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## 홍삼투여가 만성 사이클로스포린 신독성으로 유발된 autophagic cell death에 미치는 영향

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### Ginseng Treatment Attenuates Autophagic Cell Death in Chronic Cyclosporine Nephropathy

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**Aims:** Chronic cyclosporine (CsA) treatment induces autophagic cell death characterized by excessive autophagosome formation and decreased autophagic clearance. In this study, we evaluated the influence of ginseng treatment on autophagy in chronic CsA nephropathy.

**Methods:** Mice were treated with CsA (30 mg/kg) with or without Korean Red Ginseng (KRG) extract (0.2, 0.4 g/kg) for 4 weeks. The effect of KRG on CsA-induced autophagosome formation was measured using phospholipid-conjugated form of LC3-II, beclin-1, and autophagic vacuoles were visualized with electron microscopy. Autophagic clearance was evaluated by accumulation of p62/sequestosome 1 (p62) and ubiquitin, then double immunolabeling for p62 and either LC3-II or ubiquitin. To demonstrate the association between the effects of KRG treatment on autophagy and apoptosis, double immunolabeling for LC3-II and active caspase-3 was performed. Multiple autophagy pathways were also examined.

**Results:** KRG cotreatment significantly decreased the expression of LC3-II, beclin-1, and the number of autophagic vacuoles compared with the CsA group, and these changes were accompanied by improvements in renal dysfunction and fibrosis. CsA-induced accumulation of p62 and ubiquitin was also decreased by KRG treatment, and these proteins were colocalized with LC3-II and with each other. KRG treatment simultaneously reduced the expression of both active caspase-3 and LC3-II in the injured area. KRG treatment during chronic CsA nephropathy induced the expression of AKT/mTOR, which is a pathway that inhibits autophagy, and reduced AMPK expression.

**Conclusion:** Ginseng treatment attenuated CsA-induced excessive autophagosome formation and autophagic aggregates. These findings suggest that ginseng has a renoprotective effect against CsA-induced autophagic cell death.

**Key Words:** 사이클로스포린, 홍삼, 신독성, 오토파지, 산화성 스트레스  
Cyclosporine, Nephropathy, Korean red ginseng, Autophagy