Molecular imprinting for sustainable downstream processing of biopharmaceuticals

Gyorgy Szekely from the University of Manchester and Tibor Nagy from Fujifilm Diosynth Biotechnologies worked together on a project funded by a BioProNET Proof of Concept award. Their work aimed to make downstream processing more efficient.

The problem

Downstream processing — the recovery and purification of biosynthetic products after fermentation — accounts for up to 80% of the entire production costs of biopharmaceuticals due to the multi-step approaches used and high product loss.

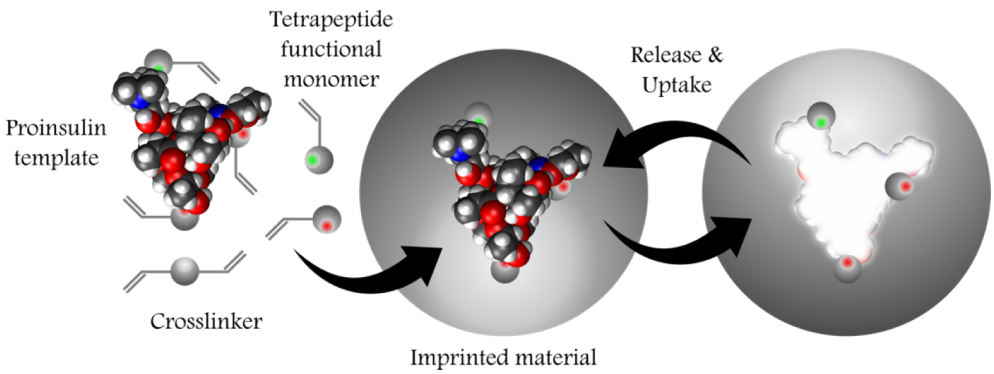
Project aims

The aim of the project is to replace the currently used multistep chromatography approaches in downstream processing with a single downstream operation unit that uses molecularly imprinted membranes.

What is molecular imprinting?
A technique that is used to create synthetic polymers containing custom-made binding sites for a specific target, such as a biological drug.

The project

This project aimed to make molecularly imprinted materials that can purify insulin from proinsulin. Insulin was chosen as an exemplar molecule to ensure a high chance of success as its physical and chemical properties, manufacturing, purification and structure and so on are all well-documented.



Results

Both pH-responsive hydrogels and microspheres were developed to capture the insulin subpart of proinsulin, and release insulin after the enzymatic digestion. The most laborious part of the work was to design and prepare a modified tetrapeptide functional monomer, which mimics the biological receptor for insulin.

Once this was achieved through a vinylbenzoic acid derivative, the tetrapeptide was characterised using NMR and MS techniques confirming its chemical structure. The tetrapeptide and the proinsulin was allowed to self-assemble, and their complex was incorporated into a polymer matrix, the imprinted material.

Rebinding studies of proinsulin and insulin were performed, confirming the success of the imprinting procedure. Finally, the pH sensitivity of the hydrogels was investigated in order to optimise the proinsulin uptake and insulin release.

Next steps

Firstly, the collaborators will consider patenting and publishing the research outcomes. They are also in discussions to apply for a larger grant to expand the scope of the project covering more complex biopharmaceuticals, and focusing more on the process aspects than materials science

"Molecular imprinting has not been used in biopharmaceutical molecule purification process. Successful implementation of the technology would fundamentally change the drug process development approach in the future."
Tibor Nagy, Fujifilm Diosynth Biotechnologies.