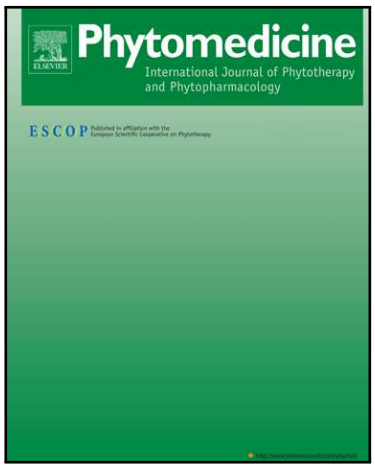

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Novel RAS inhibitor 25-O-methylalisol F attenuates epithelial-to-mesenchymal transition and tubulo-interstitial fibrosis by selectively inhibiting TGF-β-mediated Smad3 phosphorylation

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Abstract

Background: Tubulo-interstitial fibrosis (TIF) is the common pathway in the chronic kidney disease. Epithelial-to-mesenchymal transition (EMT) is a major contributor to the TIF by the increased myofibroblasts. Renin-angiotensin system (RAS) is critical mediator on EMT in progressive CKD. Angiotensin II (ANG) mediates EMT and causes TIF by stimulating transforming growth factor-β1 (TGF-β1). RAS activation could further activate TGF-β1. Inhibition of the RAS is one of the most powerful therapies for progressive CKD. 25-O-methylalisol F (MAF) is a new tetracyclic triterpenoid compound isolated from the *Alismatis rhizoma*, which is extensively used for anti-hypertensive, diuretic and anti-hyperlipidemic effects.

Methods: Inhibitory effect of MAF on EMT is investigated in both TGF-β1- and ANG-induced tubular epithelial cells (NRK-52E) and fibroblasts (NRK-49F). Western blot analyses, qRT-PCR, siRNA, immunofluorescence