[BIOINFO 2025]

Comprehensive evaluation of current network pharmacology for herbal medicine focusing on identifying mechanisms and therapeutic effects

Won-Yung Lee[1,*]

1 School of Korean Medicine, Wonkwang University, Iksan 54538, Republic of Korea

*Corresponding author: wonyung21@wku.ac.kr

Network pharmacology has gained significant traction as a tool for identifying the mechanisms and therapeutic effects of herbal medicines. However, despite the usefulness of these approaches, their diversity underscores the critical need for a systematic evaluation to ensure consistency and reliability. We aimed to evaluate the network pharmacological analyses, focusing on identifying the mechanisms and therapeutic effects of herbal medicines. We employed a comprehensive approach involving systematic data retrieval, network construction, and analysis. Herbal compounds and their targets were meticulously extracted from five distinct network pharmacology databases to ensure extensive coverage and high data reliability. Advanced network-based methods were used to identify key herbal targets and predict therapeutic effects, thereby enriching the depth and breadth of the analysis. Experimental validation was performed on prostate cancer models to substantiate the computational predictions. The results of the recapitulating task for known herbal ingredient targets revealed distinct patterns in performance and coverage based on network construction and aggregation methods. We performed the same analysis to identify herbal targets and found that network centrality, path counts, and downweighted path counts had their own pros and cons. By comparing network-based methods, we found that considering the impact on the multiscale interactome yielded the highest accuracy in discriminating known therapeutic effects. Using optimal conditions, we successfully identified new indications for herbal medicines and validated these findings through follow-up in vitro and in vivo experiments. This study presents the first comprehensive and critical evaluation of the current network pharmacology analyses in the field of herbal medicine and provides valuable guidance for continued advances in the elucidation of the mechanisms and therapeutic effects.