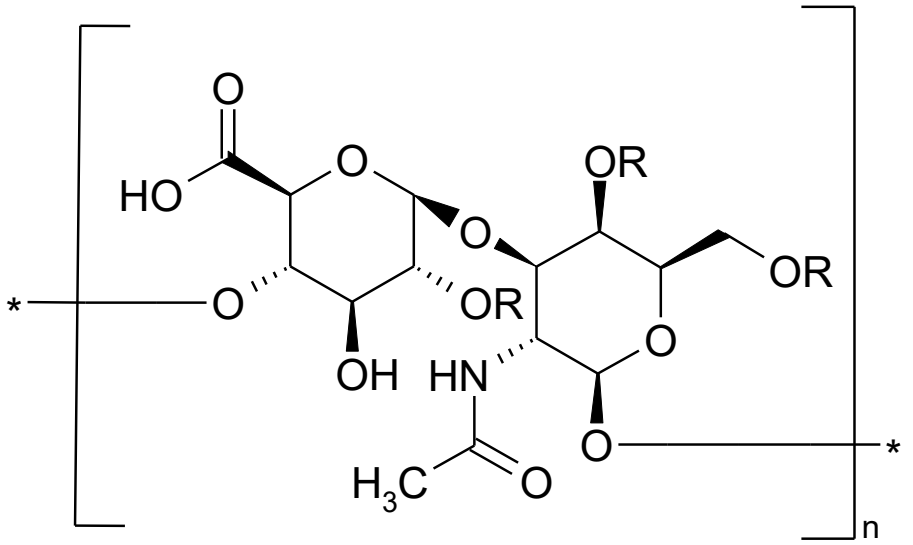
Therapeutic oligo- and polysaccharides

Therapeutics of arthrosis and arthritis



R = H or $-SO_2O^-$

chondroitine sulfate

poly-β-D-glucurono-(1→3)-2-deoxy-2-(acetylamino)-β–D-galactopyranose polysulfafe

•prepared by hydrolysis of porcine, bovine or shark cartilages; the composition of the mixture markedly depends on the both raw material and preparation procedure

•absorbed in small intestine in the amount < 10 % probably by an endocytose mechanism

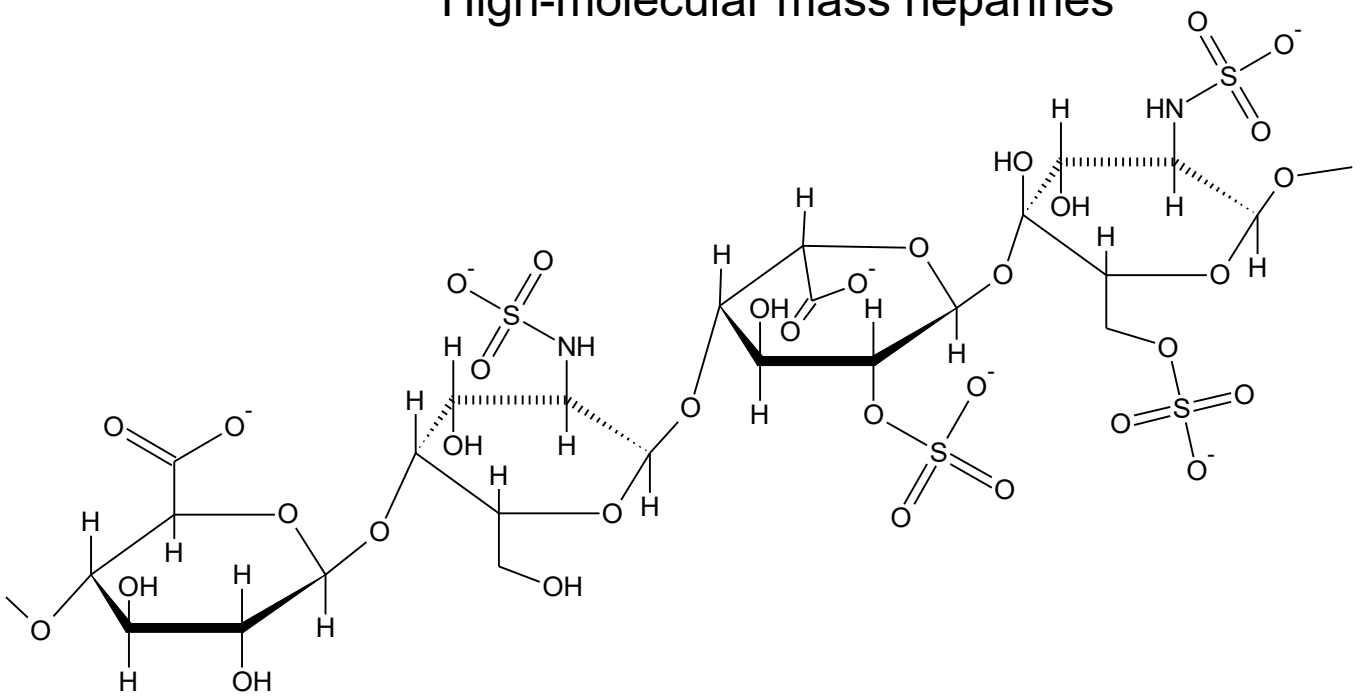
•acts as a prebiotic in the distal part of GIT and is degraded by enzymes of the intestinal microflora into na mono- and disaccharides that are peptidoglycane precursors (namely N-acetylgalaktosamine)

•recommended daily dose 800 mg

Authorized drug preparations: Condrosulf ®

Nutraceutics: Mobilin ® , Artryn ® , Gelactiv ® , GS-CS-MSM 3000 ® , GS-Condro (forte) ®, Proenzi 3 ® , Proenzi premium forte 3000 ® -combined with glucosamine and sometimes also with MSM

Anticoagulants
Heparines
High-molecular mass heparines

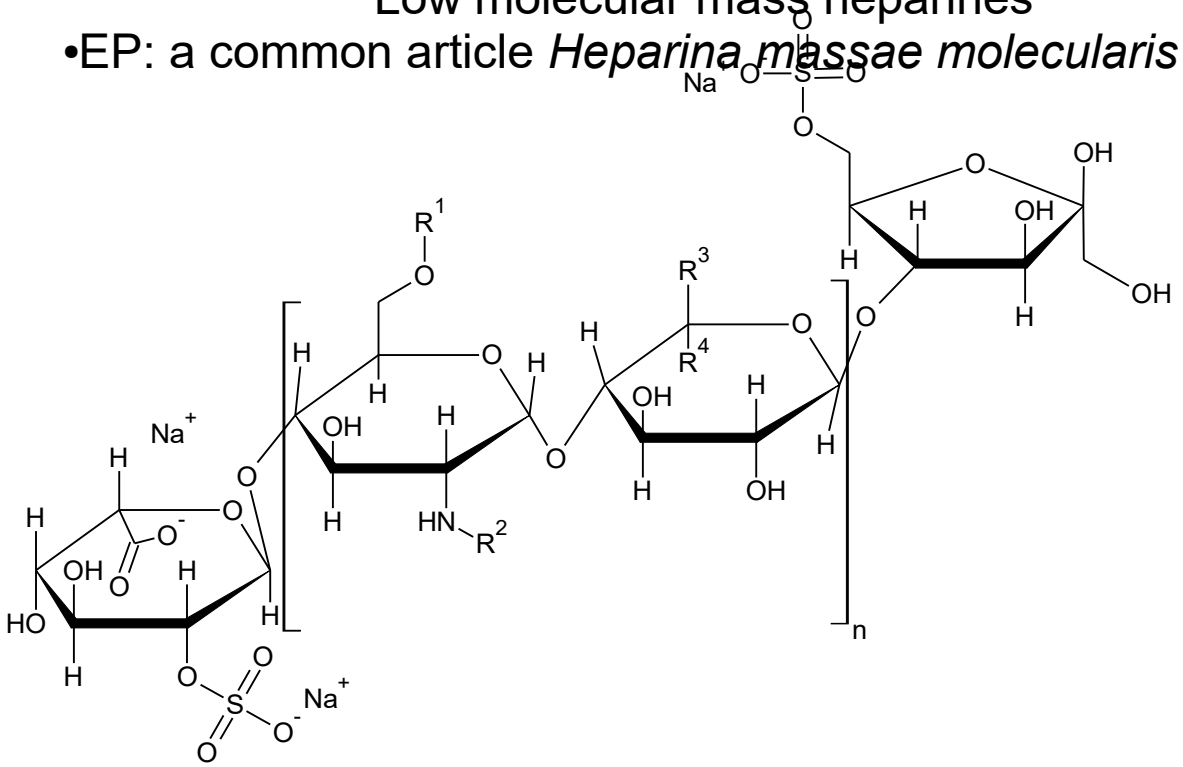


Heparine chain fragment

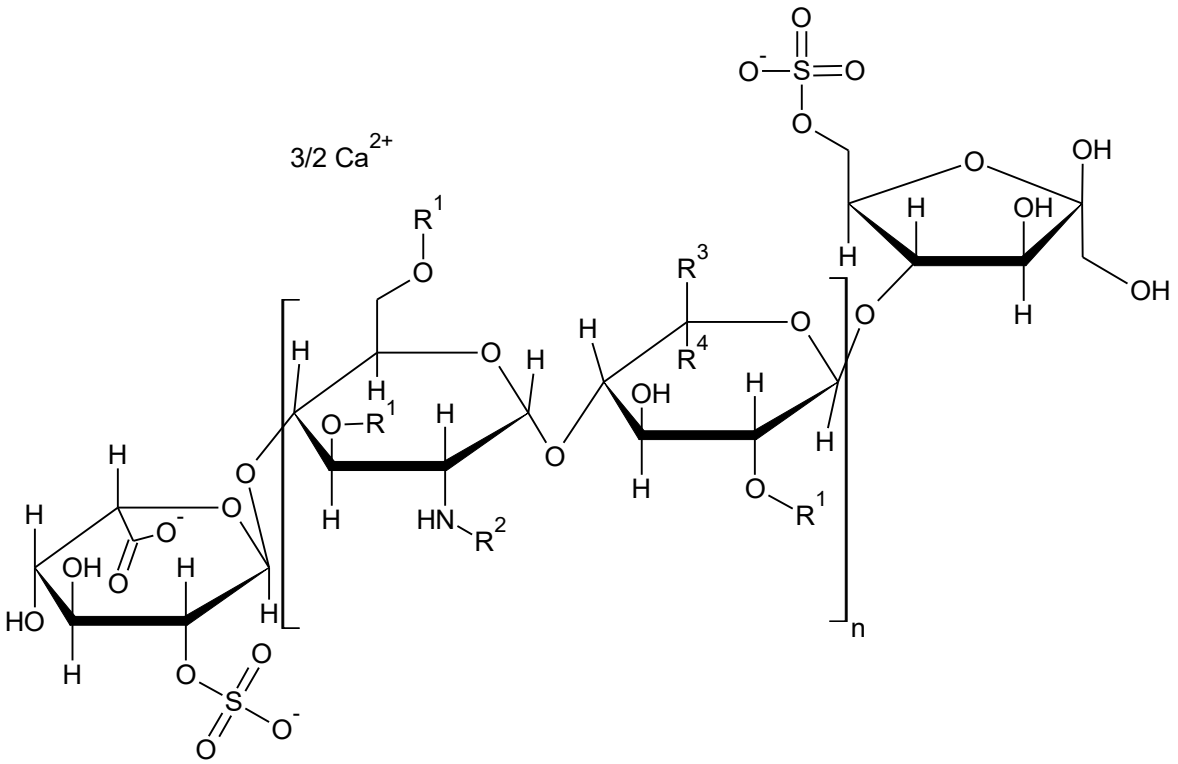
β–D-glucuronic acid (α-D-galactosamine) (α-L-iduronic acid) (α-D-glucosamine)

- 6 000 < M_r < 20 000
- < 30 % glucuronic acid
- < 70 % iduronic acid
- *Heparinum natricum, Heparinum calcicum EP*; Heparin Forte Léčiva®
- Mode of action: activates α_2-globuline antitrombin (AT III); heparin-antitrombin complex blocks then blood clotting factors and avoids thrombine formation
- acts as an „superficial catalyser“
- 5 saccharide units suffices for binding to AT III, binding of additional units stabilizes this complex
- isolated from bovine lungs or from intestinal mucous membranes of cattle, pigs or sheep

Antikoagulants
Heparines
Low molecular mass heparines
•EP: a common article *Heparina massae molecularis minoris*



dalteparine sodium salt
Dalteparinum natricum EP
$2 < n < 21$, R^1 = H or SO_3Na, R^2 = SO_3Na or $COCH_3$; R^3 = H and R^4 = COONa or R^3 = COONa and R^4 = H
Fragmin® inj. sol. (s.c.)
•treatment of deep venous thromboses and lung embolisms; prevention of blood clotting in an out-of-body system in haemodialysis and haemofiltration linked with an accute renal failure or a chronic renal insufficinecy; prophylaxis of thromboembolism linked with a surgical interventions; treatment of an unstable angina pectoris and non-Q myocardial infarction



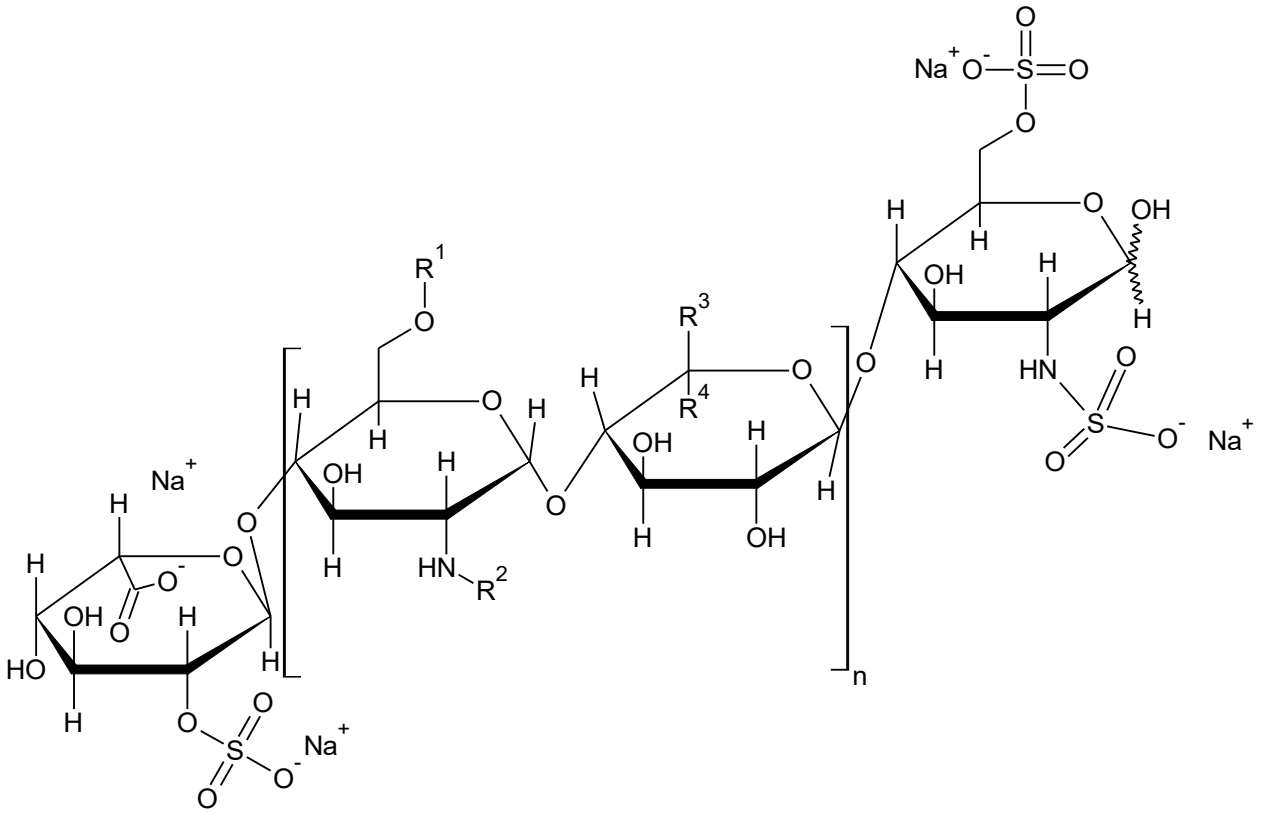
nadroparine calcium salt

Nadroparinum natricum EP

R^1 = H or SO_3(1/2Ca), R^2 = H or SO_3(1/2Ca) or $COCH_3$

R^3 = H and R^4 = COO(1/2Ca) or R^3 = COO(1/2Ca) and R^4 = H

Fraxiparin multi® inj. sol.

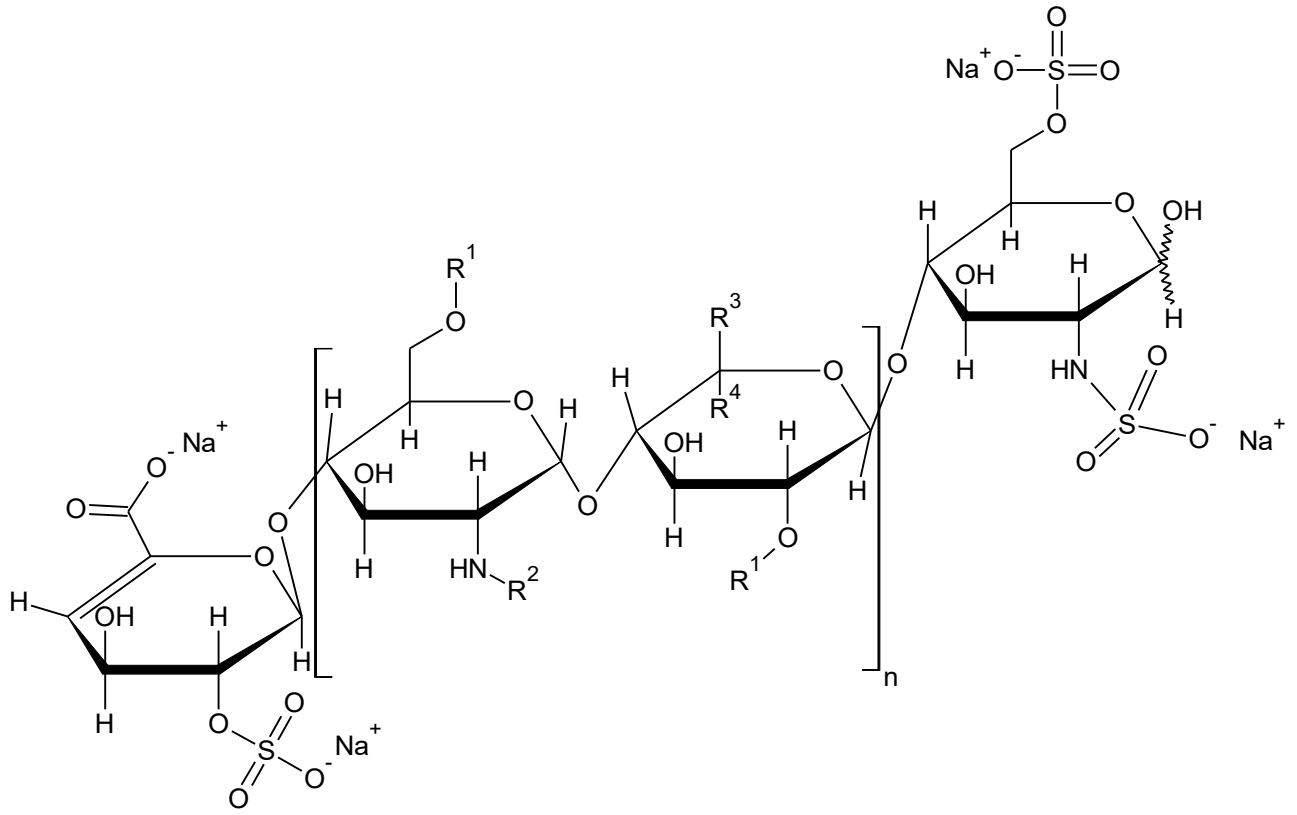


parnaparine sodium salt

Parnaparinum natricum EP

$0 < n < 22$, R^1 = H or SO_3Na, R^2 = SO_3Na or $COCH_3$ R^3 = H and R^4 = COONa or R^3 = COONa and R^4 = H

Fluxum® inj. sol.P

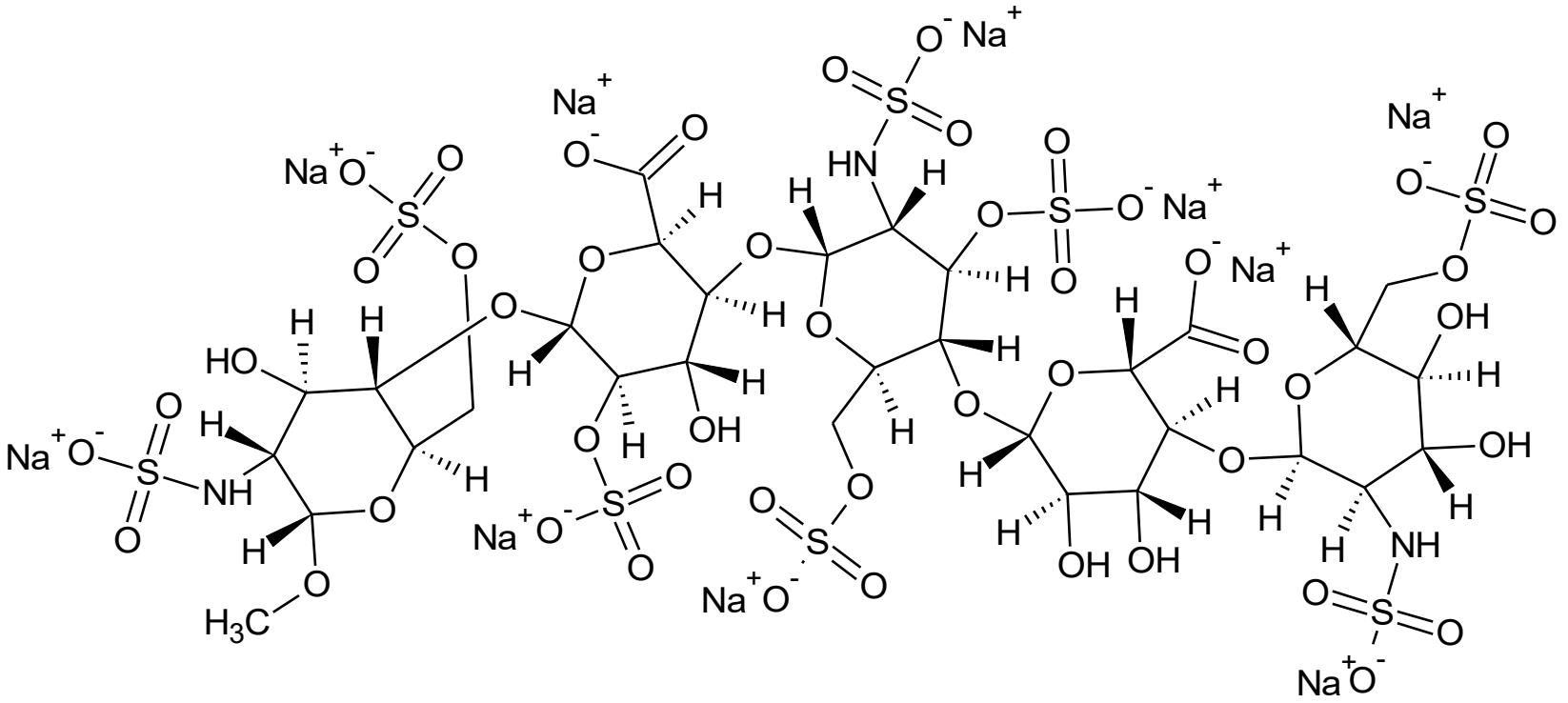


tinzaparine sodium salt

Tinzaparinum natricum EP

$0 < n < 26$, R^1 = H or SO_3Na, R^2 = H or SO_3Na or $COCH_3$, R^3 = H and R^4 = COONa or R^3 = COONa and R^4 = H

Synthetic short chain heparinoids



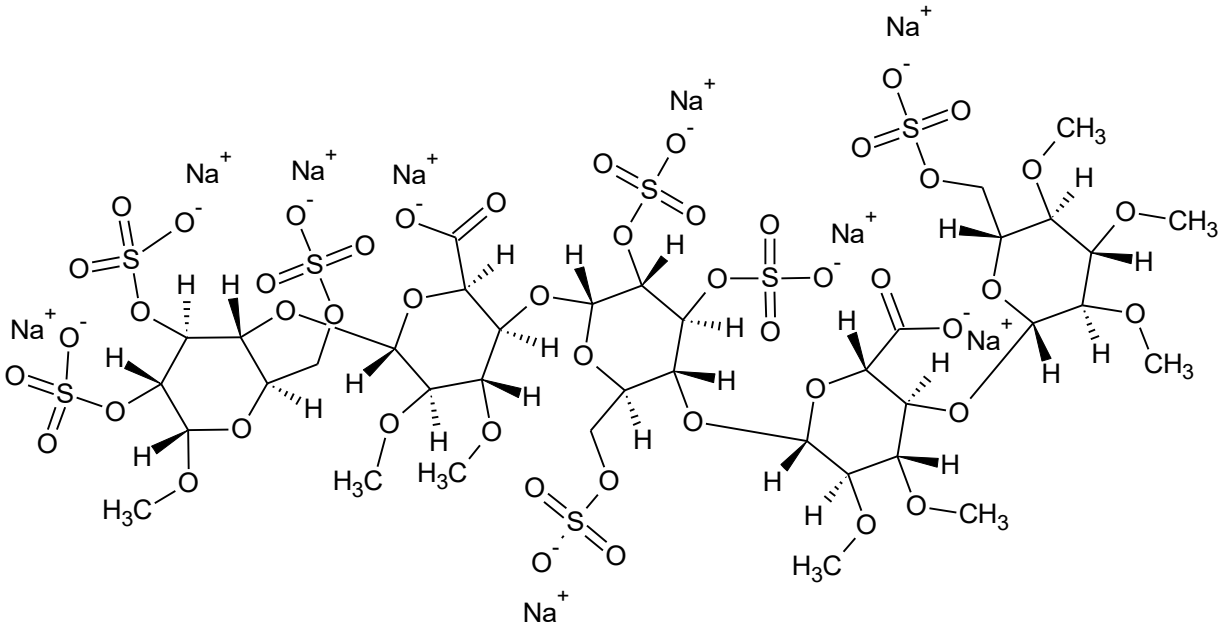
fondaparinux sodium

Arixtra®

•s.c.

•prophylaxis of deep venous thrombosis after fractures, surgical interventions etc.

Synthetic short chain heparinoids



idraparinux sodium

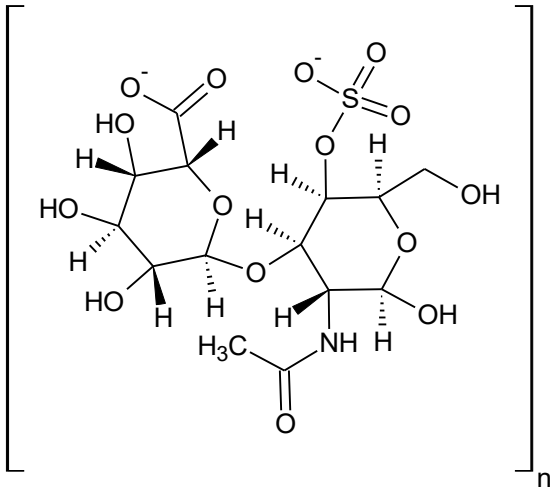
syn. SR 34006

•s.c. aplication once weekly only

•phase 3 clinical study for deep venous thrombosis or symptomatic lung embolism

Sulodexide

- a mixture containing 80 % of fast mobility heparine (FMH) and 20 % dermatan sulfate
- FMH fraction is described based on its electrophoretic mobility
- both fractions have lower degree of sulfation and lower anticoagulant activity compared to unfractionized heparin
- obtained from the porcine intestinal mucosa by a patented process
- lower $M_r \Rightarrow$ extensive oral absorption $\Rightarrow$ possibility of **oral administration**
- oral administration results in the release of tissue plasminogen activator and an increase in fibrinolytic activities
- longer $T_{1/2}$
- reduced effect on systemic clotting and bleeding
- treatment of various vascular pathologies including sudden death after MI prevention
- efficiency in treatment of deep vein thrombosis, venous leg ulcers and reduction of reperfusion injury after MI demonstrated by clinical trials
- Vessel Due ® - used
- Sulonex ® - phase 3 and 4 clinical tests for diabetic neuropathy



dermatan sulfate