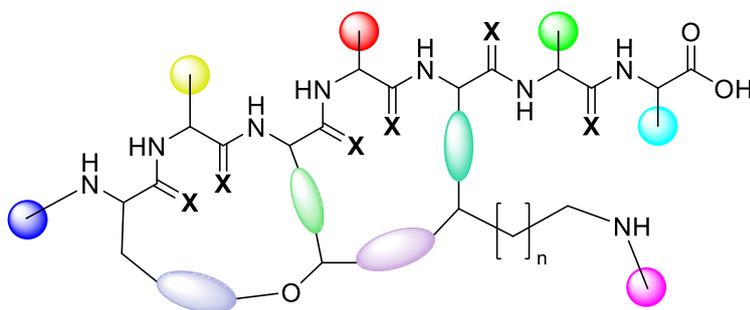


Darobactin effective as an antibiotic against gram-negative bacteria

New drug candidate for antibiotic therapy of patients

DESCRIPTION OF TECHNOLOGY

Many bacteria that cause serious infectious diseases have developed resistance to common antibiotics, so that antibiotics are no longer effective. These include in particular the Gram-negative bacteria with their stable outer membrane, such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Acinetobacter baumannii*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Shigella sonnei*, *Salmonella enterica* Typhimurium LT2, *Enterobacter cloacae*, *Bifidobacterium longum*, *Bacteroides fragilis*, *Lactobacillus reuteri*, *Enterococcus faecalis*, *Yersinia pestis* and *Klebsiella pneumoniae*.



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Darobactin is now a promising candidate for a new class of drugs with a new mechanism of action. It binds to the protein BamA, which is localised in the outer membrane of Gram-negative bacteria. This disrupts the formation of a functional outer membrane and the bacteria die. This means that darobactin does not first have to penetrate the bacterial cell to exert its antibiotic effect, but is effective and reliable from the outside. Chemically, darobactin is a peptide isolated from the extract of bacterial symbionts of threadworms, but it can also be produced recombinantly or chemically. It consists of seven amino acids and has two fused macrocyclic ring systems that form post-translationally. Darobactin is effective against typical Gram-negative bacteria both in vitro and in animal models.

AT A GLANCE ...

Application Fields

- Medicine
- Hygiene

Business

- Pharma
- Medicine
- Biotechnology

USP

- New drug candidate
- Attacks bacterial cell wall from the outside
- there is no resistance to it
- shows no cell toxicity in animal

Development Status

- in vitro and in vivo results with *E.coli* strains in mice
- Cloning of the Dar operon for recombinant production

Patent Status

Priority application filed on November 2019
International PCT Patentapplication filed on Nov. 22, 2020

ADVANTAGES OVER THE PRIOR ART

New active substance candidate against antibiotic-resistant Gram-negative bacteria such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Acinetobacter baumannii*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Shigella sonnei*, *Salmonella enterica* Typhimurium LT2, *Enterobacter cloacae*, *Bifidobacterium longum*, *Bacteroides fragilis*, *Lactobacillus reuteri*, *Enterococcus faecalis*, *Yersinia pestis* and *Klebsiella pneumoniae*.

Darobactin can be easily administered and shows reliable efficacy against infections with wild-type or antibiotic-resistant Gram-negative bacteria.

The good efficacy is shown in vivo in mice, where no cell toxicity and no development of resistance was found.

STATE OF THE PRODUCT DEVELOPMENT

First preclinical experiments are available.

MARKET POTENTIAL

In Germany, most antibiotics are prescribed in the outpatient sector (85%), the share of clinic consumption is only 15%. In medical practices, about 39 million antibiotic prescriptions were issued in 2014, which corresponds to 374 million mean daily doses (DDD) and a turnover of 699 million euros. Consumption has been relatively constant over the last few years, but reserve antibiotics are being prescribed more and more frequently. In Europe, the situation is similar: most antibiotics (90%) are consumed outside hospitals. In the outpatient sector, the average is 21.5 DDD per 1,000 inhabitants per day, compared to 2.0 DDD in hospitals. Broad-spectrum antibiotics, which are effective against many different types of bacteria, are used most frequently. The top countries for antibiotic consumption are Greece (31.9 DDD per 1,000 inhabitants and day), as well as Belgium, France and Hungary. In terms of consumption in hospitals, Finland is the frontrunner. Global antibiotic consumption increased by 36% between 2000 and 2010, with South Africa and the BRIC countries accounting for three quarters of the increase: Brazil, Russia, India and China, as they experience huge population growth. This trend has roughly continued until today.

COOPERATION OPPORTUNITIES

On behalf of its shareholder Justus-Liebig-University of Giessen TransMIT GmbH is looking for cooperation partners or licensees for distribution / further development in Germany, Europe, USA and Asia.

A TECHNOLOGY OF



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