Current Topics in Biophysics Vol 26(1), 2002

Nitrogen oxides, the good, the bad, and the ugly

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Nitric oxide, one of the most stable radicals produced by biological systems, has been extensively studied. However, other reactive nitrogen species (RNS) are also formed in mammalian cells, either enzymatically by nitric oxide synthase or nonenzymatically as a reaction product of nitric oxide with other molecules. It is well known that RNS have a high affinity for iron and iron-containing proteins. A study of the effects of RNS on several iron containing proteins indicates that while nitric oxide (NO) inhibits the biological action of most iron proteins with concomitant production of ironnitrosyl EPR signals, the effects are by and large reversible. Nitroxyl anion (NO-) does not significantly inhibit most iron-containing proteins and in fact its reducing capability often is able to prevent the inhibitory effects of nitric oxide. Peroxynitrite (ONOO-) irreversibility inhibits the activity of most iron enzymes tested without formation of EPR signals and often causes significant bleaching of the chromophores, suggesting that iron is removed from the proteins. Snitrosoglutathione (GSNO) effects mimic those of nitric oxide with both reversible inhibition of biological activity and formation of iron-nitrosyl EPR signals. In the absence of added thiols, nitrosonium cation (NO+) has little effect on iron proteins although in the presence of reduced thiols, the effects of nitrosonium are similar to those of nitric oxide, presumably due to the facile formation of S-nitrosothiols from nitrosonium and reduced thiols. At neutral pH, neither nitrite (NO2 .) nor nitrate (NO3) has a significant effect on biological activity of iron proteins and neither induces formation of EPR signals in the iron proteins tested. The bacterial molybdoenzyme, DMSO reductase forms an axial EPR signal when exposed to NO(g) but forms a rhombic EPR signal when incubated with NO-. Incubation of DMSO reductase with nitric oxide synthase (NOS) produces an EPR signal that is a combination of axial and rhombic molybdenum (V) signals. This latter result shows that NOS enzymatically produces both NO(g) and another reductive compound, possibly NO-.