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NOVEL LECTIN-TARGETING CONJUGATES FOR TREATMENT OR DIAGNOSIS OF BACTERIAL INFECTIONS

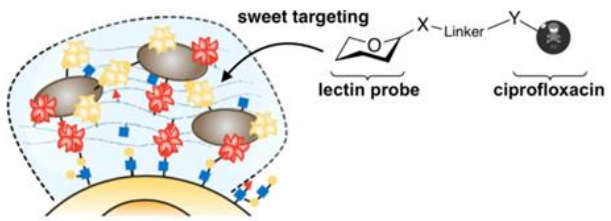
Keywords: LecA, LecB, Pseudomonas aeruginosa, biofilm, prodrug antibiotic conjugates, imaging conjugates

INVENTION NOVELTY

Provided are innovative lectin-targeting conjugates as prodrugs comprising a ligand specifically binding to a bacterial lectin, a peptide linker cleavable by a bacterial protease, and an anti-bacterial therapeutic agent for treatment or an imaging agent for diagnosis of lectin-producing bacterial pathogens, especially of *Pseudomonas aeruginosa*.

VALUE PROPOSITION

Chronic infections, in particular with Gram-negative bacteria like *Pseudomonas aeruginosa* are often severe and difficult to treat. The formation of biofilms characterises such infections and is an important virulence factor, which leads to extensive drug resistance and additionally promotes the resistance to common antibiotics, which is already frequently found e. g. in *P. aeruginosa*. The extracellular matrix of a biofilm is a complex structure of multidimensional polysaccharides, nucleic acids and proteins. Two important biofilm proteins are the quorum-sensing regulated carbohydrate-binding pathogen-specific lectin proteins, e. g. lectin A and B (LecA, LecB) of *P. aeruginosa*, which are essential for cross-linking, for which their interaction with certain sugar molecules, such as galactose and fucose, respectively, is essential. Thus, LecA and LecB represent interesting target structures for the directed application of antibiotics. Accordingly, for fluoroquinolones like ciprofloxacin, which are very effective standard antibiotics for the treatment of *P. aeruginosa* infections, but having dose-dependent rare severe side effects (such as tendon rupture, neuropathy, or heart valve insufficiency) leading to medical contraindications, such targeted application of antibiotics at the site of infection could reduce or avoid side effects.



Lectin-targeting of antibiotic conjugates (Meiers et al.,J. Med. Chem. 2020, 63, 11707−11724, modified]]

TECHNOLOGY DESCRIPTION

The invention relates to novel lectin-targeting conjugates specifically designed to bind to bacterial lectin and thus, to direct the conjugate to the site of infection. In addition, the lectin-targeting ligand is bound to a linker engineered to be cleaved by bacterial proteases, thereby releasing the antibiotic drug or diagnostic probe only in the presence of bacteria. The innovative conjugates feature several advantages compared to currently available conjugates: they are less prone to hydrolysis, possess superior stability in a patient, feature improved targeting, accumulate to higher concentrations at the site of disease, and lead to a decrease in the systemic release of the drug attached to the targeting moiety.

COMMERCIAL OPPORTUNITY

Application as antibiotic prodrug for the treatment of infections with lectin-producing bacterial pathogens, specifically for *P. aeruginosa* infections, or as diagnostic probe. The technology is offered for co-development and/or licensing.

DEVELOPMENT STATUS

Besides comprehensive *in vitro* data preliminary pharmacokinetic data obtained *in vivo* are available.

PATENT SITUATION

Priority application was filed in December 2021, an international PCT application was filed in December 2022 (WO2023/104922).

FURTHER READING

Meiers et al. 2022. Lectin-Targeted Prodrugs Activated by Pseudomonas aeruginosa for Self-Destructive Antibiotic Release. J. Med. Chem. 2022, 65, 20, 13988–14014.

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