Enzyme Engineering
ISSN: 2329-6674
Abstract

Highly Efficient and Controllable Method for Sulfation of Complex Carbohydrates

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Abstract:

Body Sulfated glycosaminoglycans (GAGs) are important biological molecules, a number of which, for example heparin, Fondaparinux Sodium (ARIXTRA®) and Pentosan Polysulfate Sodium (ELMIRON®), have been in clinical use for decades. A key step in the preparation of homogeneous sulfated carbohydrates is efficient, reproducible and scalable chemical O- and N-sulfation method. A significant difficulty that arises during attempts to sulfate polyfunctional substrates using conventional approaches is incomplete conversion and unpredictable outcome. In this presentation we describe a new chemical sulfation method [1] successfully applied to O- and N-sulfation of a wide range of substrates for synthesis of a library of discrete homogeneous heparan sulfate fragments ranging from mono to octa-saccharides which has been exploited to uncover the specific binding interactions of pure GAG fragments with proteins and in metalloorganic complexes [2,3,4]. In the meantime we exploited this new method to acquire a library of densely sulfated GAG mimetics as potent inhibitors of EV71 infection [5]. We also successfully extended this new protocol to sulfate a polyol substrate on a scale of 232 grams in the academic lab and transferred the technology to GMP production (7 kg scale) of a lead drug candidate currently in a human clinical trial for therapeutic development against sepsis.

Biography:

Chih-Wei had worked in pharmaceutical industry for 5 years before he completed his join-PhD from Université Paris-Sud, ICSN du CNRS in France and National Chiao Tung University (NCTU) in Taiwan. Postdoctoral Studies from Academia Sinica in Taiwan, mainly focus on total synthesis of natural product. He is currently research fellow of Institute for Glycomics in Griffith University in Australia since 2011. He has published more than 16 papers in reputed journals, 2 awarded and 1 granted patents.

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Citation: Chih-Wei Chang ; Highly Efficient and Controllable Method for Sulfation of Complex Carbohydrates ; Glycobiology 2020; June 24, 2020; Berlin, Germany.