

Abstract

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Docosahexaenoic acid (DHA) blunts liver injury by conversion to protective lipid mediators: protectin D1 and 17S-hydroxy-DHA.

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OBJECTIVE: Docosahexaenoic acid (DHA) is a omega-3 essential fatty acid that reduces the incidence and severity of a number of diseases. Recently, a novel series of DHA-derived lipid mediators with potent protective actions has been identified. In this study we demonstrate that dietary amplification of these DHA-derived products protects the liver from necroinflammatory injury.

METHODS AND RESULTS: In vitro, supplementation of hepatocytes with DHA significantly reduced hydrogen peroxide-induced DNA damage, evaluated by the "comet assay," and oxidative stress, determined by measurement of malondialdehyde levels. In vivo, dietary supplementation of mice with DHA ameliorated carbon tetrachloride-induced necroinflammatory damage. In addition, hepatic cyclooxygenase-2 expression and PGE2 levels were significantly reduced in mice fed DHA-enriched diets. In these animals, increased hepatic formation of DHA-derived lipid mediators (i.e., 17S-hydroxy-DHA (17S-HDHA) and protectin D1) was detected by HPLC-gas chromatography/mass spectrometry analysis. Consistent with these findings, synthetic 17-HDHA abrogated genotoxic and oxidative damage in hepatocytes and decreased TNF-alpha release and 5-lipoxygenase expression in macrophages. In a transactivation assay, 17-HDHA acted in a concentration-dependent manner as a PPARgamma agonist.

CONCLUSION: Taken together, these findings identify a potential role for DHA-derived products, specifically 17S-HDHA and protectin D1, in mediating the protective effects of dietary DHA in necroinflammatory liver injury.

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