

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

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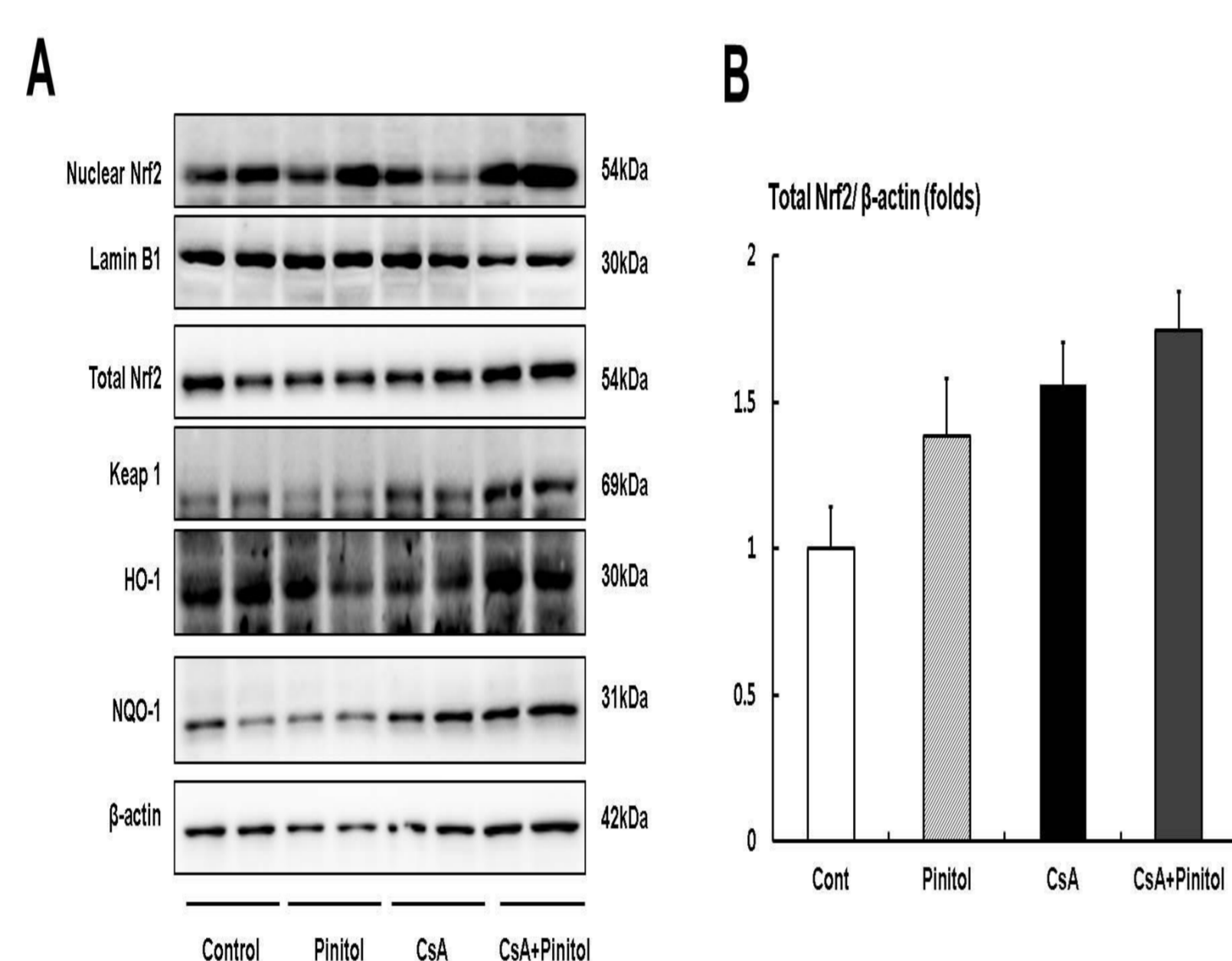
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Background

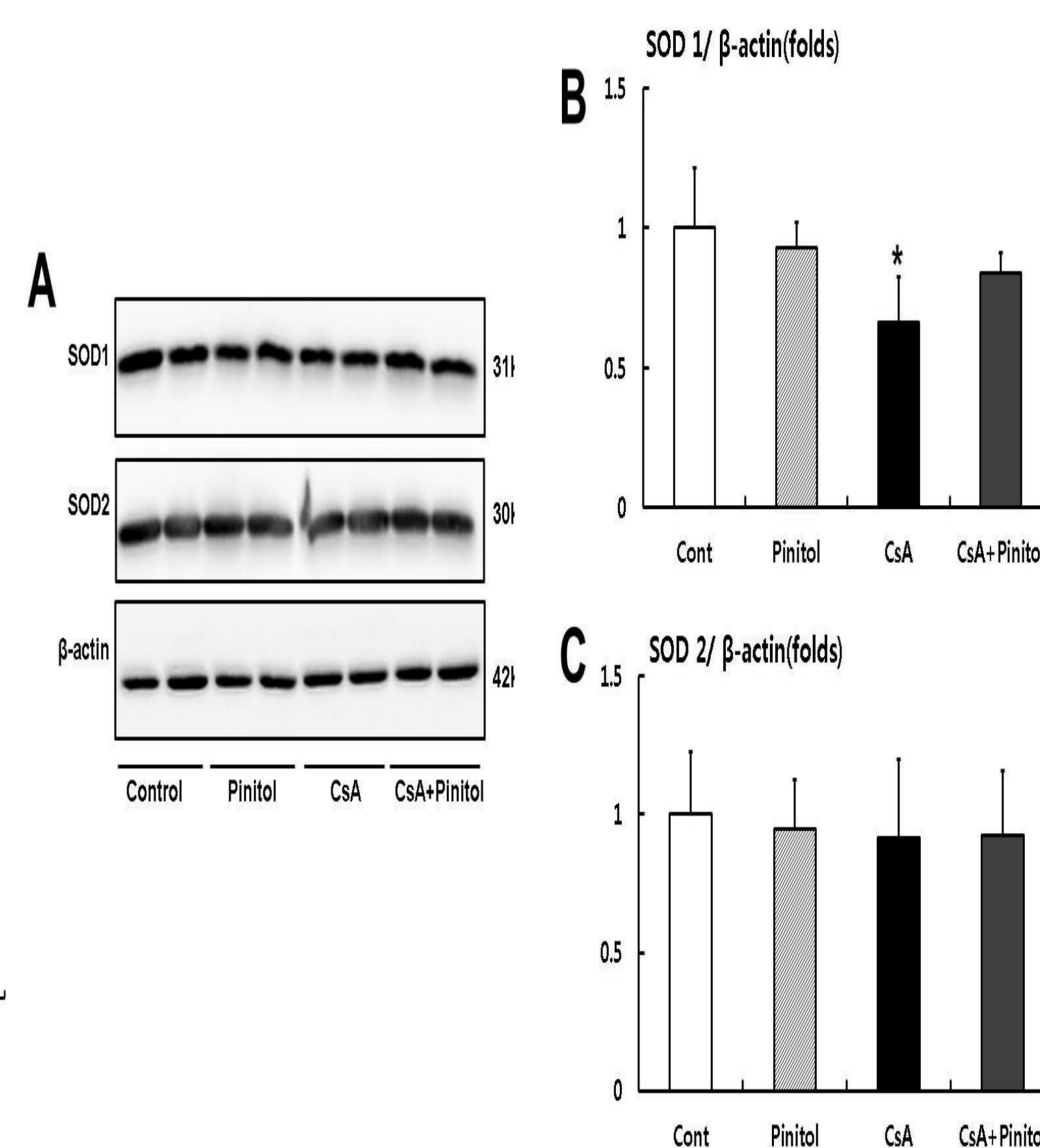
D-Pinitol, 3-methoxy analogue of D-chiroinositol, is one of the most abundant cyclitol present in soybean seeds, legumes and soy food. According to previous studies, D-pinitol has been suggested to possess multifunctional properties including anti-inflammatory, anti-lipidemic and anti-diabetic effects. 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.

Result

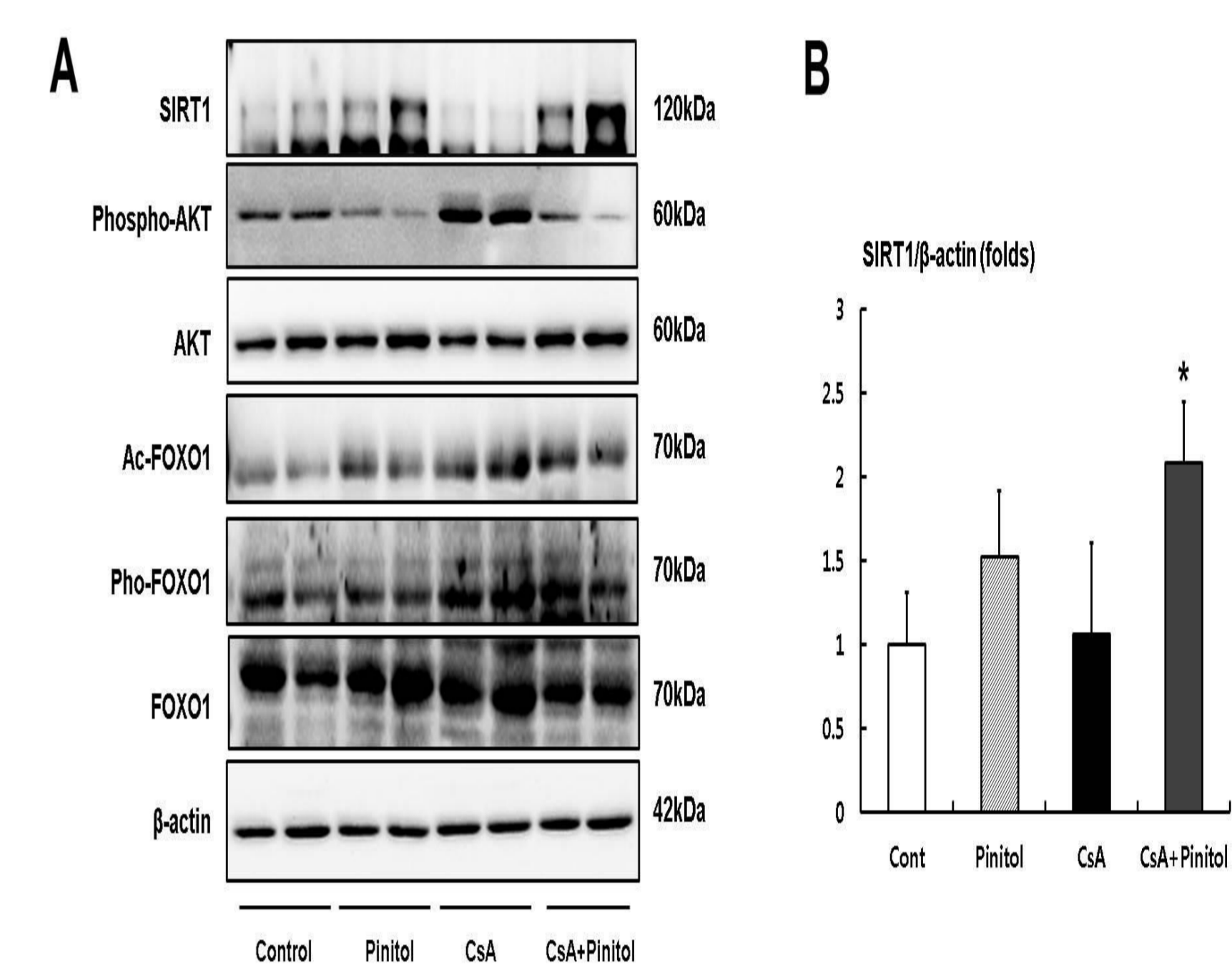
Effects of D-pinitol on Nrf-2, Keap 1 and the antioxidant defence system



Effects of D-pinitol on expressions of SODs in chronic CsA nephropathy



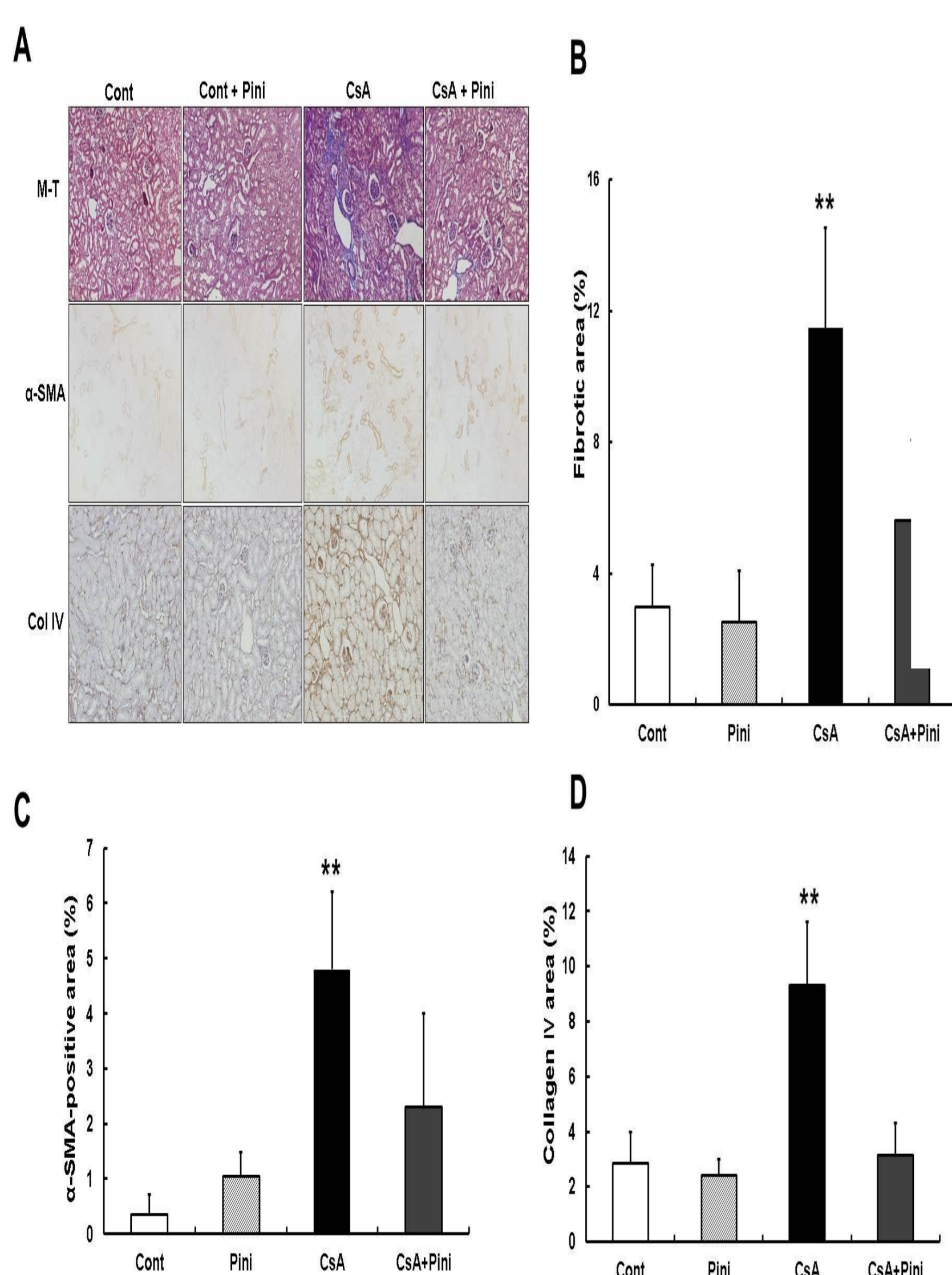
Effect of D-pinitol on Sirt1, Akt and FoxO1 in chronic CsA nephropathy



Design and Method

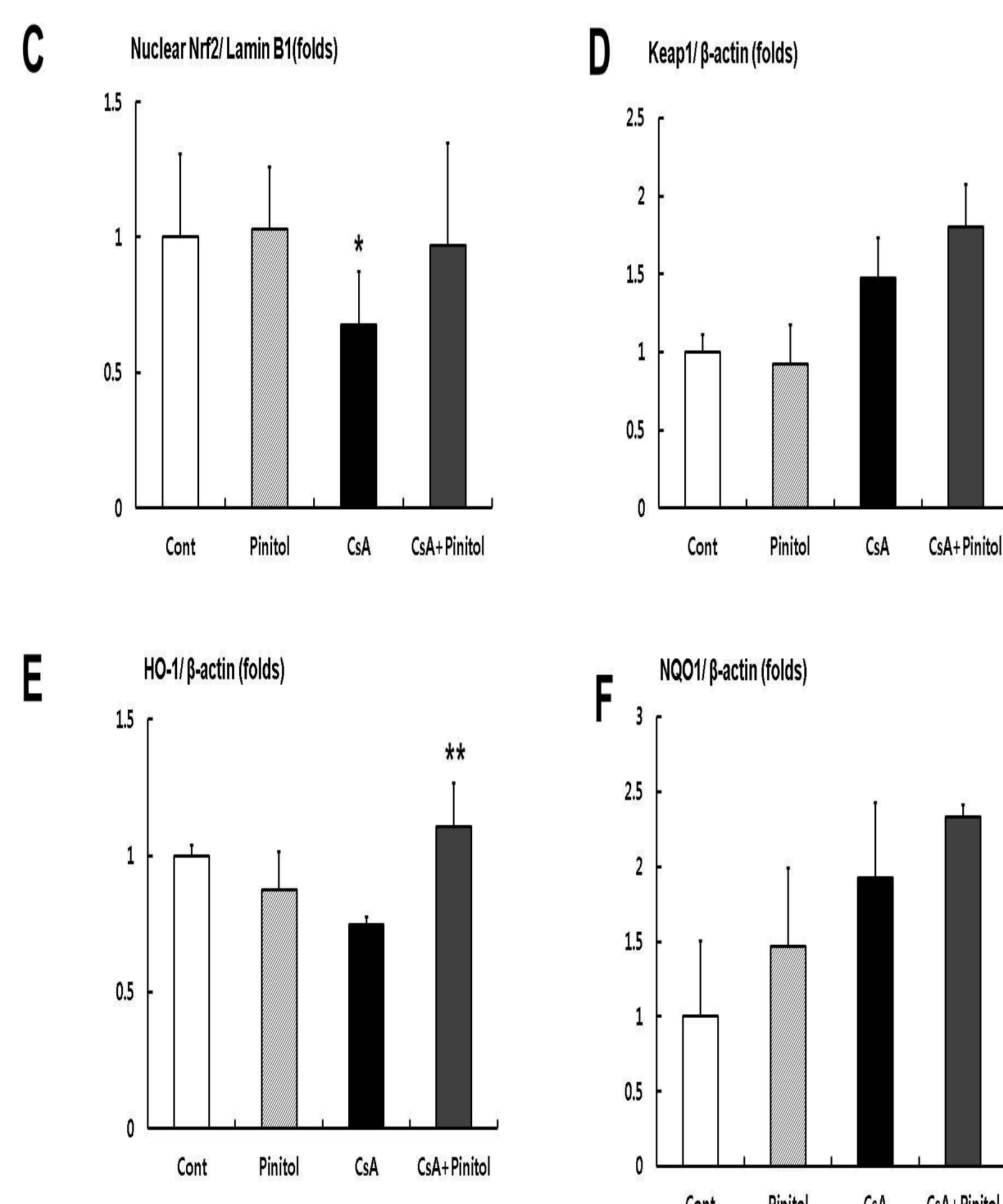
Renal effect of oral treatment of D-pinitol at 50 mg/kg body weight for 28 days was evaluated against CsA-induced renal injury in male ICR mice.

Changes of D-pinitol on renal morphological changes



(A) Representative renal sections stained With Masson-trichrome, α-smooth muscle actin and collagen IV. Quantitative analyses of the results for the tubulo-interstitial fibrosis area(B), α-SMA(C) and collagen IV (D) staining.

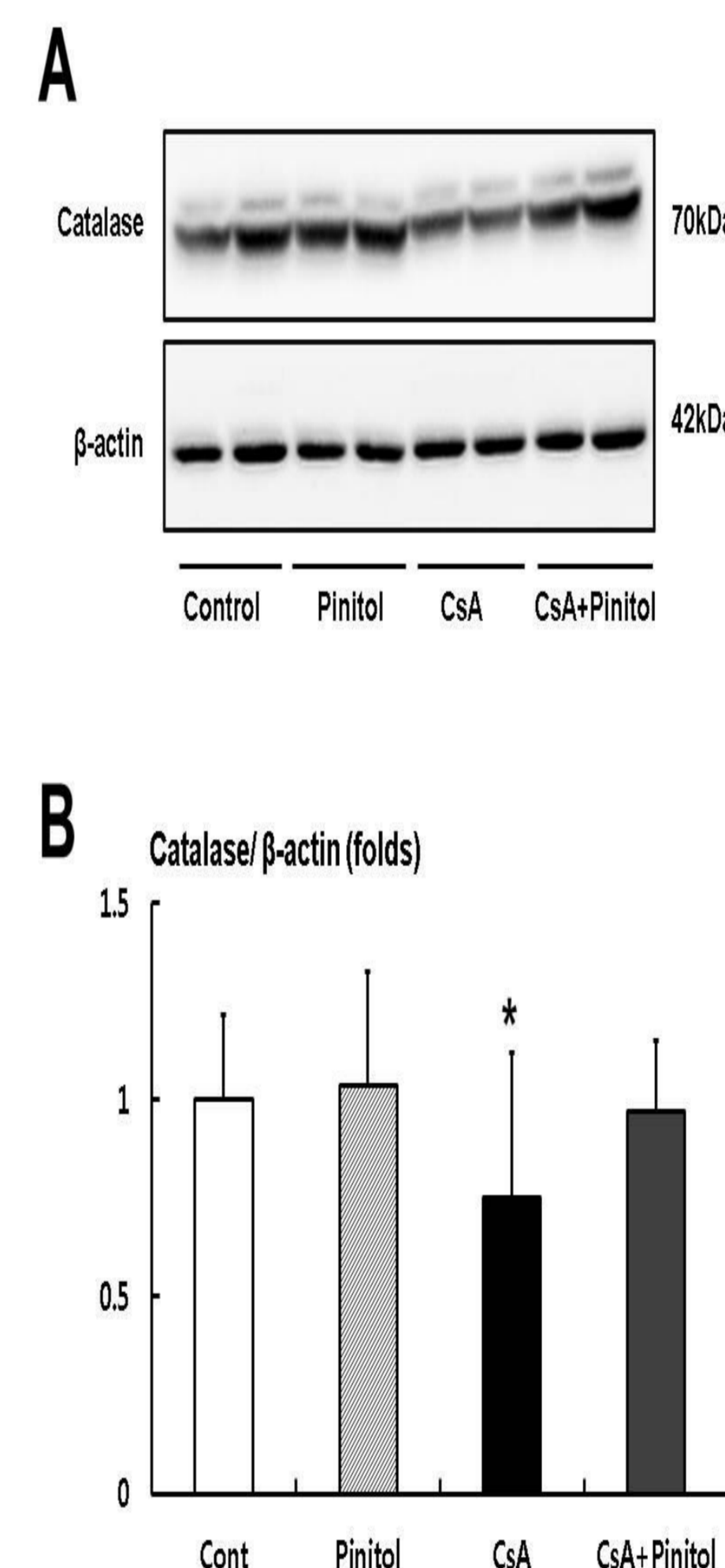
** p < 0.001 vs. other groups.



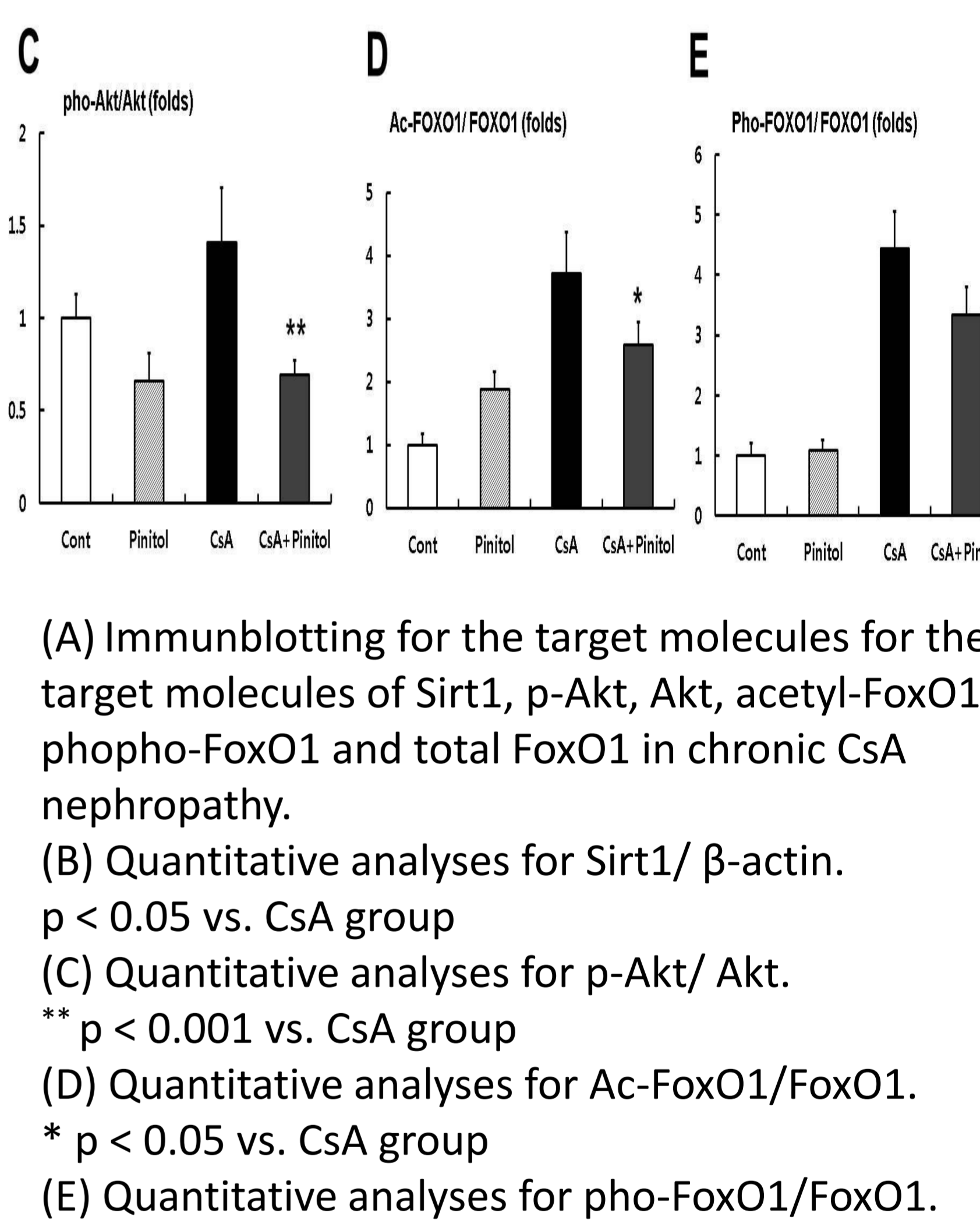
(A) Representative Western blot showing the effects of D-pinitol on nuclear/total Nrf2, Keap1, HO-1 and NQO1 expressions in chronic CsA nephropathy. Quantitative analyses of the results for total Nrf2/β-actin(B), nuclear Nrf2/ Lamin B1(C), keap1/β-actin(D), HO-1/β-actin(E) and NQO1/β-actin(F). * p < 0.05 vs. other groups. ** p < 0.001 vs. CsA group.

(A) Immunoblotting for the target molecules of SOD1 and SOD2 showing the effects of D-pinitol in chronic CsA nephropathy. Quantitative analyses for SOD1/β-actin(B) and SOD2/β-actin(C). * p < 0.05 vs. other groups.

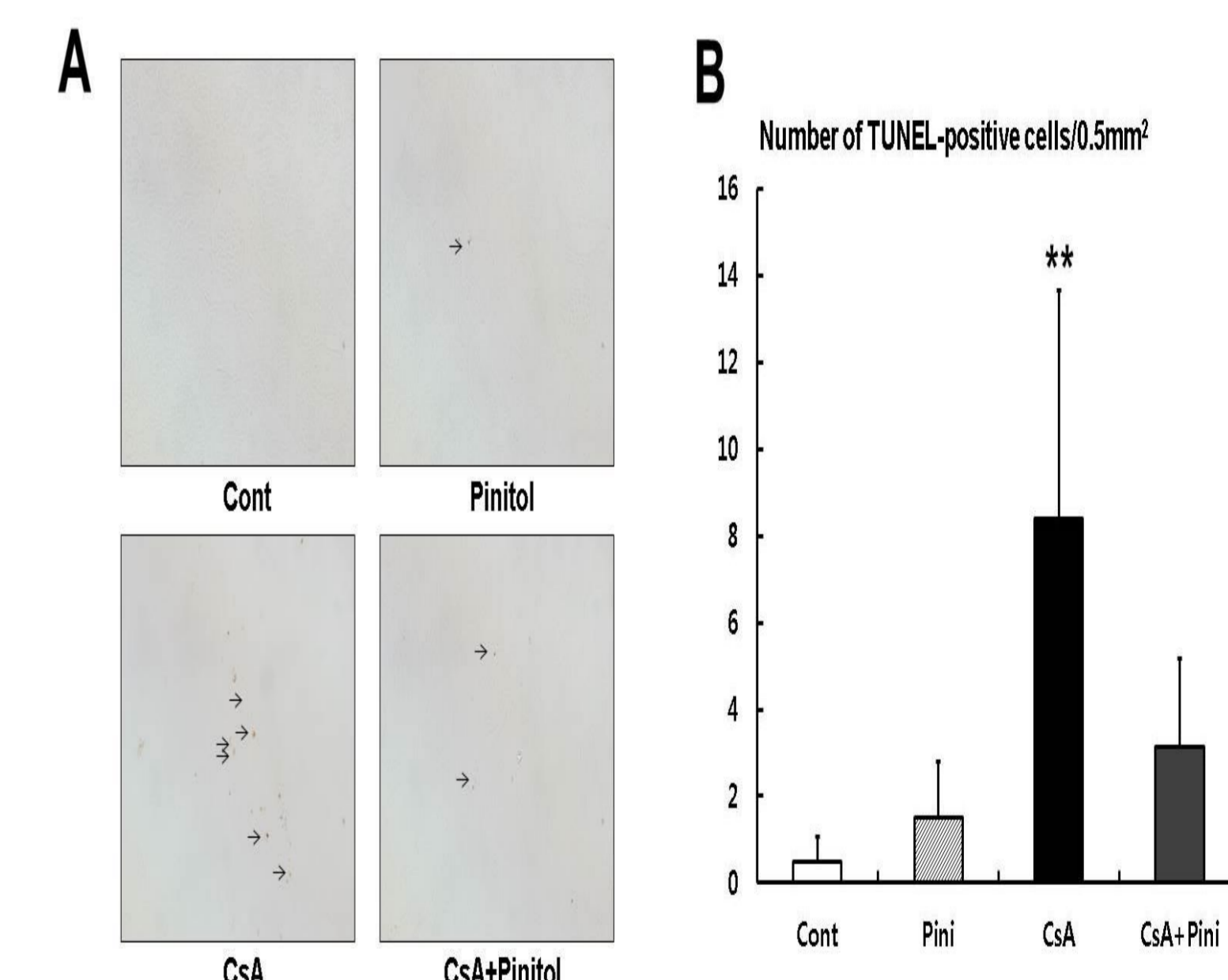
Effects of D-pinitol on catalase in CsA nephropathy



(A) Representative Western blot showing the effects of D-pinitol on catalase in chronic CsA nephropathy. (B) Quantitative analyses of the results for catalase/β-actin. * p < 0.05 vs. other groups.



Effect of D-pinitol on apoptosis in chronic CsA nephropathy



(A) TUNEL assay in kidney tissues of the experimental groups. (B) Quantitative analysis of TUNEL-positive nuclei in the experimental groups. ** p < 0.001 vs. other groups.

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.