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Theoretical Study of Effects of Changing the Metal Inos on Glyoxalase II Reaction Mechanism

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Metal ions are essential for the catalytic action of some enzymes. The most common role of metal ions is their ability to orient the substrate correctly for the reaction, exchange electrons in redox reactions, and stabilize negative charges. Glyoxalase II (GlxII) is a binuclear metalloenzyme with Zn(II) as the most frequently observed metal ion. However, cytosolic and mitochondrial GlxII from *Arabidopsis thaliana* contains varying ratios of Zn(II), Fe(II), and Mn(II) [1,2]. Human GlxII has also been shown to contain a mixed binuclear center with Zn(II) and Fe(II), although the mononuclear Zn(II) reconstituted enzyme is also active. This enzyme converts *S*-D-lactoylglutathione to D-lactic acid. In this study, using quantum mechanics/molecular mechanics (QM/MM) calculations, the effect of changing the metal ions on the reaction mechanism of GlxII was investigated. A model of the active site of GlxII was constructed based on the crystal structure of the human GlxII (1QH5 PDB ID) [3]. Besides, by changing the zinc ions of the active site with Fe^{2+} or Fe^{3+} ions, we constructed other eight active site models. The reaction mechanism of GlxII was investigated by using these active site models and obtained energy profiles (cf. Figure 1). Our results showed that the reaction mechanism of GlxII with two zinc ions in its active site has the lowest energy barrier which is in line with the higher preference of GlxII for zinc ion pairs in the active site.

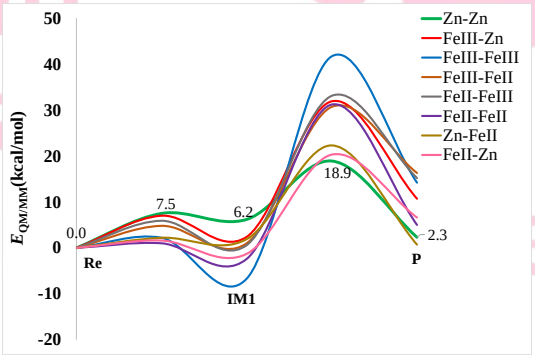


Figure 1. The energy profile of the reaction mechanism of GlxII different active site models.

Keywords: Metalloprotein, GlxII, QM/MM, DFT

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