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## **Cyclo(His-Pro) protects against gentamicin-induced cell apoptosis and cisplatin-induced acute kidney injury through inhibiting p53-mediated apoptotic pathway**

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**Objectives:** Cyclo(His-Pro) (CHP) is an endogenous cyclic dipeptide that exerts cellular protective effects against anti-oxidative damages. However, the role and mechanisms for CHP in preventing cisplatin-induced nephrotoxicity remains largely unknown. In this study, we sought to investigate whether and how cyclo(His-Pro) prevents in cisplatin-induced acute kidney injury (AKI) mouse model.

**Methods:** In this study, a single intraperitoneal injection of cisplatin (10 mg/kg) was employed to induce AKI in ICR mice. To determine the role of CHP on cisplatin-induced AKI, the mice were pretreated with at different dosage CHP (1, 3 mg/kg) orally for 7 days before cisplatin injection. To explore the cell protective effect of CHP, in vitro study was also performed with LLC-PK1 cells, gentamicin (5 mg/ml) was administered to induce cell death.

**Results:** The mice developed severe acute kidney dysfunction exhibited as elevated BUN and creatinine level at day 2 after cisplatin injection. Mice with pretreatment of CHP showed markedly attenuated cisplatin-induced acute kidney injury. Additionally, pretreatment of CHP improved the activity of superoxide dismutase (SOD) and glutathione peroxidase (GPx) which are the enzymes to defense against oxidative stresses. Comparable findings were observed in the protein expression of p53, Bax, caspase-3, and c-Jun which is associated with apoptosis, especially intrinsic apoptotic pathway. In cultured LLC-PK1 cells, which is a pig kidney proximal tubule cell line, CHP showed a protective effect on gentamicin-induced cell toxicity. This study demonstrated that CHP may protect against cisplatin-induced tubular cell apoptosis and AKI through suppression of p53 and up-regulation of antioxidant defense.

**Conclusions:** Together, this study demonstrated that CHP may protect against gentamicin-induced epithelial cell apoptosis and cisplatin-induced AKI through inhibiting apoptosis. Additionally, CHP could be a new therapeutic strategy for the patients suffering from AKI.