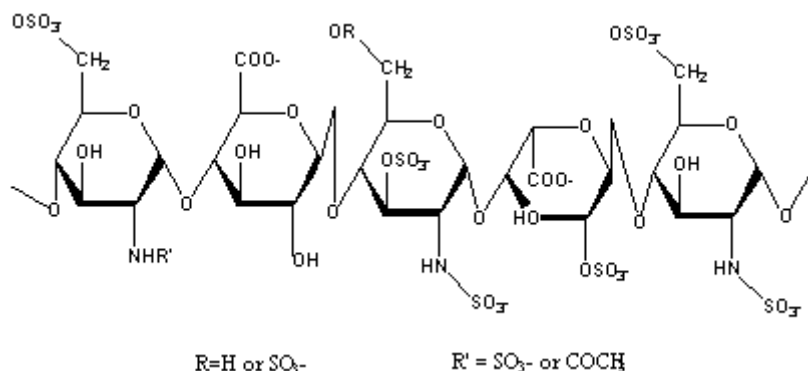


Catalog Number: 101928, 101929, 101930, 101931, 101932, 194110, 194112, 194113, 194114, 194118, 194683

Heparin

Structure: (partial - antithrombin binding site of Heparin¹)



Most of the structure of heparin can be accounted for by repeated disaccharide units consisting of 1,4-linked L-iduronic acid and D-glucosamine. The iduronic acid residues are O-sulfated at position 2, and the glucosamine residues are N-sulfated and O-sulfated at position 6. The repeated block can be interrupted or extended by residues of beta-D-glucuronic acid and 6-O-sulfated N-acetyl-alpha-D-glucosamine.^{1,38}

Heparin isolated from porcine intestinal mucosa (typically called Heparin A) is slightly different from heparin isolated from bovine lung (typically called Heparin B). Porcine heparin has several times more "extender residues" compared to the bovine heparin.¹

Molecular Weight: A mixture of polyanion chains in a relatively wide range of molecular weights. It can range from 3000 to as high as 30,000.¹ The average molecular weight tends to be 17000 - 19000. Low molecular weight fractionations are available through MP.

Form (Salt):	Ammonium	Lithium	Potassium	Calcium	Sodium
CAS #	60800-63-7	9045-22-1	9005-48-5	37270-89-6	9041-08-1

Synonym: Heparinic acid

Source: *Porcine intestinal mucosa*

Physical Description: White to off-white powder/Clear, colorless solution

Solubility: Soluble in water (50 mg/ml - clear, colorless to faint yellow solution) - essentially soluble in water up to 60% by mass; insoluble in methanol, ethanol or acetone.³⁸ Solutions are stable in the pH range 4-9 when stored at either room temperature or refrigerated temperatures. No significant change in activity is seen in solutions autoclaved at 121°C for 5 to 10 minutes²; however, autoclaving is typically not recommended for sterilization. Sterilization should be done by filtration when possible.²

Stability: Heparin salts are normally stable as a powder or in solution. It is reported to be incompatible with a number of common antibiotics.²

Activity: The USP unit is a measure of the anticoagulant properties of a given heparin product as it acts on antithrombin III (AT-III).

Description: Heparin is a polymer classified as a mucopolysaccharide or a glycosaminoglycan. It is biosynthesized and stored in mast cells of various mammalian tissues, particularly liver, lung and mucosa.¹

It is typically used as an anticoagulant. It binds to antithrombin III, a naturally occurring plasma protease inhibitor, accelerating the rate at which antithrombin III inhibits coagulation proteases (factor Xa and thrombin).^{4,8,28}

The activity of heparin as an anticoagulant has been shown to be related to the molecular weight. In the range of 6-12 kDa, heparin apparently binds to AT-III in a 1:1 stoichiometry; however, heparin with a molecular weight of 20 kDa can have two binding regions for AT-III. The probability of a third region is negligible.^{31,43} There is a correlation between molecular weight and anticoagulant activity, but it is linear only over a narrow range (8-12 kDa).⁴¹

Low molecular weight heparins (below approximately 8000; produced by oxidative depolymerization) inhibit AT-III but have a higher ratio of anti-factor Xa to anti-AT-III activity than regular heparin. They have lowered effect on platelet aggregation than normal heparin, and no significant effect on blood coagulation tests. Dosages of these low molecular weight heparins cannot be equated to those of normal molecular weight heparins.²

Typical Use: The amount of heparin needed to prevent coagulation in whole blood is between 20 units and 50 units per ml of whole blood. Typically the sodium salt is used in most blood collection.

Availability:

Catalog Number	Description	Size
101928	Heparin, Ammonium Salt; Activity approximately 100 units/mg.	50 KU 100 KU 500 KU 1000 KU
194110	Heparin, Ammonium Salt; Activity not less than 150 units/mg.	50 mg 250 mg 1 g
101929	Heparin, Lithium Salt; Activity approximately 100 units/mg	50 KU 100 KU 500 KU 1000 KU
101930	Heparin, Potassium Salt; Activity approximately 100 units/mg	100 KU 500 KU 1000 KU
194683	Heparin, Potassium Salt, cell culture reagent; Activity approximately 100 units/mg	10 KU 25 KU 50 KU 100 KU 250 KU 500 KU 1000 KU
101931	Heparin, Sodium Salt; Activity approximately 100 units/mg	25 KU 100 KU 500 KU 1000 KU
101932	Heparin, Sodium Salt Solution; Activity 1000 units/cc packed in 10 ml vials. Preserved with 1.5% benzyl alcohol.	10 ml (1 vial)
194112	Heparin, Calcium Salt; Activity not less than 150 units/mg.	250 mg 1 g
194118	Heparin, Zinc Salt; Activity not less than 150 units/mg	250 mg

		1 g
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Low Molecular Weight Heparins:

194113	Heparin, Sodium Salt, Low Molecular Weight – Average molecular weight: ~5000; Anti-Xa approximately 100–120 IU/mg	10 mg 50 mg 100 mg 250 mg
194114	Heparin, Sodium Salt, Low Molecular Weight – Average molecular weight: ~3000; Anti-Xa > 65 IU/mg	10 mg 50 mg 100 mg 250 mg

References:

1. *Merck Index*, **12th Ed.**, No. 4685.
2. *Martindale: The Extra Pharmacopoeia*, 30th Ed., J.E.F. Reynolds (ed.), Pharmaceutical Press, pp. 227-232 (1993).
3. *U.S. Pharmacopoeia*, **XXI**, p. 481.
4. "Special Report: Prevention of Venous Thromboembolism in Surgical Patients...", *Circulation*, **v. 55**, 423A-428A (1977).
5. Bágel'ová, J., et al., "Conformational stability of ferricytochrome c near the heme in its complex with heparin in alkaline pH." *Carbohydrate Polymers*, **v. 45:3**, 227-232 (2001).
6. Band, P. and Lukton, A., *Anal. Biochem.*, **v. 120**, 19 (1982) (Heparin Assay).
7. Baumann, H., et al., "Novel regio- and stereoselective O-6-desulfation of the glucosamine moiety of heparin with N-methylpyrrolidinone-water or N,N-dimethylformamide-water mixtures." *Carbohydrate Research*, **v. 308:3-4**, 381-388 (1998).
8. Bjork, I. and Lindahl, U., *Molec. Cellular Biochem.*, **v. 48**, 161 (1982).
9. Calvete, J.J., et al., "Characterisation of the conformational and quaternary structure-dependent heparin-binding region of bovine seminal plasma protein PDC-109." *FEBS Letters*, **v. 444:2-3**, 260-264 (1999).
10. Cheng, T.-J., et al., "Determination of heparin levels in blood with activated partial thromboplastin time by a piezoelectric quartz crystal sensor." *Analytica Chimica Acta*, **v. 432:1**, 101-111 (2001).
11. Capila, I., et al., "Interaction of heparin with annexin V." *FEBS Letters*, **v. 446:2-3**, 327-330 (1999).
12. Courvalin, J.C. and Dumontier, M., *J. Biol. Chem.*, **v. 257**, 456 (1982) (Solubilization of nuclear structures by the polyanion heparin).
13. Dedem, G. van, et al., *Dev. Biochem.*, **v. 12**, 19 (1981).
14. Dembny, K.D., et al., "Heparin interferes with the determination of plasma nitric oxide by inhibition of enzymatic conversion of nitrate by nitrate reductase." *Clinica Chimica Acta*, **v. 275:1**, 107-114 (1998) (Short Communication).
15. Faham, S., et al., "Diversity does make a difference: fibroblast growth factor-heparin interactions." *Current Opinion in Structural Biology*, **v. 8:5**, 578-586 (1998) (Review).
16. Fairbrother, W.J., et al., "Solution structure of the heparin-binding domain of vascular endothelial growth factor." *Structure*, **v. 6:5**, 637-648 (1998).
17. Fath, M., et al., "Interaction of soluble and surface-bound heparin binding growth-associated molecule with heparin." *FEBS Letters*, **v. 454:1-2**, 105-108 (1999).
18. Finotti, P., Pagetta, A. and Corvaja, C., "Role of reducing terminals in unfractionated and low-molecular-mass heparins in causing free radical generation and loss of structure and activity of trypsin." *International Journal of Biological Macromolecules*, **v. 26:2-3**, 135-144 (1999).
19. Gadgil, H. and Jarrett, H.W., "Heparin elution of transcription factors from DNA-Sepharose columns." *Journal of Chromatography A*, **v. 848:1-2**, 131-138 (1999).
20. Gadzekpo, V.P.Y., et al., "Development of an ion-channel sensor for heparin detection." *Analytica Chimica Acta*, **v. 411:1-2**, 163-173 (2000).
21. Gaus, K. and Hall, E.A.H., "Surface plasmon resonance sensor for heparin measurements in blood plasma." *Biosensors and Bioelectronics*, **v. 13:12**, 1307-1315 (1998).

22. Gogly, B., et al., "Influence of heparin(s) on the interleukin-1-beta-induced expression of collagenase, stromelysin-1, and tissue inhibitor of metalloproteinase-1 in human gingival fibroblasts." *Biochemical Pharmacology*, **v. 56:11**, 1447-1454 (1998).
23. Gupta, K., et al., "Mechanism of interaction of thrombospondin with human endothelium and inhibition of sickle erythrocyte adhesion to human endothelial cells by heparin." *Biochimica et Biophysica Acta/Molecular Basis of Disease*, **v. 1453:1**, 63-73 (1999).
24. Guzmán-Casado, M., et al., "Myo-inositol hexasulphate and low molecular weight heparin binding to human acidic fibroblast growth factor: a calorimetric and FTIR study." *International Journal of Biological Macromolecules*, **v. 28:4**, 305-313 (2001).
25. Hiebert, L.M., et al., "Tissue distribution and antithrombotic activity of unlabeled or ¹⁴C-labeled porcine intestinal mucosal heparin following administration to rats by the oral route." *Canadian Journal of Physiology and Pharmacology*, **v. 78:4**, 307-320 (2000).
26. Huhtala, M.T., Pentikainen, O.T. and Johnson, M.S., "A dimeric ternary complex of FGFR1, heparin and FGF-1 leads to an 'electrostratic sandwich' model for heparin binding." *Structure*, **v. 7:6**, 699-709 (1999).
27. Jiao, Q.C., et al., "Investigation on the binding site in heparin by spectrophotometry." *Talanta*, **v. 48:5**, 1095-1101 (1999).
28. Jordan, R., Beeler, D. and Rosenberg, R., "Fractionation of Low Molecular Weight Heparin Species and their Interaction with Antithrombin." *J. Biological Chemistry*, **v. 254**, 2902-2913 (1979).
29. Kinoshita, M., et al., "Identification of heparin-binding stretches of a naturally occurring deleted variant of hepatocyte growth factor (dHGF)." *Biochimica et Biophysica Acta/Protein Structure and Molecular Enzymology*, **v. 1384:1**, 93-102 (1998).
30. Krasilnikov, O.V., et al., "Heparin influence on alpha-staphylo toxin formed channel." *Biochimica et Biophysica Acta/Biomembranes*, **v. 1417:1**, 167-182 (1999).
31. Laurent, T.C., et al., *Biochem. J.*, **v. 175**, 691-701 (1978).
32. Lin, P.-H., Sinha, U. and Betz, A., "Antithrombin binding of low molecular weight heparins and inhibition of factor Xa." *Biochimica et Biophysica Acta/General Subjects*, **v. 1526:1**, 105-113 (2001).
33. Lin, Y.-H., et al., "Heparin binding to cobra basic phospholipase A2 depends on heparin chain length and amino acid specificity." *FEBS Letters*, **v. 453:3**, 395-399 (1999).
34. Lin, Y.-H., et al., "Heparin reduces the alpha-helical content of cobra basic phospholipase A2 and promotes its complex formation." *International Journal of Biological Macromolecules*, **v. 27:2**, 171-176 (2000).
35. Lindhal, U. and Hook, M., *Ann. Rev. Biochem.*, **v. 47**, 385 (1978) (Structure of heparin).
36. Mathison, S. and Bakker, E., "Improving measurement stability and reproducibility of potentiometric sensors for polyions such as heparin." *Journal of Pharmaceutical and Biomedical Analysis*, **v. 19:1-2**, 163-173 (1999).
37. Meng, F.-G., Park, Y.-D. and Zhou, H.-M., "Role of proline, glycerol, and heparin as protein folding aids during refolding of rabbit muscle creatine kinase." *The International Journal of Biochemistry and Cell Biology*, **v. 33:7**, 701-709 (2001).
38. Nachtmann, F., Atzl, G. and Roth, W.D., *Analytical Profiles of Drug Substances*, **v. 12**, K. Florey (ed.), Academic Press, pp. 215-276 (1983). Review.
39. Richman, R. and Flickinger, R.A., *Life Sci.*, **v. 35**, 911 (1984) (Stimulates cell division of cultured mammalian cells).
40. Rodén, L. and Horowitz, M.I., *The Glycoconjugates*, **v. II**, M.I. Horowitz and W. Pigman (eds.), Academic Press: New York, p. 3 (1978).
41. Rodriguez, H.J. and Vanderwielen, A.J., *J. Pharmaceutical Science*, **v. 68**, 588-591 (1979).
42. Rosenberg, R.D., *Ann. Rev. Med.*, **v. 29**, 367 (1978).
43. Rosenberg, R., et al., *Biochem. Biophys. Res. Comm.*, **v. 86**, 1319-1324 (1979).
44. Ruiz-Calero, V., Puignou, L. and Galceran, M.T., "Use of reversed polarity and a pressure gradient in the analysis of disaccharide composition of heparin by capillary electrophoresis." *Journal of Chromatography A*, **v. 828:1-2**, 497-508 (1998).
45. Sahli, A., et al., "The stability of heparin-coated liposomes in plasma and their effect on its coagulation." *Colloids and Surfaces B: Biointerfaces*, **v. 10:4**, 205-215 (1998).
46. Shuvaev, V.V., et al., "Glycation of apolipoprotein E impairs its binding to heparin: identification of the major glycation site." *Biochimica et Biophysica Acta/Molecular Basis of Disease*, **v. 1454:3**, 296-308 (1999).
47. Sibinga, C.T.S., et al., *Thromb. Haemostasis*, **v. 51**, 12 (1984) (Increases yield of factor VIII in the purification and concentration process).
48. Varshavskaya, M.Ya., et al., *Anal. Biochem.*, **v. 95**, 449 (1979) (production and immobilization of heparin).
49. Zhou, H., et al., "The solution structure of the N-terminal domain of hepatocyte growth factor reveals a potential heparin-binding site." *Structure*, **v. 6:1**, 109-116 (1998).