

Chance meeting leads to creation of antibiotic spider silk

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Credit: University of Nottingham

A chance meeting between a spider expert and a chemist has led to the development of antibiotic synthetic spider silk.

After five years' work an interdisciplinary team of scientists at The University of Nottingham has developed a technique to produce chemically functionalised spider silk that can be tailored to applications used in drug delivery, regenerative medicine and wound healing.

The Nottingham research team has shown for the first time how 'click-chemistry' can be used to attach molecules, such as antibiotics or fluorescent dyes, to artificially produced spider silk synthesised by *E. coli* bacteria. The research, funded by the Biotechnology and Biological Sciences Research Council (BBSRC) has been published in the online journal *Advanced Materials*.

The chosen molecules can be 'clicked' into place in soluble silk protein before it has been turned into fibres, or after the fibres have been formed. This means that the process can be easily controlled and more than one type of molecule can be used to 'decorate' individual silk strands.

Nottingham breakthrough

In a laboratory in the Centre of Biomolecular Sciences, Professor Neil Thomas from the School of Chemistry in collaboration with Dr Sara

Goodacre from the School of Life Sciences, has led a team of BBSRC DTP-funded PhD students starting with David Harvey who was then joined by Victor Tudorica, Leah Ashley and Tom Coekin. They have developed and diversified this new approach to functionalising 'recombinant'—artificial—spider silk with a wide range of small molecules.

They have shown that when these 'silk' fibres are 'decorated' with the antibiotic levofloxacin it is slowly released from the silk, retaining its anti-bacterial activity for at least five days.

Neil Thomas, a Professor of Medicinal and Biological Chemistry, said: "Our technique allows the rapid generation of biocompatible, mono or multi-functionalised silk structures for use in a wide range of applications. These will be particularly useful in the fields of tissue engineering and biomedicine."

Remarkable qualities of spider silk

Spider silk is strong, biocompatible and biodegradable. It is a protein-based material that does not appear to cause a strong immune, allergic or inflammatory reaction. With the recent development of recombinant spider silk, the race has been on to find ways of harnessing its remarkable qualities.

The Nottingham research team has shown that their technique can be used to create a biodegradable mesh which can do two jobs at once. It can replace the extra cellular matrix that our own cells generate, to accelerate growth of the new tissue. It can also be used for the slow release of antibiotics.

Professor Thomas said: "There is the possibility of using the silk in advanced dressings for the treatment of slow-healing wounds such as diabetic ulcers. Using our technique infection could be

prevented over weeks or months by the controlled release of antibiotics. At the same time tissue regeneration is accelerated by silk fibres functioning as a temporary scaffold before being biodegraded."

The medicinal properties of spider silk recognised for centuries.

The medicinal properties of spider silk have been recognised for centuries but not clearly understood. The Greeks and Romans treated wounded soldiers with spider webs to stop bleeding. It is said that soldiers would use a combination of honey and vinegar to clean deep wounds and then cover the whole thing with balled-up [spider webs](#).

There is even a mention in Shakespeare's *Midsummer Night's Dream*: "I shall desire you of more acquaintance, good master cobweb," the character 'Bottom' said. "If I cut my finger, I shall make bold of you."

'I think we could make that!'

The idea came together at a discipline bridging university 'sandpit' meeting five years ago. Dr Goodacre says her chance meeting at that event with Professor Thomas proved to be one of the most productive afternoons of her career.

Dr Goodacre, who heads up the SpiderLab in the School of Life Sciences, said: "I got up at that meeting and showed the audience a picture of some spider silk. I said 'I want to understand how this silk works, and then make some.'

"At the end of the session Neil came up to me and said 'I think my group could make that.' He also suggested that there might be more interesting 'tweaks' one could make so that the silk could be 'decorated' with different, useful, compounds either permanently or which could be released over time due to a change in the acidity of the environment."

The approach required the production of the silk proteins in a bacterium where an amino acid not normally found in proteins was included. This amino acid contained an azide group which is widely used in 'click' reactions that only occur at

that position in the protein. It was an approach that no-one had used before with spider silk—but the big question was—would it work?

Dr Goodacre said: "It was the start of a fascinating adventure that saw a postdoc undertake a very preliminary study to construct the synthetic silks. He was a former SpiderLab PhD student who had previously worked with our tarantulas. Thanks to his ground work we showed we could produce the silk proteins in bacteria. We were then joined by David Harvey, a new PhD student, who not only made the silk fibres, incorporating the unusual amino acid, but also decorated it and demonstrated its antibiotic activity. He has since extended those first ideas far beyond what we had thought might be possible."

David Harvey's work is described in this paper but Professor Thomas and Dr Goodacre say this is just the start. There are other joint SpiderLab/Thomas lab students working on uses for this technology in the hope of developing it further.

David Harvey, the lead author on this their first paper, has just been awarded his PhD and is now a postdoctoral researcher on a BBSRC follow-on grant so is still at the heart of the research. His current work is focused on driving the functionalised spider silk technology towards commercial application in wound healing and tissue regeneration.

Where will we be in 5 years' time?

Dr Goodacre said: "It is likely that this paper is just the start of a very exciting range of studies using the new [spider silk](#) material. Some of the future work will also be supported by other, neat ideas from the world of spiders and their silk, which the SpiderLab is currently trying to unravel."

More information: David Harvey et al. Antibiotic Spider Silk: Site-Specific Functionalization of Recombinant Spider Silk Using "Click" Chemistry, *Advanced Materials* (2016). DOI: [10.1002/adma.201604245](https://doi.org/10.1002/adma.201604245)

Provided by University of Nottingham

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