Modeling and confirmation of copper-ion induced hydroxylation and subsequent oxidation of catechol as a proposed model of beta-amyloid blocking in Alzheimer's pathology

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Beta-amyloid proteins as well as transition metal dications such as copper(II), iron(II), and zinc accumulate in the brain of patients diagnosed with Alzheimer's Disease. It has been suggested that these proteins have a role in eliminating excess metal ions from the brain, but they end up being retained in the brain after reaction with dications. The exact cause of the disease is uncertain, and it may be associated with the accumulation of beta-amyloids or with redox reactions that affect synapsis. Catechol serves as a model for beta-amyloid proteins, and its interaction with dications may shed light on Alzheimer's pathology. By modeling this reaction we can elucidate the hydroxylation and oxidation of these proteins. Reactions with copper(II), iron(II) and zinc ions were considered in this study and were compared to reaction profiles suggested by da Silva and Ming. An analysis of five density functional theory methods using three basis sets suggests that electron affinities and reduction of the transition metals relevant to this problem are best obtained using mPW1PW91, while the popular functional DGDZVP yields acceptable results. The reaction model confirms da Silva and Ming's work by calculating approximate energy values for each of the transition states in the five-step process they suggest.

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