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Inulin Ameliorates Alcoholic Liver Disease via Suppressing LPS-TLR4-M ψ Axis and Modulating Gut Microbiota in Mice

Xiaoli Yang^{1, 2}, Fang He², Yanting Zhang², Jing Xue³, Ke Li¹, Xiaoxia Zhang⁴, Lili Zhu³, Zhen Wang¹, Hao Wang³, Shaoqi Yang²

Affiliations

Affiliations

- 1 Clinical Medical College, Ningxia Medical University, Yinchuan, Ningxia, China.
- 2 Department of Gastroenterology, General Hospital of Ningxia Medical University, Yinchuan, Ningxia, China.
- 3 Department of Pathogenic Biology and Medical Immunology, School of Basic Medical Sciences, Ningxia Medical University, Yinchuan, Ningxia, China.
- 4 College of Traditional Chinese Medicine, Ningxia Medical University, Yinchuan, Ningxia, China.

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Abstract

Background: Alcoholic liver disease (ALD) represents a chronic liver disorder caused by alcohol abuse. Numerous studies have demonstrated that gut microbiota dysbiosis plays a critical role in ALD pathogenesis. Application of prebiotic, probiotic, and dietary supplementation to the modulation of gut microbiota contributes to a novel approach to the management of ALD. Inulin, a natural prebiotic found in plants, can restore gut dysbiosis in ALD. However, the exact mechanism of dietary inulin in ALD remains largely unknown.

Methods: Sixty female C57BL/6J mice were randomly divided into 4 groups: pair-fed (PF) group (PF/CON); alcohol-fed (AF) group (AF/CON); PF with inulin (INU) group (PF/INU); and AF with INU group (AF/INU). All mice were fed with isocaloric modified Lieber-DeCarli liquid diets with or without alcohol.

Results: After 6 weeks of feeding, mice were euthanized and associated indications were investigated. The results showed that chronic ethanol (EtOH) intake led to the loss of body weights, abnormal levels of transaminases, and inflammatory indicators (lipopolysaccharide [LPS], interleukin [IL]-6, IL-10, tumor necrosis factor- α , IL-17A), while inulin administration ameliorated these effects. To further understand the underlying mechanism, we investigated macrophages (M ψ s) and gut microbiota in diverse groups. The number of M ψ s was reduced after dietary inulin treatment in chronic EtOH exposure. Hepatic Toll-like receptor 4 (TLR4⁺) M ψ s in AF/INU group were lower than AF/CON group. 16S rRNA sequencing and analysis of gut microbiota indicated the reduction of *Allobaculum*, *Lactobacillus*, and *Lactococcus*, as well as the increase of *Parasutterella* in AF group compared with PF

control. Increased Allobaculum, Lactobacillus, and Lactococcus but reduced Parasutterella in AF/INU group were confirmed that dietary inulin rectified gut dysbiosis to attenuate ALD.

Conclusions: Dietary inulin ameliorates ALD via suppressing LPS-TLR4-M ψ axis and modulating gut microbiota in mice, thus potentially provides theoretical foundation for inulin intervention in the prevention and treatment of ALD.

Keywords: Alcoholic Liver Disease; Gut Microbiota; Inulin; LPS-TLR4-M ψ Axis.

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