Inclusion complexes between β-cyclodextrin and the anticancer drug 5-Fluorouracil: a Molecular dynamics study of its solubilization

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Abstract.
Cyclodextrins (CDs) can solubilize hydrophobic drugs in water enhancing their bioavailability. In this theoretical study based on Molecular Mechanics and Molecular Dynamics methods using a simulation protocol used in previous work the non-covalent inclusion complexes formation thanks to favorable intermolecular interactions between β-cyclodextrin and 5-Fluorouracil (5FU) were investigated. The 5FU is a hardly soluble in water anticancer drug. It is important to determine possible stable inclusion complexes considering different drug concentration enhancing the anticancer activity with lower dose. At first the host-guest complexes formation with native *β*-CD in a 1:1 stoichiometry are studied, then in a 2:1 stoichiometry were considered. Moreover, their complexes formations in explicit water are investigated. The inclusion complexes formation is found as well the stability also in presence of explicit water. Fluorouracil complex with natural or synthetic cyclodextrins permit the solubilization of this poor soluble anticancer drug. The intermolecular interactions in the complex during the time can prolonged the release profile. Molecular dynamics simulations are an interesting tool to continue to evaluate possible favorable interactions between hydrophobic anticancer drug and hydrophilic carrier with an internal hydrophobic cavity such as cyclodextrins.