Evaluating Kanchner Guggulu's Therapeutic Potential in Polycystic Ovary Syndrome: A Comprehensive Approach with Network Pharmacology, Transcriptomics, Docking, and MD Simulation.

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Introduction: Kanchnar Guggulu (KG) is a potent Ayurvedic remedy for hormonal imbalances, PCOS, ulcers, cystic swelling, and tumors. PCOS is clinically significant, impacting one in five women during their reproductive years, leading to infertility, hyperandrogenism, and metabolic issues like insulin resistance and obesity. This study aims to explore KG's mechanism of action and investigate its potential therapeutic targets for PCOS.

Methodology: The formulation's phytochemicals were screened utilizing online databases such as IMPPAT, TCMSP, and literature mining. Subsequently, ADME analysis was performed to screen the drug potential of phytochemicals. Targets of the active ingredients were identified using databases like Similarity Ensemble Approach (SEA) and Swiss Target Prediction (STP). Transcriptomics analysis validated therapeutic targets, followed by gene ontology, pathway enrichment analyses, and PPI network establishment. Molecular docking was performed to visualize the interactions between the active molecules and network hub genes. The top three docked complexes were subjected to 250 ns MD simulation and GBMV analysis.

Results: The initial database-based screening identified 643 active ingredients, with 413 remaining post-ADME analysis. Initially, 171 potential targets were identified from STP and SEA, of which 55 were differentially expressed in PCOS based on transcriptome analysis. Top enriched pathways encompassed lipid and atherosclerosis, HIF-1 signaling, estrogen signaling, insulin signaling, etc. The toxicology-based screening process efficiently narrowed down a conclusive set of 83 bioactive molecules. These molecules were then subjected to computational docking with 8 targets identified as hubs in the PPI analysis. The top three docked complexes identified were – Retinoic acid receptor(RAR)-Curcumene, Estrogen

receptor(ESR)-Shogaol, and Platelet-activating factor receptor(PTAFR)-Siphonodiol. Finally, the relative stability of the docked complexes was validated by MD simulation.

Conclusion: Our results not only validate the clinical efficacy of KG in treating PCOS but also establish a basis for subsequent experimental investigations.