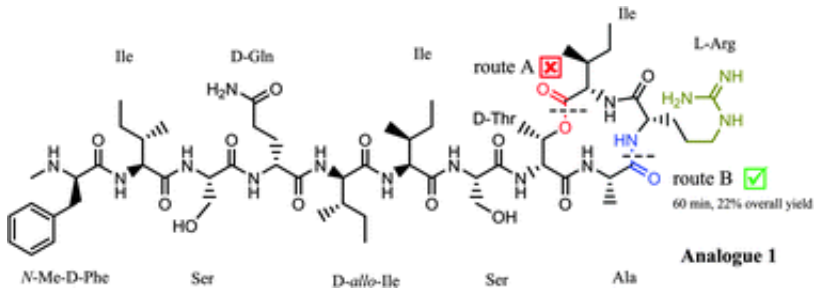
UK scientists pioneer synthetic forms of 'game-changing' antibiotic

April 27 2016, by Elizabeth Allen



Scientists at the University of Lincoln, UK, have successfully produced two synthetic derivatives of Teixobactin – the world's first known antibiotic capable of destroying 'drug resistant' bacteria.

Last year, the discovery of the antibiotic Teixobactin by researchers in the USA was hailed as a 'game-changer' in the fight against antimicrobial resistance.

Teixobactin, which kills a range of pathogens without detectable resistance, was isolated from microorganisms (which do not grow under laboratory conditions) found in soil – the natural source of nearly all antibiotics developed since the 1940s.

However in order for it to be developed as a potential drug treatment,

several versions of the antibiotic must be produced via chemical synthesis in order to overcome the hurdles of drug development. Researchers in laboratories around the world have been working towards this objective since last year's breakthrough.

Now Dr Ishwar Singh from the University of Lincoln and his colleagues have become the first group of scientists to synthetically produce two derivatives of Teixobactin.

Dr Singh, a specialist in novel drug design from Lincoln's School of Pharmacy, said: "Teixobactin originally evolved in soil to kill the bacteria around it, so our challenge was to produce the antibiotic synthetically. The method we created to do this uses commercially available 'building blocks' and has a single purification step, and we are delighted with the results – we are now able to present the total synthesis of two derivatives of Teixobactin.

"We have also been able to identify some of the properties of the antibiotic which are critical for its antimicrobial activities. This is a very important stepping stone towards an in-depth study of Teixobactin and the quest for synthesising similar molecules which could prove vital in our fight against drug resistant bacteria. Breakthroughs such as this via organic chemistry have to be made to keep the drug resistance problem in check."

The bacteria against which Teixobactin is effective have, thus far, not shown any detectable resistance and given its mechanisms of attack, scientists are also confident that this is unlikely to occur in the future.

It has been predicted that by 2050 an additional 10 million people will succumb to drug resistant infections each year. The development of new antibiotics which can be used as a last resort when other drugs are ineffective is therefore a crucial area of study for healthcare researchers

around the world. This new study by Dr Singh and his team represents an important step towards this end goal.

The processes they used produced a yield of 22% for one of the derivatives of Teixobactin, making Dr Singh's methods highly efficient.

Once Dr Singh's synthesis of the different Teixobactin derivatives was complete, Dr Edward Taylor from the University of Lincoln's School of Life Sciences was able to test them. Their findings are published in the Royal Society of Chemistry journal, *Chemical Communications*. The work is available online as an open access article.

Dr Singh and his colleagues will now carry out further tests to more clearly understand the chemical properties of Teixobactin and to simplify the molecule so that other derivatives can be produced. He hopes to create a library of Teixobactin derivatives which could prove vital for the future development of the antibiotic.

Dr Singh added: "The process of bringing an antibiotic to clinic is an extremely lengthy one and can often take around 10-15 years. There is much more extensive research and testing to be carried out before we can even consider Teixobactin as a viable medical treatment. This is a very rare occurrence - the last new class of antibiotics was discovered nearly 30 years ago – and a far-off possibility, however we are certainly making great strides in our work against drug resistant bacteria."

Dr Deirdre Black, Science Manager at the Royal Society of Chemistry, said: "This is another exciting development in the fight against antimicrobial resistance, which is such a huge threat to us all. I am very pleased to see this paper in one of our journals especially in the lead up to the final report from the O'Neill Review of Antimicrobial Resistance, expected to make recommendations for global solutions this summer.

"Research on understanding the mechanisms of antimicrobial resistance, as well as on ways of preventing, diagnosing and treating microbial infection, is crucial if we want to continue to do things we currently take for granted."

More information: Anish Parmar et al. Efficient total syntheses and biological activities of two teixobactin analogues, *Chem. Commun.* (2016). DOI: 10.1039/C5CC10249A

Provided by University of Lincoln