FASEB J. 2019 Mar 8:fj201802316R. doi: 10.1096/fj.201802316R. [Epub ahead of print]

Berberine alleviates nonalcoholic fatty liver induced by a high-fat diet in mice by activating SIRT3.

Xu X[1], Zhu XP[1], Bai JY[1], Xia P[1,2], Li Y[3], Lu Y[1,2], Li XY[1,2], Gao X[1,2].

Author information

1 Department of Endocrinology and Metabolism, Affiliated Zhongshan Hospital of Fudan University, Shanghai, China.
2 Fudan Institute for Metabolic Diseases, Shanghai, China; and.
3 Key Laboratory of Nutrition and Metabolism, Institute for Nutritional Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, University of Chinese Academy of Sciences, Shanghai, China.

Abstract

Berberine (BBR) shows promising effects in the treatment of nonalcoholic fatty liver disease (NAFLD) by influencing various metabolic aspects. Inhibition of mitochondrial β-oxidation (β-OX) participates in the pathogenesis of NAFLD. Silent mating-type information regulation 2 homolog 3 (SIRT3) has been reported to regulate mitochondrial β-OX by deacetylating its substrate, long-chain acyl-coenzyme A dehydrogenase (LCAD). This study aimed to explore whether BBR can promote mitochondrial β-OX and the role of SIRT3 as well as the mechanisms underlying the effects of BBR on hepatic lipid metabolism in mice fed a high-fat diet (HFD). BBR can significantly improve systematic and hepatic lipid metabolism in HFD-fed mice. Metabolomics analysis revealed that β-OX was inhibited in HFD-induced mice, as indicated by the reduced production of short and medium carbon chain acyl-carnitines, the activated form of free fatty acids, via β-OX, which was reversed by BBR intervention. Exploration of the mechanism found that BBR intervention reversed the down-regulation of SIRT3 and decreased the LCAD hyperacetylation level in HFD-fed mice. SIRT3 knockout (KO) mice were used to identify the role of SIRT3 in the BBR's influence of β-OX. The beneficial effects of BBR on systemic and hepatic metabolism were profoundly attenuated in KO mice. Moreover, the promotive effect of BBR on β-OX in HFD-induced mice was partially abolished in KO mice. These results suggested that BBR alleviates HFD-induced inhibition of fatty acid β-OX partly through SIRT3-mediated LCAD deacetylation, which may provide a novel mechanism and support BBR as a promising therapeutic for NAFLD.-Xu, X., Zhu, X.-P., Bai, J.-Y., Xia, P., Li, Y., Lu, Y., Li, X.-Y., Gao, X. Berberine alleviates nonalcoholic fatty liver induced by a high-fat diet in mice by activating SIRT3.

KEYWORDS: BBR; LCAD; mitochondrial β-OX

PMID: 30848932 DOI: 10.1096/fj.201802316R