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Structural Evidence of the Conversion of Nitric Oxide (NO) to Nitrite Ion ($NO2^-$) by Lactoperoxidase (LPO): Structure of the Complex of LPO with $NO2^-$ at 1.89å Resolution

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Abstract : Lactoperoxidase (LPO) is a heme containing mammalian enzyme which uses hydrogen peroxide (H2O2) to catalyze the conversion of substrates into oxidized products. LPO is found in body fluids and tissues such as milk, saliva, tears, mucosa and other body secretions. The previous structural studies have shown that LPO converts substrates, thiocyanate (SCN^-) and iodide (I^-) ions into oxidized products, hypothiocyanite ($OSCN^-$) and hypoiodite (IO^-) ions, respectively. We report here a new structure of the complex of LPO with an oxidized product, nitrite ($NO2^-$). This product was generated from NO using the two step reaction of LPO by adding hydrogen peroxide (H2O2) in the solution of LPO in 0.1M phosphate buffer at pH 6.8 as the first step. In the second step, NO gas was added to the above mixture. This was crystallized using 20% (w/v) PEG-3350 and 0.2M ammonium iodide at pH 6.8. The structure determination showed the presence of $NO2^-$ ion in the distal heme cavity of the substrate binding site of LPO. The structure also showed that the propionate group, which is linked to pyrrole ring D of the heme moiety, was disordered. Similarly, the side chain of Asp108, which is covalently linked to heme moiety, was also split into two components. As a result of these changes, the conformation of the side chain of Arg255 was altered, allowing it to form new interactions with the disordered carboxylic group of propionate moiety. These structural changes are indicative of an intermediate state in the catalytic reaction pathway of LPO.

Keywords : lactoperoxidase, structure, nitric oxide, nitrite ion, intermediate, complex
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