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Luteolin Ameliorates Cisplatin-Induced Acute Kidney Injury in Mice by Regulation of p53-Dependent Renal Tubular Apoptosis

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Background: Cisplatin chemotherapy often causes acute kidney injury in cancer patients. The causative mechanisms of cisplatin-induced acute kidney injury include renal inflammation, activation of p53 tumor suppressor protein, and tubular apoptosis. Luteolin, a flavones found in medicinal herbs and plants, has been reported to exhibit anti-inflammatory, anti-oxidant, and anti-carcinogenic activities. The purpose of this study was to investigate the anti-apoptotic effect of luteolin on cisplatin-induced acute kidney injury and the molecular mechanism.
Methods: C57BL/6 mice were treated with cisplatin (20 mg/kg) with or without treatment with luteolin (50 mg/kg for 3 d). Renal function, histological changes, degree of oxidative stress, and tubular apoptosis were examined. The effects of luteolin on cisplatin-induced expression of renal p53, PUMA-α, and Bcl-2 family protein were evaluated.
Results: Treatment of mice with cisplatin resulted in renal damage, showing an increase in BUN and creatinine levels, tubular damage, oxidative stress and apoptosis. Treatment of cisplatin-treated mice with luteolin significantly improved renal dysfunction, reducing tubular cell damage, oxidative stress and apoptosis. Examination of molecules involving apoptosis of the kidney revealed that treatment of cisplatin increased levels of p53 and its phosphorylation, PUMA-α, Bax, and caspase-3 activity that were significantly decreased by treatment with luteolin.
Conclusion: These results indicate that cisplatin induces acute kidney injury by regulation of p53-dependent renal tubular apoptosis and that luteolin ameliorates the cisplatin-mediated nephrotoxicity through down-regulation of p53-dependent apoptotic pathway in the kidney.

Key Words: 급성신장손상, 세포사멸, 시스플라틴, 루테올린, P53
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