Computational study on the interaction of phosphoethanolamine in MCR-1 using molecular dynamics simulation
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Abstract: Recently the scientists had found a gene which resists to last-resort antibiotic called colistin. Normally, the positively charged colistin bound to negatively charged lipid A can disrupt the gram-negative bacteria outer cell membrane. The mobile colistin resistance gene mcr-1 have been reported that MCR-1 acts as phosphoethanolamine (PEA) transfer reaction to lipid A on the gram-negative bacterial outer membrane which neutralizes the negative charge on bacterial membrane and reduces the colistin binding consequently causing the bacteria resistance to colistin. We performed the 100-ns molecular dynamics simulations on MCR-1 in mono-zinc and di-zinc forms with different protonation states of T285, H395 and H478 residues in water solution at 310 K to examine the zinc coordination and PEA binding. The obtained information of this study suggested that the active conformation may require only a single zinc ion. Model of MCR-1 with PEA binding could be further used for the QM/MM study on enzymatic reaction of PEA transfer and design of competitive inhibitors.

Keywords: MCR-1; Molecular dynamic simulation; Antibiotic resistant