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Synthetic oligosaccharides can replace animal-sourced low-molecular weight heparins

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Low-molecular weight heparin (LMWH) is used clinically to treat clotting disorders. As an animal-sourced product, LMWH's supply chain reliability is a concern for regulatory agencies. Here, we demonstrate the synthesis of heparin dodecasaccharides (12-mers) at gram-scale. *In vitro* and *ex vivo* experiments demonstrate that the anticoagulant activity of the 12-mers could be reversed using protamine. The 12-mer-1 reduced the size of blood clot in the mouse model of deep vein thrombosis, and attenuated circulating procoagulant markers in the mouse model of sickle-cell disease. The 12-mer-1 was examined in a non-human primate model to determine its pharmacodynamic parameters. A 7-day toxicity study in a rat model showed no toxic effects. The data suggest that a synthetic homogeneous oligosaccharide can replace animal-sourced LMWHs. In this seminar, the synthesis of homogenous LMWH, *in vitro* and *ex vivo* studies which demonstrate that the anticoagulant activity and reversibility of synthetic dodecasaccharides, and animal studies which suggest a synthetic homogeneous oligosaccharide can replace animal-sourced LMWHs will be discussed.

Biography

Yongmei Xu has her expertise in synthesis of heparin and heparin sulfate. She developed a chemoenzymatic method to synthesize structurally defined heparin analog. The method dramatically improved the synthesis efficiency and the product yield especially for larger size and diverse sulfate patterns. Now she is working on library synthesis and biologic function of heparin sulfate. It opens a new opportunity to develop synthetic heparin-based therapeutics.

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