

Mangiferin promotes uric acid excretion and kidney function improvement and modulates related renal transporters in hyperuricemic mice.

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Abstract

The effects of mangiferin on uric acid excretion, kidney function and related renal transporters were investigated in hyperuricemic mice induced by potassium oxonate. Mice were divided into normal control group, and 5 hyperuricemic groups with model control, 50, 100, and 200 mg x kg⁽⁻¹⁾ mangiferin, and 5 mg x kg⁽⁻¹⁾ allopurinol. Mice were administered by gavage once daily with 250 mg x kg⁽⁻¹⁾ potassium oxonate for seven consecutive days to create the model. And 3 doses of mangiferin were orally initiated on the day 1 h after potassium oxonate was given, separately. Serum uric acid, creatinine and urea nitrogen levels, as well as urinary uric acid creatinine levels were measured. Mouse uromodulin (mUMOD) levels in serum, urine and kidney were determined by ELISA method. The mRNA and protein levels of related renal transporters were assayed by RT-PCR and Western blotting methods, respectively. Compared to model group, mangiferin significantly reduced serum uric acid, creatinine and urea nitrogen levels, increased 24 h uric acid and creatinine excretion, and fractional excretion of uric acid in hyperuricemic mice, exhibiting uric acid excretion enhancement and kidney function improvement. Mangiferin was found to down-regulate mRNA and protein levels of urate transporter 1 (mURAT1) and glucose transporter 9 (mGLUT9), as well as up-regulate organic anion transporter 1 (mOAT1) in the kidney of hyperuricemic mice. These findings suggested that mangiferin might enhance uric acid excretion and in turn reduce serum uric acid level through the decrease of uric acid reabsorption and the increase of uric acid secretion in hyperuricemic mice. Moreover, mangiferin remarkably up-regulated expression levels of renal organic cation and carnitine transporters (mOCT1, mOCT2, mOCTN1 and mOCTN2), increased urine mUMOD levels, as well as decreased serum and kidney mUMOD levels in hyperuricemic mice, which might be involved in mangiferin-mediated renal protective action.