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Exploration of Ethnomedicinal Plants for Skin Diseases: A Network Pharmacology Approach to Revealing the Molecular Mechanisms of Traditional Herbs

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ABSTRACT

Improving the prevalence of skin disease is multifactorial. And limitations therapy conventional push exploration. Ethnomedicine uses a systems approach to discover more effective and safe drug candidates. This study aims to analyse and synthesise scientific evidence on the use of ethnomedicinal plants for the treatment of skin diseases and to identify the relationship between ethnomedicine and drug use. between bioactive compounds and target biologicals through a *network pharmacology approach*. The method used is qualitative research with an *integrative review approach*, drawing on data from Google Scholar, Elicit, Scite.ai, Scispace, DOAJ, and Scopus. Inclusion criteria are articles published from 2016 to 2026, relevant, written in English and Indonesian, and available *in full text*. The results of the study indicate that plants with high ethnobotanical value contain secondary metabolites, such as flavonoids, alkaloids, and terpenoids, which contribute to antioxidant, antimicrobial, and anti-inflammatory activities. The *network pharmacology approach* reveals multi-target interactions through biological pathways such as inflammation, apoptosis, and metabolism, which are further strengthened by bioinformatics and *molecular docking analyses*. The conclusion of this study confirms that integrating ethnomedicine and *network pharmacology* can explain the comprehensive molecular mechanisms of medicinal plants. The implementation has the potential to support the development of evidence-based, drug-related scientific research and to serve as the basis for innovation in modern dermatological therapy.

1. INTRODUCTION

Ethnomedicine is a traditional knowledge system that uses plants to treat various ailments, including skin diseases, passed down from generation to generation and based on the community's empirical experience. In the modern context, ethnomedicine is recognized as an important resource for discovering new drugs, as it contains various bioactive compounds with complex, multi-target mechanisms of action. This approach aligns with the concept of systems pharmacology, which emphasizes interactions. between various component bioactives with target biological in the body. Because of that, the integration of ethnomedicine with modern scientific approaches is very relevant to reveal the therapeutic potential of plants more comprehensively (Huang et al., 2019; Bai et al., 2025; Elmi et al., 2023)

With advances in technology, the network pharmacology approach has emerged as an innovative method for systematically elucidating the mechanisms of action of ethnomedicinal plants. This approach enables analysis of the relationships among active compounds, protein targets, and biological pathways. something network complex, capable of explaining the characteristics of multi-component, multi-target systems in medicinal plants. In the context of multifactorial skin diseases, such as psoriasis and dermatitis, network pharmacology provides deeper insights into the underlying mechanisms of plant-based therapies. Thus, integrating ethnomedicine and network pharmacology has become a strategic approach in modern pharmacological research (Huang et al., 2019; Yang et al., 2024; Zhou et al., 2024).

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Various studies show that the use of plants in ethnomedicine has significant potential for treating skin diseases through complex biological mechanisms. Bibliometric studies have shown a significant increase in publications on the use of medicinal plants for skin diseases over the last decade, with the research focus shifting from traditional uses to network pharmacology-based exploration of molecular mechanisms. Furthermore, studies have shown that network pharmacology approaches are capable of identifying interactions between active plant compounds and relevant biological targets in skin diseases such as psoriasis, including inflammatory and immunological pathways (Yang et al., 2024; Li et al., 2025; Huang et al., 2019; Zhou et al., 2024; Bai et al., 2025).

More carry on, a study shows that integrating network pharmacology and metabolomics approaches can identify key active components and metabolic pathways involved in the therapeutic effects of ethnomedicinal plants. For example, a study by Zhou et al. (2024) identified dozens of biomarkers and metabolic pathways that modulate the immune system through a network-based approach. Besides that, studies show that plant drugs have an anti-inflammatory, antimicrobial, and immunomodulatory effect, which is relevant in the treatment of skin, and work through interaction with multiple targets (Which et al., 2024; Huang et al., 2019; Bai et al., 2025; Elmi et al., 2023; Li et al., 2025).

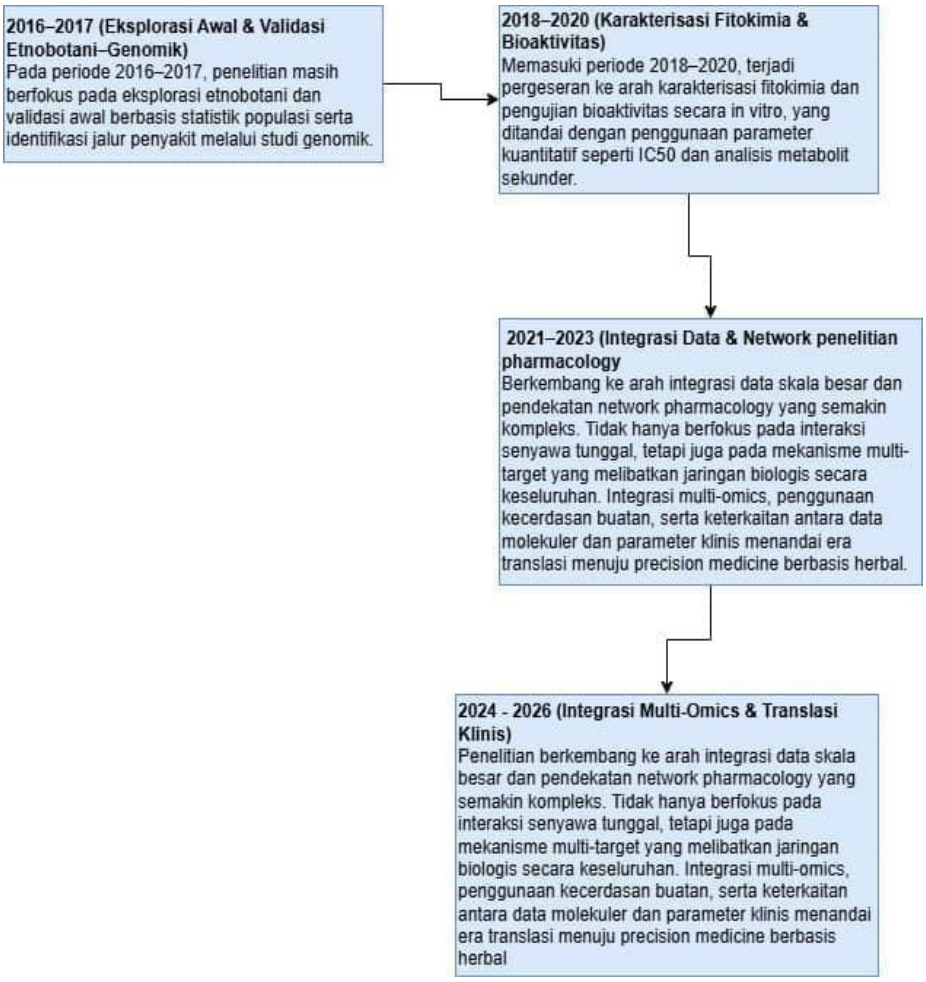
Ethnomedicine of plants for the treatment of skin diseases combines traditional knowledge documentation and quantitative verification to identify the potential of species, assess informant consensus, and ensure security, so that the focus of research is pharmacological and clinical. For example, a survey in Ilorin notes 57 species reported by 62 respondents, with an informant consensus factor (ICF) ranging from 0.923 for insect bites to 0.263 for general skin conditions. A quantitative study in Pakistan interviewed 180 participants and recorded 106 species, with relative citation frequency (RFC) of 0.07–0.25% and fidelity level (FL) of 36.8–100%. A review in Zimbabwe identified 93 species across 21 skin conditions and reported that 40.9% had evidence of low toxicity, while 8.6% were associated with high toxic risk. while other community studies documented local inventories, such as 60 species in Uttarkashi and 28 in Mukundara Hills. For support diversification, source therapy candidate traditional

2. METHOD

This study employed a qualitative approach using a library research or integrative review. This approach aimed to analyse and synthesise scientific evidence on the use of ethnomedicinal plants for the treatment of skin diseases and to identify the relationships between bioactive components and their biological targets. This method enabled the integration of various empirical and conceptual research findings to gain a comprehensive understanding of the mechanisms of action. Work plant drug-based. A network pharmacology approach was used. The data sources for this study were obtained from various reputable scientific databases, namely Google Scholar, Elicit, Scite.ai, Scispace, the Directory of Open Access Journals (DOAJ), and Scopus, which provide journal articles, reviews, and scientific publications relevant to the research topic. (Snyder, 2019).

The inclusion criteria in this study include: (1) scientific articles discussing ethnomedicinal plants for disease skin, (2) study Which use or study network pharmacology approach, bioinformatics, or analysis molecular related, (3) article Which published in range year 2016–2025, (4) article speaking English or Indonesia, and (5) article Which available in text complete (full-text). Meanwhile, the exclusion criteria include: (1) articles that are not relevant to the research topic, (2) publications in the form of non-peer-reviewed proceedings, editorials, or opinions, and (3) articles with incomplete data. Alternatively, No can access, as well as (4) duplicate publication. Process search literature done systematically using a combination of keywords such as "ethnomedicine", "medicinal plants", "skin diseases", "network pharmacology", and "bioactive compounds" and using Boolean operators (AND, OR) to optimize the results of the relevant literature search.

The literature selection procedure comprises several stages: identification, screening, eligibility assessment, and final inclusion, in accordance with the Preferred Reporting Items for Systematic Reviews guidelines. Reviews and Meta-Analyses (PRISM). An article was selected and analyzed using thematic analysis and narrative synthesis to identify relationships among bioactive compounds, protein targets, and biological pathways involved in the therapeutic mechanisms of skin diseases. Data validity and reliability were maintained through source triangulation, article quality evaluation based on journal reputation and indexing, and consistency. results between studies. Additionally, verification is conducted by comparing findings across sources to ensure the accuracy and credibility of the data used in the research. (Page et al., 2021).



2016–2017 (Eksplorasi Awal & Validasi Etnobotani–Genomik)
Pada periode 2016–2017, penelitian masih berfokus pada eksplorasi etnobotani dan validasi awal berbasis statistik populasi serta identifikasi jalur penyakit melalui studi genomik.

2018–2020 (Karakterisasi Fitokimia & Bioaktivitas)
Memasuki periode 2018–2020, terjadi pergeseran ke arah karakterisasi fitokimia dan pengujian bioaktivitas secara in vitro, yang ditandai dengan penggunaan parameter kuantitatif seperti IC50 dan analisis metabolit sekunder.

2021–2023 (Integrasi Data & Network penelitian pharmacology
Berkembang ke arah integrasi data skala besar dan pendekatan network pharmacology yang semakin kompleks. Tidak hanya berfokus pada interaksi senyawa tunggal, tetapi juga pada mekanisme multi-target yang melibatkan jaringan biologis secara keseluruhan. Integrasi multi-omics, penggunaan kecerdasan buatan, serta keterkaitan antara data molekuler dan parameter klinis menandai era translasi menuju precision medicine berbasis herbal.

2024 - 2026 (Integrasi Multi-Omics & Translasi Klinis)
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3. RESULT AND DISCUSSION

Result

1. Identification and Characterisation of Plant Ethnomedicine for Skin Diseases

Overall, the findings indicate a close relationship between knowledge-based ethnomedicinal experience and scientific evidence from phytochemical analyses of ethnomedicines and proof of phytochemical analysis and bioactivity. Plants with high ethnobotanical value often contain secondary metabolites, such as flavonoids, alkaloids, and terpenoids, which exhibit antioxidant, antimicrobial, and enzyme-inhibitory activities. This indicates a correlation between the frequency of traditional use and the pharmacological potential that can be explained at the molecular level. Variation in IC50 values across species also shows that the biological activity of the active compound is strongly influenced by its composition and extract concentration, which opens up opportunities for formulation optimisation. Thus, integrating ethnomedicinal data and phytochemical approaches provides a strong basis for further development by applying modern techniques, such as network pharmacology, to identify molecular targets and biological pathways underlying the mechanisms of action of medicinal plants, especially in the therapy of skin diseases.

Ethnomedicinal research in various regions of Indonesia shows the richness of biodiversity and knowledge. significant local data, with the number of subjects or informants ranging from 30 to 387, identifying 42 to 149 medicinal plant species (Silalahi et al., 2019; Syarifuddin et al., 2022; Tefu et al., 2023). Statistically, the highest Use Value (UV) was reported at 3.44 for Eurycoma longifolia, indicating a high level of utilisation by the local community (Silalahi et al., 2019). In addition, quantitative tests through the Relative Frequency of Citation (RFC) show numbers as high as 0.63 for Curcuma longa, the Temporary Species Use Value. The SUV for Zingiber officinale was recorded at 0.97, reinforcing the position of these two plants as the most essential herbs in traditional medicine (Tefu et al., 2023; Utaminingrum et al., 2022). Informant Consensus Factor (ICF) values approaching 1.00 across various disease categories also demonstrate strong agreement among informants regarding the efficacy of certain plants in ethnomedicinal systems (Silalahi et al., 2019; Syarifuddin et al., 2022).

Research on the phytochemical profiles of plants in Indonesia consistently shows the presence of key bioactive compounds, including phenolics, flavonoids, alkaloids, tannins, saponins, and terpenoids, which contribute to various biological activities. For example, testing on five Litsea species originating from East Kalimantan showed strong inhibitory activity against the enzymes α-amylase and α-glucosidase, with IC50 values of 52.1 ± 1.01 µg/mL and 55.21 ± 1.46 µg/mL, respectively (Phytochemical and Screening, 2023). In line with this, Eusideroxylon zwageri stem bark extract showed a DPPH antioxidant IC50 of 44.90 µg/mL and significant antidiabetic potential via α-amylase inhibition (IC50 = 9.04 µg/mL; Kusuma et al., 2018). In addition to its antidiabetic potential, Acanthus ilicifolius leaves tested at various concentration levels showed antidiabetic activity. antioxidant with an IC50 of 49.73 ± 1.14 µg/mL and capable of inhibiting the growth of Aeromonas hydrophila bacteria by 9.09% (Aisiah et al., 2022). Similar results were also found on the extract of the methanol leaf

Aquilaria malaccensis, which has a total flavonoid content of 14.71 ± 0.15 mg QE/g and an antioxidant IC50 value as high as 45.17 ± 0.55 µg/mL (Flag et al., 2025). In a way, collective data confirmed that variations in the concentration of plant extracts significantly affect their bioactivity in neutralising free radicals and inhibiting enzymatic activities associated with metabolic diseases.

2. Analysis Network Pharmacology in Revealing Target Molecular

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Overall, these various approaches complement each other in building a comprehensive understanding of compound–target–disease interactions at scale. Ligand-based methods provide a foundation for early, highly accurate predictions based on chemical structure similarity. temporary transcriptomics enrichment analysis with information on dynamic, related responses and biological effects of compounds. Domain-based and knowledge graph-based approaches then expand the interaction network by integrating heterogeneous data sources, enabling the identification of new relationships and previously undetected ones. Matter. This reflected a large-scale network encompassing tens of thousands of entities and millions of interactions, capable of predicting hundreds to thousands of new relationships, as in the Salvia miltiorrhiza and fraxetin study. However, the variation in performance across methods suggests that integrating multiple approaches is the optimal strategy, in which the predictions from one method can be validated and enriched by those from another. Thus, this combination of approaches not only improves predictive accuracy but also enhances biological relevance, particularly when linked to clinical parameters such as statistical significance for survival. patient's life ($p < 0.05$), thus providing a basis for exploring molecular mechanisms and for developing herbal-based therapies.

Ligand-based, transcriptomics, and knowledge-graph/embedding approaches were applied to map target protein and interaction compound activity, produce a large dataset, and achieve strong metric performance. The following is a summary of numeric and metric data from relevant studies.

- **Training dataset**: 589,107 compounds and 2,507 target proteins used in PASS Targets training to predict ligand-target interactions
- **Model accuracy**: PASS Targets reported an AUC ROC of ≈96% on leave-one-out and 20-fold cross-validation and an average AUC of ≈90% on the external set (~700 drugs and 206 targets)
- **Target prediction accuracy**: A transcriptomics-based pipeline achieved top-10/top-100 validation accuracies of 26% and 41% across 152 FDA drugs and 3,104 potential targets.
- **Domain scale and association**: The DRUIDom method processes ~2.9 million active/inactive data points, produces 27,032 associations between 250 domains and 8,165 compounds, as well as ≈5 million predicted protein-compound interactions
- **Experimental validation**: A knowledge graph-based method in perturbation transcriptomics (PertKGE) discovered and confirmed multiple targets, with an experimental hit rate of 10.2% for ALDH1B1 inhibitor discovery.

3. Mechanism, Molecular, and Track Biological in Therapy of Skin Diseases

Overall, integrating signalling pathway analysis with clinical data provides a comprehensive picture of how molecular mechanisms contribute to the effectiveness of therapies, including herbal therapies. Pathways identified from large-scale genomic studies serve as a biological map outlining potential intervention points. At the same time, herbal therapies act through a multi-target approach, modulating multiple pathways simultaneously, including insulin signalling, inflammation, apoptosis, and angiogenesis.

This explains why herbal therapeutic effects can be clinically significant, as interventions are not limited to a single specific target but encompass the entire biological network relevant to the disease. The association between changes in clinical parameters (such as HbA1c, LVEF, and functional capacity) with the activation or inhibition of specific pathways suggests a link. Which is measurable between the molecular level and the clinical outcome? Thus, the network pharmacology approach, which integrates genomic data, pathway analysis, and clinical evidence, provides a robust framework for elucidating the mechanisms of action of herbs in a scientific, time-sensitive manner, opening opportunities for the development of more targeted, evidence-based therapies.

Analysis of track signals (pathway analysis) across various genomic studies has provided crucial insights into disease mechanisms by integrating extensive statistical data and large sample sizes. For example, a meta-analysis in European populations involving 19,809 type 2 diabetes (T2D) cases and 111,181 controls identified 43 globally significant signalling pathways after Bonferroni correction (Zhang et al., 2016). In line with that, a study of type 1 diabetes (T1D) with 7,514 case subjects and 9,045 controls identified 31 pathways that showed enrichment at a False Discovery Rate (FDR) of 5% (Evangelou et al., 2014). In the metabolic disease analysis, the track on 40 wild pigs and 123 domestic pigs shows significant differences in the signal transduction pathway, especially the ITPR3 gene, as well as the ovarian steroidogenesis pathway, as identified by statistics Fst and nSL (Leno, Colorado et al., 2017). Studies on the cohort 500 subject, Healthy, also highlight the role of the Vasoactive Intestinal Peptide track, which showed a significant association with body mass index (BMI) and obesity risk (Evangelou et al., 2012).

The implications of molecular mechanisms on the effectiveness of herbal therapy are significantly demonstrated through modulation of various signalling pathways, which contribute to repair parameters in clinical patients. For example, a meta-analysis involving 7,318 participants showed that traditional Chinese medicine (TCM) For diabetes capable lower glucose fast in a way significant (MD = −0.53 mmol/L; $P < 0.00001$) and HbA1c (MD = −0.40%; $P = 0.0001$) through activation of the PI3K-AKT insulin signaling pathway and regulation of inflammatory factors such as TNF and IL-17 (Tang et al., 2025). In addition to that, studies on 5,216 patients with coronary heart disease and heart failure reported that herbal therapy increased left ventricular ejection fraction (LVEF) with a value of SMD = 0.70 ($p < 0.00001$) and six-minute walk capacity

(6-MWT) with SMD = 0.72 ($p < 0.0001$), which, in a way, molecularly pushes a mechanism anti-inflammatory, anti-apoptotic, and stimulatory of angiogenesis (Teng et al., 2023). Integration between analysis network pharmacology and clinical data. This confirms that the effectiveness of herbs is not just a phenomenon, but the result of multi-target interactions at a statistically measurable molecular level.

Discussion

Based on the overall findings, this study confirms that the exploration of ethnomedicinal plants for skin diseases has a strong scientific basis, integrating traditional knowledge, phytochemical analysis, and network pharmacology. Plants with high ethnobotanical value have been shown to contain bioactive secondary metabolites that contribute to pharmacological activity, which can then be systematically mapped through compound-target-disease interactions. Computational approaches such as ligand-based, transcriptomics, and knowledge graphs strengthen this. Identification of target molecular targets with wide coverage and high accuracy, and temporal path analysis of signals and clinical data demonstrate the effectiveness of herbs through a multi-target mechanism involving various biological pathways, such as inflammation, cell proliferation, and immune response. Thus, this multi-level data integration not only bridges empirical and scientific knowledge but also provides a comprehensive framework for uncovering the molecular mechanisms of traditional herbs in a more targeted, evidence-based manner, particularly in the development of therapies for skin diseases.

4. CONCLUSION AND RECOMMENDATION

Further research is needed to experimentally and clinically validate the predicted molecular targets, ensuring the biological relevance and safety of herbal use. diseased skin. Besides that, the development approach is integrative, based on multi-omics, and Artificial intelligence is becoming important to improve prediction accuracy and accelerate the translation of network pharmacology results into clinical applications.

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