魚油の多価不飽和脂肪酸を取り込んだ培養ラット肝細胞における脂質過酸化

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Toxicol. Apple. Pharmacol. **126**(1) 124～128 (1994)

High Peroxidative Susceptibility of Fish oil Polyunsaturated Fatty Acid in Cultured Rat Hepatocytes.

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The peroxidative susceptibility in cultured rat hepatocytes of eicosapentaenoic acid (EPA) and other polyunsaturated fatty acids (PUFA) with different numbers of double bonds was examined. Lipid peroxidation was evaluated using a newly developed HPLC procedure which includes the determination of malondialdehyde (MDA). Following exposure to 0.25–1.0 mM EPA adsorbed to BSA (EPA–BSA), cultured hepatocytes produced MDA in the fatty acid concentration- and incubation time-dependent manner. The rate of MDA production by hepatocytes varied greutly with the degree of PUFA unsaturation, and ranked as follows: docosahexaenoic acid > EPA > arachidonic acid > α-linolenic acid = γ-linolenic acid > linoleic acid > oleic acid. Prolonged exposure of cultured hepatocytes to 1.0 mM EPA–BSA resulted in substantial leakage of LDH into the medium. The cell injury was associated with the loss of cellular GSH and protein thiol groups. Cotreatment of the EPA-supplemented hepatocytes with a GSH-depleting agent, diethylmaleate, promoted the cellular protein thiol loss and LDH leakage. An iron chelator, deferoxamine, and other antioxidants such as *N,N'*-diphenyl-*p*-phenylenediamine and γ-tocopherol efficiently prevented MDA production and consequently LDH leakage in the EPA-supplemented hepatocytes. These results show that peroxidative deterioration in excess of GSH-dependent defense mechanisms may occur in hepatocytes loaded with highly peroxidizable fish oil PUFA.

初代培養ラット肝細胞に、EPAを添加すると、EPA濃度依存的に、また経時的に、脂質過酸化の指標であるMDAが産生された。1mMのEPAを添加した肝細胞は、6時間後からLDH漏出が始まり、24時間後には80%のLDH漏出に達した。この細胞障害は、細胞内GSHや蛋白質SHの減少を伴い、GSH枯渇剤DEM処理により促進された。鉄キレート剤であるdeferoxamineや抗酸化剤であるDPPD、V.Eは、EPA処理細胞における脂質過酸化と、それに伴う細胞障害を効果的に抑制した。種々の不飽和脂肪酸を培養肝細胞に取り込ませ、MDAの産生量を比較したところ、不飽和度の高い脂肪酸ほど、培養肝細胞の過酸化に対する感受性が高かった。