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### **ACCEPTED MANUSCRIPT**

Oxidant-Specific Biomarkers of Oxidative Stress. Association with Atherosclerosis and Implication for Antioxidant Effects

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#### ABSTRACT

The unregulated oxidative modification of lipids, proteins, and nucleic acids induced by multiple oxidants has been implicated in the pathogenesis of many diseases. Antioxidants with diverse functions exert their roles either directly or indirectly in the physiological defense network to inhibit such deleterious oxidative modification of biological molecules and resulting damage. The efficacy of antioxidants depends on the nature of oxidants. Therefore, it is important to identify the oxidants which are responsible for modification of biological molecules. Some oxidation products produced selectively by specific oxidant enable to identify the responsible oxidants, while other products are produced by several oxidants similarly. In this review article, several oxidant-specific products produced selectively by peroxyl radicals, peroxynitrite, hypochlorous acid, lipoxygenase, and singlet oxygen were summarized and their potential role as biomarker is discussed. It is shown that the levels of specific oxidation products including hydroxylinoleate isomers, nitrated and chlorinated products, and oxysterols produced by the above-mentioned oxidants are elevated in the human atherosclerotic lesions, suggesting that all these oxidants may contribute to the development of atherosclerosis. Further, it was shown that the reactivities of physiological antioxidants toward the above-mentioned oxidants vary extensively, suggesting that multiple antioxidants effective against these different oxidants are required, since no single antioxidant alone can cope with these multiple oxidants.

Graphical abstract

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