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Effects of Conjugated Linoleic Acid (CLA) Isomer, t10c12, c9t11-CLA and Mixed Form on Rat Hepatic Stellate Cells (HSC-T6) and Hepatic Fibrosis

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Rat hepatic stellate cells (HSC-T6) were incubated for 24 h with 10-180 ìM of t10c12 (98%), c9t11 (96%), and a mixed form (c9,t11:t10,c12; 41%:44%) of conjugated linoleic acid (CLA). MTS dye reduction was measured to verify the cell viability in a dose-dependent manner. Among the three CLAs, c9,t11-CLA exhibited the most intense cytotoxic affect on HSCs, whose survival was reduced to 60% under 80 ìM treatment, while cell survival was slightly affected by the mixed form. Three CLA-induced cell deaths were determined by measuring DNA fragmentation using DAPI staining. The degrees of DNA fragmentation were the most severe in HSC treated with 80 ìM c9,t11-CLA. MAPK/extracellular signal regulated kinase-kinase and MEK1 and 2 were not activated in t10,c12-CLA treatment, suggesting that the MEK- dependent apoptosis signal is crucial in HSC induced by c9,t11 and mixed CLA. In order to evaluate the protective effect of CLA on carbon tetrachloride (CCl4) induced hepatic fibrosis in vivo, animals were treated with 10% CCl4 to induce hepatic fibrosis during all experimental periods. Rats were divided into two treatment groups: (1) control diet with tap water *ad libitum* (n=15), (2) 1% CLA diet with tap water *ad libitum* (n=15). In the CLA-supplemented rat liver, -smooth muscle actin (á-SMA) positive cells around the portal vein were significantly reduced. Additionally, collagen fibers were not detected in the CLA-treated group. These results suggest that 9c,11t-CLA but not 10t,12c-CLA exerts a potent cytotoxic effect on HSC in an MEK-dependent manner, resulting in prevention of liver fibrosis.

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