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Berberine treatment increases Akkermansia in the gut and improves high-fat diet-induced atherosclerosis in Apoe$^{-/-}$ mice.

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Abstract

BACKGROUND AND AIMS: Gut microbiota plays a major role in metabolic disorders. Berberine is used to treat obesity, diabetes and atherosclerosis. The mechanism underlying the role of berberine in modulating metabolic disorders is not fully clear because berberine has poor oral bioavailability. Thus, we evaluated whether the antiatherosclerotic effect of berberine is related to alterations in gut microbial structure and if so, whether specific bacterial taxa contribute to the beneficial effects of berberine.

METHODS: Apoe$^{-/-}$ mice were fed either a normal-chow diet or a high-fat diet (HFD). Berberine was administered to mice in drinking water (0.5 g/L) for 14 weeks. Gut microbiota profiles were established by high throughput sequencing of the V3-V4 region of the bacterial 16S ribosomal RNA gene. The effects of berberine on metabolic endotoxemia, tissue inflammation and gut barrier integrity were also investigated.

RESULTS: Berberine treatment significantly reduced atherosclerosis in HFD-fed mice. Akkermansia spp. abundance was markedly increased in HFD-fed mice treated with berberine. Moreover, berberine decreased HFD-induced metabolic endotoxemia and lowered arterial and intestinal expression of proinflammatory cytokines and chemokines. Berberine treatment increased intestinal expression of tight junction proteins and the thickness of the colonic mucus layer, which are related to restoration of gut barrier integrity in HFD-fed mice.

CONCLUSIONS: Modulation of gut microbiota, specifically an increase in the abundance of Akkermansia, may contribute to the antiatherosclerotic and metabolic protective effects of berberine, which is poorly absorbed orally. Our findings therefore support the therapeutic value of gut microbiota manipulation in treating atherosclerosis.

KEYWORDS: Akkermansia; Atherosclerosis; Berberine; Gut microbiota; Inflammation

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