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NOVEL OXYSTEROL SULFATES ALLEVIATE INJURED-LIVER FUNCTION AND DECREASE MORTALITY IN LPS-INDUCED MOUSE MODEL

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Background: Novel oxysterol sulfates, 25-hydroxycholesterol 3-sulfate (25HC3S) and 25-hydroxycholesterol 3, 25-disulfate (25HCDS) have been demonstrated to be potent regulators of lipid metabolism, inflammatory response, cell apoptosis, and cell survival. In the present study, we tested the chemicals' potential to treat LPS-induced acute liver failure in a mouse model.

Methods: Acute liver failure mouse model was established by intravenous injection with LPS. The injured liver function was treated with intraperitoneal administration of 25HC3S or 25HCDS. Serum enzymatic activities were determined in our clinic laboratory. ELISA assays were used to detect pro-inflammatory factor levels in sera. Western blot, real-time quantitative PCR and RT2 profiler PCR Array analysis were used to determine levels of gene expression.

Results: Administration of 25HC3S/25HCDS decreased serum liver-impaired markers; suppressed secretion of pro-inflammatory factors; alleviated liver, lung, and kidney injury; and subsequently increased the survival rate in the LPS-induced mouse model. These effects resulted from the inhibition of the expression of genes involved in the pro-inflammatory response and apoptosis and the simultaneous induction of the expression of genes involved in cell survival. Compared to 25HC, 25HC3S and 25HCDS exhibited significantly stronger effects in these activities, indicating that the cholesterol metabolites play an important role in the inflammatory response, cell apoptosis, and cell survival *in vivo*.

Conclusions: 25HC3S/25HCDS have potential to serve as novel biomedicines in the therapy of acute liver failure and acute multiple organ failure.

Biography

Shunlin Ren, Professor of Medicine and Research Career Scientist, received his Medical Degree from Shanghai First Medical College, and his PhD degree from Virginia Commonwealth University. He is a Principal Investigator. His research has been supported by NIH R01 and VA Merit Review grants, Research Career Scientist Award, American Liver Scholar Award, and Durect Corporation Research Agreement. He has published more than 50 papers in reputed journals and 55 US and World patents and patent application. He is serving as an Editorial Board Member of repute. His research has focused on the role of oxysterols and oxysterol sulfation in lipid metabolism, inflammatory responses and cell proliferation.

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