

Abstract

Arterioscler Thromb Vasc Biol. 2003 Oct 1;23(10):1881-8.

Small, dense HDL particles exert potent protection of atherogenic LDL against oxidative stress.

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OBJECTIVE: The relationship of the structural and functional heterogeneity of HDL particles to protection of LDL against oxidative stress is indeterminate.

METHODS AND RESULTS: HDL subfractions of defined physicochemical properties were isolated by density gradient ultracentrifugation from normolipidemic human serum (n=8), and their capacity to protect LDL from oxidation was evaluated. Under mild oxidative stress induced by AAPH or Cu(II), HDL subfractions (at equal cholesterol or protein concentration or equal particle number) significantly decreased LDL oxidation rate (-20% to -85%) in the propagation phase (234 nm), which was prolonged by up to 82% with decreased maximal diene formation. Antioxidative activity of HDL subfractions increased with increment in density, as follows: HDL2b<HDL2a<HDL3a<HDL3b<HDL3c (confirmed by thiobarbituric acid-reactive substance content and LDL electrophoretic mobility). Concordantly, antioxidative activity of small HDL prepared by FPLC was significantly higher (+56%) than that of large HDL. Antioxidative action of HDL subfractions was primarily associated with inactivation of LDL lipid hydroperoxides. The potent protective activity of small HDL could not be accounted for exclusively by enzymatic activities (PON1, platelet-activating factor acetylhydrolase, and lecithin-cholesterol acyltransferase).

CONCLUSIONS: Small, dense HDL exhibit potent antioxidant activity, which may arise from synergy in inactivation of oxidized LDL lipids by enzymatic and nonenzymatic mechanisms, in part reflecting distinct intrinsic physicochemical properties.

PMID: 12920049

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