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Effect of free radicals on brain protein cystatin and their defense by involvement of antioxidants

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Hypochlorous acid [HOCl] is a potent oxidant formed by myeloperoxidase that causes aggregation of many proteins and the damage of proteins by reaction with amino acid side-chains or backbone cleavage. HOCl is supposed to be the major oxidant produced by neutrophils under physiological conditions. It reacts with wide variety of biological molecules and is known to cause tissue damage. Reaction of HOCl with amino acids, peptides and proteins has been the subject of extensive study. Active myeloperoxidase enzymes identified in human atherosclerotic plaque tissue has HOCl modified apolipoprotein B-100 (Low-Density Lipoproteins, LDLs) and other proteins. HOCl results in oxidative damage to the structure of protein by alteration of amino acid side chains, protein fragmentation and dimerization causing the protein further susceptible to degradation by proteolytic enzymes. Protein aggregation due to HOCl could contribute to inflammatory tissue injury counting the early stages of atherosclerosis. Oxidation and production of free radicals is an integral part of human metabolism. Oxygen is the ultimate electron acceptor linking electron flow system with energy production in the form of ATP. Under certain conditions the electron flow becomes uncoupled leading to the production of free radicals. The molecules with unpaired electrons are highly reactive. They oxidize other molecules to gain electrons and stabilize themselves. The reaction produces another free radical initiating a domino effect of free radical stabilization and formation. The oxidative damage created by free radicals is referred as oxidative stress and has been associated with several degenerative diseases including Alzheimer, cardiovascular and inflammatory diseases, cancer, aging and stroke. Reactive Oxygen Species (ROS) that are produced during several pathological conditions such as inflammation, Alzheimer and damage of various biological molecules are controlled by antioxidants. Cystatins are the inhibitors of thiol proteinases and are ubiquitously present in mammalian system. In brain, they put off unwanted proteolysis and are also involved in several neurodegenerative diseases. In the present study, it was demonstrated that photo-activated HOCl induced modifications in brain cystatin leading to its inactivation and degradation due to hydroxyl radicals. It has been predicted that oxidation of cystatin by ROS *in vivo* may leads to oxidative modification which may direct the damage of this significant protein, as it is so well pronounced *in vitro*. The interplay between free radicals, antioxidants and co-factors is important in maintaining health, aging and age-related diseases. Body's endogenous antioxidant system stabilizes free radicals induced oxidative stress by the ingestion of exogenous antioxidants. If the generation of free radicals goes beyond the protective effect of antioxidants, this can cause oxidative damage which accumulates during the life cycle and has been implicated in aging and age related diseases such as cardiovascular disease, cancer, neurodegenerative disorders and other chronic conditions. Activation of neutrophils, in certain diseases (e.g. inflammatory conditions and atherosclerosis) results in the production of highly reactive species, such as OH and the release of the enzyme myeloperoxidase. Stimulated monocytes and neutrophils generate hypochlorite (HOCl) via the release of the enzyme myeloperoxidase and hydrogen peroxide which may leads to further damage of cystatin.

Biography

Fakhra Amin had completed her PhD from Aligarh Muslim University and did Postdoctoral degree of three years from the same university. She is currently working as a Young Scientist in the Department of Zoology, Aligarh Muslim University. She had published 15 papers in reputed international journals.

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