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The molecular mechanisms of the attenuation of cisplatin-induced acute renal failure by CM-EH in mice

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Abstract

The clinical use of cisplatin (*cis*-diamminedichloro-platinum II, CDDP) is highly limited by its nephrotoxicity. CM-EH was isolated from *Cordyceps sinensis* (CS). CS has benefits in immunoregulation and anti-inflammation, the precise mechanism by which CS is still unclear. We investigated the effects of CM-EH on oxidative stress and oxidation- associated signals, such as p38 mitogen-activated protein kinase (MAPK), NF-κB and TNF-α, in RAW264.7 macrophages and CDDP-induced acute renal failure (ARF) mice. When RAW264.7 macrophages were treated with CM-EH together with LPS, a significant concentration-dependent inhibition of NO production was detected. Western blotting revealed that CM-EH blocked the protein expression of iNOS, and NF-κB. CM-EH blocked the protein expression of COX-2, iNOS, and NF-κB in LPS-stimulated RAW264.7 macrophages, significantly. CM-EH also inhibited LPS-induced JNK, and p38 phosphorylation in LPS-stimulated RAW264.7 macrophages, significantly. CDDP-triggered NF-κB translocation into the nucleus and TNF-α mRNA increase in the kidney were also inhibited in CM-EH -treated mice. These data suggest that CM-EH might be related to decrease the levels of iNOS through the suppression of NO. In the pathogenesis of CDDP-induced ARF, and negative regulation of MAPK activation through inhibition of inflammation appears to play a central role in the beneficial effects of CM-EH.

Key words: CDDP-induced acute renal failure, *Cordyceps sinensis,* CM-EH, MAPK