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Mechanism of Formation of EPR-Active Mononitrosyl-Iron Complexes with Dithiocarbamates in Biosystems.

Anatoly F. Vanin, Alexander P. Poltorakov, Vasak D. Mikoyan, Lioudmila N. Kubrina, Ernst Van Faassen

The in-vivo mechanism of NO trapping by iron-dithiocarabamate complexes is revised. Contrary to common belief, we find that in biological systems the NO radicals are predominantly trapped by ferric iron-dithiocarbamates. Therefore, the trapping leads to diamagnetic mononitrosyl complexes which cannot be directly detected with Electron Paramagnetic Resonance spectroscopy. The diamagnetic mononitrosyl complexes are far easier reduced with L-cysteine, glutathione or ascorbate to ferrous state than their non-nitrosyl counterpart. The reduction could also proceed through the mechanism of reductive nitrosylation that could be accompanied with the accumulation of EPR-silent S-nitrosylated dithiocarbamate molecules. The latter as well as diamagnetic mononitrosyl iron complexes with dithio-carbamate compose the majority of the compounds in biological systems containing trapped NO molecules as com-pared with the amount of EPR-detectable paramagnetic mononitrosyl iron complexes with dithiocarbamates. The ex-ogenous reductant, dithionite being added to tissue preparations ex-vivo initiated sharp increase in the amount of paramagnetic mononitrosyl iron complexes with dithiocarbamates. This treatment led to significantly higher yields from NO trapping experiments on mice. Concomitant background signal from copper-dithiocarbamate complexes was eliminated, thereby facilitating the quantification of yields from NO trapping.