DFT analysis of water clusters, dopaminergic derivatives, and their desolvation energies

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Our current research explores the synthesis, metabolism, and excretion of novel catecholamines which could serve as drugs in the dopaminergic pathway. By studying all of the enzymes involved in the dopaminergic pathway, we can paint a comprehensive picture of how these catecholamines will behave in our bodies which will help us find novel drugs that could treat conditions such as Parkinson's disease. Computational models of dopaminergic analogs were used to examine the substrates' binding in the enzymatic active site. The binding of a ligand to an enzyme not only involves the interaction between the ligand and the enzyme but also the energy lost or gained by desolvation of the ligand. Desolvation of dopaminergic derivatives was examined using a series of hydration shells that increase in size. The desolvation energies were calculated using M062X with the aug-cc-pvdz, cc-pvdz, and cc-pvtz basis sets. Ligands with the carboxylic acid and nitro substituents exhibited the least favorable energies, whereas the nitrile substituents exhibited the most favorable desolvation energies in each of the explicit water models. The implicit Polarizable Continuum Model was also used together with explicit solvation to calculate desolvation energies of dopaminergic ligands. The use of implicit and explicit models was compared. This information will be combined with prior research done on ligand/enzyme interaction in order to get a more comprehensive understanding of ligand binding in this system.