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Bioinformatics investigation of potential natural bioactive compounds targeting TGF-β1 receptor to treat kidney fibrosis

Reny Rosalina[1], Rian Ka Praja[2]
[1]Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Palangka Raya, Indonesia
[2]Department of Microbiology, Faculty of Medicine, Universitas Palangka Raya, Indonesia

Objectives: Kidney fifibrosis is a typical pathophysiological process in the development of chronic kidney disease (CKD). Transforming growth factor-1 (TGF-β1) has been identified as the 'master regulator' in renal fibrosis, influencing extracellular matrix (ECM) accumulation, epithelial dysfunction, and pro-inflammatory responses. TGF-β1 has also been identified as the most potent inducer of the epithelial-to-mesenchymal transition (EMT). Treatment methods targeted at inhibiting TGF-β1 itself or TGF-β1 signaling have been predicted to be potential treatments and have been actively researched in recent decades. Natural product compounds have emerged as a promising resource for identifying lead compound candidates in the course of drug research. This study aimed to investigate potential natural bioactive compounds targeting TGF-β1 receptor to treat kidney fibrosis.

Methods: This study used a virtual screening strategy to look for possible TGF-β1 receptor inhibitors derived from natural bioactive compounds and analyzed their molecular mechanism. The AutoDockTools were used to screen and dock 10 natural bioactive compounds in the group of flavonoids, alkaloids, terpenoids, and phenyl propanoids that have been found to have kidney protective effects via antioxidant, anti-inflammatory, and antifibrotic mechanisms.

Results: The anthraquinone compound (rhein) and two flavonoid compounds (calycosin and epigallocatechin gallate) had the lowest free energy binding of -7.54, -7.54, and 6.24 kcal/mol, respectively. Their interaction with the TGF-β1 receptor (1PY5) binding site was mostly through the aromatic ring's hydrophobic interaction and the oxygen moiety's hydrogen bond. The absence of aromatic rings and the bulky structure, as in the astragaloside IV compound, lowers the binding affinity to the receptor.

Conclusions: It can be concluded that phenolic compounds with non-bulky structures can be the potential candidate as the inhibitor of the TGF-β1 receptor. Further research to investigate the pharmacophore model needs to be performed to obtain the novel lead compounds.

Figure 1. Interaction of various natural bioactive compounds with TGF-β1 receptor .

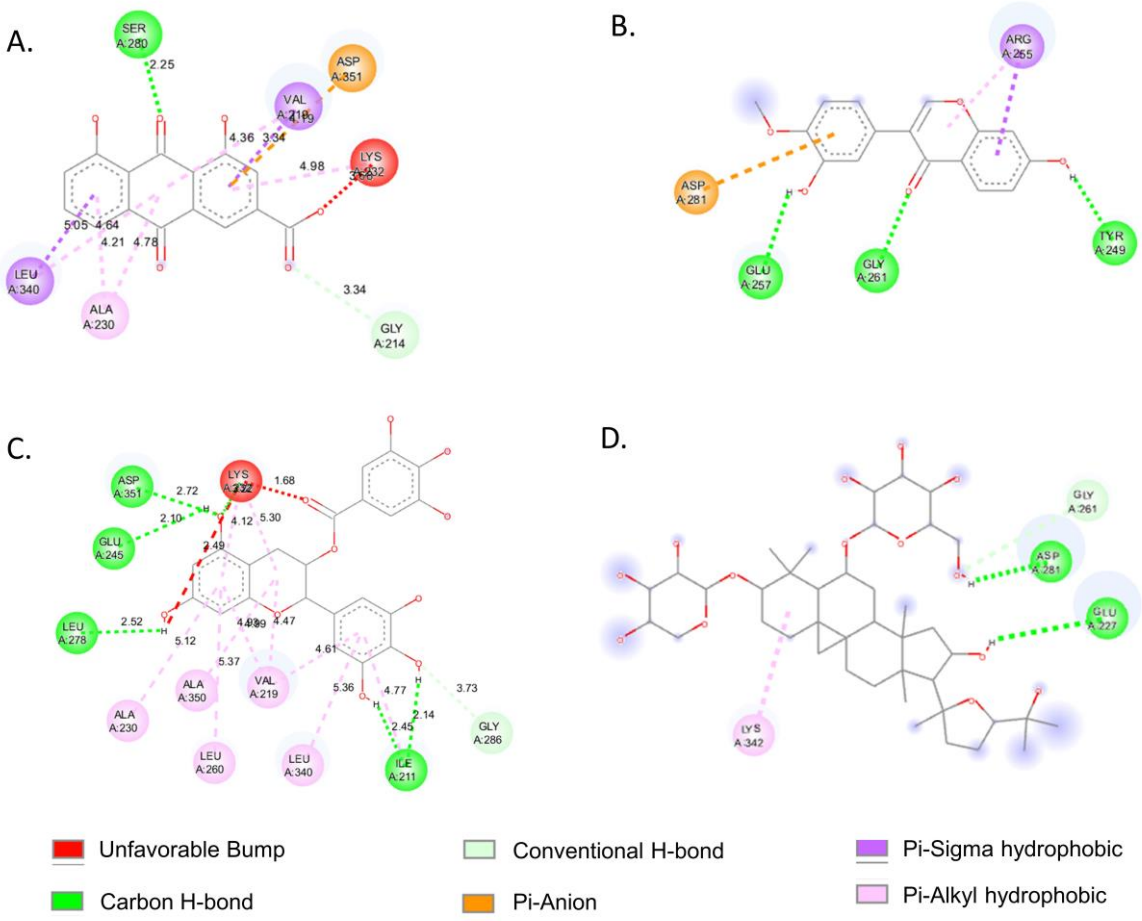

Figure 1. Interaction of rhein (A), epigallocatechin-gallate (B), and calycosin (C) with TGF-β1 receptor via hydrogen bond and hydrophobic interactions, and (D) lesser binding of astragaloside IV with TGF-β1 receptor.