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As traditional medicine continues to gain recognition in modern healthcare, there is a growing need to scientifically validate and understand the therapeutic effects of these ancient remedies. Jamu, a traditional Indonesian herbal medicine, has been used for centuries to treat a wide variety of ailments. Determining the precise mechanisms by which jamu functions is difficult due to its complexity, as it frequently consists of a blend of various plant-based compounds. To investigate the active ingredients in jamu and comprehend their molecular mechanisms, network pharmacology has proven to be an effective tool in this regard.

Network pharmacology represents a shift from the traditional "one drug, one target" paradigm to a more holistic "multi-compound, multi-target" approach. This discipline integrates systems biology with pharmacology to map out the networks of interactions that various bioactive compounds engage in, aiming to understand how these compounds influence multiple targets and pathways simultaneously. This is particularly relevant for herbal medicine, which often involves complex mixtures of bioactive compounds (Li et al., 2023). The purpose of this editorial is to highlight the importance of network pharmacology as a method to validate and

## Network Pharmacology Approach to Explore Active Compounds and Molecular Mechanisms of Jamu

Pendekatan Farmakologi Jejaring Untuk Identifikasi Senyawa Aktif dan Mekanisme Molekular Jamu

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understand the therapeutic effects of jamu. By examining recent studies, we aim to showcase how this approach can systematically explore the interactions between the multiple bioactive compounds in jamu and their molecular targets. This not only enhances our understanding of how jamu works at a molecular level but also opens up new avenues for the development of novel therapeutic agents derived from traditional medicine.

Recent studies have successfully applied network pharmacology to investigate the active compounds and mechanisms of action in traditional Chinese medicine (TCM). For instance, research published in 2021 used network pharmacology to understand the effects of jamu on metabolic disorders. Gegen in TCM is one of the most prevalent Chinese herbs for treating metabolic disorders. The key active ingredients of Gegen that are responsible for its anti-diabetic and antihyperlipidemic effects are isoflavones, such as daidzein, genistein, and puerarin, as well as  $\beta$ -sitosterol. These ingredients primarily target AKR1B1, EGFR, ESR, TNF, NOS3, MAPK3, PPAR, CYP19A1, INS, IL6, and SORD, as well as multiple pathways, including the PI3K-Akt signaling pathway, the AGE-RAGE signaling pathway in diabetic complications, fluid shear stress, and atherosclerosis, the

PPAR signaling pathway, insulin resistance, the HIF-1 signaling pathway, and the TNF signaling pathway. (Yuan et al., 2021).

The polypharmacological nature of jamu, where individual compounds can interact with multiple molecular targets, has also been a focus of recent research. Quercetin, a compound commonly found in jamu, can influence various pathways associated with oxidative stress, inflammation, and apoptosis. This study highlights quercetin's potential role in preventing or treating cancer (Fu et al., 2023), providing a scientific basis for the traditional use of traditional medicine in cancer prevention (Lu et al., 2020).

The practice of integrative medicine has made significant progress in increasing treatment precision and efficiency by incorporating global trends in network pharmacology. The comprehensive methodology of integrative medicine is enhanced by network pharmacology, which studies the complex relationships between pharmaceuticals and biological molecular mechanism networks. This synergy is especially helpful in the field of herbal medicine, where it can be difficult to verify the safety and efficacy of treatments. Herbal formulations are complicated and frequently contain several active compounds, which makes it challenging to standardize dosages and guarantee reliable therapeutic effects. Novel approaches to investigate these interactions, determine active components, and forecast possible synergies are provided by recent advancements in network pharmacology. Standardized procedures and carefully planned clinical trials are necessary for strong validation before these insights can be implemented in clinical practice. (Wang et al., 2021).

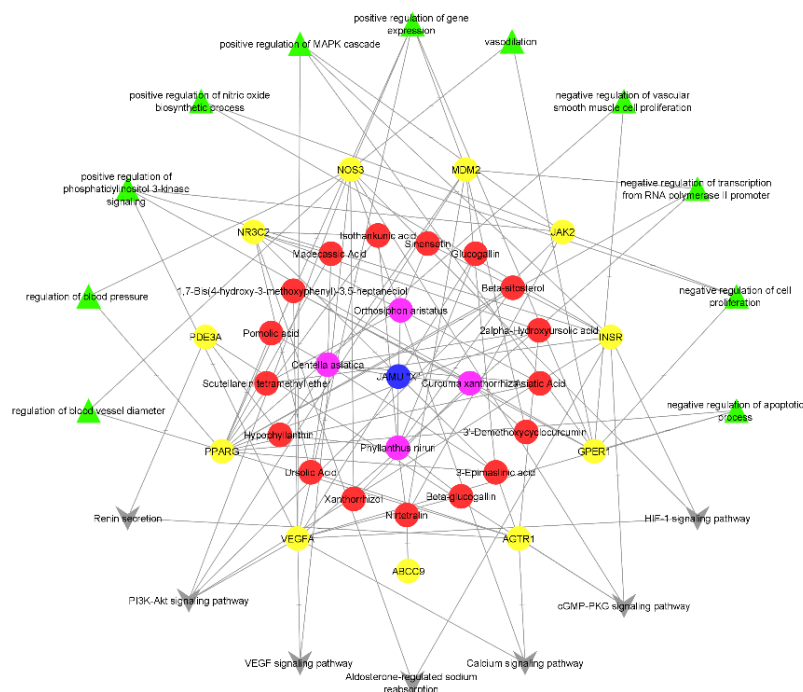
Network pharmacology has also been utilized to predict potential interactions between jamu and conventional drugs, which is crucial for ensuring the safe integration of traditional and modern medicine. For example, a study in 2024 used this approach to explore how fitofarmaka product (DLBS2411). Preclinical and clinical research have demonstrated the anti-ulcer properties of DLBS2411, a bioactive fraction of *Cinnamomum burmannii*. P-cymene, copaene, and cinnamondehyde—three DLBS2411 compounds—were chosen as highlighted compounds in this study for their ability to treat gastritis. These compounds primarily target seven target proteins: PTGS1, PTGS2, HPGD, NOS2, APT4A, HRH2, and EGFR. The primary ways in

which these proteins work are through mucosal defense, cell regeneration, and proton pump down regulator pathways. (Rustan et al., 2024).

The fundamental difference between traditional pharmacology and network pharmacology lies in their approach to understanding and utilizing complex herbal mixtures. Traditional pharmacology typically focuses on isolating single active compounds from herbs and studying their effects on specific biological targets. In contrast, network pharmacology considers the intricate interactions between multiple compounds within an herbal mixture and their collective impact on various biological networks. This holistic approach acknowledges the synergistic effects and potential for multiple targets, making it particularly well-suited for analyzing and validating the complex formulations used in herbal medicine. (Heinrich et al., 2020)

In the case of hypertension, a study investigates the molecular mechanisms of the Indonesian scientific jamu used to treat hypertension. Utilizing databases such as the Kyoto Encyclopedia of Genes and Genomes (KEGG), the researchers employed network analysis to investigate the underlying mechanisms after identifying the active compounds, evaluating the bioavailability, and comparing the medications. **Figure 1** illustrates the relationship between the mechanisms of scientific jamu hypertension and network pharmacology pathways. The study found that 44 compounds had relevant bioavailability metrics and drug similarities. Pathway analysis revealed that the antihypertensive effects of this herbal drug involve several signal pathways, including HIF-1, Relaxin, PI3K, and MAPK, which are associated with vascular endothelial and atherosclerosis. (Setiani et al., 2024).

In conclusion, network pharmacology provides a comprehensive framework for exploring the active compounds and molecular mechanisms of jamu. By integrating traditional knowledge with modern scientific techniques, this approach not only validates the therapeutic uses of jamu but also uncovers new possibilities for drug discovery and development. As research in this field continues to grow, network pharmacology will likely play an increasingly important role in bridging the gap between traditional and modern medicine, ultimately leading to safer and more effective therapeutic options.



**Figure 1.** Visualization of Networks Pharmacology and Kyoto Encyclopedia of Genes and Genomes (KEGG) Analysis in Jamu

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