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PBI-4050, an antifibrotic/metabolic compound, reduces liver steatosis, ballooning and fibrosis in various metabolic and fibrotic models

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Background & Aim: Chronic liver diseases are a major cause of mortality and morbidity worldwide. Liver fibrosis is characterized by progressive accumulation of extracellular matrix proteins, resulting in destruction of the hepatic architecture. This study investigates the effect of anti-fibrotic/metabolic compound PBI-4050 on NASH and liver fibrosis using three animal models.

Methods: C57BL/6 mice were fed with either a standard or a high-fat diet for 14 weeks and treated with PBI-4050 (200 mg/kg, oral once a day) for an additional six weeks. Liver fibrosis was induced by 10% CCl4 in (2 mL/kg), twice a week for 8 weeks. Mice were treated from day 1 to 58 with oral administration of PBI-4050 (200 mg/kg). Bile Duct Ligation (BDL) was performed on male Wistar rats on day 0 and treated with PBI-4050 (200 mg/kg) (day 1 to 21).

Results: PBI-4050 reduced steatosis and ballooning as well as improved glycogen deposition in HFD-induced NASH. Extensive collagen accumulation was observed in the liver of CCl4-treated animals compared to control. PBI-4050 significantly reduced collagen deposition as measured by histological examination of the liver (H&E, Masson's trichrome staining and histomorphometric analysis of collagen deposition). Treatment with PBI-4050 also reduced liver fibrosis in BDL, as shown by a reduction of collagen in histological analysis.

Conclusion: PBI-4050 reduced liver fibrosis induced by CCl4 and BDL and attenuated steatosis and ballooning in a HFD-induced NASH model. These data suggest that PBI-4050 could be a potential novel therapy for hepatic fibrosis and NASH.

Biography

Ramon M Corpuz has completed his PhD from The University of Tokyo, Japan. He is the Pathologist of Liminal R&D BioSciences Inc (fka Prometic Biosciences Inc.), Canada. He served as a diligent and dependable Veterinary/Toxicologic/Preclinical Pathologist of GLP and non-GLP toxicology and pharmacology non-clinical studies (100+ studies) for more than 10 years. He is a Member of the Society of Toxicologic Pathology with an American College of Veterinary Pathologists board eligibility, a Member of the Charles Louis Davis DVM Foundation for the Advancement of Veterinary Pathology (2007-2009), a Board of Director of the Philippine College of Veterinary Pathology (1998-2000) and a Member of the Japanese Veterinary Science Society (1990-1994). He was a former Monbusho Scholar of the Japanese Government (1987-1994), a Scholar of the International Congress of Virology (1993, Glasgow, UK) and a Scholar of the Philippine Veterinary Drug Association (1981-1982).

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