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Breaking Ground in CKD Therapy: Harnessing Resveratrol Derivatives to Combat Renal Fibrosis via Transforming Growth Factor Beta 1 Receptor Inhibition

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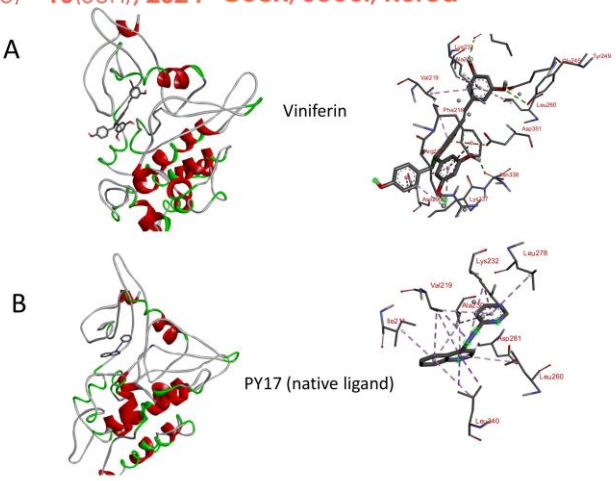
Objectives : Chronic kidney disease (CKD) often involves kidney fibrosis as a typical pathophysiological process. Transforming growth factor-1 (TGF-β1) serves as a key regulator in renal fibrosis, impacting extracellular matrix (ECM) accumulation, epithelial dysfunction, and pro-inflammatory responses. TGF-β1 is recognized as a potent inducer of epithelial-to-mesenchymal transition (EMT). Research has actively explored treatments targeting TGF-β1 or its signaling pathway to combat CKD progression. In recent decades, natural product compounds have emerged as a promising resource for identifying lead compounds in drug research. This study aimed to explore potential natural bioactive compounds targeting the TGF-β1 receptor for renal fibrosis treatment.
Methods : Using a virtual screening strategy, we sought TGF-β1 receptor inhibitors derived from resveratrol derivative bioactive compounds and analyzed their molecular mechanisms. AutoDockTools were employed to screen and dock nine natural bioactive compounds, resveratrol derivatives known for kidney protective effects through antioxidant, anti-inflammatory, and antifibrotic mechanisms. Additionally, online pkCSM prediction assessed adsorption, distribution, and toxicity (ADMET) characteristics.
Results : All resveratrol derivatives exhibited lower binding energies, ranging from -8.7 to -11.3 kcal/mol, in comparison to galunisertib, a TGF-β1 inhibitor, with a binding energy of -7.5 kcal/mol. Their interaction with the TGF-β1 receptor (1PY5) binding site primarily involved hydrophobic interactions from the aromatic ring and hydrogen bonding from the oxygen moiety. Resveratrol derivatives also demonstrated drug-like properties based on ADMET predictions.
Conclusions : In conclusion, resveratrol derivatives show promise as potential TGF-β1 receptor inhibitors. Further research is needed to explore the pharmacophore model for novel lead compounds. These findings hold significance for utilizing resveratrol derivatives as potential candidates for TGF-β1 inhibition and may assist researchers in developing natural bioactive compounds in everyday foods as anti-fibrotic agents.

Figure 1. Interaction of Viniferin (A) and PY17 (B) with TGF-β1 receptor via hydrogen bond.jpg



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