Whey-hydrolyzed peptide-enriched immunomodulating diet prevents progression of liver cirrhosis in rats

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Abstract

Objective: Liver fibrosis and subsequent cirrhosis is a major cause of death worldwide, but few effective anti-fibrotic therapies are reported. Whey-hydrolyzed peptide (WHP), a major peptide component of bovine milk, exerts anti-inflammatory effects in experimental models. A WHP-enriched diet is widely used for immunomodulating diets (IMD) in clinical fields. However, the impact of WHP on liver fibrosis remains unknown. Here, we investigated the anti-fibrotic effects of WHP in a rat cirrhosis model.

Methods: Progressive liver fibrosis was induced by repeated intraperitoneal administration of dimethylnitrosamine (DMN) for 3 wk. Rats were fed either a WHP-enriched IMD (WHP group) or a control enteral diet (Control group). The degree of liver fibrosis was compared between groups. Hepatocyte-protective effects were examined using hepatocytes isolated from rats fed a WHP diet. Reactive oxygen species (ROS) and glutathione (GSH) in liver tissue were investigated in the DMN cirrhosis model.

Results: Macroscopic and microscopic progression of liver fibrosis was remarkably suppressed in the WHP group. Elevated serum levels of liver enzymes and hyaluronic

acid, and liver tissue hydroxyproline content were significantly attenuated in the WHP group. Necrotic hepatocyte rates with DMN challenge, isolated from rats fed a WHP-enriched IMD, were significantly lower. In the DMN cirrhosis model, ROS were significantly lower, and GSH was significantly higher in whole liver tissue in the WHP group.

Conclusion: A WHP-enriched IMD effectively prevented progression of DMN-induced liver fibrosis in rats via a direct hepatocyte-protective effect and an antioxidant effect through GSH synthesis.

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