DOI: 10.7860/JCDR/2026/87622.23469

Original Article

Ayurveda Section

Unveiling the Therapeutic Potential of Khadira (*Acacia Catechu*) Against Vitiligo: A Computational Study

PRIYANKA NYAMTI[1], RAJENDRASWAMI HIREMATH[2], RASHMI MOTNALI[3]

ABSTRACT

Introduction: Vitiligo is characterised by a loss of skin pigmentation, resulting in white patches or spots. It happens when the cells called melanocytes, the cells responsible for producing skin pigment, are harmed or killed. Although it is not communicable or fatal, vitiligo can be emotionally taxing for people who have it. Although *Khadira* is the most well-known traditional remedy for treating skin conditions, its underlying Protein Protein Interaction (PPI) and signalling pathway remain unknown. The network pharmacology approach was used to investigate the molecular basis of action of *Khadira*.

Aim: To explore the molecular mechanisms of *Acacia catechu* in the treatment of vitiligo using network pharmacology analysis.

Materials and Methods: This study was a computational network pharmacology analysis conducted in the Department of RSBK, KLE Shri B M Kankanawadi Ayurveda Mahavidyalaya, Belagavi, Karnataka, India between May 2025 and June 2025. Phytochemicals were obtained from earlier research works from PubMed and Google Scholar, Dr. Dukes, and the Indian Medicinal Plants, Phytochemistry and Therapeutics (IMPPAT) databases. Swiss Absorption, Distribution, Metabolism and Excretion (ADME) was used to assess the drug-likeness of phytochemicals linked to PubChem Criminal Investigation Department (CID) based on Lipinski's criteria. Binding Database (BindingDB) was used to predict targets, and Gene Identifier (Gene ID) was obtained using the Uni Prot database. The String database was used to analyse Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways, and Cytoscape 3.7.2 was used to construct the networks.

Results: A total of 125 phytochemicals were identified from *Acacia catechu*, of which 31 fulfilled the drug-likeness criteria. Target prediction analysis yielded 111 potential protein targets, and 42 overlapping genes associated with vitiligo were identified. PPI network analysis highlighted key hub genes, including Xanthine Oxidoreductase (XDH), Mitogen-Activated Protein Kinase 14 (MAPK14) and Janus Kinase 1 (JAK1). Pathway enrichment analysis revealed significant involvement in immune and inflammation-related pathways, such as insulin resistance and prolactin signalling, suggesting multi-target mechanisms underlying the therapeutic potential of *Khadira*.

Conclusion: The present study suggests that *Acacia catechu* (*Khadira*) may exert therapeutic effects in vitiligo through multi-target interactions involving quercetin and kaempferol, particularly with proteins such as XDH, MAPK14, and JAK1 that are linked-to immune and inflammatory pathways. These computational findings support its traditional use; however, experimental and clinical validation is required.

Keywords: Melanocytes, Network pharmacology, Pathways, Targets

INTRODUCTION

Vitiligo was originally described in ancient literature as *Kilasa* during the Aushooryan period (around 2200 BC). It is an autoimmune depigmentary disorder characterised by the destruction of melanocytes, leading to the development of depigmented macules and patches of varying shapes and sizes. The global prevalence of vitiligo ranges from 0.06% to 2.28% in the general population and from 0.0% to 2.16% among children and adolescents [1]. The exact aetiology of vitiligo remains unclear. It is frequently associated with other autoimmune disorders and is considered a multifactorial condition with a complex pathogenesis. Several hypotheses have been proposed to explain its development. The disease is characterised by multiple susceptibility loci, genetic heterogeneity, and incomplete penetrance. Twin and family studies suggest that vitiligo inheritance is complex and influenced by both genetic and environmental factors. Genetic predisposition may also affect the age of onset. Genes involved in melanin synthesis, immune regulation, autoantibody production, and oxidative stress response are believed to contribute to disease susceptibility [2].

Khadira (*Acacia catechu* (L.f.) Willd.; AC) is a deciduous tree belonging to the family Fabaceae. In Ayurveda, *Khadira* is described as possessing *tikta* (bitter) and *kashaya* (astringent) rasa with *sita virya* (cool potency), which is traditionally believed to alleviate *pitta* and *kapha* doshas. The *kashaya rasa* (astringent taste) is traditionally considered to have immunomodulatory properties beneficial for skin conditions. *Khadira* is also described as *twak-prasadaka* (enhancing skin complexion) and *rakta-shodhaka* (blood purifying). Additionally, it exhibits antibacterial and antifungal activities, which may contribute to its therapeutic potential in managing various skin disorders [3]. It is regarded as one of the most effective remedies for skin disorders in classical Ayurvedic literature [4].

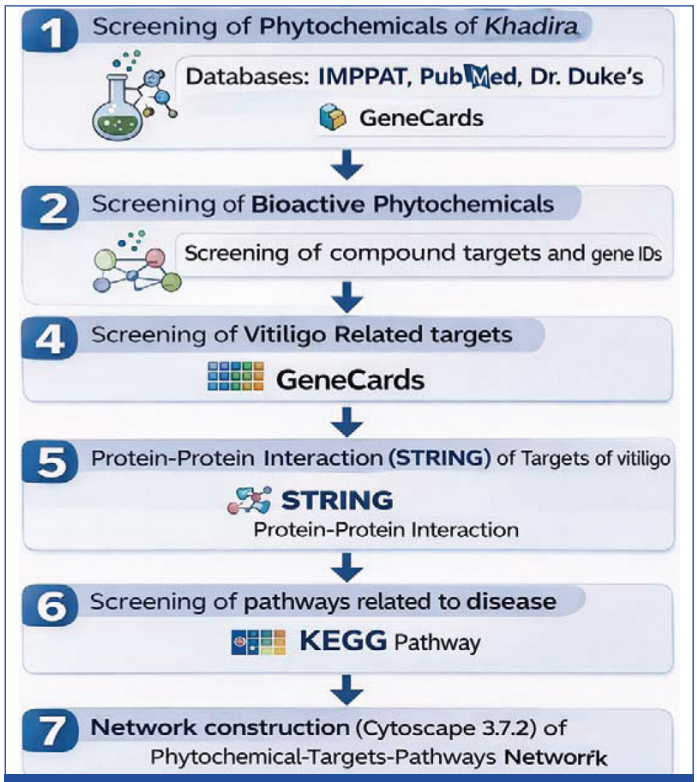
Network pharmacology, an interdisciplinary area that combines computer science, bioinformatics, and network science, helps with drug development and treatment by clarifying how medications interact with genes, proteins, metabolites, and signalling pathways linked to disease. Integrating and analysing networks, it helps find new drug targets and therapeutic approaches [5]. The traditional *one drug-one target-one disease* paradigm is widely used in drug discovery because it simplifies compound screening and reduces adverse effects. However, herbal medicines often act through multiple bioactive compounds targeting several pathways. Network pharmacology provides a systematic approach to understand these multi-component and multi-target interactions. Therefore, the present study aimed to explore the molecular mechanisms of *Acacia catechu* in vitiligo using a network pharmacology approach.

MATERIALS AND METHODS

The present study was a computational network pharmacology analysis conducted in the Department of RSBK, KLE Shri B M Kankanawadi Ayurveda Mahavidyalaya, Belagavi, Karnataka, India between May 2025 and June 2025.

Study Procedure

Publicly available databases and bioinformatics tools were used to identify phytochemicals, predict targets, analyse PPIs, and perform pathway enrichment analysis, followed by network construction using Cytoscape 3.7.2 [Table/Fig-1].



[Table/Fig-1]: Study flowchart

Bioactive phytochemical screening: The Latin name of the plant, *Acacia catechu* (L.f.) Willd., was used to search phytochemical databases such as IMPPAT (assessed on May 15) and Dr. Duke's database (assessed on May 17), as well as research articles available on PubMed and Google Scholar, to identify its phytochemical constituents. All retrieved phytochemicals were compiled, and duplicate entries were removed to obtain a final list of unique compounds for further analysis.

Estimating the Drug-likeness of chemicals from *acacia catechu*: Each phytochemical associated with PubChem CID was evaluated for drug-likeness using Lipinski's "rule of five" and the Swiss ADME database (assessed on May 21). A molecule's oral absorption and bioavailability are determined by its molecular weight (less than 500), number of hydrogen bond donors (less than five), number of hydrogen bond acceptors (less than ten), and LogP value (less than five).

Target identification: After removing duplicate compounds, the canonical Support for Marginalised Individuals for Livelihood and Enterprise scheme (SMILES) and PubChem IDs of the phytochemicals were retrieved from the PubChem database (assessed on May 22). These canonical SMILES were used to identify potential protein targets based on similarity. Target information was obtained from the BindingDB database (assessed on May 25), which provides experimentally validated ligand–protein interactions, and the SwissTargetPrediction database, which predicts targets based on chemical similarity. The species was limited to *Homo sapiens*. The corresponding gene names, gene IDs, and UniProt IDs of the identified protein targets were retrieved from the UniProt database (assessed on June 1) to ensure standardised target identification for further analysis.

Computation of genes that overlap: Overlapping genes are those that appear in both pharmacological targets and disease genes. Disease-related genes and predicted drug targets were uploaded into Venny 2.1 to identify overlapping genes.

Establishment of PPI network maps of possible therapeutic targets: The STRING database (version 12.5; accessed on June 15) was used to construct the PPI network, with the minimum required interaction score set at 0.7 (high confidence). KEGG pathway enrichment analysis was performed to identify pathways associated with vitiligo, and pathways with a FDR ≤0.05 were considered statistically significant.

Establishing and analysing networks: To construct the network linking phytoconstituents, targets, and pathways, Cytoscape 3.7.2 was utilised. All redundancies were removed throughout the network's construction procedure. Using the "Network Analyser" tool, the produced network was evaluated by setting it up as instructed and analysing the complete network based on edge count. The quantity of nodes for chemicals, targets, and pathways may differ based on the material used and the retrieval time.

STATISTICAL ANALYSIS

Statistical analysis and enrichment studies were performed using bioinformatics tools. PPI analysis was carried out using the STRING database with the species restricted to *Homo sapiens* and a confidence score of 0.7. Network visualisation and topological analysis were performed using Cytoscape (version 3.7.2). KEGG pathway enrichment analyses were conducted, and pathways with a FDR ≤0.05 were considered statistically significant.

RESULTS

Bioactive Phytochemical Screening

The Latin name of the plant, *"Acacia catechu(L.f) Willd"* (AC), was used to search databases like IMPPAT and Dr. Duke as well as research articles on PubMed and Google Scholar, to determine the phytochemical contents of AC. A total of 125 phytochemicals were initially identified. After removing compounds without PubChem CID, 63 compounds remained, of which 31 satisfied Lipinski's Rule of Five and were included for further analysis. Shown in [Table/Fig-2].

Drug name	Total phytochemicals	After screening from PubChem CID	Compounds satisfying Lipinski's rule
Acacia catechu (L.f) Willd	125	63	31

[Table/Fig-2]: Total number of phytochemicals of *Khadira*.

Target Identification

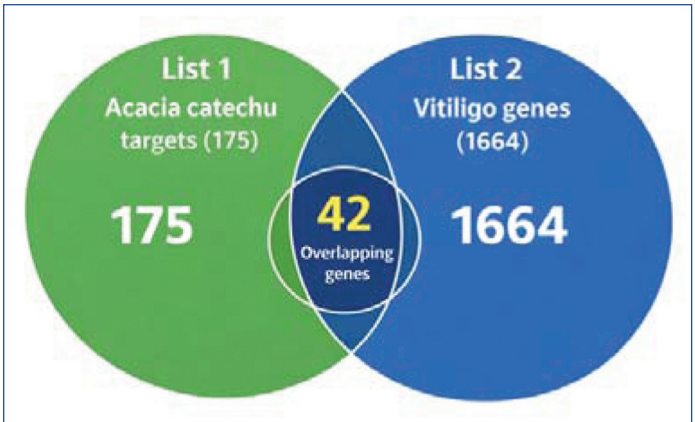
The BindingDB and SwissTargetPrediction databases initially generated 475 potential protein targets associated with the selected phytochemicals. After removing duplicate entries and standardising the gene names using the UniProt database, 111 unique protein targets were obtained for further analysis.

Estimation of Overlapping Genes

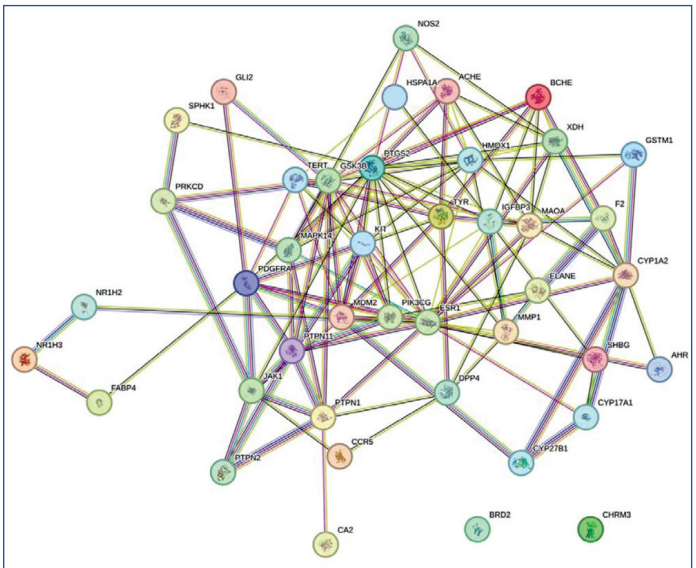
Total 42 overlapping/common genes were identified by VENNY 2.1 for *"Acacia catechu (L.f) Willd"* [Table/Fig-3].

Protein-Protein Interaction (PPI) and KEGG Pathway Analysis

The overlapping targets were uploaded to the STRING database (version 12.5) (assessed on June 17) to construct a PPI network, with species restricted to *Homo sapiens* and a minimum interaction score of 0.7 [Table/Fig-4]. KEGG pathway enrichment analysis was carried out using the STRING database revealed



[Table/Fig-3]: Venn diagram showing overlapping targets between *Khadira* phytochemicals and vitiligo-associated genes.



[Table/Fig-4]: PPI network of overlapping targets constructed using the STRING database (confidence score ≥0.7).

several pathways related to melanogenesis, immune regulation, and cancer-related signalling. All identified pathways were statistically significant with FDR ≤0.05, suggesting their potential involvement in the therapeutic mechanism of *Acacia catechu* against vitiligo. The network was visualised and analysed using Cytoscape 3.7.2.

The overlapping targets of *Acacia catechu* (L.f.) Willd and its metabolites were analysed using the STRING database to generate a PPI network in order to identify the top 10 genes associated with vitiligo.

Estimating the *Acacia catechu* Pharmacological Resemblance (Drug likeness).

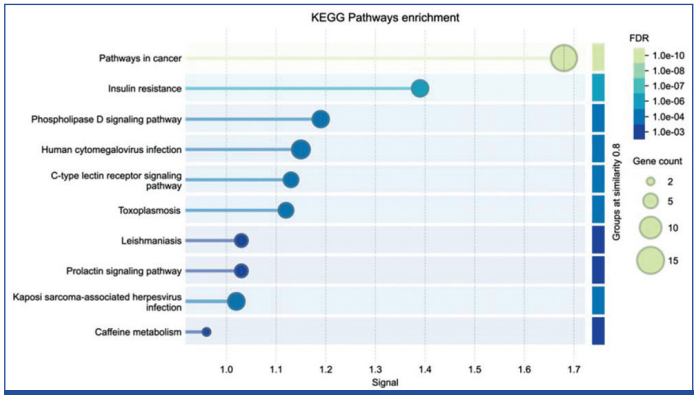
A total of 31 phytochemicals were identified from *Acacia catechu* (*Khadira*) after screening based on pharmacokinetic parameters, including high gastrointestinal absorption, oral bioavailability ≥0.55, and compliance with Lipinski's Rule of Five. These screened phytochemicals were considered for further target prediction analysis. The potential protein targets associated with the selected phytochemicals were obtained from the BindingDB and SwissTargetPrediction databases.

Gene Collection for Vitiligo

A total of 1706 vitiligo-associated genes were retrieved from the GeneCards database using a relevance score cut-off ≥1. The UniProt IDs of the predicted phytochemical targets were used to standardise the target genes. The overlapping genes between *Khadira*-associated targets and vitiligo-related genes were identified using Venny software.

KEGG Pathway Analysis

To know protein–protein interactions and to perform KEGG pathway analysis, a total of 42 genes were retrieved for KEGG analysis, and the overlapping genes were uploaded to the Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database. KEGG pathway enrichment analysis identified 10 significantly enriched pathways. Subsequently, the role of these pathways in the pathophysiology of vitiligo was analysed. The 10 *Khadira* pathways linked to vitiligo are listed in [Table/Fig-5,6].



[Table/Fig-5]: KEGG pathway enrichment analysis of overlapping target genes. (The bubble plot shows enriched pathways of overlapping target genes. Bubble size represents gene count, and colour indicates statistical significance.)

Term ID	Pathways	No. of targets	Targets
hsa05200	Pathways in cancer	14	HMOX1, PDGFB, PDGFRA, MDM2, KIT, F2, TERT, GSTM1, MMP1, GSK3B, NOS2, PTGS2, GLI2, JAK1
hsa04931	Insulin resistance	6	GSK3B, PRKCD, PTPN1, NR1H3, PTPN11, NR1H2
hsa05163	Human cytomegalovirus infection	7	MAPK14, PDGFRA, MDM2, CCR5, GSK3B, PTGS2, JAK1
hsa04072	Phospholipase D signaling pathway	6	PDGFRA, KIT, F2, SPHK1, PIK3CG, PTPN11
hsa04625	C-type lectin receptor signaling pathway	5	MAPK14, MDM2, PRKCD, PTGS2, PTPN11
hsa05145	Toxoplasmosis	5	MAPK14, CCR5, NOS2, PIK3CG, JAK1
hsa05167	Kaposi sarcoma-associated herpesvirus infection	6	MAPK14, CCR5, GSK3B, PTGS2, PIK3CG, JAK1
hsa04917	Prolactin signaling pathway	4	MAPK14, GSK3B, CYP17A1, ESR1
hsa05140	Leishmaniasis	4	MAPK14, NOS2, PTGS2, JAK1
hsa00232	Caffeine metabolism	2	CYP1A2, XDH

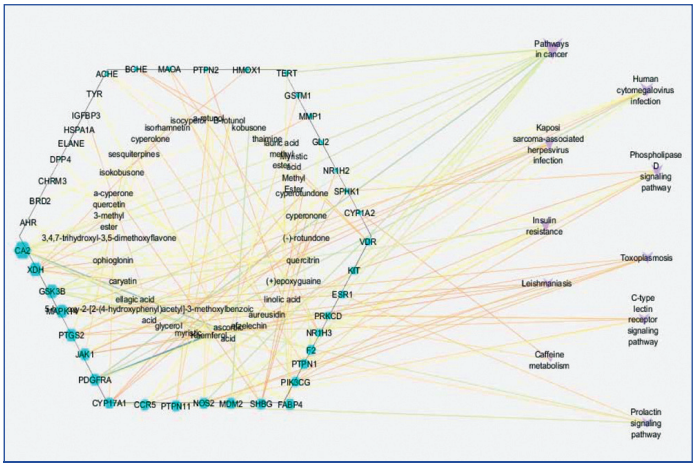
[Table/Fig-6]: Gene-set enrichment analysis of vitiligo disease pathway.

Network Construction

Out of 31 Phytochemicals examined in the network linking phytochemicals, targets, and pathways associated with vitiligo, all were found to be implicated. The network constructed includes 82 nodes, 148 edges representing 10 pathways [Table/Fig-7].

DISCUSSION

Vitiligo is a chronic depigmentary disorder characterised by the progressive destruction of melanocytes, leading to depigmented macules on the skin. Its pathogenesis is multifactorial, involving autoimmune mechanisms, oxidative stress, genetic susceptibility, and dysregulated cellular signalling pathways. These complex interactions contribute to melanocyte dysfunction and loss, resulting in the clinical manifestations of the disease [6,7]. Increasing evidence suggests that immune-mediated melanocyte destruction,



[Table/Fig-7]: Phytochemical-target-pathway interaction network of *Acacia catechu* in vitiligo.

particularly through interferon-γ–driven inflammatory responses, plays a central role in disease progression [8].

In the present study, a network pharmacology approach was employed to investigate the potential molecular mechanisms of *Khadira* (*Acacia catechu*) in the management of vitiligo. Network pharmacology provides a systems-level perspective on the interactions among multiple phytochemicals, target proteins, and biological pathways [9]. This approach is particularly suitable for herbal medicines, which typically exert therapeutic effects through multi-component and multi-target interactions rather than single-target mechanisms.

The PPI network analysis identified several hub genes with high connectivity, including JAK1, MAPK14, and XDH, suggesting their potential involvement in vitiligo-related biological processes. The JAK-STAT signalling pathway plays an important role in mediating inflammatory responses and autoimmune reactions associated with melanocyte destruction. Clinical evidence supporting the relevance of this pathway includes the recent development of JAK inhibitors, such as ruxolitinib cream, which has demonstrated efficacy in vitiligo treatment [10,11].

Oxidative stress is another key mechanism implicated in vitiligo pathogenesis. Increased production of reactive oxygen species and impaired antioxidant defence systems contribute to melanocyte damage and apoptosis [12,13]. Previous studies have reported reduced catalase activity and increased oxidative stress markers in vitiligo patients, further supporting the role of oxidative imbalance in disease development [14].

In addition to immune dysregulation and oxidative stress, intracellular signalling pathways also contribute to melanocyte survival and apoptosis. MAPK signalling pathways are known to regulate cellular responses to stress and inflammation, and their dysregulation may lead to melanocyte dysfunction [15]. Another enzyme identified in the present network analysis, XDH, plays a role in oxidative metabolism and can contribute to reactive oxygen species generation under pathological conditions [16].

Pathway enrichment analysis was performed using KEGG databases and network analysis tools to identify biological pathways associated with the predicted targets [17]. PPI networks were constructed using the STRING database and visualised using Cytoscape software to better understand molecular interactions [18]. These bioinformatics approaches allow the identification of biologically relevant signalling pathways and potential therapeutic targets involved in disease pathogenesis.

Among the phytochemicals identified in *Khadira*, flavonoid compounds such as quercetin demonstrated interactions with multiple targets within the network. Quercetin is widely recognised for its antioxidant and anti-inflammatory activities and has been reported to modulate several cellular signalling pathways associated with oxidative stress and inflammation [19,20]. Flavonoids in general are known to act as potent antioxidants capable of scavenging reactive oxygen species and protecting cells from oxidative damage [21].

Overall, the findings of the present network pharmacology analysis suggest that *Khadira* may exert potential therapeutic effects in vitiligo through multi-target and multi-pathway mechanisms, including modulation of immune responses, regulation of oxidative stress, and influence on intracellular signalling pathways. These results provide a theoretical basis for the traditional use of *Khadira* in dermatological disorders and highlight potential molecular targets for future experimental validation.

Limitation(s)

The present study is limited by its reliance on in-silico bioinformatics analyses and publicly available databases such as the STRING database and KEGG. The predicted targets and pathways require further validation through experimental and clinical studies to confirm their therapeutic relevance.

CONCLUSION(S)

The present study demonstrated the potential mechanisms of *Khadira* (*Acacia catechu*) based on predicted interactions between phytochemicals, target proteins, and associated signalling pathways. Among the identified compounds, quercetin and kaempferol showed notable predicted interactions with target proteins such as XDH, MAPK14, and JAK1, which are involved in pathways including insulin resistance and prolactin signalling, both implicated in vitiligo pathophysiology. These findings suggest possible molecular mechanisms through which *Khadira* phytochemicals may influence immune regulation and melanocyte function. However, these results are based on computational analysis and do not establish direct therapeutic effects. The study provides mechanistic support for the traditional use of *Khadira* in skin disorders and highlights its potential relevance in vitiligo. Further experimental and clinical studies are required to validate these predicted interactions and determine their biological and clinical relevance.

Authors' contribution: PN: Conceptualisation, methodology, writing, review and editing; RH: Supervision and validation; RM: Data curation and software.

Acknowledgement

Authors would like to acknowledge their guide and seniors for their contribution in conducting present study. AI tools were only used for language improvement and editing during manuscript preparation.

REFERENCES

[1] Al-Smadi K, Imran M, Leite-Silva VR, Mohammed YH. Vitiligo: A review of aetiology, pathogenesis, treatment, and psychosocial impact. *Cosmetics*. 2023;10(3):84. Doi: 10.3390/cosmetics10030084.
[2] Ahmed N, Jan A. Vitiligo. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559149/.
[3] Kumari M, Kumar M, Zhang B, Zhang B, Amarowicz R, Puri S, et al. *Acacia catechu* (L.f.) Willd.: A review on bioactive compounds and health-promoting functionalities. Plants. 2022;11(22):3091.
[4] Shashirekha HK. *Charaka Samhita: Sutra Sthana*. English commentary. New Delhi: Chaukhamba Publications; Part 1, Chapter 25: p.399.
[5] Wei W, Wu S, Zhou C, Chen T, Zhu J, Feng S, et al. Network pharmacology combined with molecular docking and experimental validation to explore the potential mechanism of *Cinnamomi ramulus* against ankylosing spondylitis. *Ann Med*. 2023;55(2). Doi: 10.1080/07853890.2023.2290741.
[6] Ezzedine K, Eleftheriadou V, Whitton M, van Geel N. Vitiligo. Lancet. 2015;386(9988):74-84.
[7] Frisoli ML, Essien K, Harris JE. Vitiligo: Mechanisms of pathogenesis and treatment. Annu Rev Immunol. 2020;38:621-48.
[8] Harris JE. Vitiligo and the immune response. Pigment Cell Melanoma Res. 2016;29(5):546-58.
[9] Hopkins AL. Network pharmacology: The next paradigm in drug discovery. Nat Chem Biol. 2008;4(11):682-90.

[10] Rosmarin D, Passeron T, Pandya AG, Grimes P, Harris JE, Desai SR, et al. Two phase 3 trials of ruxolitinib cream for vitiligo. N Engl J Med. 2022;387(2):144-55.
[11] Damsky W, King BA. JAK inhibitors in dermatology: The promise of a new drug class. J Am Acad Dermatol. 2017;76(4):736-44.
[12] Kaur S, Zilmer K, Leping V, Zilmer M. Serum markers of oxidative stress in vitiligo. Free Radic Biol Med. 2004;37(11):1960-69.
[13] Dell'Anna ML, Ottaviani M, Albanesi V, Vidolin AP, Leone G, Ferraro C, et al. Membrane lipid alterations in vitiligo. J Invest Dermatol. 2007;127(5):1226-33.
[14] Schallreuter KU, Wood JM, Berger J. Low catalase levels in vitiligo epidermis. J Invest Dermatol. 1991;97(6):1081-85.
[15] Kyriakis JM, Avruch J. Mammalian MAPK signal transduction pathways activated by stress and inflammation. Physiol Rev. 2012;92(2):689-737.
[16] Battelli MG, Bortolotti M, Polito L, Bolognesi A. Xanthine oxidoreductase in disease. Redox Biol. 2018;14:254-65.
[17] Kanehisa M, Goto S. KEGG: Kyoto encyclopedia of genes and genomes. Nucleic Acids Res. 2000;28(1):27-30.
[18] Szklarczyk D, Gable AL, Lyon D, Junge A, Wyder S, Huerta-Cepas J, et al. STRING v11: Protein-protein association networks with increased coverage. Nucleic Acids Res. 2019;47(D1):D607-D613.
[19] Boots AW, Haenen GR, Bast A. Health effects of quercetin. Eur J Pharmacol. 2008;585(2-3):325-37.
[20] Calderón-Montano JM, Burgos-Morón E, Pérez-Guerrero C, López-Lázaro M. A review on the dietary flavonoid quercetin. Mini Rev Med Chem. 2011;11(4):298-344.
[21] Pietta PG. Flavonoids as antioxidants. J Nat Prod. 2000;63(7):1035-42.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Scholar, Department of Rasashastra and Bhaishajya Kalpana (RSBK), KAHER's, Shri B M Kankanawadi Ayurveda Mahavidyalaya, Postgraduate Studies and Research Centre, Belagavi, Karnataka, India.
2. Professor and Head, Department of Rasashastra and Bhaishajya Kalpana (RSBK), KAHER's Shri B M Kankanawadi Ayurveda Mahavidyalaya, Postgraduate Studies and Research Centre, Belagavi, Karnataka, India.
3. Postgraduate Scholar, Department of Rasashastra and Bhaishajya Kalpana (RSBK), KAHER's, Shri B M Kankanawadi Ayurveda Mahavidyalaya, Belagavi, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Priyanka Nyamti,
Postgraduate Scholar, Department of Rasashastra and Bhaishajya Kalpana (RSBK), KAHER's Shri B M Kankanawadi Ayurveda Mahavidyalaya, Post Graduate Studies and Research Centre, Belagavi-590001, Karnataka, India.
E-mail: drrshiremath.pub@gmail.com, priyankarn87@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Feb 02, 2026
- Manual Googling: Mar 14, 2026
- iThenticate Software: Mar 17, 2026 (3%)

ETYMOLOGY: Author Origin

EMENDATIONS: 8

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? No
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Jan 21, 2026**
Date of Peer Review: **Feb 16, 2026**
Date of Acceptance: **Mar 19, 2026**
Date of Publishing: **Jun 01, 2026**