Effects of Dietary Components on Acetaminophen-induced Liver Injury and Human Liver Cancer Cell Lines

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ABSTRACT

In the first part of this study, protective effects of carnosine or histidine against acetaminophen-induced hepatotoxicity in Balb/cA mice were examined. Each compound, at 0.5, 1, or 2 g/L, was added into the drinking water for 4 weeks. Acute liver injury was induced by acetaminophen treatment intraperitoneally. Acetaminophen treatment significantly depleted hepatic GSH and ascorbic acid levels, increased hepatic level of malonyldialdehyde (MDA), reactive oxygen species (ROS), and oxidized glutathione (GSSG), as well as decreased hepatic activity of glutathione peroxidase (GPX), catalase, and superoxide dismutase (SOD) ($P < 0.05$). However, the pre-intake of carnosine or histidine significantly alleviated acetaminophen-induced oxidative stress by increasing GSH content, decreasing MDA, ROS, and GSSG formations, and retaining activity of GPX, catalase, and SOD in liver ($P < 0.05$). Acetaminophen treatment increased the hepatic levels of interleukin (IL)-6, IL-10, tumor necrosis factor (TNF)-alpha, and monocyte chemoattractant protein (MCP)-1 ($P < 0.05$). The pre-intake of carnosine or histidine significantly diminished acetaminophen-induced elevation of these cytokines ($P < 0.05$). However, these two compounds reduced viability and increased DNA fragmentation in Huh7 cell only at 4 and 8 μmol/L ($P < 0.05$). OA or UA treatments concentration-dependently lowered MMP in HepG2, Hep3B and HA22T cell lines ($P < 0.05$). These two compounds also concentration-dependently diminished Na+ – K+-ATPase activity and VEGF level in four test cell lines ($P < 0.05$). Besides Huh7 cell, OA or UA treatments concentration-dependently elevated caspase-3 and caspase-8 activities in other three cell lines ($P < 0.05$). Besides HA22T cell, these two compounds concentration-dependently inhibited cell adhesion and decreased ICAM-1 level in other three cell lines ($P < 0.05$). These findings support that OA and UA are potent anti-cancer agents to cause apoptosis in these liver cancer cell lines.

Keywords : carnosine、histidine、acetaminophen、liver injury、oleanolic acid、ursolic acid、apoptosis、liver cancer

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