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D-Pinitol Alleviates Cyclosporine-Induced Renal Fibrosis via the Activation of Sirt1 and Nrf2 Antioxidant Pathways

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Background: D-Pinitol, 3-methoxy analogue of D-chiroinositol, is one of the most abundant cyclitol present in soybean seeds, legumes and soy food. According to previous studies, D-pinitol has been suggested to possess multifunctional properties including anti-inflammatory, anti-lipidemic and anti-diabetic effects. The aim of this study was to evaluate of the effect of D-pinitol on renal fibrosis through the antioxidant signaling pathway in an experimental model of cyclosporine A (CsA)-induced nephropathy.

Methods: Renal effect of oral treatment of D-pinitol at 50 mg/kg body weight for 28 days was evaluated against CsA-induced renal injury in male ICR mice.

Results: Treatment with D-pinitol significantly prevented the rise in albuminuria, urine volume and urine osmolality and the decrease in renal function as compared to CsA control group. Additionally, D-pinitol attenuated CsA-induced tubulointerstitial fibrosis and inflammation as assessed by Masson's trichrome and α-SMA staining. Administration of D-pinitol increased the expression of heme oxygenase-1, NAD(P)H:quinone oxidoreductase 1 and catalase in CsA-treated kidneys. These renoprotective effects of OA were attributed to the increase in level of sirtuin 1 (Sirt1) and total and nuclear expressions of nuclear erythroid factor 2-related factor 2 (Nrf2), as well as an elevated level of Kelch-like ECH-associated protein 1, indicating that Sirt1 increased by D-pinitol regulates Nrf2 and in turn the activated Nrf2 affects the cellular antioxidant system.

Conclusion: These findings show that the renoprotective effect of D-pinitol against renal fibrosis in CsA-induced nephrotoxicity may result from the inhibition of oxidative stress through Sirt1 and Nrf2 activation and subsequent enhancement of antioxidant enzymes.

Keywords: Cyclosporine, Fibrosis, Kidney, Oxidative stress, Transcription factor