Studies on the interaction of mycotoxins and macrocycles by molecular modelling

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Abstract
The goal of our work is to develop a selective sensor to detect the gene wrecking and carcinogenic mycotoxins [1,2]. Hence our research group applies functionalized gold nanoparticles and thin films to measure these analytes. In this investigation modified macrocycle molecules (mainly cyclodextrins) were applied to functionalise the gold surfaces on the nanoparticles. The cyclodextrins contains α-D-glucopyranoside unites, which connect to a ring with 1,4 glycosidic bonds. The best known three cyclodextrins are the α-, β- and γ-cyclodextrin, these form six-, seven- and eight glucopyranose molecules, respectively. In the inner cavity, there are hydrogen atoms and the oxygens of the 1,4 glycosidic bonds. The hydroxyl groups are placed on the flange of the hoop. So, the inner cavity of the cyclodextrins is hydrophobic, and the outer surface is hydrophilic. This property makes cyclodextrin molecules able to form inclusion complexes with hydrophobic molecules like the aflatoxins. The hydrophobic character and the hydrogen donor hydroxyl groups warrants the relatively strong binding. The modification of cyclodextrins with the suitable chemical groups gives the selectivity of the sensors. To choose of the appropriate modified cyclodextrin molecules and predict the binding affinities to mycotoxins, we investigated the complexes with molecular modelling. To improve our fundamental understanding of the nanomaterials functionalized with macrocycle molecules, we use the tools of the molecular docking, molecular mechanics (MM) and semiempirical quantum chemistry methods.

Keywords: sensors, mycotoxins, macrocycles, docking.

To prepare the cyclodextrin structures, we optimized them with PM6-DH+ COSMO method, added an r = 12 Å water sphere. The cyclodextrin coordinates were fixed and the sphere was pre optimized with the SP4 force field (VegaZZ). Finally the cyclodextrin in the sphere was optimized with the PM6-DH+ method. These cyclodextrin structures were used in the further calculations.

On the right huge table, we summarize the results of AutoDock VINA virtual screening. We used Gasteiger charges. These quantities are relative scores from the AutoDock VINA score. The colour indicates the strength of the binding: (yellow: above -20.0 / green: between -25.0 and -30.0 / red: between -30.0 and white: below -30.0.) Molecules in the white cells limits strongly.

The best docked poses were optimized with the semiempirical PM6-DH+ and PM6-DH2 dispersion-hydrogen bond interaction corrected methods, with the COSMO implicit solvation model. The energies shows the size selective property of CDs.

The complex of the beta-cyclodextrin and Aflatoxin B1 molecule. The aflatoxins binds in this way, the methoxy group do not moves to the cavity.

We investigated the binding of the thiolated cyclodextrins on gold surface. The gold surface model was a gold (111) lattice plane (one layer gold atoms). The cyclodextrin – aflatoxin complexes.

On the left side picture (ACD and GCD on gold model, with Aflatoxin B1 molecule), can be seen, that the Aflatoxins molecules are too large to bind to the alpha-cyclodextrin cavity. In the gamma-cyclodextrin, the ligand is too far from the wall of the cavity, so the binding is weak. The beta-cyclodextrin has the optimal size to bind Aflatoxin molecules. The AutoDock VINA scores are show this too in the table above. We need more sophisticated calculations to explain the differences between the binding of aflatoxin molecules to modified gold surfaces.

We used random conformation search (SP4 force field, VegaZZ), and the best conformations were optimized with the new PM7 semiempirical method implemented in the MOPAC software, using the COSMO implicit solvation model.

We started to investigate the aflatoxin adsorption, and the mycotoxin - cyclodextrin interaction with semiempirical quantum chemistry and molecular docking.

These calculations are the early attempt, to understand these systems.

To get better result we need to use MD (REMD) and DFT methods, to investigate the conformation space of modified cyclodextrines and the thiol-gold interactions.

References: