MOLECULAR DYNAMICS STUDY OF CONFORMATIONAL FREEDOM OF VANCOMYCIN, ORITAVANCIN AND TELAVANCIN

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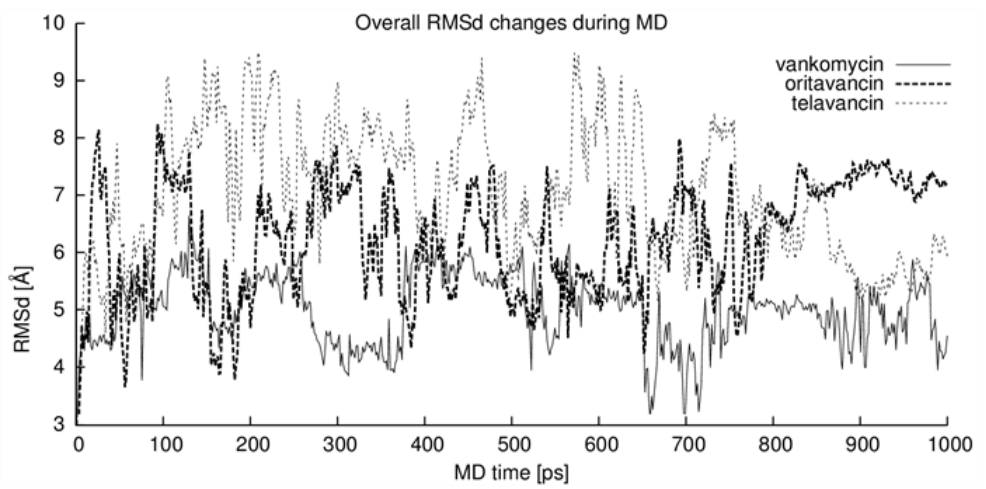
Vancomycin is a glycopeptide antibiotic used in the treatment of serious and multi-drug-resistant infections caused by Gram-positive bacteria. It is composed of a disaccharide, with monosaccharides D-glucose and vancosamine, and a heptapeptide core. Oritavancin and telavancin are semisynthetic derivatives of vancomycin. They all bind to D-alanyl-D-alanine stem termini on the peptidoglycan precursors on the cell wall in Gram-positive bacteria. This binding inhibits cross-linking between peptides and subsequently cell wall synthesis. The sugar moieties attached to the aglycon basket are able to assume a variety of orientations by rotation. In this study some of the aspects of conformational restrictions from the modifications of vancomycin structure introduced into oritavancin and telavancin are presented and discussed. Fully hydrated, unrestricted molecular dynamics of vancomycin, oritavancin and telavancin have been conducted. The resulting trajectories, RMSd changes of aglycon as well as the saccharide moieties, N-4-(4-chlorophenyl)benzyl in the oritavancin, and decylaminoethyl side chain or (phosphonomethyl)aminomethyl substituent groups in the telavancin have been measured and analyzed. The discussion of advantages and disadvantages of these and other possible modifications is provided.



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