

Article

Network pharmacology approach for validation of traditional claims of Ayurvedic medicines

Suvarna Ingale¹, Tejal Bele¹, Pramod Ingale²

¹Department of Pharmacology, SCES's Indira College of Pharmacy, Pune-411033, India

²Department of Pharmaceutical Chemistry, SGMSPM's Dyanvilas College of Pharmacy, Dudulgaon, Pune-412105, India

E-mail: suvarnaingale@gmail.com, suvarna.ingle@indiraicp.edu.in

Received 27 August 2023; Accepted 17 October 2023; Published online 20 October 2023; Published 1 June 2024



Abstract

Ayurveda, an ancient holistic healing system originating from India emphasizes balance and harmony between body, mind, and spirit. Ayurvedic medicines offer diverse therapeutic claims, spanning preventive care, disease treatment, and overall well-being. This traditional system significantly influences global healthcare and complements modern medicine. However, scientific validation of Ayurvedic claims remains a challenge. Network pharmacology, an interdisciplinary approach, has emerged as a promising tool for this purpose. Network pharmacology explores complex interactions in biological systems. It aligns well with Ayurveda's holistic philosophy and offers potential in validating Ayurvedic medicines. This review covers successful case studies of justification of Ayurvedic claims using network pharmacology approach. We further outlined key steps for such validation, including literature review, compound identification, data collection, network construction, and enrichment analysis. The approach aligns traditional knowledge with modern scientific findings, enhancing the credibility of both. The integration of Ayurvedic principles with network pharmacology can shed light on the mechanisms of action underlying Ayurvedic medicines. In conclusion, network pharmacology holds immense potential in validating the traditional claims of Ayurvedic medicines. It provides a framework for understanding complex interactions, confirming traditional knowledge, and potentially unlocking novel therapeutic mechanisms. Collaboration between traditional practitioners and scientists, along with advancements in data integration and analysis, can drive this integration, enriching global healthcare with Ayurvedic insights.

Keywords Ayurvedic medicines; network pharmacology; validation.

Network Biology
ISSN 2220-8879
URL: <http://www.iaees.org/publications/journals/nb/online-version.asp>
RSS: <http://www.iaees.org/publications/journals/nb/rss.xml>
E-mail: networkbiology@iaees.org
Editor-in-Chief: WenJun Zhang
Publisher: International Academy of Ecology and Environmental Sciences

1 Overview of Ayurveda and Ayurvedic Medicines

Ayurveda is an ancient holistic healing system originating from India, with roots dating back over 5,000 years. It is based on the concept of balance and harmony between the body, mind, and spirit (Patwardhan and

Mashelkar, 2009). Ayurvedic medicine encompasses various practices, including herbal remedies, dietary guidelines, lifestyle modifications, and therapeutic techniques. Ayurvedic medicine has a vast repository of traditional knowledge passed down through generations. It is founded on the principles of observation, experience, and documentation of healing practices over centuries (Jaiswal and Williams, 2017).

Ayurvedic medicines are known for their diverse therapeutic claims, targeting a wide range of health conditions. These claims cover a broad spectrum, including preventive care, treatment of diseases, and promotion of overall well-being. Ayurvedic medicine considers the individual, focusing on the balance between the body, mind, and spirit. Traditional claims often emphasize the restoration of harmony and equilibrium in the body for optimal health (Pandey et al., 2013).

Ayurvedic medicine has played a significant role in shaping healthcare practices in India and other parts of the world. It has influenced various traditional healing systems, including Tibetan medicine and Traditional Chinese Medicine (TCM). Ayurveda is deeply embedded in the cultural fabric of India and continues to be widely practiced and accepted. Traditional claims of Ayurvedic medicines hold significant value for individuals seeking alternative and complementary approaches to healthcare (Ravishankar and Shukla, 2007).

In recent years, there has been an increasing interest in complementary and alternative medicine (CAM) and natural remedies globally. Ayurvedic medicines are sought after by individuals looking for holistic and natural approaches to health and well-being. There is a growing trend towards integrating traditional systems of medicine, such as Ayurveda, with modern healthcare. Validating the traditional claims of Ayurvedic medicines can facilitate their integration into evidence-based healthcare practices (Patwardhan, 2014). Ayurvedic medicines, often derived from natural sources, have the potential to provide cost-effective and accessible healthcare options, particularly in resource-limited settings (WHO, 2013).

Validating the traditional claims of Ayurvedic medicines can contribute to preserving cultural heritage and safeguarding traditional knowledge for future generations. The network pharmacology approach has emerged as a valuable tool for validating the efficacy and mechanisms of action of traditional Chinese medicines (TCMs). TCMs are complex mixtures of bioactive compounds that often exert their therapeutic effects through multi-target and multi-pathway interactions. Network pharmacology enables the systematic analysis of the interactions between TCM compounds, target proteins, and disease pathways, providing a comprehensive understanding of their pharmacological effects. Studies have successfully applied network pharmacology to explore the molecular targets, biological pathways, and therapeutic potential of various TCMs, such as Danshen (*Salvia miltiorrhiza*), Huangqi (*Astragalus membranaceus*), and Ganoderma lucidum. These investigations have contributed to the validation and development of TCMs as effective therapeutic agents for various diseases (Zhang et al., 2019; Li et al., 2013; Lai et al., 2020). Overall, network pharmacology served as a valuable approach for elucidating the complex mechanisms of TCMs and facilitating their integration into modern medicine. Similarly, Indian Ayurvedic medicines have been used for centuries to treat various diseases. One of the main challenges with their use is limited scientific evidence supporting the use of Ayurvedic medicines in the management of diseases, and there is a need for further research to establish their safety and effectiveness. Furthermore, the molecular targets and pathways underlying their therapeutic effects are not fully understood. Addressing these challenges can help to improve the use of Ayurvedic medicines in managing various diseases and disorders. Validating traditional claims using scientific approaches like network pharmacology can help identify potential lead compounds and targets for drug development. Thus, Ayurvedic medicines may hold untapped sources of novel bioactive compounds (Patwardhan and Chandran, 2015; Patwardhan, 2000).

2 Traditional Claims of Ayurvedic Medicines

2.1 Overview of Ayurveda and its historical background

Ayurveda, often referred to as the "science of life," is an ancient system of medicine in India based on a holistic approach to healthcare that encompasses physical, mental, and spiritual well-being. Ayurvedic medicine views the human body as a complex network of interconnected systems and emphasizes the balance between body, mind, and spirit for optimal health (Patwardhan and Chandran, 2015). The historical context of Ayurveda is rooted in ancient texts known as the Vedas, particularly the Atharva Veda and the Charaka Samhita. These texts provide detailed descriptions of various diseases, their causes, and treatment modalities using medicinal plants, minerals, and other natural substances. Ayurveda has evolved over centuries, incorporating knowledge from diverse sources, and adapting to different cultural contexts (Patwardhan, 2000).

2.2 Traditional claims associated with Ayurvedic medicines

Ayurvedic medicines are known for their extensive use of plant-based formulations, minerals, and herbo-mineral combinations. Traditional claims associated with Ayurvedic medicines cover a wide range of health conditions and therapeutic effects including disease management and prevention. Ayurvedic medicines are believed to support the body's natural healing mechanisms and help manage various diseases, such as respiratory disorders, digestive issues, musculoskeletal problems, skin conditions, and mental health disorders. Ayurvedic medicines aim to restore the balance of bodily humors (doshas) - Vata, Pitta, and Kapha - which are believed to govern physiological and psychological functions. Achieving balance is thought to promote overall vitality, energy, and well-being (Patwardhan, 2000). Ayurvedic medicines are often prescribed in combination with lifestyle modifications, dietary recommendations, and practices such as yoga and meditation. This holistic approach is believed to promote not only physical health but also mental and spiritual well-being (Patwardhan, 2000).

Ayurveda possesses remarkable potential in addressing various chronic ailments including arthritis, asthma, cancer, diabetes, and more. Ayurveda possesses a considerable capacity to effectively address both chronic/non-communicable and communicable diseases. However, the absence of scientific validation for Ayurvedic concepts has resulted in this invaluable ancestral treasure for human health falling behind (Sahu et al., 2023).

2.3 Importance of validating traditional claims of Ayurvedic medicines

It is of utmost importance to delve deeper into the realm of traditional medicines such as Ayurveda to gain insights into their active constituents, activity profiles, characterization, and understanding of their modes of action. These challenging aspects can be unraveled through research at the intersection of *in silico* biology, which refers to computer-based work related to biological experiments. This represents a paradigm shift from traditional *in vitro* and *in vivo* drug discovery processes to *in silico* drug discovery screening, transforming the reliance on "wet lab" experiments to computational resources, automation, and cost-effective research. *In silico* based high-throughput screening methods align well with the principles of refinement, reduction, and mechanistic research in Ayurveda. The global expansion of *in silico* biology encompasses the development of software tools to capture, analyze, and integrate biological and medical data from diverse sources. By utilizing untapped information through computational models, Ayurvedic medicine can generate hypotheses, validate them, and ultimately advance in the field of therapeutics (Ekins et al., 2007). Validating the traditional claims associated with Ayurvedic medicines holds significant importance in modern healthcare for several reasons:

(1). Safety and efficacy: By subjecting Ayurvedic medicines to rigorous scientific validation, their safety and efficacy can be accurately assessed. This ensures that the medicines are reliable and effective for the

conditions they claim to treat, minimizing potential risks or adverse effects (Patwardhan and Chandran, 2015).

(2) Integration with mainstream medicine: Validating Ayurvedic claims can help integrate this ancient system of medicine with modern healthcare practices. It allows for evidence-based collaborations between Ayurvedic practitioners and conventional healthcare providers, facilitating a comprehensive and personalized approach to patient care (Chauhan et al., 2015).

(3) Identification of active compounds and mechanisms of action: Through validation, the active compounds present in Ayurvedic formulations can be identified and their pharmacological actions elucidated. This knowledge contributes to a better understanding of the mechanisms of action of Ayurvedic medicines, allowing for targeted therapies and potential drug development (Patwardhan and Chandran, 2015; Lele, 2010).

(4) Cultural preservation and global recognition: Validating Ayurvedic claims help preserve and promote traditional knowledge and practices. It acknowledges the cultural heritage associated with Ayurveda and enables its integration into global healthcare systems, fostering cross-cultural collaborations and facilitating the exchange of medicinal knowledge (Chaturvedi et al., 2023).

3 Network Pharmacology: An Overview

Network pharmacology is an interdisciplinary field that combines network science, computational biology, and pharmacology to understand the interactions between biological entities at systems level. It focuses on studying the complex relationships among genes, proteins, metabolites, and other molecular components within biological networks. The principles of network pharmacology involve analyzing and modeling these networks to gain insights into the mechanisms of drug action and disease pathogenesis (Hopkins, 2008; Zhang, 2016, 2017).

Traditional pharmacology approaches often focus on individual molecular targets and their effects. In contrast, network pharmacology recognizes that biological systems are inherently complex and interconnected. By utilizing network-based analyses, it becomes possible to unravel the intricate relationships and interactions within these systems. Network pharmacology provides a holistic understanding of the molecular mechanisms underlying diseases, drug actions, and therapeutic interventions (Hopkins, 2007; Zhang, 2016).

Network pharmacology has significant implications for drug discovery and development processes. It aids in identifying potential drug targets by exploring the connectivity and centrality of molecules within biological networks. By integrating data from various sources, including genomics, proteomics, and metabolomics, network pharmacology enables the identification of key nodes or hub molecules that play crucial roles in disease processes. This information can guide the rational design of targeted therapies and the repurposing of existing drugs for new indications (Li et al., 2011).

Additionally, network pharmacology allows for the prediction of drug-drug interactions and adverse effects by considering the network context of drug targets. It aids in optimizing drug combinations and improving therapeutic outcomes by identifying synergistic interactions and reducing potential toxicities. Furthermore, network pharmacology can provide insights into the personalized treatment of patients by considering individual variations in molecular networks and responses to drugs (Wu et al., 2008).

The use of network pharmacology offers several advantages in understanding complex biological systems and drug discovery. It provides a comprehensive view of the interactions and relationships within biological networks, enabling a more holistic understanding of disease mechanisms and drug actions (Hopkins, 2008). Network pharmacology helps identify key molecules and pathways involved in diseases,

which can serve as potential drug targets or biomarkers (Menche et al., 2015). It also facilitates the repurposing of existing drugs for new indications by identifying their effects on specific network components. Additionally, it aids in predicting potential drug-drug interactions and adverse effects based on network connectivity and molecular interactions (Li et al., 2011).

However, network pharmacology also has limitations. Integrating data from diverse sources and database interactions is challenging due to differences in data formats, quality, and availability. Analyzing large-scale biological networks requires advanced computational tools and algorithms, which can be computationally intensive and time-consuming. Furthermore, network pharmacology predictions often require experimental validation to confirm the functional relevance and accuracy of the network-based findings (Hopkins, 2008; Zhang, 2016).

3.1 Network pharmacology in validating Ayurvedic medicines

Network pharmacology provides a valuable framework for integrating the principles of Ayurveda with modern scientific approaches. Ayurveda, an ancient system of medicine, emphasizes a holistic understanding of health and disease and focuses on personalized and preventive healthcare. By combining Ayurvedic principles with network pharmacology, it becomes possible to explore the complex interactions between Ayurvedic medicines and biological systems at a systems level. This integration allows for a deeper understanding of the therapeutic effects of Ayurvedic medicines and their potential mechanisms of action (Patwardhan et al., 2004).

One of the challenges in validating traditional claims of Ayurvedic medicines is understanding their mechanisms of action at a molecular level. Network pharmacology plays a crucial role in unraveling these mechanisms by analyzing the interactions between the bioactive components of Ayurvedic formulations and cellular networks. By constructing and analyzing network models, it becomes possible to identify key molecular targets, signaling pathways, and biological processes that are modulated by Ayurvedic medicines. This knowledge helps in elucidating the pharmacological basis of Ayurvedic formulations and provides insights into their therapeutic effects (Patwardhan and Chandran, 2015).

Network analysis techniques are instrumental in identifying the active compounds and molecular targets in Ayurvedic medicines. By analyzing the network connectivity patterns and interactions, it becomes possible to identify the key components that contribute to the overall pharmacological activity of the formulation. Network-based approaches aid in identifying the target proteins and pathways that are modulated by Ayurvedic medicines, thereby providing a scientific basis for their traditional claims. This information is essential for validating the efficacy and therapeutic potential of Ayurvedic formulations (Bhatia et al., 2022).

Network pharmacology offers the potential for predictive modeling to assess the efficacy and safety of Ayurvedic medicines. By integrating data on chemical structures, pharmacological activities, and network interactions, computational models can be developed to predict the efficacy of Ayurvedic formulations against specific disease targets. These models aid in identifying potential synergistic interactions between multiple components of Ayurvedic medicines and their targets. Furthermore, network-based approaches can also be employed to predict potential adverse effects or drug-drug interactions, enabling safety assessments of Ayurvedic formulations (Patwardhan & Mashelkar, 2009).

3.2 Case studies

In recent years, network pharmacology has emerged as a powerful approach for validating the traditional claims of Ayurvedic medicines. By applying network analysis techniques and computational modeling, researchers have successfully explored the complex interactions between Ayurvedic formulations and biological systems, shedding light on their therapeutic efficacy and mechanisms of action. Several case studies have demonstrated the potential of network pharmacology in validating Ayurvedic claims and

providing scientific evidence for their traditional use.

One notable case study was focused on the validation of an Ayurvedic formulation called "Triphala," which consists of three medicinal plants: *Embllica officinalis*, *Terminalia chebula*, and *Terminalia bellirica*. Triphala has been traditionally used for various ailments, including digestive disorders and inflammatory conditions. Through network pharmacology, researchers investigated the molecular targets and pathways associated with Triphala's therapeutic. The study involved the construction of a network model that integrated information on the chemical constituents of Triphala, their interactions with target proteins, and their modulation of key biological pathways. The network analysis revealed the potential targets and pathways involved in Triphala's antioxidant, anti-inflammatory, and immunomodulatory activities, providing scientific validation for its traditional claims (Patwardhan and Chandran, 2015).

Another case study focused on Ayurvedic formulations used for the management of cancer. Researchers presented the potential of network pharmacology to understand the mechanisms of action of Ayurvedic medicines Triphala. By integrating data on the chemical composition of the Triphala and their interactions with target proteins, a network-based approach identified the key molecules and pathways involved in the anti-cancer effects of Triphala. This pioneering effort might open new possibilities to know pharmacodynamics of Ayurvedic drugs like Triphala and help in the discovery of new leads and targets for various diseases (Chandran et al., 2015).

Another study employed a network pharmacology-based approach to investigate the protective mechanism of Triphala, a traditional therapeutic formula, against cardio-cerebral vascular diseases (CCVDs). By analyzing compound-target gene networks and pathways, key targets (PTGS2, MMP9, and IL6) and potential therapeutic pathways were identified. In vitro experiments supported the findings, indicating that Triphala inhibits the expression of PTGS2, MMP9, and IL6. This study provided valuable insights into the components and pharmacological mechanism of Triphala and offers potential targets for developing new CCVD treatments (Wang et al., 2019).

A study by Vinothkanna et al. (2023) exploited pharmacological network analysis on Chandanasava, an Ayurvedic fermented traditional medicine to uncover its mode of action and functional targets for chronic kidney disease and cardiovascular disease. They identified 10 bioactive compounds in Chandanasava that exhibit strong binding affinity with target proteins involved in chronic kidney disease and cardiovascular disease. Gene Ontology and KEGG analysis provided insights into the target pathways, and molecular docking suggested piperine and melatonin as effective inhibitors/regulators of CKD and CVD hub genes.

Wadhawan et al. (2021) investigated the pharmacological mechanism of Nisha Amalaki, an herbal formulation used for treating Type 2 diabetes mellitus (T2DM). Through a network pharmacology-based approach, potential targets of Nisha Amalaki were identified, and a protein-protein interaction network was analyzed. Enrichment analysis revealed multiple biological processes and pathways associated with its anti-diabetic effects, including glucose and lipid metabolism, insulin resistance, inflammation, apoptosis, and cell cycle regulation.

Jethalia et al. (2021) investigated the neuroprotective role of the Ayurvedic formulation Saraswatarishta (SWRT) in neurological disorders using a network pharmacology approach. Five ingredients and nine active phytoconstituents were analyzed for their gene targets and interactions. The networks revealed associations with major neurological disorders, and the phytoconstituents showed potential therapeutic effects. Additionally, the study found significant expression of gene targets in various central nervous system regions and indications that the phytoconstituents can cross the blood-brain barrier.

Another study focused on Nisakathakadi Kashaya (NK), an Ayurvedic anti-diabetic formulation, to identify its potential as a DPP4 inhibitor and its modulation of diabetes-associated gene networks. In vitro

and in silico methods were used to study Nisakathakadi Kashaya's DPP4 inhibitory potential and identify bioactive compounds. Network pharmacology analysis revealed Nisakathakadi Kashaya's interactions with diabetes-related proteins and pathways. The study provides insights into Nisakathakadi Kashaya's mechanism of action and its potential for diabetes management (Thottappillil et al., 2022).

3.3 Steps for validation of traditional claims of Ayurvedic medicines using network pharmacology approach

Network pharmacology approach combines the principles of network biology, systems pharmacology, and bioinformatics to understand the complex interactions between multiple herbal components in ayurvedic formulations. In terms of Ayurvedic medicines, they contain multiple molecules that can target multiple genes/proteins and therefore can affect multiple pathways with overall positive impact against a disease condition. Depending on experiments/available datasets of molecules in ayurvedic formulation, one could build and analyze networks and characterize various properties. The following steps involved can be followed for validation of traditional claims of Ayurvedic medicines using network pharmacology approach.

3.3.1 Selection of Ayurvedic medicine

Choose an Ayurvedic medicine with specific therapeutic claims that one wants to validate. Ensure that there's enough historical documentation and traditional knowledge available about the medicine's usage.

3.3.2 Literature review

Conduct an extensive literature review to gather information about the selected Ayurvedic medicine, including its composition, traditional uses, constituents, formulations, and therapeutic claims. This step helps in understanding the medicine's context and potential mechanisms of action. This can be done using Ayurvedic literature, traditional texts, and modern scientific databases.

3.3.3 Identification of active compounds

Based on the composition of ayurvedic medicine, identify the active compounds (bioactives / phytoconstituents) present in Ayurvedic medicine. This can be done by referring to traditional texts, Ayurvedic experts, or databases of Ayurvedic herbs like Universal natural products database (UNPD), Dr Dukes phytochemical and ethnobotanical database (U.S. Department of Agriculture, Agricultural Research Service. 1992-2016), Medicinal plants database for drug designing (MPD3) (Mumtaz et al., 2017), Indian medicinal plants phytochemistry and therapeutics (IMPPAT) (Mohanraj et al., 2018), etc.

3.3.4 Data collection to predict protein targets, pathways, and interactions

Collect biological data related to the identified active compounds. This includes information about protein targets, pathways, and interactions. This can be done using literature, some relevant databases and web tools. Protein targets of identified bioactives / phytoconstituents can be mined using Binding DB, the first public molecular recognition database, accessible at <https://www.bindingdb.org> (Gilson et al., 2015) or SwissADME web tool accessible at <http://www.swissadme.ch/> (Daina et al., 2017).

Information about pathways associated with identified bioactives / phytoconstituents can be mined using KEGG PATHWAY Database accessible at <https://www.genome.jp/kegg/>. Similarly, information of protein targets of diseases can be mined from various databases like Therapeutic Target Database (TTD) accessible at <https://db.idrblab.net/ttd/>, DrugBank accessible at <https://go.drugbank.com/>, OMIM (Online Mendelian Inheritance in Man) accessible at <https://www.omim.org/>, DisGeNET accessible at <https://www.disgenet.org/>, STRING accessible at <https://string-db.org/>, etc.

3.3.5 Network construction and analysis

Build and analyze protein-protein interactions, compound-protein interactions, and pathway networks that represent interactions between the active compounds and their protein targets (Yang and Zhang, 2023). Protein-protein interactions network can be constructed and analyzed using STRING database (von Mering et

al., 2003). Further Cytoscape, an open-source software platform, can be used for visualizing and analyzing complex networks. Network analysis tools help to identify central nodes (highly connected proteins) and clusters (groups of closely interacting proteins) (Shannon et al., 2003). This step helps in understanding the potential biological significance of the interactions. This enables the identification of novel targets, prediction of drug effects, and the exploration of intricate relationships that contribute to disease and drug response.

3.3.6 Gene function and pathway enrichment analysis

Perform Gene Function and pathway enrichment analysis to identify biological pathways that are significantly enriched among the target proteins. This provides insights into the pathways influenced by the active compounds and their potential therapeutic relevance. Pathway enrichment analysis tools help researchers understand the biological significance of a set of genes or proteins by identifying overrepresented biological pathways. Some popular pathway enrichment analysis tools used include DAVID (Database for Annotation, Visualization, and Integrated Discovery), KEGG Pathway Database, Reactome, STRING, etc.

3.3.7 Validation and hypothesis generation

Validation involves comparing network findings with traditional claims to affirm alignment, validating both knowledge sources. Comparing network and pathway analysis with Ayurvedic medicine's traditional claims is vital in network pharmacology. It validates alignment between network findings and Traditional knowledge. This confirms network pharmacology's ability to identify pathways consistent with historical uses. It may unveil new insights and address discrepancies. Integrating traditional wisdom with modern approaches builds a comprehensive understanding of medicine's action. Cross-validation via experiments enhances credibility. Hypothesis generation stems from unexplained pathways identified in the analysis, allowing new insights into mechanisms of action.

This seven step harmonization underscores network pharmacology's potential to validate Ayurvedic medicine while revealing novel mechanisms (Noor et al., 2022; Srikanth, 2021). It is important to note that network pharmacology is an emerging field, and while it shows promise for validating traditional claims of Ayurvedic medicines, further research and validation are needed.

4 Challenges and Future Directions

The application of network pharmacology to Ayurvedic medicines faces several challenges. One challenge is the complexity and diversity of Ayurvedic formulations, which often contain multiple herbs and compounds, making it difficult to decipher the interactions and mechanisms of action. Another challenge is the lack of comprehensive data on Ayurvedic herbs and their active compounds in existing databases, hindering accurate network analysis. Additionally, the integration of Ayurvedic concepts, such as holistic approaches and individualized treatments, into network pharmacology frameworks poses challenges in terms of standardization and reproducibility (Patwardhan et al., 2004).

An important aspect of validating Ayurvedic claims using network pharmacology is the integration of traditional knowledge and modern scientific approaches. This requires bridging the gap between traditional Ayurvedic concepts and the language and methodologies of modern science. Collaboration between Ayurvedic practitioners, traditional healers, and scientists is crucial to ensure a comprehensive understanding of Ayurvedic medicines and their mechanisms of action (Patwardhan, 2000).

Regulatory considerations and standardization are significant challenges in the application of network pharmacology to Ayurvedic medicines. The regulatory framework for traditional medicine products varies across different countries and regions, and there is a need for standardized guidelines for the evaluation, safety assessment, and quality control of Ayurvedic formulations. Developing standardized protocols and criteria for conducting clinical trials and establishing quality control parameters for Ayurvedic medicines are

essential for their acceptance and integration into mainstream healthcare systems (Patwardhan and Mashelkar, 2009).

The field of network pharmacology holds great potential for advancing the validation of Ayurvedic claims. Future directions include the integration of multi-omics data, such as genomics, transcriptomics, and metabolomics, to gain a comprehensive understanding of the molecular mechanisms and interactions underlying Ayurvedic medicines. Additionally, the development of databases specific to Ayurvedic herbs and compounds, combined with advanced data mining and machine learning techniques, will enhance the accuracy and reliability of network analysis. Furthermore, the utilization of network-based predictive modeling and systems biology approaches can aid in personalized treatment strategies and the identification of potential drug targets (Li S et al., 2011; Wu et al., 2008).

Acknowledgements

The authors are thankful to the management of SCES's Indira College of Pharmacy, Pune, Maharashtra, India for encouraging and providing necessary facilities.

References

- Bhatia N, Mokashi A, Nathore N, Nathore A. 2022. Network pharmacology: An emphasis on traditional Chinese medicines and its adaptability for Ayurveda medicines in India. *International Journal Of Medical Science And Clinical Research Studies*, 2(12): 1608-1620. doi:10.47191/ijmscrs/v2-i12-40. <http://dx.doi.org/10.47191/ijmscrs/v2-i12-40>
- Chandran U, Mehendale N, Tillu G, Patwardhan B. 2015. Network pharmacology of Ayurveda formulation Triphala with special reference to anti-cancer property. *Comb Chem High Throughput Screen*, 18(9): 846-854. doi:10.2174/1386207318666151019093606
- Chaturvedi S, Porter J, Gopalakrishna Pillai GK, Abraham L, Shankar D, Patwardhan B. 2023. India and its pluralistic health system - a new philosophy for Universal Health Coverage. *Lancet Regional Health Southeast Asia*, 10(100136): 100136. doi:10.1016/j.lansea.2022.100136
- Chauhan A, Semwal DK, Mishra SP, Semwal RB. 2015. Ayurvedic research and methodology: Present status and future strategies. *Ayu*, 36(4): 364-369. doi:10.4103/0974-8520.190699. <http://dx.doi.org/10.4103/0974-8520.190699>.
- Daina A, Michielin O, Zoete V. 2017. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific Reports*, 7(1). <http://dx.doi.org/10.1038/srep42717>
- Ekins S, Mestres J, Testa B. 2007. In silico pharmacology for drug discovery: methods for virtual ligand screening and profiling. *British Journal of Pharmacology*, 152(1): 9-20. doi:10.1038/sj.bjp.0707305.
- Gilson MK, Liu T, Baitaluk M, Nicola G, Hwang L, Chong J. 2016. BindingDB in 2015: A public database for medicinal chemistry, computational chemistry and systems pharmacology. *Nucleic Acids Research*, 44(D1): D1045-1053. <http://dx.doi.org/10.1093/nar/gkv1072>
- Hopkins AL. 2007. Network pharmacology. *Nature Biotechnology*, 25(10): 1110-1111. doi:10.1038/nbt1007-1110
- Hopkins AL. 2008. Network pharmacology: the next paradigm in drug discovery. *Nature Chemical Biology*, 4(11): 682-690. doi:10.1038/nchembio.118
- Jaiswal YS, Williams LL. 2017. A glimpse of Ayurveda - The forgotten history and principles of Indian traditional medicine. *Journal of Traditional and Complementary Medicine*, 7(1): 50-53. doi:10.1016/j.jtcme.2016.02.002

- Jethalia V, Hasyagar SV, Bhamidipati K, Chatterjee J. 2021. Analysing the role of Saraswatarishta in the treatment of neurological disorders based on network pharmacology. *Neuroscience Research Notes*, 3(5): 23-35. doi:10.31117/neuroscirn.v3i5.106
- Lai X, Wang X, Hu Y, Su S, Li W, Li S. 2020. Editorial: Network pharmacology and traditional medicine. *Frontiers in Pharmacology*, 11: 1194. doi:10.3389/fphar.2020.01194
- Lele RD. 2010. Beyond reverse pharmacology: Mechanism-based screening of Ayurvedic drugs. *Journal of Ayurveda and Integrative Medicine*, 1(4): 257-265. doi:10.4103/0975-9476.74435
- Li S, Zhang B, Zhang N. 2011. Network target for screening synergistic drug combinations with application to traditional Chinese medicine. *BMC Systems Biology*, 5(Suppl 1): S10. doi:10.1186/1752-0509-5-S1-S10
- Li S, Zhang B. 2013. Traditional Chinese medicine network pharmacology: theory, methodology and application. *Chinese Journal of Natural Medicines*, 11(2): 110-120. doi:10.1016/S1875-5364(13)60037-0
- Menche J, Sharma A, Kitsak M, Ghiassian SD, Vidal M, Loscalzo J, Barabasi A-L. 2015. Uncovering disease-disease relationships through the incomplete interactome. *Science*, 347(6224): 1257601-1257601. doi:10.1126/science.1257601
- Mohanraj K, Karthikeyan BS, Vivek-Ananth RP, Chand RPB, Aparna SR, Mangalapandi P, et al. 2018. IMPPAT: A curated database of Indian Medicinal Plants, Phytochemistry And Therapeutics. *Scientific Reports*, 8(1): 4329. <http://dx.doi.org/10.1038/s41598-018-22631-z>
- Mumtaz A, Ashfaq UA, ul Qamar MT, Anwar F, Gulzar F, Ali MA, et al. 2017. MPD3: a useful medicinal plants database for drug designing. *Natural Product Research*, 31(11): 1228-1236. <http://dx.doi.org/10.1080/14786419.2016.1233409>
- Noor F, Tahir UI, Qamar M, Ashfaq UA, Albutti A, Alwashmi ASS, Aljasir MA. 2022. Network pharmacology approach for medicinal plants: Review and assessment. *Pharmaceuticals (Basel)*, 15(5): 572. doi:10.3390/ph15050572
- Pandey MM, Rastogi S, Rawat AKS. 2013. Indian traditional ayurvedic system of medicine and nutritional supplementation. *Evidence-Based Complementary and Alternative Medicine*, 2013: 376327. doi:10.1155/2013/376327
- Patwardhan B, Chandran U, 2015. Network ethnopharmacology approaches for formulation discovery. *Indian Journal of Traditional Knowledge*, 14(4): 574-580
- Patwardhan B, Chandran U, 2015. Network ethnopharmacology approaches for formulation discovery. *Indian Journal of Traditional Knowledge*, 14(4): 574-580
- Patwardhan B, Mashelkar RA. 2009. Traditional medicine-inspired approaches to drug discovery: can Ayurveda show the way forward? *Drug Discovery Today*, 14(15-16): 804-811. doi:10.1016/j.drudis.2009.05.009
- Patwardhan B, Vaidya ADB, Chorghade M. 2004. Ayurveda and natural products drug discovery. *Current Science*, 86(6):789-799. <http://www.jstor.org/stable/24109136>.
- Patwardhan B. 2000. Ayurveda: The 'designer' medicine: A review of ethnopharmacology and bioprospecting research. *Indian Drugs*, 37(5): 213-227
- Patwardhan B. 2014. Bridging Ayurveda with evidence-based scientific approaches in medicine. *EPMA Journal*, 5(1): 19. doi:10.1186/1878-5085-5-19
- Ravishankar B, Shukla VJ. 2007. Indian systems of medicine: a brief profile. *African Journal of Traditional, Complementary and Alternative Medicines*, 4(3): 319-337. doi:10.4314/ajtcam.v4i3.31226
- Sahu R, Gupta PK, Mishra A, Kumar A. 2023. Ayurveda and in silico approach: A challenging proficient confluence for better development of effective traditional medicine spotlighting network pharmacology. *Chinese Journal of Integrative Medicine*, 29(5): 470-480. doi:10.1007/s11655-022-3584-x

- Shannon P, Markiel A, Ozier O, Baliga NS, Wang JT, Ramage D, et al. 2003. Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome Research*, 13(11): 2498-2504. <http://dx.doi.org/10.1101/gr.1239303>
- Srikanth N. 2021. Bioinformatics and network pharmacology: Scope and relevance in Ayurveda research. *Journal of Drug Research in Ayurvedic Sciences*, 6: 197-199. DOI: 10.4103/jdras.jdras_28_22
- Thottappillil A, Sahoo S, Chakraborty A, Kouser S, Ravi RV, Garawadmath S, Banvi PG, Kukkupuni SK, Mohan S S, Vishnuprasad CN. 2022. In vitro and in silico analysis proving DPP4 inhibition and diabetes associated gene network modulation by a polyherbal formulation –Nisakathakadi Kashaya. *bioRxiv*, doi:10.1101/2022.07.15.500175
- U.S. Department of Agriculture, Agricultural Research Service. 1992-2016. Dr. Duke's Phytochemical and Ethnobotanical Databases. <http://phytochem.nal.usda.gov/>
<http://dx.doi.org/10.15482/USDA.ADC/1239279>
- Vinothkanna A, Prathiviraj R, Sivakumar TR, Ma Y, Sekar S. 2023. GC-MS and network pharmacology analysis of the Ayurvedic fermented medicine, Chandanasava, against chronic kidney and cardiovascular diseases. *Applied Biochemistry and Biotechnology*, 195(5): 2803-2828. doi:10.1007/s12010-022-04242-7
- von Mering C, Huynen M, Jaeggi D, Schmidt S, Bork P, Snel B. 2003. STRING: a database of predicted functional associations between proteins. *Nucleic Acids Research*, 31(1): 258-261. <http://dx.doi.org/10.1093/nar/gkg034>
- Wadhawan M, Chhabra V, Katiyar A, Sharma V, Khuntia BK, Rathore S, Kaur P, Sharma G. 2021. A network pharmacology-based approach to explore therapeutic mechanism of Indian herbal formulation Nisha Amalaki in treating Type 2 diabetes mellitus. *Research Square*, doi:10.21203/rs.3.rs-954990/v1
- Wang W, Liu T, Yang L, Ma Y, Dou F, Shi L, Wen A, Ding Y. 2019. Study on the multi-targets mechanism of triphala on cardio-cerebral vascular diseases based on network pharmacology. *Biomedicine and Pharmacotherapy*, 116(108994): 108994. doi:10.1016/j.biopha.2019.108994
- WHO traditional medicine strategy. 2014-2023. Geneva, World Health Organization, 2013 https://apps.who.int/iris/bitstream/handle/10665/92455/9789241506090_eng.pdf
- Wu X, Jiang R, Zhang MQ, Li S. 2008. Network-based global inference of human disease genes. *Molecular Systems Biology*, 4(1):189. doi:10.1038/msb.2008.27
- Yang S, Zhang WJ. 2022. Systematic analysis of olfactory protein-protein interactions network of fruitfly, *Drosophila melanogaster*. *Archives of Insect Biochemistry and Physiology*, 110(2): e21882
- Zhang R, Zhu X, Bai H, Ning K. 2019. Network pharmacology databases for Traditional Chinese Medicine: Review and assessment. *Frontiers in Pharmacology*, 10: 123. doi:10.3389/fphar.2019.00123
- Zhang WJ. 2016. Network pharmacology: A further description. *Network Pharmacology*, 1(1): 1-14
- Zhang WJ. 2017. Network pharmacology of medicinal attributes and functions of Chinese herbal medicines: (II) Relational networks and pharmacological mechanisms of medicinal attributes and functions of Chinese herbal medicines. *Network Pharmacology*, 2(2): 38-66