

Publication

Anti-adhesion therapy for urinary tract infections - a balanced PK/PD-profile proved to be key for success

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 1534849

Author(s) Jiang, Xiaohua; Abgottspon, Daniela; Kleeb, Simon; Rabbani, Said; Scharenberg, Meike; Wittwer, Matthias; Haug, Martina; Schwardt, Oliver; Ernst, Beat

Author(s) at UniBasel [Ernst, Beat](#) ; [Jiang, Xiaohua](#) ; [Abgottspon, Daniela](#) ; [Kleeb, Simon](#) ; [Rabbani, Said](#) ; [Scharenberg, Meike](#) ; [Wittwer, Matthias](#) ; [Schwardt, Oliver](#) ;

Year 2012

Title Anti-adhesion therapy for urinary tract infections - a balanced PK/PD-profile proved to be key for success

Journal Journal of Medicinal Chemistry

Volume 55

Number 10

Pages / Article-Number 4700-4713

The initial step for the successful establishment of urinary tract infections (UTIs), predominantly caused by uropathogenic Escherichia coli, is the adhesion of bacteria to urothelial cells. This attachment is mediated by FimH, a mannose-binding adhesin, which is expressed on the bacterial surface. To date, UTIs are mainly treated with antibiotics, leading to the ubiquitous problem of increasing resistance against most of the currently available antimicrobials. Therefore, new treatment strategies are urgently needed, avoiding selection pressure and thereby implying a reduced risk of resistance. Here, we present a new class of highly active antimicrobials, targeting the virulence factor FimH. When the most potent representative, an indolinyphenyl mannoside, was administered in a mouse model at the low dosage of 1 mg/kg (corresponding to approximately 25 µg/mouse), the minimal therapeutic concentration to prevent UTI was maintained for more than 8 h. In a treatment study, the colony-forming units in the bladder could be reduced by almost 4 orders of magnitude, comparable to the standard antibiotic treatment with ciprofloxacin (8 mg/kg, sc).

Publisher American Chemical Society

ISSN/ISBN 0022-2623 ; 1520-4804

edoc-URL <http://edoc.unibas.ch/dok/A6070817>

Full Text on edoc No;

Digital Object Identifier DOI 10.1021/jm300192x

PubMed ID <http://www.ncbi.nlm.nih.gov/pubmed/22519985>

ISI-Number WOS:000304338800014

Document type (ISI) Article