Griffith UNIVERSITY
Institute for Glycomics
Queensland, Australia

Sulfated Polysaccharides for Wound Management

Using novel intermediates, we have developed a synthetic method to readily access homogenous synthetic heparan mimetics.

Sulfated polysaccharides have been long-recognised for their biological activity. Glycosaminoglycan (GAG) and heparin mimetics are now being used to treat indications such as cancer, inflammatory diseases and blood disorders, among others. Sulfated GAGs are able to act as anti-cancer agents by inhibiting heparanase, a protein that facilitates the spread of tumour cells, and retarding angiogenesis by binding to growth factors. Synthetic heparin mimetics are also being pursued to mitigate off-target effects and maximise therapeutic benefits.

Additionally, sulphated polysaccharides are emerging as high-value drugs and biomaterials for use in wound management and tissue engineering. Many naturally-derived sulphated polysaccharides used in wound healing are derived from plants, seaweed and algae. Typically, these materials show low toxicity and good biocompatibility with human tissue, however suffer significant inherent variability, which makes commercial production challenging. Alternatively, synthetic biomolecules demonstrate excellent physical properties but can be difficult to manufacture. This is particularly the case for complex sulphated polysaccharides, where incomplete sulfation on polyfunctional substrates is a significant problem.

Our approach to carbohydrate and sulfation chemistry overcomes the main issues of synthetically-derived sulphated polysaccharide. Using our proprietary methods and expertise allows synthesis of polymers with (a) a variety of repeating sequences or backbone chemistry, (b) specific sulfation patterns (O- or N-sulfated), (c) varied sulfation frequency, (d) improved purity and (e) a safe, simplified synthesis.

The Technology

Using our world-leading expertise in carbohydrate chemistry, we have developed a series of key oligosaccharide intermediates that allow for versatile synthesis of heparin and heparan mimetics.

Our novel sulfation method enables selective or complete conversion to sulfated functional groups on a range of carbohydrate templates. The method provides a general means for synthesis of O- or N-sulfated materials with significant improvement in yield and ease of purification. We have used this process to produce, in the lab, gram-scale quantities of heparin mimetic, fondaparinux, reducing the number of steps by 10% and improving the yield.

The Market

Acute wounds typically progress through the three stages of healing (inflammation, proliferation and matrix remodelling) with or without intervention, within a short period. Chronic wounds, however, are those that are arrested in one of these stages and remain unhealed after approximately four weeks. Chronic wounds require long-term treatment at significant cost. Increases in the frequency of causal morbidities such as obesity and diabetes, along with an increasing aging population is resulting in an increase in the socieo-economic burden of chronic wounds. In 2009 an estimated 6.5 million US patients were affected by chronic

wounds, causing an annual economic burden of $25 billion. Additionally, recurrence rates between 23 – 60 % have been reported for pressure, venous and diabetic ulcers.

The global wound care market is estimated to reach US$20.4 billion by 2021. This market is divided into three segments including: basic products, such as bandages and Band-Aids; surgical products, such as sutures and staples; and, advanced products, such as bioengineered skin, hydrocolloids and growth factors. Advanced wound care is typically required for the treatment of chronic wounds and its associated market is estimated to reach US$10.08 billion by 2020, up from US$8.25 billion in 2015.

Comparable polysaccharides alginate, carrageenan and agar extracted from seaweed, are frequently used in pharmaceutical products, including those for wound management. Together they have a gross market value of US$47.5 million/year for pharmaceutical applications alone. Quality controlled, synthetic manufacture of equivalent compounds for medical applications would capture a significant portion of this market.

Intellectual Property

A provisional patent application has been filed on our unique sulfation method, describing significant yield improvement, ease of purification and ease of access to heparin mimetics and poly-sulfated compounds. The Provisional patent was filed in December 2017. Additional patents will be filed on newly developed intellectual property around novel intermediates and derivatives of heparan mimetics.

Our Development Capacity

The Institute boasts a strong carbohydrate chemistry program, ranging from small molecule drug development to novel oligosaccharide synthesis. We have undertaken pilot scale sulfated oligosaccharide synthesis programs with a number of biotech companies. Subsequent technology transfer of our chemistry processes to GMP manufacturing facilities resulted in production of lead compounds that have emonstrated success in Phase I human clinical trials.

Led by Professor Mark von Itzstein, our synthetic carbohydrate chemistry team possesses many years of industry experience and a proven track record of developing drugs for market.

Opportunity for Partnership

We are seeking an industry partner with an interest in the use of sulfated polysaccharides for tissue engineering and wound management, with the opportunity to extend the program to other applications. The partner would be offered an exclusive option to license our proprietary methods for the synthesis of novel intermediates *en route* to heparin/heparan mimetics and other sulfated polyssacharides, together with discrete lead molecules developed during the funded co-development program.

RESEARCH LEADER

Professor Mark von Itzstein is widely recognised as a world leader in antiviral drug discovery, glycobiology and glycochemistry. He led the discovery of the world's first influenza drug Zanamivir, now marketed by GSK with sales reaching US$1.1 billion per annum. Prof. von Itzstein's use of a carbohydrate template to make an anti-viral drug was revolutionary and he continues to publish in leading journals such as Nature Chemical Biology.

ABOUT US

The Institute for Glycomics is a flagship biomedical research institute at Griffith University's Gold Coast Campus in Queensland, Australia. The Institute is one of only six of its kind worldwide and has a strategic focus on translating drug and vaccine discovery research into clinical outcomes. We have a strong track record in commercialisation and industry engagement, and our research leaders and business personnel have extensive experience in developing technologies for the commercial market. With over 230 multidisciplinary researchers and support staff, the Institute for Glycomics is well positioned to deliver tangible clinical solutions for infectious diseases and cancer.

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