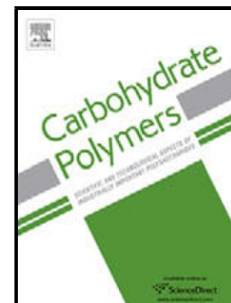


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Probing cleavage promiscuity of heparinase III towards chemoenzymatically synthetic heparan sulfate oligosaccharides

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Highlights

- A serial of synthetic HS oligosaccharides was used as substrates of Hep III.
- The primary sites of trisaccharides was different reactive to Hep III cleavage.
- Variably modified substrates was much less reactive to Hep III cleavage.
- Hep III size-dependently cleaved substrates and preferred for internal linkages
- Cleavage promiscuity arose from distinct affinity or incorrect binding to Hep III.

Abstract

An insightful investigation into specificity of bacterial heparinase III has been intriguingly difficult due to heterogeneity of polymeric substrates. Herein, we chemoenzymatically synthesized a tailored library of HS oligosaccharides as substrates. A ~15-fold reactivity difference to heparinase III was found between trisaccharides bearing different primary cleavage sites. Variable glucosamine modification decreased reactivity of trisaccharides by >20-fold compared with their counterpart primary substrates, while iduronate-containing secondary linkage showed slightly less sensitivity. The 2-sulfated iduronate residue extremely reduced reactivity to its adjacent primary site at reducing end of oligosaccharides, but showed marginal influence on the non-reducing site. Moreover, oligosaccharide susceptibility to digestion was size-dependent and had an obvious preference for the internal linkages over those near to non-reducing/reducing ends. Surface plasmon resonance revealed cleavage promiscuity attributed to different affinities or incorrect binding

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