$^{1}H/^{27}Al$ NMR investigation of siderophore complexes with trivalent metal ions: the case of acinetobactin

I. Serra[1], E. Desarbre[2], M. G. P. Page[3], M. Ceccarelli[1], M.A. Scorciapino[4]

[1]Department of Physics, University of Cagliari, Italy
[2]Basilea Pharmaceutical International, Basel, Switzerland
[3]Jacobs University, Bremen, Germany
[4]Department of Biomedical Sciences, University of Cagliari, Italy

E-mail: ilaria.serra@unica.it

Multi-drag-resistant (MDR) Gram-negative bacteria represent one of the most pressing global healthcare threats.[1,2] The presence of the outer membrane provides an efficient physical barrier to the permeation of antibacterials. Despite it is crucial to understand the chemico-physical features for a drug not to be effectively recognized by efflux pumps and degradative enzymes, the reduced accumulation in the periplasm is the first limiting factor impairing drug's efficacy. Beside the efforts focused on general porins, another possible intriguing approach is to exploit the bacterial Fe(III) uptake system. A "Trojan Horse" strategy in which either an endogenous or exogenous siderophore (a small molecule with high affinity for the ferric ion) is conjugated to an antibiotic moiety. The metal-complex formed by such a bifunctional conjugate is recognized and uptaken by specific receptors. Nuclear Magnetic Resonance (NMR) is a suitable technique to characterize equilibria of complexes formation in solution,[3] providing stability constants and stoichiometry. Also, geometrical parameters can be derived to obtain a 3D molecular model. Finally, when different signals are observed for the different complexes formed, it is also possible to monitor their interaction with the protein receptor independently. This is a molecular level information difficult to obtain with other spectroscopic techniques. In this work, acinetobactin was taken as an example. This is one of the siderophores secreted by Acinetobacter baumannii.

References

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