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Peroxynitrite: Reactive Nitrogen Species damaging Effects and Protection against it

Peroxynitrite is a potent nitrogen reactive species (RNS) that induces oxidative and nitrosative stress. It can be caused from excessive NO or excessive O₂⁻ and is common in metabolic disturbances and neurodegenerative diseases including brain injury. The focus of this conference proceeding is to discuss natural agents able to scavenge and neutralize it.

Peroxynitrite (ONOO⁻) is a potent nitrogen reactive species (RNS) that induces oxidative and nitrosative stress including typical oxidative stress induced damaged proteins, DNA, and lipid peroxidation and through nitration of tyrosine (Nitrotyrosine) which disrupts tyrosine kinase cellular signaling and depending on the level of generation has cytotoxic effects including apoptosis, while at higher levels causes necrosis and autophagy ending in cell death. (1-5) It is generated rapidly when Nitric Oxide (NO) interacts with Superoxide Anion (O₂⁻) and can occur intracellularly compartmentalized in cytosol or mitochondrial (1,2), extracellularly (3), and can diffuse through membranes (4) with a half-life of 10-20 seconds. (1,5)

Peroxynitrite can be caused from excessive NO or excessive O₂⁻ where insignificant basal levels are appropriately managed and non-damaging (1,2), however small rises above basal levels create the environment for its stress and cytotoxicity owing to the rapid reaction rate which occurs faster than the intrinsic antioxidant enzyme Superoxide Dismutase (SOD) whose function is to neutralize O₂⁻ free radicals by converting them to hydrogen peroxide (H₂O₂). It's therefore important to understand sources of excessive NO or O₂⁻ generation. (1-3)

Nitric Oxide is generated by the enzyme Nitric Oxide Synthase (NOS) which has 3 isoforms; two are constitutively expressed endothelial (eNOS) for vasodilation and neuronal (nNOS) during neuroplasticity and many brain function activities, where the third inducible (iNOS) is during infection and inflammation. During iNOS activity or during increased stimulation of eNOS/nNOS excessive amounts of NO can be generated. (1,2) Over activity of NADPH-oxidases is associated with high levels of O₂⁻ and coincidentally is part of the structure of the NOS. (1,6) Superoxide is generated during endothelial dysfunction when the eNOS doesn't have appropriate amounts of the precursor Arginine or its cofactor tetrahydrobiopterin (BH₄) which is highly susceptible to oxidative stress and inert as a cofactor upon oxidation, which commonly occurs in hypertension, hyperglycemia, and hyperlipidemia (Diabetes Mellitus, Metabolic Syndrome).

Biography:

Dr. Gantzer is a doctor of chiropractic (DC) with a post-doctorate specialty in clinical nutrition. She is a board-certified diplomate of nutrition (DACBN), fellow of the American Nutrition Association (FACN), earned a masters of nutrition (MS), and is currently pursuing a PhD in nutrition. She is additionally the chair of the Exam Committee for the American Clinical Board of Nutrition (ACBN) as well as the Director of the Mentorship Program for the ACA's Council on Nutrition.

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