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Network pharmacology speaking to ethnopharmacology: new data on an ancient remedy

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Abstract

Network pharmacology as a "green approach", predicting metabolite behaviours chemically and biologically and guiding biological experimental design, is a new strategy aiming to uncover the mechanism of action of natural products as drug candidates. It provides a powerful way to identify novel mechanisms of natural products with potential therapeutic effects. This approach has emerged as a powerful tool to overcome the limitations of traditional methods, such as the ability to predict the adverse effects of a drug and the likelihood of failure during clinical trials, by applying systems biology principles to the field of pharmacology. This method combines the multi-omics dataset, computer modeling, and chemical biology so as to reveal pharmaceutical actions and guide drug discovery. Therefore, computer-aided drug design combined with network pharmacology can be viewed as a novel *in silico* screening approach to drug discovery, by utilising chemoinformatics, bioinformatics, structure biology, and chemical biology. This strategy includes target-based virtual screening - molecular docking, ligand similarity-based virtual screening, and inverse screening (Inver-dock), providing a powerful tool for target identification of drug candidates, multitarget discovery, and natural bioactive product profiling. It can also be used for selectivity profiling of drugs, drug repositioning, safety profiling, and metabolism profiling prediction (ADMET).

KEYWORDS

network pharmacology, computer-aided drug design, molecular docking, virtual screening, ethnopharmacology

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MAIN MESSAGE

Network pharmacology is a predictive tool that utilizes computational methods to predict botanicals' chemical behavior and biological targets, thereby informing experimental lab activities [1]. This green approach combines network biology principles with pharmacology to uncover the natural products' mechanism of action (MOA) as potential drug candidates. By integrating multi-omics datasets, computer modeling, chemical biology, and computing chemistry, network pharmacology provides insights into the pharmaceutical actions of botanicals and guides drug discovery. Computer-aided drug design is a key component of network pharmacology, involving computational techniques such as molecular docking, ligand similarity-based virtual screening, and inverse screening. These

methods aid target identification, multitarget discovery, and the profiling of natural bioactive products. By utilizing computer-based predictions, researchers can prioritize and select botanicals for further investigation, thereby reducing the time, cost, and environmental impact of traditional experimental approaches. Traditional drug discovery and development processes often involve extensive laboratory experiments, which can be resource-intensive and time-consuming. In contrast, network pharmacology allows for the virtual screening and prediction of botanicals' chemical behavior and biological targets, thereby reducing the need for large-scale experimental testing [2,3]. This approach minimizes using laboratory resources, such as chemicals, reagents, and laboratory animals, leading to a more environmentally friendly and sustainable research process.

Moreover, network pharmacology enables researchers to explore a wide range of botanicals and their potential therapeutic effects without requiring extensive laboratory experiments. By utilizing computational models and databases, researchers can analyse and predict the pharmacological properties of botanicals, including their chemical behavior and potential biological targets. This approach allows for the identification of promising candidates for further experimental validation, reducing the number of unnecessary experiments and minimizing the overall environmental impact of the research process. In addition, network pharmacology can contribute to developing more sustainable and eco-friendly drug discovery strategies. By providing insights into the MOA and the potential therapeutic effects of botanicals, this approach can guide the selection and optimization of drug candidates with reduced toxicity and adverse effects. This can help develop safer and more environmentally friendly drugs, minimizing the negative impact on human health and the environment [4]. Network pharmacology adds value to experimental work by providing a predictive tool to inform and guide experimental lab activities. By integrating computational predictions with experimental validation, network pharmacology enhances drug discovery and development efficiency and success rate. Therefore, it serves as a green approach by reducing the reliance on extensive experimental testing and contributing to more sustainable research practices.

In addition, combining artificial intelligence (AI) and network pharmacology can also help elucidate the MOA of herbs or compounds used in treating diseases [5]. For example, graph neural networks can predict potential targets and infer the relationships between compounds and targets. At the same time, network pharmacology can provide information on the known targets and pathways associated with a disease. Combining these approaches makes identifying new targets and pathways involved in the disease condition and potential interactions between different compounds and targets possible. This can lead to the discovery of new drugs or the repurposing of existing drugs or therapies to treat the disease. This approach can help to reduce the time and cost associated with traditional therapy discovery methods. Generative adversarial networks are one of the most promising generative AI algorithms for generating new molecules with desired properties, such as high potency and low toxicity in recent years, which can significantly accelerate the therapy discovery process by developing potential candidates for testing and reducing the time and cost associated with traditional methods [6]. The framework based on an integrative strategy of network pharmacology to investigate pharmacological mechanisms is shown in the following steps: (i) pharmacokinetic parameters (ADMET, drug-likeness, *etc*.) and drug targets (PharmMapper, TargetNet, SwissPredicition, SEA, *etc*.) are predicted for the analysis, (ii) targets related to different diseases are selected from public gene databases (GEO, GeneCards, DisGeNET, *etc*.), (iii) the intersected gene list is obtained by overlapping drug targets and diseases targets, (iv) the mechanism of action analysis is performed using Metascape, STRING, and Cytoscape, and (v) the critical targets of medicinal herbs treating diseases are validated by molecular docking, molecular dynamics, and *in vitro* and *in vivo* experiments.

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CONFLICT OF INTEREST STATEMENT

The author declares no conflicts of interest.

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