Binding mode and binding affinity prediction of inclusion complex between flavonoid and ß-cyclodextrin

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Although fisetin, a flavonoid compound, possess a wide range of important pharmacological activities, its low water solubility is a major problem for pharmaceutical application. β-cyclodextrin (βCD) can be used to improve the solubility of poorly soluble organic compounds by encapsulating hydrophobic molecule inside its cavity. Herein, the multiple molecular dynamic simulations were applied to study the binding mode and affinity between the fisetin guest molecule and the βCD host molecule. Fisetin was firstly docked into the βCD cavity using molecular docking approach and the four different fisetin/βCD complexes (I-IV) resulted were consequently used as the starting structures for classical molecular dynamics study in aqueous solution for 70 ns. The complexes III and IV are relative complexes I and II with 180 degree rotated torsion angle. For complex I, translocation of fisetin molecule inside the cavity was observed. In contrast, the B-ring strongly interacts with the βCD in complexes II and IV. The radial distribution function indicated that the water solubility of fisetin is significantly increased by complexation with βCD. Based on MM/PB(GB)SA and QM/PB(GB)SA calculations, complexes II and IV are likely more stable than the others.