



Supplementary Figure 1: FTIR-ATR spectra. 1st derivative plots; 5 x 32 scans for both precursor and sulphated carbohydrates that possess high inhibitory activity.

Supplementary Material

Table S1: Modified heparin-like molecules tested in assays

Mucosal Heparin (porcine) (MH)
MH tNAc total deNS/reNAc (tNAc)
MH gc (glycol split) periodate treated/NaBH ₄ reduced.
MH gc deNS
MH gc (pNAc) i.e. partial deNS/reNAc (has NS/NAc)
MH gc (tNAc)
MH gc Smith deg ~4-5kDa 16mers
MH gc de2S
MH gc de2S pNAc i.e. partial deNS/reNAc (has NS/NAc)
MH gc de2S tNAc
MH gc epoxide i.e. part de2S
MH de2S
MH de2S part deNS/NAc
MH de2S total deNS/NAc
MH de6S
MH gc de6S
MH gc de2S de6S
MH deS, reNS
MH gc deS, reNS
MH part de2S
MH gc butyrate (hydroxyl groups acylated)
MH gc hexyl
MH CR (carboxyl reduced)
MH fully deS i.e. GlcNH-IdoA-
LH (Bovine lung heparin) Calbiochem (90% GlcNS6S-IdoA2S)
LH de2S (GlcNS6S-IdoA)
LH de2S pNAc
LH de2S tNAc (GlcNAc6S-IdoA)
LH de2S part gc split (A) 40-50% of UA residues split open
LH de2S gc split part deNS/NAc
LH de2S gc split total deNS/NAc (GlcNAc6S-Ido)
MH 5kDa LMWH (sigma)
MH 5kDa gc split
MH 5kDa gc split part deNS/NAc
MH 5kDa gc de2S
MH 5kDa part de2S gc
MH 5kDa de2S
MH 5kDa de6S
LMWH ~3kDa,
MH H ₂ O ₂ 3-4kDa
MH H ₂ O ₂ 3-4kDa part deNS/NAc
MH H ₂ O ₂ 3-4kDa gc split
MH H ₂ O ₂ 3-4kDa gc de2S
MH H ₂ O ₂ 3-4kDa gc de2S part deNS/NAc
MH Sigma 3kDa
MH Sigma 3kDa gc
MH Sigma 3kDa de2S
MH 3kDa gc de2S Sigma
Enoxaparin 3kDa LMWH
Enoxaparin gc 3kDa
Bemiparin LMWH 3kDa
Bemiparin gc
MH 3kDa-CHO ~3kDa
MH gc-3kDa-reduced
MH gc-3kDa-NAc (deNS/reNAc)

MH 3kDa gc-CHO + 4-phenylsemicarbazide
MH 3kDa gc-CHO + Benzhydrazide
MH 3kDa gc-CHO + Anthranilic acid (NH₂-Qm-COOH)
MH 3kDa gc-CHO + ANTS (1,3,6 triSO₃-aminonaphthaline)
MHS Celsus #10595 12-15kDa Highly sulfated HS
MHS Celsus HS1098 15kDa lowly sulfated HS
Sulodexide (low sulfated heparin/low MW DS 80:20, orally available)
Arixtra (Synthetic heparin pentasaccharide)
Arixtra de2/3 deS
Arixtra gc
CS A (4S) whale cartilage
CS A peroxide cleaved 2hr ~10kDa
CS A peroxide cleaved 4hr ~5kDa
CS B dermatan S (skin)
CS C shark cartilage
CS C peroxide cleaved 2hr ~10kDa
CS C peroxide cleaved 4hr ~5kDa
CS D shark cartilage
Fucoidan

Abbreviations;

MH: Mucosal heparin (porcine),

MHS: Mucosal heparin sulfate (porcine)

LH: lung heparin (bovine) ~12.5kDa 90% GlcNS6S-IdoA2S (bovine)

gc: periodate treated (glycol split) to open non-sulfated GlcA/IdoA rings resulting in higher flexibility and no anticoagulant activity

de2S: removal of 2S group from IdoA2S resulting in low/no anticoagulant and less protein binding

de6S: removes 6S from GlcNS6S i.e. GlcNS-IdoA2S

pNAc: partially deNS (~50%) to replace NS residues with NAc resulting in 50% less N-sulfation

NAc: fully deNS and reNAc resulting in compounds with no anticoagulant activity and reduced protein binding

CR : decarboxylated, that is -COOH motifs become -CH₂OH resulting in no anticoagulation activity

MH-butyrate: OH groups are esterified with the corresponding anhydride

Supplementary Table 2: Source of compound precursor and preparation method of sulfated polysaccharides

Compound	Source	Preparation method(s)
i-carrageenan	Sigma-Aldrich	Chlorosulfonic acid
k-carrageenan	Dextra Laboratories	Chlorosulfonic acid
λ-carrageenan	Dextra Laboratories	Chlorosulfonic acid or Pyridine sulfur trioxide [†]
Agarose sulfate	Sigma-Aldrich	Chlorosulfonic acid or Pyridine sulfur trioxide [†]
Alginic sulfate	Sigma-Aldrich	Chlorosulfonic acid or Piperidine-N-sulfonic acid ^{\$}
Amylopectin sulfate	Sigma-Aldrich	Chlorosulfonic acid
Amylose sulfate	Sigma-Aldrich	Chlorosulfonic acid
Arabic sulfate	Sigma-Aldrich	Chlorosulfonic acid or Piperidine-N-sulfonic acid ^{\$}
Ardeparin	Celsus Glycoscience	N/A
Carboxymethyl cellulose sulfate	Sigma-Aldrich	Chlorosulfonic acid
Certoparin	Novartis	N/A
Chitosan sulfate	Dextra Laboratories	Chlorosulfonic acid or Pyridine sulfur trioxide [†]
Curdlan sulfate ^{\$}	WAKO Chemicals	Piperidine-N-sulfonic acid ^{\$}
Cyclodextrin sulfate	Sigma-Aldrich	Chlorosulfonic acid
Danaparoid	EDQM (Conseil de l'Europe)	N/A
Ethyl cellulose sulfate	Sigma-Aldrich	Chlorosulfonic acid
Fucogalactan sulfate	Dextra Laboratories	Chlorosulfonic acid
Gellan sulfate	Sigma-Aldrich	Chlorosulfonic acid
Ghatti Sulfate	Sigma-Aldrich	Chlorosulfonic acid or Pyridine sulfur trioxide [†]
Glycogen sulfate	Sigma-Aldrich	Chlorosulfonic acid
Guar sulfate	Sigma-Aldrich	Chlorosulfonic acid or Pyridine sulfur trioxide [†]
Gum Rosin sulfate	Sigma-Aldrich	Chlorosulfonic acid
Hydroxyethyl cellulose sulfate	Sigma-Aldrich	Chlorosulfonic acid
Hypromellose sulfate	Sigma-Aldrich	Chlorosulfonic acid
Inulin sulfate	Sigma-Aldrich	Chlorosulfonic acid
Karaya sulfate	Sigma-Aldrich	Chlorosulfonic acid
Konjac glucomannan sulfate	Dextra Laboratories	Chlorosulfonic acid
Levan sulfate	Sigma-Aldrich	Chlorosulfonic acid
Locust bean gum sulfate	Sigma-Aldrich	Chlorosulfonic acid or Pyridine sulfur trioxide [†]
Methylcellulose sulfate	Sigma-Aldrich	Chlorosulfonic acid
Paramylon sulfate	WAKO Chemicals	Chlorosulfonic acid
Pectin sulfate	Sigma-Aldrich	Pyridine sulfur trioxide or Piperidine-N-sulfonic acid ^{\$}
Penoxyacetyl cellulose sulfate	Sigma-Aldrich	Chlorosulfonic acid
Propyleneglycol alginic sulfate	Dextra Laboratories	Chlorosulfonic acid
Propylmethyl sulfate	Sigma-Aldrich	Chlorosulfonic acid
Psyllium seed gum sulfate	Dextra Laboratories	Chlorosulfonic acid
Psyllium sulfate	Sigma-Aldrich	Chlorosulfonic acid
Pullulan sulfate	Sigma-Aldrich	Pyridine sulfur trioxide

Scleroglucan sulfate	Dextra Laboratories	Chlorosulfonic acid or Pyridine sulfur trioxide [†]
Starch sulfate	Sigma-Aldrich	Chlorosulfonic acid
Storax sulfate	Sigma-Aldrich	Chlorosulfonic acid
Sulodexide	Celsus Glycoscience	Chlorosulfonic acid
Tara sulfate	Sigma-Aldrich	Chlorosulfonic acid
Taramind sulfate	Sigma-Aldrich	Chlorosulfonic acid
Tinzaparin	EDQM (Conseil de l'Europe)	N/A
Tragacanth sulfate	Sigma-Aldrich	Chlorosulfonic acid
Tylose sulfate	Sigma-Aldrich	Chlorosulfonic acid
Welan sulfate	Dextra Laboratories	Chlorosulfonic acid
Xanthan sulfate	Sigma-Aldrich	Chlorosulfonic acid
Xylan sulfate	Sigma-Aldrich	Chlorosulfonic acid

Supplementary Table 3: Anticoagulant potential of sulfated compounds possessing potent inhibitory potential as assessed by activated partial thromboplastin time.

Compound	EC₅₀ aPTT (ug.mL⁻¹)	Ratio EC₅₀^{Compound} / EC₅₀^{Hep}
Porcine Mucosal Heparin (Na ⁺ ; Applichem)	0.27	1
Dextran sulfate [†]	40.12	149
Chemically over-sulfated i-carrageenan	7.56	28
Inulin sulfate	1151.00	4263
Chemically over-sulfated λ-carrageenan [†]	4.13	15
Propyleneglycol alginic sulfate	6.29	23
Psyllium sulfate	2.64	10
Pullulan sulfate [†]	2.59	10
Scleroglucan sulfate	5.43	20
Tragacanth sulfate	4.85	18
Xylan sulfate [#]	0.53	2