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시스플라틴에 의한 급성신손상에서 Genistein의 보호 효과

전북대학교 의학전문대학원 신장재생연구실 내과학교실[1], 한국식품연구원 식품기능본부[2]

정유진[1] · 성미정[2] · 김덕훈[1] · 강경표[1] · 이애신[1] · 이 식[1] · 김 원[1]
Munkhtugs Davaatseren[2] · 황진택[2] · 김현진[2] · 김명선[2] · 권대영[2] · 박성광[1]

Protective Role of Genistein in Cisplatin-Induced Renal Injury

Yu Jin Jung[1], Mi Jeong Sung[2], Duk Hoon Kim[1], Kyung Pyo Kang[1], Ae Sin Lee[1]
Sik Lee[1], Won Kim[1], Munkhtugs Davaatseren[2], Jin-Taek Hwang[2], Hyun- Jin Kim[2]
Myung Sunny Kim[2], Dae Young Kwon[2] and Sung Kwang Park[1]

Renal Regeneration Laboratory Department of Internal Medicine Chonbuk National University[1]
Food Function Research Center Korea Food Research Institute[2]

Oxidative stress and inflammation have been implicated in the pathogenesis of cisplatin- induced nephrotoxicity. Genistein, a polyphenolic nonsteroidal isoflavonoid with estrogen- like activity, has anticancer, antioxidant, and some anti- inflammatory effects. Here, we investigated the protective effect of genistein on cisplatin- induced renal injury and the mechanism of this protection. We treated mice with cisplatin, genistein, or cisplatin plus genistein and examined histological changes, the expression of intercellular adhesion molecule- 1 (ICAM- 1) and monocyte chemoattractant protein- 1 (MCP- 1), the nuclear binding activity of nuclear factor- κ B (NF- κ B), and the infiltration of macrophages. We also evaluated the effect of genistein on the generation of reactive oxygen species (ROS) in cisplatin- treated normal human kidney (HK- 2) cells. Pretreatment of mice with genistein protected against cisplatin nephrotoxicity, as reflected by significant decreases in Blood urea nitrogen (BUN), serum creatinine, and tubular necrosis score. Genistein significantly reduced cisplatin- induced ROS production, the protein levels of ICAM- 1 and MCP- 1, the translocation of the p65 subunit of NF- κ B into the nucleus, and the number of macrophages infiltrating into renal tissue. Genistein reduced ROS production and restored glutathione concentrations in cisplatin- treated HK- 2 cells. Genistein also decreased cisplatin- induced apoptosis by regulating p53 phosphorylation in kidney. Thus, genistein markedly ameliorated the renal damage caused by cisplatin through anti- inflammatory, antioxidant, and antiapoptotic effects, suggesting that genistein could be used therapeutically to prevent cisplatin- induced renal injury.

Key Words : 시스플라틴, 염증, 급성신부전
Cisplatin, Genistein, Inflammation