

Title: Exploring the therapeutic targets of stevioside in management of type 2 diabetes by network pharmacology and in-silico approach

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Abstract: The main objective of the current study is to investigate the pathways and therapeutic targets linked to stevioside in the management of T2D using computational approaches. We collected RNA-seq datasets from NCBI, then employed GREIN to retrieve differentially expressed genes (DEGs). Computer-assisted techniques DAVID, STRING and NetworkAnalyst were used to explore common significant pathways and therapeutic targets associated with T2D and stevioside. Molecular docking and dynamics simulations were conducted to validate the interaction between stevioside and therapeutic targets. Gene ontology and KEGG analysis revealed that prostaglandin synthesis, IL-17 signaling, inflammatory response, and interleukin signaling were potential pathways targeted by stevioside in T2D. Protein-protein interactions (PPI) analysis identified six common hub proteins (PPARG, PTGS2, CXCL8, CCL2, PTPRC, and EDN1). Molecular docking results showed best binding of stevioside to PPARG (−8 kcal/mol) and PTGS2 (−10.1 kcal/mol). Finally, 100 ns molecular dynamics demonstrated that the binding stability between stevioside and target protein (PPARG and PTGS2) falls within the acceptable range. This study reveals that stevioside exhibits significant potential in controlling T2D by targeting key pathways and stably binding to PPARG and PTGS2. Further research is necessary to confirm and expand upon these significant computational results.

Keywords: Stevioside, T2D, PTGS2, PPARG, Molecular docking, Molecular dynamics simulation

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