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
組氨酸和肌酸在乙酰胺酚引起的肝损伤的保护作用

組氨酸和肌酸在乙酰胺酚导致的肝损伤中的保护作用

4.1 組氨酸和肌酸在乙酰胺酚引起的肝损伤的保护作用

4.1.1 組氨酸或肌酸處理對ALT和AST的影響

4.1.2 組氨酸或肌酸處理對CRP的影響

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表格目錄

表1 攝食0.5、1 或 2 g/L 組氨酸 (His) 或肌酸 (Car)的小鼠, 在第1週及第4週的飲水量(WI, mL/mouse/d) 以及體重(g)

表2 以0.5、1 或 2 g/L 組氨酸 (His) 或肌酸 (Car) 前處理之後再給予或不給予乙醯胺酚(APAP) 的小鼠,其肝中GSH (nmol/mg protein),GSSG (nmol/mg protein),α-tocopherol (nmol/g tissue),以及 ascorbic acid (nmol/mg tissue) 的含量

表3 以0.5、1 或 2 g/L 組氨酸 (His) 或肌酸 (Car) 前處理之後再給予或不給予乙醯胺酚(APAP) 的小鼠,其肝中MDA (μmol/L) 及ROS(nmol/mg protein) 的含量

表4 以0.5、1 或 2 g/L 組氨酸 (His) 或肌酸 (Car) 前處理之後再給予乙醯胺酚(APAP)的小鼠,其肝中TNF-α,IL-6,IL-10,以及MCP-1的含量

REFERENCES


90. Kiyosawa, K., Sodeyama, T., Tanaka, E. et al. 1990. Interrelationship of blood transfusion, non-A, non-B hepatitis and

89. Kim, R., Emi, M., Pratsinis, H. et al. 2007. Ursolic acid, a naturally occurring triterpenoid, demonstrates anticancer activity on human prostate cancer cells. Journal of


80. Ives, N. 2004. By reconsidering its message and its mission, the maker of Tylenol


