THE KOREAN SOCIETY OF NEPHROLOGY
APCN & KSN 2024
June 13(Thu) - 16(Sun), 2024 Coex, Seoul, Korea
Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

Abstract Submission No.: A-0048

Network Pharmacology and in Vitro Experimental Verification Reveal the Mechanism of Hederagenin in Suppressing Podocyte Injury in Focal Segmental Glomerular Sclerosis

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Objectives : Podocyte injury in FSGS is a complex process in chronic kidney disease (CKD). Hederagenin (HDG) shows potential for treating CKD but its role in FSGS-induced podocyte injury and its characteristics need further elucidation.
Methods : In this study, researchers identified targets of HDG and FSGS from Genecards database. A drug-disease network revealed the relationship between HDG, FSGS, and their targets. Mechanism of HDG on FSGS was confirmed through molecular docking. In vitro experiments on MPC5 cell line verified HDG's inhibitory effect on podocyte injury in FSGS.
Results : Our systematic analysis via the protein-protein interaction (PPI) network revealed the potential mechanisms of HDG in treating FSGS. Consequently, we extracted two therapeutic targets strongly related to FSGS; IL-6 and NOS2, which were found to be bound to HDG via molecular docking, providing the basis for its inhibitory effect on FSGS. Additionally, our in vitro experiments demonstrated that HDG could alleviate TGF-β1-induced injury in MPC5 cells, and significantly reduce the mRNA and protein levels of IL-6 and NOS2.The above research workflow is shown in Figure 1.
Conclusions : This study utilized network pharmacology along with experimental validation to promote the application of HDG in FSGS and to interpret and understand the molecular biological mechanisms involved.

figure 1.jpg