

Ferrioxamine B analogues: targeting the FoxA uptake system in the pathogenic *Yersinia enterocolitica*.

Autorzy

H. Kornreich-Leshem
C. Ziv
Elżbieta Gumienna-Kontecka
R. Arad-Yellin
Yujing Chen
M. Elhabiri
A.-M. Albrecht-Gary
Yitzhak Hadar
Abraham Shanzer

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Streszczenie

A series of ferrioxamine B analogues that target the bacterium *Yersinia enterocolitica* were prepared. These iron carriers are composed of three hydroxamate-containing monomeric units. Two identical monomers consist of *N*-hydroxy-3-aminopropionic acid coupled with β -alanine, and a third unit at the amino terminal is composed of *N*-hydroxy-3-aminopropionic acid and one of the following amino acids: β -alanine (**1a**), phenylalanine (**1b**), cyclohexylalanine (**1c**), or glycine (**1d**). Thermodynamic results for representatives of the analogues have shown a strong destabilization (3–4 orders of magnitude) of the ferric complexes with respect to ferrioxamine B, probably due to shorter spacers and a more strained structure around the metal center. No significant effect of the variations at the N-terminal has been observed on the stability of the ferric complexes. By contrast, using in vivo radioactive uptake experiments, we have found that these modifications have a substantial effect on the mechanism of iron(III) uptake in the pathogenic bacteria *Yersinia enterocolitica*. Analogues **1a** and **1d** were utilized by the ferrioxamine B uptake system (FoxA), while **1b** and **1c** either used different uptake systems or were transported to the microbial cell nonspecifically by diffusion via the cell membrane. Transport via the FoxA system was also confirmed by uptake experiments with the FoxA deficient strain of *Yersinia enterocolitica*. A fluorescent marker, attached to **1a** in a way that did not interfere with its biological activity, provided additional means to monitor the uptake mechanism by fluorescence techniques. Of particular interest is the observation that **1a** was utilized by the uptake system of ferrioxamine B in *Yersinia enterocolitica* (FoxA) but failed to use the ferrioxamine uptake route in *Pseudomonas putida*. Here, we present a case in which biomimetic siderophore analogues deliberately designed for a particular bacterium can distinguish between related uptake systems of different microorganisms.

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