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Suppressive Effect of Modified Arabinoxylan from Rice Bran (MGN-3) on D-Galactosamine-Induced IL-18 Expression and Hepatitis in Rats

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We investigated in this study the effect of modified arabinoxylan from rice bran (MGN-3) and its fractions on D-galactosamine (D-GalN)-induced IL-18 expression and hepatitis in rats. Male Wistar rats were pretreated with MGN-3 or fractions of the MGN-3 hydrolysate, or with saline 1 h before administering D-GalN (400 mg/kg B.W.). The serum transaminase activities, IL-18 mRNA expression level in the liver and IL-18 concentration in the serum were determined 24 h after injecting D-GalN. Both the oral and intraperitoneal administration of MGN-3 (20 mg/kg B.W.) alleviated D-GalN-induced hepatic injury under these experimental conditions. The low-molecular-weight fraction (LMW) of MGN-3 showed the strongest protective effect on D-GalN-induced liver injury, its main sugar component being glucose. Moreover, the D-GalN-induced IL-18 expression was significantly reduced by treating with MGN-3 and LMW. The results suggest that MGN-3 and LMW could provide significant protection against D-GalN liver injury, and that IL-18 might be involved in their protective influence.

Key words: modified arabinoxylan; MGN-3; D-galactosamine; hepatitis; IL-18

MGN-3 is a modified water-soluble hemicellulose from rice bran that can be obtained by partial hydrolysis with enzymes from a basidiomycete. The main chemical constituent of MGN-3 is arabinoxylan, with a xylose in its main chain and an arabinose polymer in its side chain (Fig. 1).[1] MGN-3 also contains β-1,3-glucan and has a variety of physiological functions. NK cell, T cell, and B cell functions are augmented by MGN-3 both *in vitro* and *in vivo*.[1–3] In addition, when MGN-3 is administered in conjunction with conventional chemotherapeutic agents, it has been highly effective in inducing cancer remission in animal models.[4] However, its effect on liver dysfunction in rats induced by D-galactosamine (D-GalN) has not been fully investigated.

Liver injury induced by D-GalN has been used as the animal model for liver injury, since its morphological and pathophysiological characteristics are similar to those of human hepatits B.[5,6] Hepatitis induced by D-GalN in rats is considered to be mediated by the inhibition of protein and mRNA biosynthesis through the depletion of cellular UTP[7] and by the enhanced absorption of endotoxins from the intestines to the blood stream.[8,9] The precise mechanism for D-GalN-induced hepatitis has not yet been elucidated. Recent investigations have also demonstrated that D-GalN hepatotoxicity in rats involved the release of cytokines related to apoptosis and necrosis.[10–12]

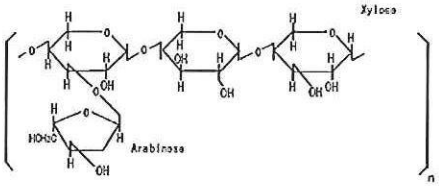

Fig. 1. Main Chemical Structure of MGN-3.

We found in our previous study that IL-18 expression was elevated in D-GalN-induced hepatitis.[13] IL-18 is a potent inflammatory cytokine which regulates autoimmune and inflammatory diseases.

However, the effects of MGN-3 and its hydrolysate on D-GalN-induced IL-18 expression and hepatitis, as well as their mechanism, have not yet been clarified. We therefore investigated in this study the effect of MGN-3 and its hydrolysate on the development of D-GalN-induced hepatitis in rats.

Materials and Methods

Reagents. The following materials were commercially obtained: D-galactosamine hydrochloride (D-GalN) from Sigma Chemicals (St. Louis, MO, USA); the SV Total RNA isolation system from Promega (USA); the first-strand cDNA synthesis kit for RT-PCR (AMV) from Roche Diagnostics (Germany); the SYBR® Premix Ex Taq™ II kit (perfect real-time PCR) from Takara Bio (Otsu, Japan); and the reaction mixture for PCR, Absolute™ QPCR SYBR Green mixes from Abgene (United Kingdom). The rat IL-18 ELISA kit was purchased from Abnova Corporation (Jhongli, Taiwan) and MGN-3 was provided by Daiwa Pharmaceutical Co. (Tokyo, Japan).

Fractionation of MGN-3 by gel filtration. MGN-3 (1 g) was hydrolyzed in boiling water at 100 °C for 1 h in 100 mL (final volume) of 1 N hydrochloric acid. The hydrolysate was cooled under running tap water for 10 min and neutralized with 1 N sodium hydroxide. The solution was evaporated to dryness under decreased pressure by using a rotary evaporator.

The cation-exchange resin used was DOWEX 50W-X8 (Dow Chemicals). To this resin was added 1 N NaOH, and the mixture was stirred. The resin was washed with distilled water (D.W.) and then packed into a column (55 mm × 250 mm). The column was washed with D.W. after sufficient 1 N HCl had flowed through.

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