

Demethyleneberberine attenuates isoniazid-induced-liver injury by reducing CYP2E1 expression and preventing endoplasmic reticulum stress

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Introduction: With the wide clinical application of isoniazid (INH) for tuberculosis treatment, its hepatotoxicity is emerging as a most common adverse effect. Demethyleneberberine (DMB) is a natural product existing in Chinese herb, which plays an important role in protecting against liver disease.

Aim: To investigate the potential effect of DMB against INH-induced liver injury by reducing CYP2E1 expression and preventing endoplasmic reticulum stress.

Methods: To investigate the potential effect of DMB against INH-induced liver injury, 8-week-old male C57 mice were given INH (150 mg/kg) for 3 weeks. The mice were administrated DMB (10 and 20 mg/kg) or a positive control drug tiopronin (50 mg/kg) via enterocelia concurrently. Serum levels of aspartate aminotransferase (AST), and liver homogenate glutathione (GSH), malondialdehyde (MDA), total cholesterol (TC) and triglyceride (TG) were measured. The expression levels of CYP2E1 and ER stress associative protein were determined. Section of livers was collected for photographic and microscopic observation by hematoxylin and eosin (HE) staining.

Results: DMB protected the liver function with significantly low serum AST level. Lipid-lowering effect of DMB was observed with reductions in liver TG and TC, which consisted of HE stained sections (with the observation), reflected that DMB dose-dependently reversed the INH-induced-liver injury, as there were much less lipid droplets depositing inside the parenchyma cells. The benefits of DMB were associated with increased GSH and decreased MDA activity and CYP2E1 expression in the livers. Furthermore, DMB remarkably inhibited ER stress by down-regulating UPR (GRP78) and ATF4-CHOP pathway.

Conclusion: DMB exerts protective effect against INH-induced-liver injury in mice, which may be associated with its regulation of lipid metabolism, reduction of CYP2E1 expression and inhibition of ER stress.

Biography

Lulu Xu is an MD-PhD working at the China Pharmaceutical University, China. She has completed her Bachelor's degree from China Pharmaceutical University, China.

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