Membrane Interaction and Permeability of Prodigiosin – A Molecular Dynamics Study

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Abstract

Prodigiosin is a tripyrrollic red pigment produced by many strains of Serratia marcescens. Prodigiosin is also an antimicrobial and acts against certain Gram positive and Gram negative bacteria. The minimum inhibitory concentration has been observed to be 1 μg/mL, while the minimum bactericidal concentrations was around 5 μg/mL. It has been shown that Prodigiosin was observed to be internalized into bacterial cells and was localized predominantly in the membrane fraction, thus, facilitating intracellular trafficking and then binding of prodigiosin to the bacterial DNA. In the present study we have performed molecular dynamics simulations to explore the interactions between prodigiosin and a bilayer. Molecular dynamics (MD) simulations were performed on the hydrated bilayer with BPAs. Prodigiosin was modelled using parameters from the ATB server. In the simulation the prodigiosin molecule was placed in the middle of the hydrophobic region of the membrane. Another simulation was carried out placing prodigiosin in the solvated region outside the membrane. The simulation shows that prodigiosin can easily enter the membrane from the aqueous phase within a couple of nanoseconds. Thus at low concentrations, the molecule can readily penetrate into the membrane and positions itself at the interface between water and lipids, with its polar groups towards the lipid headgroups and its carbon chain in the lipid tails. It assumes this final conformation even when the molecule is placed in the hydrophobic core of the membrane and is then subjected to further simulation. Further displacement of the molecule is lateral. This location and orientation enables electrostatic interactions between the polar groups of prodigiosin and the polar headgroups of the bilayer as well as water. Prodigiosin exhibits low water solubility and hence may not be present as individual molecules in the aqueous phase. When the concentration of prodigiosin in the aqueous phase is increased, prodigiosin tends to aggregate and form into cluster. With high concentration, prodigiosin clusters first and then enters the membrane, leaving a hole at the entrance. The results provide detailed atomic mechanism of the interactions between prodigiosin and a model cell membrane.

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