Interaction of Peroxynitrite with Hemoproteins: Focus on Hemoglobin

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Peroxynitrite, the product of the diffusion-controlled radical-radical reaction between $^{\bullet}NO$ and $O_2^{\bullet-}$, is a strong oxidant involved in cell injury. Hemoproteins are one of the major targets of peroxynitrite in vivo, but it is unclear if these proteins are the peroxynitrite physiological scavengers. It has been proposed that the heme-peroxynitrite interaction results in both peroxynitrite inactivation [1] and catalysis of tyrosine nitration [2]. In fact, the reaction of peroxynitrite with porphyrins and some hemoproteins is faster than that with CO_2 and prevents the formation of highly reactive radical species, such as $^{\bullet}OH$, $CO_3^{\bullet-}$ and $^{\bullet}NO_2$. However, the reaction of peroxynitrite with heme can cause toxic reactions characteristic of peroxides such as the formation of ferryl or perferryl species. In the case of oxygenated hemoglobin visible spectroscopy, direct EPR and spin trapping with 2-methyl-2-nitrosopropane (MNP) suggested the formation of ferryl species and tyrosyl radical(s). Tyrosyl radical(s) can further react with $^{\bullet}NO_2$ produced by peroxynitrite leading to 3-nitrotyrosine formation on both the alfa and beta chains (Tyr130 in the beta chain, Tyr42, Tyr140 and, to a lesser extent, Tyr24 in the alfa chain). 3-Nitrotyrosine content, however, sharply increased only in molar excess of peroxynitrite, suggesting that hemoglobin is not a catalyst of nitration. In the case of methemoglobin, the bimolecular reaction with peroxynitrite was slower and outcompeted by CO_2. Moreover, a different pattern of tyrosine nitration and a lower amount of tyrosyl radical(s) were observed. We hypothesize that the formation of tyrosyl radicals from methemoglobin does not reflect the formation of ferryl/perferryl species, but is largely due to a peroxynitrite-dependent one-electron oxidation.

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