# A MOLECULAR SIMULATION STUDY ON BETA-CYCLODEXTRIN POLYMERIC MEMBRANES

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## ABSTRACT

Molecular dynamics simulations have been performed on β-cyclodextrins octyl-derivative (b-CD) encapsulated into a polymer matrix of glassy poly(ether ether ketone) (PEEK-WC) material to investigate the effects of the complexation of *p*-nitrophenilacetate and naringin molecules with the aim to study the recognition properties of b-CD.

## INTRODUCTION

Cyclodextrins are cyclic α (1-4) linked glucose oligomers having six (α), seven (β) and eight (γ) glucose units. These molecules have a torus shape and characteristic dimensions which increase going from α-CD to γ-CD. Because of their geometry, and as the surface of the internal cavity is relatively hydrophobic, in contrast to the hydrophilic character of the external hydroxyl faces, these molecules form inclusion complexes with a wide range of molecules being extremely attractive component of biomimetic materials [1-3].

## METHODS

The investigated structures were boxes of amorphous PEEK-WC with b-CDs encapsulated onto the surfaces of the membrane materials. The InsightII/Discover software of Accelrys with pcff forcefield was used for the construction of models. The polymer chains were constructed at 303 K under 2D periodic boundary conditions.

To have chain effects reduced, only one long chain, containing 80 monomer units (about 4000 atoms), instead of several shorter chains segments were filled in each simulation box. This procedure was chosen to come closer to reality where polymer chains are typically composed of at least several thousand atoms. In order to avoid packing algorithm related catenations and spearings of aromatic units, it was necessary to start the packing at low density with inserted "solvent" molecules in the initial phase of amorphous cell construction. To reach the experimental density of the cells, several stages of compression and of equilibrations with MD NVT at high temperatures were performed, using a penalty surface potential on the non-periodic *z*- direction. Subsequently, feed-mixtures of *p*-nitrophenilacetate (PNPA) and Naringin (NAR) respectively, were added to the PEEK-WC/β–CD system to study the interaction of β-CD with host molecules [4-5]. The polymer and the solvent boxes were layered onto each other along the *z*-axis and combined into a single simulation cell. The equilibrated packing models were then subjected to NVT-MD date production runs with

simulation performed at 303 K for 1 ns each. Newton's equation of motion was solved with a time step of 1 fs [6].

## RESULTS AND DISCUSSION

The analysis of PNPA/β–CD models show that some PNPA molecules approach to the cyclodextrins cavity and one entered with the preferential orientation of nitro groups into the β–CD cavity. To check the reason of the preferential orientation of PNPA molecules, useful to study the 1:1 complexation process of β–CD, molecular mechanics calculations have been performed to obtain the relative binding energy, $E_{binding}$ (Figure 1).

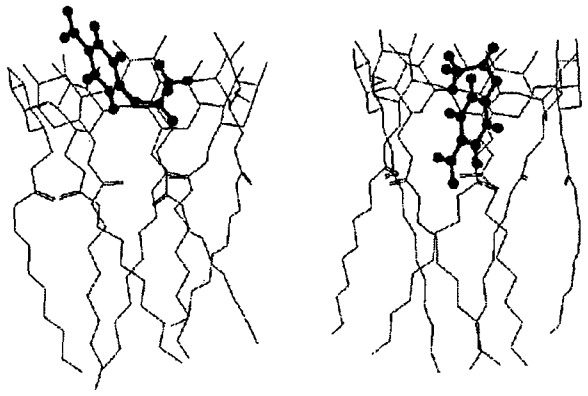

**Figure 1** **(a)** $E_{binding}$ = -18,8 Kcal/mol **(b)** $E_{binding}$ = -34,3 Kcal/mol

The $E_{binding}$ was obtained as the difference between the potential energy of the ß-CD:PNPA complex and the sum of the potential energies of isolated β–CD and PNPA molecules in the same conformation. PNPA approaches the cavity in both direction, with the nitro (PNPA-$NO_2$) and the acetyl (PNPA-Ace) groups; when PNPA enter with the $NO_2$ group into the cavity $E_{binding}$ is –34.3 Kcal/mol while that of PNPA-Ace is -18.8 Kcal/mol.

The structure of β–CD:PNPA-$NO_2$ complex indicate that PNPA penetrate deeply into the β–CD cavity with its longitudinal axis almost perpendicular to the β–CD ring and also the acidic moiety do not interact with the –OH groups of β–CD. When PNPA-Ace approaches the CD cavity the benzene ring result partly inserted into the cavity and the acetyl moiety is more distorted that in the PNPA-$NO_2$minimum. In this case the $E_{binding}$ is the half with respect to that of PNPA-$NO_2$: β–CD complex suggesting that the hydrophobic effect is of lower importance. In both structures no hydrogen bond have been found with the –OH of the β–CD due to the dimension of the guest molecule. In β–CD most of the hydrogen bonds are intramolecular, forming a bend around the molecule.

Docking approach have been also applied to provide information on the inclusion processes of the nitro group and the acetyl group approaching the cavity in PNPA/β–CD model. The minimum energy is lower for PNPA-$NO_2$ indicating that the complex with nitro group down is more stable than the alternative.

The investigations performed on NAR/β–CD system will be also presented.

## ACKNOWLEDGEMENT

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