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Abstract

Role of Gal-3 on cisplatin-induced acute liver injury model†

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Abstract:

Oxidative stress is a common mechanism in the cytotoxicity of cisplatin, a widely used antineoplastic agent related to hepatotoxicity. In this context, we highlight galectin-3 (Gal-3), a β-galactoside binding protein that regulates the inflammatory response and oxidative stress, and modified citrus pectin (MCP), an inhibitor of Gal-3. Thus, this study evaluates the effect of Gal-3 inhibition with MCP on cisplatin-induced acute liver injury in Wistar rats. Animals were divided into 4 groups (n = 5/group): SHAM – intraperitoneal (i.p.) injection of saline for 3 days; CIS – i.p. injection of cisplatin (10 mg/kg/day) for 3 days; MCP - orogastric gavage with MCP (100 mg/kg/day) for 7 days, followed by saline via i.p.; and MCP+CIS - gavage with MCP for 7 days, followed by cisplastin via i.p. for 3 days. Cisplatin administration caused a significant weight loss in the animals from CIS and MCP+CIS, an effect corroborated by a marked reduction in the glycogen storage in hepatocytes compared to their control groups. Cisplatin also provoked a marked increase in the influx of leukocytes, liver degeneration, ROS production and STAT3 activation in the hepatocytes, plasma levels of cytokines (IL-6, IL-10), and hepatic toxicity biomarkers (ARG1, GSTα, SDH). Cisplatin per se reduced Gal-3 levels, especially in the mitochondria of hepatocytes. On the other hand, the MCP+CIS group also showed increased levels of IL-1β, TNF-α, and GOT1, as well as raised hepatic levels of MDA production and mitochondrial respiratory complex I. In conclusion, inhibition of Gal-3 with MCP did not protect the liver against the deleterious effects of cisplatin, indicating that Gal-3 is important for tissue, cellular and molecular maintenance of the liver.

Keywords: cytokines, hepatotoxicity, inflammation, mitochondria, modified citrus pectin, ROS.

Abbreviations ARG1, hepatic arginase 1; GOT1, aspartate transaminase 1; GSTα, α-glutathione S-transferase; IL, interleukin; MCP, modified citrus pectin; MDA, malondialdehyde; ROS, reactive oxygen species; SDH, sorbitol dehydrogenase; TNF-α, tumor necrosis factor-α; STAT3, signal transducer and activator of transcription 3.

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