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Title:

***Ziziphus jujuba* Mill. polysaccharide attenuates MASLD through multi-organ regulation of lipid metabolism, inflammation, fibrosis, and gut microbiota**

Authors & affiliations:

Jiamei Cui[1,2,3], Minhyeok Kang[1,2,4], Yunpeng Wang[2,3], Eunyoung Kim[1,2], Kayeon Ko[1,2], Guiguo Zhang[2,3], Yunkyoung Lee[1,2,4]**

[1] *Department of Food Science and Nutrition, Jeju National University, Republic of Korea*

[2] *China-South Korea International Joint Laboratory of Functional Polysaccharides in Shandong Province, China*

[3] *Department of Animal Nutrition, Shandong Agricultural University, China*

[4] *Interdisciplinary Graduate Program in Advanced Convergence Technology & Science, Jeju National University, Republic of Korea*

Abstract: (Your abstract must use **Normal style** and must fit in this box. Your abstract should be no longer than 300 words. The box will 'expand' over 2 pages as you add text into it.)

Preparation of Your Abstract

1. The title should be as brief as possible but long enough to indicate clearly the nature of the study. Capitalise the first letter of the first word ONLY (place names excluded). No full stop at the end.
2. Abstracts should state briefly and clearly the purpose, methods, results and conclusions of the work.

Introduction: Clearly state the purpose of the abstract

Methods: Describe your selection of observations or experimental subjects clearly

Results: Present your results in a logical sequence

Discussion: Emphasize new and important aspects of the study and conclusions that are drawn from them

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a growing global health concern characterized by hepatic lipid accumulation, inflammation, and fibrosis, and is closely associated with metabolic syndrome, diabetes, and cardiovascular disease. *Ziziphus jujuba* Mill. (jujube) has long been used in traditional medicine and is increasingly recognized as a functional food due to its diverse nutritional and medicinal properties. Among its active components, jujube-derived polysaccharides (JP) exhibit antioxidant, anti-inflammatory, and gut-modulating effects. However, their therapeutic potential in MASLD remains largely unexplored. Therefore, this study aimed to comprehensively investigate the protective effects and underlying mechanisms of JP against MASLD.

Methods: MASLD was induced in C57BL/6 mice by feeding a high-fat, high-fructose diet for 17 weeks, with or without 5% JP supplementation. Assessments included physiological parameters, serum biochemistry, hepatic lipid metabolism, inflammation, fibrosis-related pathways, multi-organ histopathology, gut microbiota profiling, and hepatic transcriptomics.

Results: JP improved body composition, particularly by reducing fat mass, and alleviated hepatic steatosis by suppressing triglyceride accumulation and modulating PPARγ and SREBP1 pathways. JP attenuated hepatic inflammation by limiting macrophage infiltration and inhibiting NF-κB activation, reduced hepatocellular ballooning, and mitigated fibrosis, as reflected by decreased α-SMA expression. In adipose tissue, JP reduced $F4/80^{+}$ macrophage infiltration and inflammation, while in the intestine it enhanced MUC2 expression and goblet cell activity, thereby improving barrier integrity. JP further modulated the gut microbiota by enriching beneficial bacteria such as *Faecalibaculum*, *Bifidobacterium*, *Coriobacteriaceae*, and *Lachnoclostridium*. Moreover, JP restored hepatic transcriptomic profiles related to lipid metabolism, inflammation, and fibrosis. Integrated analysis identified core microbes and genes contributing to JP's protective effects.

Discussion: This study demonstrates that JP confers protection against MASLD through multi-organ regulation and gut–liver axis modulation, highlighting its potential as a promising dietary intervention for MASLD.