Oxidative Stress: Plasma Lipoprotein Oxidation and the Protective Role of Micronutrients

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Oxidative modification of plasma lipoproteins appears to be a key process in the development of cardiovascular diseases. Thus, the plasma level of oxidized LDL (oxLDL) has been reported to correlate with the risk of cardiovascular complications. Several enzymes are capable of oxidizing LDL *in vitro*, such as 15- and 5-lipoxygenases and myeloperoxidase, but the major *in vivo* catalysts are still far from clear. OxLDL is taken up by vascular endothelial cells and monocyte/macrophages via scavenger receptors, followed by oxidative stress-related metabolic changes in these cells leading, in turn, to endothelial dysfunction and favoring of atherogenesis. Dietary polyphenols such as the flavan-3-ol (–)-epicatechin, contained in cocoa, red wine and green and black tea, protect by several mechanisms. They inhibit LDL oxidation induced by several catalysts in vitro (copper ions, 15-lipoxygenase, 5-lipoxygenase, myeloperoxidase) as well as cell-mediated LDL oxidation. The protection is caused by either direct inhibition of enzyme activity (lipoxygenases) or interference with the catalytic cycle (myeloperoxidase) [1]. Moreover, dietary polyphenols counteract oxidative-stress-related damage to vascular endothelial cells elicited by oxLDL [2]. Endothelial NADPH oxidase activity is the probable target for the latter action [3]. A wide array of phenolics proved to be inhibitors of endothelial NADPH oxidase acting in an apocynin-like fashion [4]. (–)-Epicatechin is substrate of catechol-O-methyl transferase (COMT), which also occurs in vascular endothelial cells capable of forming the apocynin-like metabolite 3'-O-methyl epicatechin. This reaction is assumed to be involved in improvement or preservation of bioavailability and bioactivity of nitric oxide, which has been demonstrated in several clinical studies [1, 4 and refs. therein].

[1] H. Sies, T. Schewe, C. Heiss, M. Kelm, *Am. J. Clin. Nutr.* 81 (2005) 304S–312S.

[2] Y. Steffen, T. Schewe, Y. Steffen, H. Sies, *Free Radic. Res* 40 (2006) 1076–1085.

[3] Y. Steffen, T. Jung, L.-O. Klotz, T. Schewe, T. Grune, H. Sies,. *Free Radic. Biol. Med.* 42 (2007) 933–970.

[4] T. Schewe, Y. Steffen, H. Sies, *Arch. Biochem. Biophys* 476 (2008) 102–106.