Probing the specific interactions and structures of gas-phase vancomycin antibiotics with cell-wall precursor through the combination of Ion Mobility Mass Spectrometry and IRMPD spectroscopy

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Vancomycin is a naturally occurring glycopeptide antibiotic active against Gram-positive bacteria and is considered as a drug of last resort for the treatment of penicillin-resistant *Staphylococcus aureus*. Vancomycin binds to the bacteria cell-wall peptidoglycan precursor through noncovalent interactions with the C terminal part containing the ^{D}Alanyl-^{D}Alanine sequence. Vancomycin and its peptide receptor analogues $Ac_2{}^{L}K^{D}A^{D}A$ have been widely used as model systems for investigating biomolecular recognition processes through pure mass spectrometric approaches. In particular, the energetics of dissociation of vancomycin-receptor complexes strongly change in positive and negative ion modes although no direct structural investigation has been yet carried out. We are thus mostly concerned with the binding site of the receptor peptide to vancomycin and more precisely to question whether the structure known in the condensed phase is preserved upon desolvation during electrospray.

Biomolecular recognition of vancomycin antibiotics with its cell-wall precursor analogue $Ac_2{}^{L}K^{D}A^{D}A$ has been investigated in the gas phase through a combined laser spectroscopy (IRMPD), ion mobility mass spectrometry (IMS) and theoretical modeling approach. The two experimental methods are highly complementary: the global shape of the system is probed by ion mobility, and IRMPD spectroscopy is directly sensitive to the intra and inter molecular interactions. Structural assignment has been achieved through comparisons with the low-energy conformers obtained from replica-exchange molecular dynamics simulations, for which IR spectra were calculated using a hybrid quantum mechanics/semi-empirical (QM/SE) method at the DFT/B3LYP/6-31+G*/AM1 level.[1] Both theoretical and experimental findings provide strong evidence that the native structure of the $V+Ac_2{}^{L}K^{D}A^{D}A$ complex is only preserved in the deprotonated species and is lost in protonated complex.[2,3]

[1] J.C. Poully *et al.*, J. Phys. Chem. A **113**, 8020 (2009)

[2] J. C. Poully *et al.*, Phys. Chem. Chem. Phys. (Submitted 2010)

[3] J. C. Poully *et al.*, Int. J. Mass. Spectrom. (Submitted 2010)