Novel Chemoenzymatic Synthesis Of Heparin And Heparan Sulfate

Tech ID: 23616 / UC Case 2010-207-0

ABSTRACT

Heparin and heparan sulfate (HS) are complex polysaccharides with incredible diversity. They play important roles in many physiological and pathological processes such as regulating cancer growth, blood coagulation, inflammation, assisting viral and bacterial infections, and cell differentiation. Heparin and low molecular weight heparin are the leading therapeutic of choice for use as anticoagulants or antithrombotics today. Researchers at UC Davis have developed a very cost effective and highly efficient method to synthesize heparin and HS oligosaccharide analogs.

FULL DESCRIPTION

While Heparin, low molecular weight Heparin, and ultralow molecular weight synthetic heparin are used quite frequently, current synthetic methods are quite difficult and do not create all possible heparin or HS oligosaccharide sequences. While chemical synthesis provides a greater variety of homogenous heparin and HS, they are time consuming, tedious, and have quite insufficient yields. Comparatively an enzymatic synthesis is dependent on polysaccharide modification, inevitably leads to the formation of inherently heterogeneous products, which are not as desirable as homogenous products.

Researchers at the University of California, Davis have developed a highly efficient and convenient one-pot multi-enzyme chemoenzymatic approach for synthesizing heparin and HS oligosaccharide analogs of designed sequences by assembling inexpensive chemically modified monosaccharides. This method efficiently combines the diversity of organic synthesis and the highly efficient, regio- and stereo-selective enzymatic approaches in a very cost effective manner.

APPLICATIONS

▶ Method to manufacture synthetic homogenous oligosaccharide analogs for use as therapeutics.

FEATURES/BENEFITS

▶ Methodology is dependent on an enzyme system with broad substrate specificity to ensure homogenous products.
▶ High yield with complete regio- and stereo-control
▶ Simplified isolation and purification of desired products.
▶ Reactions are carried out in water, which can decrease exposure to otherwise environmentally unfriendly organic solvents
▶ Very expensive sugar nucleotides, such as UDP-GlcNAc and UDP-uronic acid, can be generated in situ from inexpensive starting materials.

PATENT STATUS

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ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

▶ Automated Chemoenzymatic Synthesis Of Glycans And Glycoconjugates
▶ A Photobacterium Sp. Alpha2-6-Sialytransferase 9Psp2.6St) A366g Mutant With Increased Expression Level And Improved Activity In Sialylating Tn Antigen
▶ Synthesis of Capsular Polysaccharides
▶ Using Escherichia coli to Produce Human Milk Oligosaccharide Lactodifucotetraose
▶ Stable N-acetylated analogs of Sialic Acids and Sialosides
▶ Alpha1–2-Fucosyltransferase for Enzymatic Synthesis of Alpha1–2-linked Fucosylated Glycans
▶ One-Pot Multienzyme Synthesis of Sialidase Reagents, Probes and Inhibitors