Impact of mercury(II) on proteinase K catalytic center: investigations via classical and Born-Oppenheimer molecular dynamics.

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Streszczenie

Mercury(II) has a strong affinity for the thiol groups in proteins often resulting in the disruption of their biological functions. In this study we present classical and first-principles, DFT-based molecular dynamics (MD) simulations of a complex of Hg(II) and proteinase K, a well-known serine protease with a very broad and diverse enzymatic activity. It contains a catalytic triad formed by Asp39, His69, and Ser224, which is responsible for its biological activity. It was found previously by X-ray diffraction experiments that the presence of Hg(II) inhibits the enzymatic action of proteinase K by affecting the stereochemistry of the triad. Our simulations predict that (i) the overall structure as well as the protein backbone dynamics are only slightly affected by the mercury cation, (ii) depending on the occupied mercury site, the hydrogen bonds of the catalytic triad are either severely disrupted (both bonds for mercury at site 1, and the His69-Ser224 contact for mercury at site 2) or slightly strengthened (the Asp39-His69 bond when mercury is at site 2), (iii) the network of hydrogen bonds of the catalytic triad is not static but undergoes constant fluctuations, which are significantly modified by the presence of the Hg(II) cation, influencing in turn the triad's ability to carry out the enzymatic function--these facts explain the experimental findings on the inhibition of proteinase K by Hg(II).

Słowa kluczowe

poteinase, K, Hg(II), catalytic triad, classical MD, ab initio MD

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