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Aqueous solvation of α-, β-, and γ-cyclodextrins: from first principles to classical force fields

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Cyclodextrins (CDs) are cyclic oligosaccharides of α-D-glucose naturally produced by the action of a family of enzymes on starch. One of the most prominent features of CDs is their ability to form inclusion complexes with a wide range of guest molecules in aqueous solution. This inclusion allows increasing water solubility of normally hydrophobic compounds or protecting compounds from degradation reactions. CDs and their derivatives have been used widely in chemical, cosmetics, food, pharmaceutical and other industrial areas. Three major classes of CDs are the α-, β-, and γ-cyclodextrins, comprising of 6, 7, and 8 glucopyranose residues (Fig. 1). These CDs exhibit "doughnut" or "truncated cone" macrocycle structures with the hydrophobic cavity and hydrophilic hydroxyl groups on both rims of the macrocycle. Their solvation structures and properties play a critical role in the inclusion phenomena in the aqueous solution.

We present a comprehensive investigation of the gas and aqueous solvation properties of CDs. Extensive sampling of the gas phase conformations of gas phase CD monomers and dimers as well as the CD-water interaction are investigated using electronic structure theory (DFT and MP2) in order to establish accurate benchmarks that are used to assess the accuracy of classical force fields that are used for probing their solvation properties. We investigated the performance of existing (GLYCAMM) and new force fields (in collaboration with the developers) for sugars (CHARMM) in reproducing the electronic structure results. Overall the new parametrization of the CHARMM force field was found to reproduce the electronic structure results to the degree possible. We will finally present preliminary results of MD simulations using this force field for the solvation and interaction between CDs in aqueous solution.

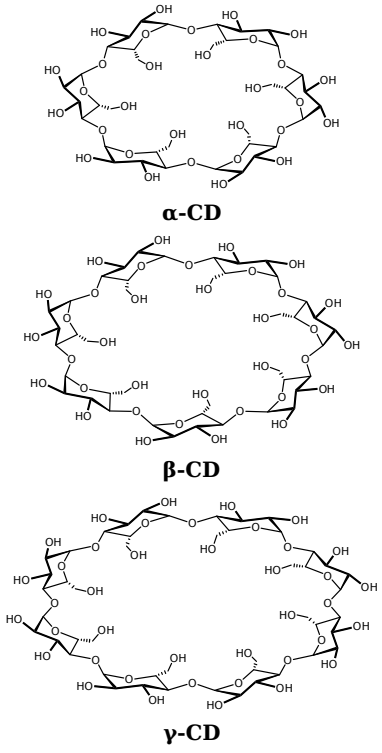

Fig 1. Chemical structures of CDs