

Polygonum cuspidatum attenuates high-fat diet-induced NAFLD in rats: impact on untargeted serum metabolomics and liver lipidomics

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Abstract:

Introduction: The dried rhizome and root of *Polygonum cuspidatum* Sieb. et Zucc. (PCRR) has long been used to treat atherosclerosis, gastrointestinal disorders and liver disease. However, the underlying mechanism of PCRR against liver steatosis remains unclear.

Materials and Methods: A high-fat diet (HFD)-induced simple steatosis model in rats will be used to evaluate the therapeutic effect of polyphenol-rich water extract from PCRR. Its underlying mechanisms were revealed using untargeted mass spectrometry-based serum metabolomics, hepatic lipidomics profiling approaches and Western blotting assays.

Results: Our study showed that PCRR-treated rats displayed significant reduction of serum TC and LDL-C, hepatic TG, TC levels and total liver lipid contents under a high-fat diet feeding condition. Untargeted metabolomics showed that PCRR significantly restored overall levels of eight lipid classes in liver tissues and elevates the bile acids levels in the serum. We demonstrated that PCRR protected from steatosis by promoting hepatic triglyceride export and decreasing de novo lipogenesis via regulating AMPK/ACC/FAS/PPAR α signaling pathway. Moreover, the anti-steatotic effects of PCRR were related to increased cholesterol uptake and increased bile acids synthesis from cholesterol via regulating LDLR/CYP7A1 signaling pathway. Moreover, resveratrol and/or polydatinderived metabolites were solely detected in the serum of the PCRR-treated group,

indicating these microbial transformed metabolites might partly contribute to the beneficial effects of PCRR.

Conclusions: Our findings suggest that PCRR could treat hepatic steatosis and its related dyslipidemia via multiple pathways.