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Unveiling The Wound-Healing Potential Of *Scaevola Taccada* Through Network Pharmacology Approaches

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ABSTRACT

The multi-target effects of bioactive compounds and their therapeutic potential are well explained by a network pharmacology framework. Computational network pharmacology methods were applied in this research to evaluate *Scaevola taccada* leaf extract's wound-healing activity. The GC-MS analysis identified a total of 20 active phytoconstituents, and Lipinski's rule was applied to filter for drug-likeness. 192 target-identified relevant genes were contrasted with 5,482 wound healing-related genes retrieved from the GeneCards database. 86 overlapping targets were determined through Venn analysis and are considered to be candidate therapeutic targets for wound healing. Essential hub genes were obtained through protein–protein interaction (PPI) analysis and included PPARG, ESR1, HIF1A, and MAPK1 as being essential regulators.

GO enrichment analysis identified their involvement in inflammation, proliferation, and tissue remodelling through significant roles in nuclear receptor activation, transcription factor binding, and cell migration. Participation of putative targets in significant pathways like estrogen signaling, HIF-1 signaling, MAPK signaling, and regulation of lipid/atherosclerosis was again confirmed by KEGG pathway enrichment. The complex interaction between phytochemicals and molecular targets was demonstrated by the compound–target–pathway network constructed with Cytoscape.

All of these findings indicate the prospective use of *Scaevola taccada* as a natural medicinal compound by showing it to modulate multi-gene and multi-pathway interactions to achieve wound-healing effects. This article emphasizes the employment of network pharmacology in validating traditional medicinal

herbs for modern drug discovery, aside from providing molecular evidence for the pharmacological basis of *Scaevola taccada.*

Key words: network pharmacology, *Scaevola taccada*, wound healing, genes, molecular targets.

INTRODUCTION

Outside of the classical "one drug–one target" concept, a new discipline called network pharmacology (NP) examines how drugs are interacting with various molecular targets within biological systems. NP meticulously documents these interactions through computational methods to better understand the intricate relationship between drugs, herbal formulas, and the human body. This strategy facilitates the identification of new drug leads, repurposing of existing drugs for a range of diseases, and finding new therapeutic targets. Notably, in choosing appropriate targets and pharmacological scaffolds, traditional medical wisdom can serve as a resource. Through the integration of systems biology and NP, scientists aim to design multi-target drugs that are more potent and less toxic but consider the multifaceted nature of human diseases. [1]

To explore complex interactions between genes, proteins, and signaling pathways, it combines molecular biology, biochemistry, genomics, and bioinformatics. Increased clinical efficacy rates, reduced side effects, improved therapeutic activity, and reduced attrition in the process of drug development have all been shown with this technique. Network pharmacology enhances the number of potential clinical leads by identifying key disease nodes and drug repurposing. Network pharmacology is now applied in about 40% of drug discoveries, making it a powerful tool for modern drug design. [2]

METHODOLOGY

Network pharmacology analysis

- **Collection of active ingredients of *Scaevola taccada* leaf:**

The active phyto ingredients of *scaevola taccada* leaf extract is collected from the data obtained through GC-MS analysis. SMILES of active ingredients were retrieved using pubchem (https://pubchem.ncbi.nlm.nih.gov/) and the parameters chosen for the screening of active ingredients were set at drug likeness and the molecules that defies three rules listed by Lipinski were excluded in the study. [3]

- **Target prediction of Phytomolecule:**

Phytoconstituents related targets are predicted using Swiss Target prediction (https://swisstargetprediction.ch) and the uniprot ID given to STRING data base (https://string-db.org/) to get the preferred name of the target genes. [4]

- **Wound healing related target selection:**

Target genes of wound healing is collected from Gene card data base (https://www.genecards.org/) by searching the keyword "wound healing". Then the obtained data is filtered with gift score greater than 60. So we obtained total of 5482 genes. [5]

- **Venn Diagram:**

The overlapping targets were identified by using venny 2.1.0 (https://bioinfogp.enb,esic.es/tools/venny/).The overlappimg target genes obtained were used for bioinformatic analysis. [6]

- **Protein protein interaction:**

Using the settings of Homo sapiens analysis of overlapping genes of *Scaevola taccada* and wound healing was done in STRING (https://string-db.org/), where they made a protein- protein Interaction (PPI) network. The node-node data which was exported is visualized using the software Cytoscape 3.7.2. [7]

- **GO enrichment analysis:**

To expand the results of the overlapping genes, gene ontology (GO) enrichment analysis was conducted by uploading the results into the ShinyGo 0.80. [8]

- **KEGG enrichment analysis:**

Overlapping genes were next analysed in the KEGG enrichment that was conducted by importing them into the ShinyGo 0.80 (https://bioinformatics.sdstate.ed/go80/) database. In the descending order of gene number enriched in each pathway, we tabulated the top 20 signaling pathways in a lollipop plot. [9]

- **Network Construction:**

Cytoscape 3.7.2 is used to construct the herb ingredient core drug target was constructed. Then performed the topological analysis and using degree value important targets are analysed. [10]

RESULTS AND DISCUSSION

Network pharmacology analysis

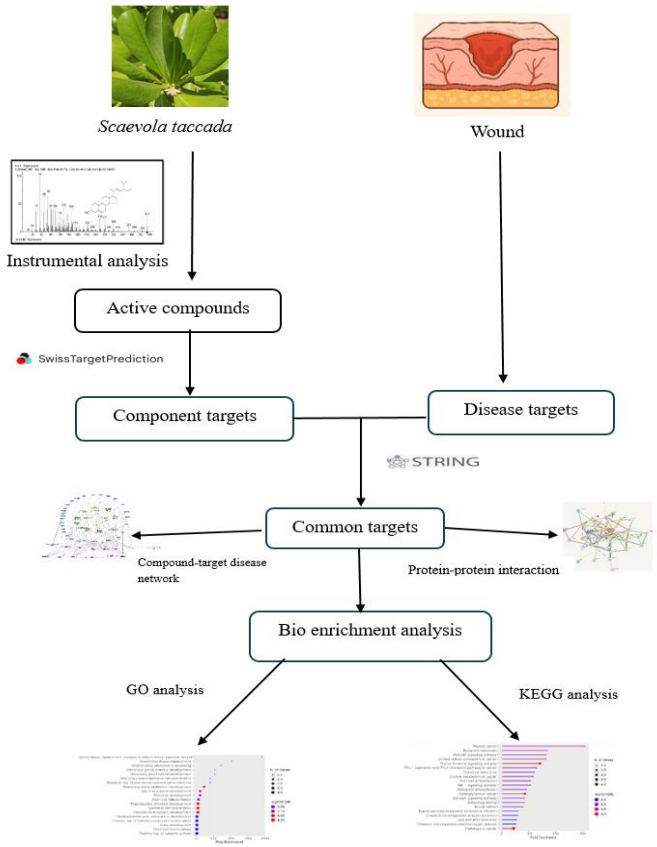


Fig 1: Schematic diagram of the utilization strategy of network pharmacology in wound healing

1) Prediction of active ingredients and target genes of *scaevola taccada*

Through instrumental analysis a total 20 active ingredients were identified from S*caevola taccada* leaf. These ingredients were used to get the related targets using target prediction system. We obtained 192 target genes from *Scaevola taccada* leaf.

2) Overlapping targets with *Scaevola taccada* and wound healing

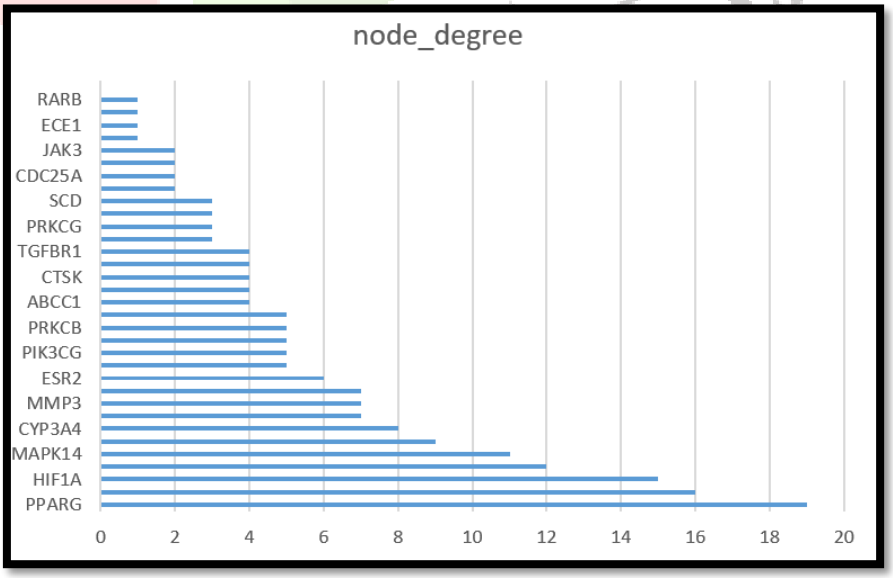
We searched "wound healing" in Gene card data base and obtained 5482 target genes. By giving target genes of in *Scaevola taccada* and wound healing in Venn diagram we got total of 86 overlapping genes that were regarded as the therapeutic targets of *Scaevola taccada* and wound healing.

3) Identification of *Scaevola taccada* core target against wound healing

A total of 86 overlapping genes of *Scaevola taccada* against wound healing were uploaded in string database. Homosapienes was set as organization and obtained the key targets. PI network obtained with 187 nodes. The obtained date of PPI were imported to cytoscape software and target node degree is taken as important parameter and the top 20 genes were tabulated in Table number 1. The top four genes involved in wound healing were **PPARG, ESR1, HIF1A** and **MAPK1**.

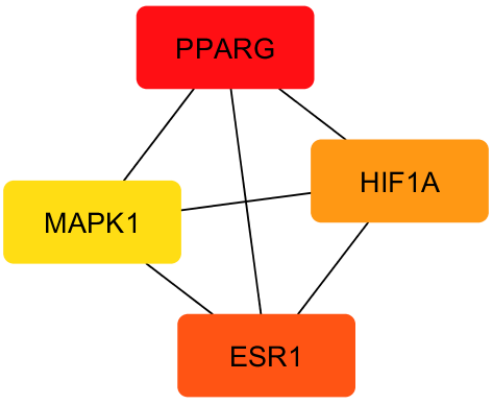
Table 1: Node degree of genes

SL	#NODE	NODE_DEGREE
1	**PPARG**	**19**
2	**ESR1**	**16**
3	**HIF1A**	**15**
4	**MAPK1**	**12**
5	MAPK14	11
6	MDM2	9
7	CYP3A4	8
8	ABCB1	7
9	MMP3	7
10	NOS2	7
11	ESR2	6
12	OPRM1	5
13	PIK3CG	5
14	PLAU	5
15	PRKCB	5
16	TERT	5
17	ABCC1	4
18	ACACA	4
19	CTSK	4
20	PTPN1	4

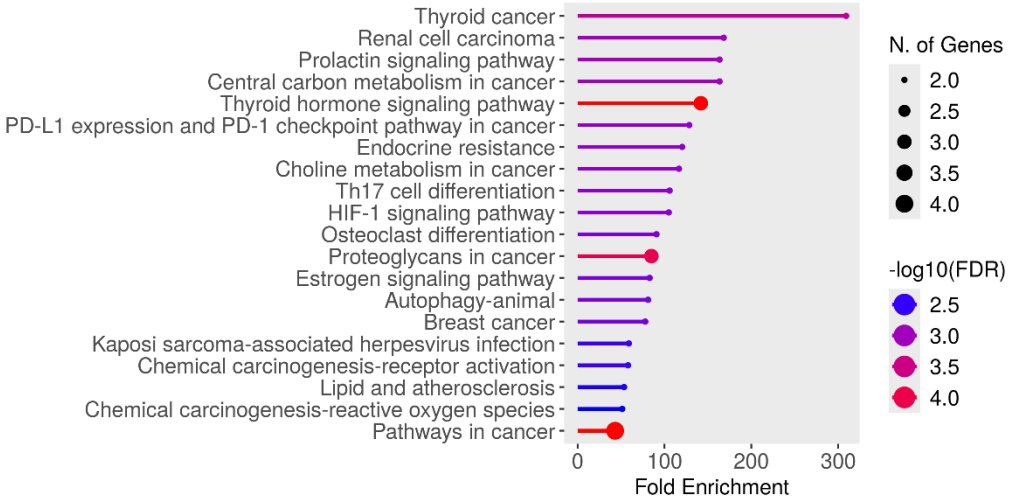


Graph 1: Node degree of genes

Fig 2: Genes involved in wound healing



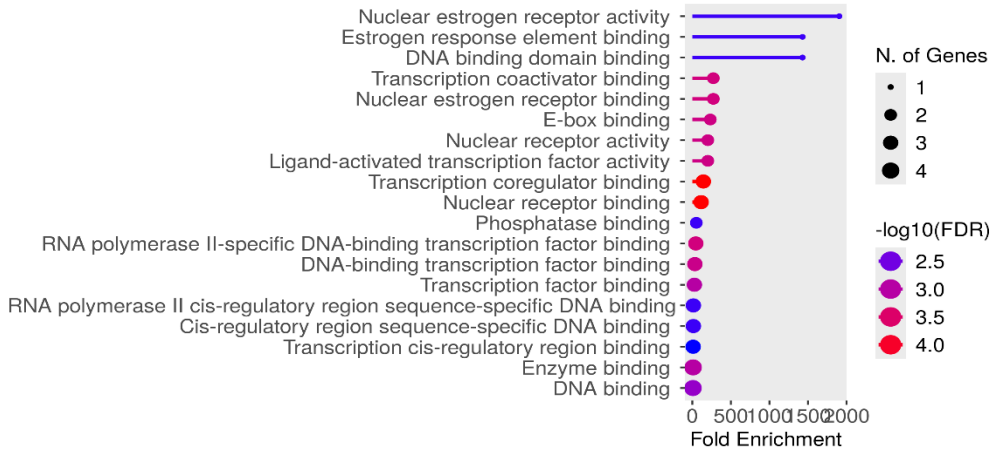
KEGG pathway enrichment output



Graph 2: KEGG pathway enrichment

KEGG pathway enrichment output lists several pathways like Estrogen signaling pathway, HIF-1 signaling pathway, MAPK signalling (indirect via cancer/ proliferation) and lipid/atherosclerosis pathways. These overlap well with the four genes you mentioned (PPARG, ESR1, HIF1A, MAPK1) and can indeed be tied to wound healing. Together, these enriched pathways suggest that your gene set is highly relevant to the different phases of wound healing (inflammatory → proliferative → remodelling).

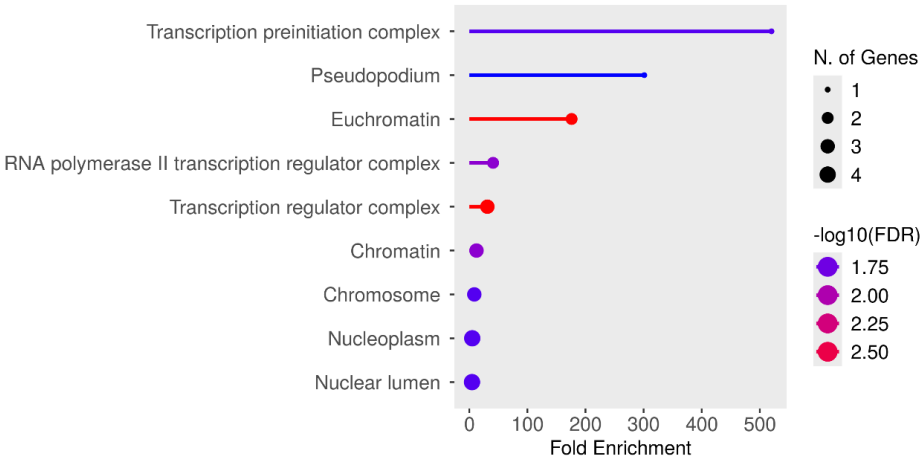
GO molecular function enrichment chart



Graph 3: GO molecular function enrichment

It highlights functions such as DNA binding, transcription factor binding, nuclear receptor activity, estrogen receptor binding, and ligand-activated transcription factor activity. This chart shows that your gene set is enriched in molecular functions related to transcriptional regulation and nuclear receptor signaling. These functions are essential for wound healing because they control inflammation, angiogenesis, cell proliferation, and tissue remodeling at the genetic level.

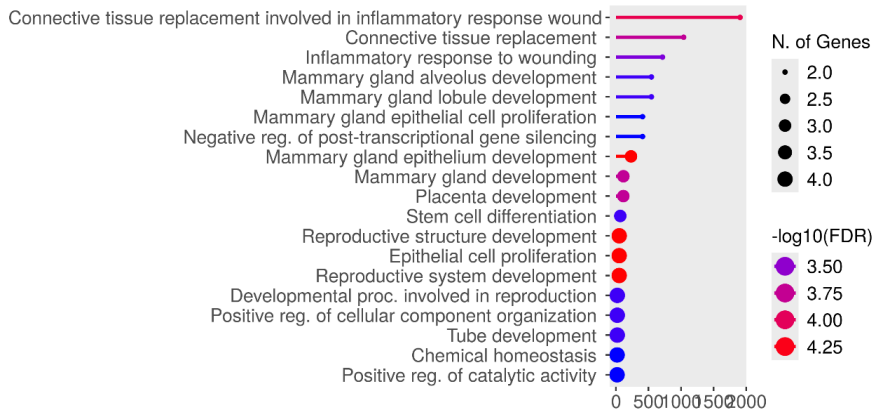
GO cellular component enrichment chart



Graph 4: GO cellular component enrichment

It shows enrichment in nuclear lumen, nucleoplasm, chromatin, transcription regulator complex, RNA polymerase II complex, euchromatin, and pseudopodium. This chart shows that your gene set is mainly localized in the nucleus (for gene regulation) and in cell structures involved in migration (pseudopodia). Both functions are essential for wound healing: activating genes that control repair and enabling cells to physically move into the wound site.

GO Biological Process enrichment chart



Graph 5: GO biological process enrichment

It highlights processes such as inflammatory response to wounding, connective tissue replacement, epithelial cell proliferation, stem cell differentiation, tube development, and chemical homeostasis.

This chart shows that your genes are directly associated with all major phases of wound healing:

1. Inflammation (immune response regulation),
2. Proliferation (epithelial growth, stem cell activation, angiogenesis), and
3. Remodelling (connective tissue replacement and collagen deposition).

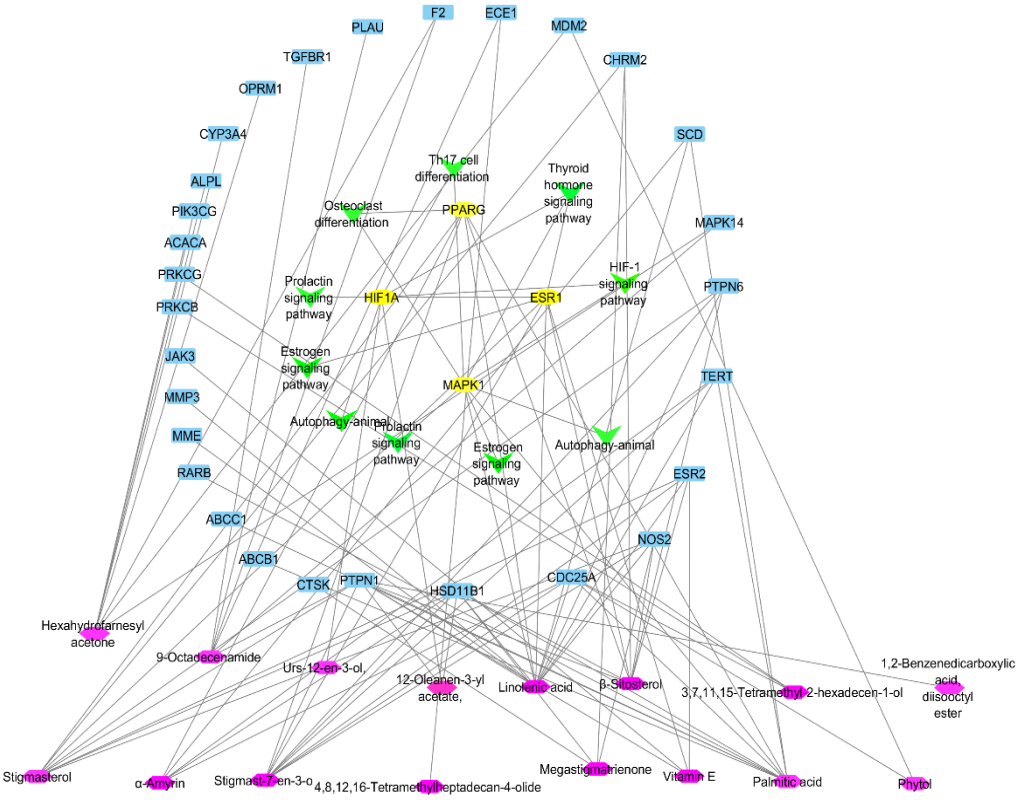


Fig 2: Compound–Target–Pathway Network of Bioactive Constituents and Their Potential Targets

CONCLUSION

The present research applied a network pharmacology method to detect the molecular mechanisms responsible for *Scaevola taccada's* ability to facilitate wound healing. After the detection of twenty bioactive phytoconstituents, 86 co-target genes associated with wound healing were examined through a systematic analysis. PPARG, ESR1, HIF1A, and MAPK1 were recognized as core hub genes among them, highlighting their critical regulatory roles in tissue remodeling, inflammation, angiogenesis, and proliferation. Participation of these targets in significant pathways such as estrogen signaling, HIF-1 signaling, and MAPK signaling—all of which are directly involved with wound-repair processes—was confirmed through enrichment studies. *Scaevola taccada's* multi-target, multi-pathway medicinal value was revealed through the integration of compound–target–pathway networks, validating its historical medicinal value. Everything considered, this work provides scientific evidence for *Scaevola taccada's* wound-healing capacity and the value of network pharmacology as a powerful method for identifying novel therapeutic pathways in traditional Chinese medicinal plants.

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