This dissertation focuses on theoretical studies of the interaction between protein kinases and their inhibitors. Studied protein kinases, cyclin-dependent kinase 2 (CDK2) and CK2 kinase (casein kinase 2) play an important role in regulating cellular processes in eukaryotic organisms. Their abnormal function in human cells can lead to serious diseases. This process can be stopped by blocking the aberrant protein kinases using specific low molecular weight inhibitors. Inhibitors of protein kinases typically bind to the active site of the enzyme by noncovalent interactions. Theoretical description of these interactions using quantum-chemical and molecular mechanical methods can help in understanding the biophysical principles governing the binding. These, in turn, can be subsequently used for a rational drug design of more effective and more specific inhibitors. The stabilization energy of the complex of CDK2 with inhibitor roscovitine is predominantly formed by the dispersion energy. DFT methods, which do not describe the dispersion energy was thus completely inappropriate for the treatment of such a system. When an empirical term is included to correct for the description of dispersion, such methods, as e.g. the SCC-DFTB-D, can be recommended for computation of this or similar complexes. The dominant part of the overall interaction is due to a limited number of amino acids, that contribute to binding of roscovitine with CDK2. Their mutations can thus be crucial to destabilize the complex. It was also shown that the AMBER force field was able to describe the interaction of roscovitine with CDK2. The drug design community often employs scoring functions based on the principle of force field to describe the interaction between proteins and their inhibitors. However, the force fields methods are not able to describe quantum phenomena such as polarization or charge transfer. In contrast, the designed scoring functions based on the semiempirical method PM6-DH2 method was shown to give satisfactory results for the group of 15 structurally diverse inhibitors of CDK2. The strongest correlation with experimental inhibition constants was obtained using the interaction enthalpy (R^2=0.87) calculated by the PM6-DH2 method. After the inclusion of all the terms of the scoring functions (including the entropy term), the correlation deteriorated (R^2=0.52) probably due to the inaccuracies in the calculation of the entropy term in AMBER force field. Due to very good correlation with the interaction enthalpy, it appears that the calculations using the scoring functions based on SQM method will be a promising approach for future drug design, enabled by the rapid development of information technology. In last part of study, the scoring function based on the PM6-DH2X method was used for halogenated inhibitors that are able to form halogen bonding with CK2 protein kinase. Structures optimized using PM6-D2X agreed very well with the crystal structures, while the structures optimized by the AMBER force field were dissimilar, due to the inability to describe the halogen bonding. For halogenated CK2 inhibitors, based on the crystal and modeled structures, a strong correlation was found between the inhibitory constant and the interaction enthalpy calculated in water. After the inclusion of the entropic term, the correlation deteriorated, due to the inability of the empirical potential to describe the halogen bonding. The correct description of halogenated compounds in complexes with halogen bonding is one of the conditions for the possibility of finding more effective inhibitors.

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