



DEVELOPMENT OF SYNTHETIC HEPARIN MIMETICS

Using novel intermediates, we have developed a synthetic method to readily access fondaparinux and other synthetic heparin mimetics.

Fondaparinux Sodium is an anticoagulant medication chemically related to low molecular weight heparins (LMWH). It is marketed as Arixtra by GlaxoSmithKline with generic versions now available worldwide.

For over 30 years, fondaparinux has been used extensively for the prevention of thrombosis in surgery patients and the treatment of deep vein thrombosis and pulmonary embolism.

Increasingly, glycosaminoglycan (GAG) and heparin mimetics are being used to treat other indications, including cancer and inflammatory disease. 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 now being pursued to reduce unwanted off-target effects and maximise therapeutic benefits.

The Technology

Through our world-leading carbohydrate chemistry expertise, we have developed a series of key pentasaccharide intermediates that provide direct access to fondaparinux and allow for versatile synthesis of heparin mimetics.

Our novel synthetic process to make gram-scale amounts of fondaparinux, which is further scalable, reduces the number of

synthetic steps by 10% compared to most methods, and improves the overall yield up to 1.0%. This ultimately could be used to reduce the cost of synthesising commercial amounts of fondaparinux.

Synthetic Heparin Market

The global market value of fondaparinux in 2013 was around US\$475 million and is expected to grow to nearly US\$700 million by 2024. Driving this growth is the increasing geriatric population and rising prevalence of thrombosis worldwide. In China, there is a growing demand for fondaparinux due to the increased burden of chronic diseases witnessed by those of middle-to-high socioeconomic standing.

While the market for fondaparinux is growing rapidly, low molecular weight heparin (LMWH) is more commonly used to prevent thrombosis. This is despite fondaparinux being more cost-effective as a prophylaxis regimen and exhibiting fewer adverse effects than LMWH. Reduced costs of fondaparinux may drive greater acceptance in the clinic, increasing market share.

The global market for heparin products is around US\$10 billion, with strong growth predicted to extend revenue to over \$US14 billion by 2023. The market for heparin in the oncology space has yet to be substantiated due to the lack of any approved drug on the market. There are heparin mimetics currently in clinical trials for the treatment of various cancers, and these compounds are seen as a viable and exciting therapeutic strategy for cancer. A potent anti-cancer heparin mimetic would be expected to achieve blockbuster global sales.

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 and conducted technology transfer of chemistry processes to GMP manufacturing facilities for other lead compounds that have subsequently been evaluated in Phase 1 human clinical trials.

Led by Professor Mark von Itzstein AO, our synthetic heparin 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 synthetic heparin space to co-develop fondaparinux and heparin mimetics for the anti-coagulation and oncology markets, 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 fondaparinux and heparin mimetics together with discrete lead molecules developed during the funded co-development program.



Research Leader

Professor Mark von Itzstein AO 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.

Professor 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 in the world 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 200 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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