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Structure and dynamics of the monomer of protein E of dengue virus type 2 with unprotonated histidine residues

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ABSTRACT. The surface of the dengue virus is composed of 180 copies of a multifunctional envelope glycoprotein that acts at several stages of viral infection. When the virus is in the endosome, these glycoproteins undergo major conformational rearrangements owing to the protonation of histidine side chains. This protonation allows for the formation of trimers, thereby triggering fusion between the viral and the host membranes. In this study, we examined the behavior of a monomer of this key protein containing unprotonated histidine side chains before the stage of trimer formation using explicit solvent molecular dynamics at various ionic strengths. The extended secondary structures, which contribute to protein stabilization, are smaller than those observed in a previous study involving monomers containing the protonated histidine. However, the structure of the monomer investigated herein is extremely stable under ionic strengths ranging from 0 to 225 mM. The results show that a protein surface frozen owing to interactions between charged groups is mainly responsible for this stabilization. Thus, focusing on binding sites and ligands that destabilize these properties can aid the search for dengue virus inhibitors.

Key words: Dengue glycoprotein E; Molecular simulation; Flavivirus; Ionic strength; Unprotonated histidine residues

