



ORIGINAL RESEARCH PAPER

Ayurveda

REVIEW ON NETWORK PHARMACOLOGY APPROACH THROUGH COMPARATIVE ANALYSIS OF RESEARCH WORK DONE ON MARICHA (PIPER NIGRUM)

KEY WORDS:

Prof. Dr. Aparna M. Ghotankar

HOD Dravyaguna Dept., CSMSS, Ayurved Mahavidyalaya And Rugnalaya-Chh.Sambhajinagar

Dr. Rajashri A. Bomble

Associate Professor Dravyaguna Dept., GJPIASR, New V.V.Nagar.

ABSTRACT

Ayurvedic drugs have played a crucial part in treatment of various disorders due to their rasa panchak attributes which are responsible in binding at modulated cellular levels and targets the disease involved. Ayurvedic plants hold a variety of bio-active scaffolds like guna karma of their various attributes for the treatment of multiple ailments. The very less harmful effects, affordability, and easy availability make the traditional remedies easy and beneficial for use at various aspects of patients and Vaidya's demand. Targets to be identified on pharmacological aspects of active ingredients or phytochemical compounds of medicinal plants has become a trend for today's research to develop and uplift the new possible therapies. This gives new scope of research to traditional ayurvedic drugs to undergo new research heights for its systematic examination and new advances like network pharmacology becoming a front line research of drug discovery and advancement of Ayurvedic science. The upcoming researches in network pharmacology has put forward new advances for understanding the complex bioactive compounds and phytochemicals found in various medicinal plants. This comparative review study is highlighting to a comprehensive summary of network pharmacology involves current research, comparing it with work done on maricha, which will well relate with the research to be established on basis of Network Pharmacology. Brihatraye extensively described maricha (Piper nigrum) plant as appetizer, carminative and antimicrobial. Sharangdhar quoted it as the example for chedana and pramathi group of drugs.

INTRODUCTION

To discover useful compounds to explore its utilisation and importance as chemical constituents with biological potential of traditionally used plants. This attempt to review the use of Maricha on new aspects of network pharmacology based on its utilisation and earlier research work done which has a base as per authentic granthokta reference proven its useful aspects and utilisation in various disease attempted to cover this vast topic in the review form. Which further will be significantly important for researches to prove the plants on new protocols of network pharmacology. The classical text and scriptures describe Marich as by CHARAK---Deepaniya, Shoola prashamana, Krimighna, Shirovirechanopaga, Shirovirechan, aharopayogi SUSHRUT---Pippaliyadi, Trikatu, Shirovirechan VAGBHATT---Shirovirechanagana, Vatsakadi, Pippaliyadi, Deepaniya

It is a need of the hour to focus or tackle the major concerns that the world has been confronted which is making us face the world wide health challenges to keep the world a better healthy place to live. Threatening epidemics and diseases like covid cancer diabetes, etc., make the researchers to work harder with attention because these diseases hamper the quality of global health status

Networking implements a strong base in screening the goods pharmacological or efficient way by work of herbal medications in drug discovery. One unique way to learn more about how active substances perform At present, one can say that network pharmacology has begun to grow and is a commonly used approach in this modern era-drug discovery process [17]. The advances are of the paradigm from a "one-target, one-drug" mode to a "network-target, multiple-component-therapeutics" mode. One unique method to understand learn more about how active substances perform their therapeutic effect is to predict the gene networks that are being regulated by active compounds of medicinal plants [9].

Methodology

Drug Research As Per Ancient Literatures

Network pharmacology deals with pharmacology drug research linking the one drug one disease concept with mutually correlates the proven theories of various drugs to be

used in various diseases explained as further.

Dravya Pariksha Vidhi as per Charaka Samhita

तस्यापीयं पीक्षा - इदमेवंद्रित्येवंगुणमेवंप्रभावमक्तिदेश जातमक्तिन्तावेवं गृहीतमेव मुपस्कृतमनया च मात्रया युक्तिं व्याप्तिं वेवधविस्य पुरुषेभ्य तावन्तं दोषमपिषत्पुशमयधत वा ; यदन्यदधप चैवधविं भेषजं भवेत तत्त्वानेन धवशेषेण युधिधमधत // (च.ध.8/87)

Acharya Charaka has given guidelines for drug standardization, which are as relevant in today's era too. It indicates that a drug should be studied as follows:

- 1. Prakruti:** Name, Natural order of drug and botanical morphology.
- 2. Guna:** Rasa, Virya, Gunas and chemical properties
- 3. Prabhava:** Therapeutic actions.
- 4. Desha:** Botanical distribution
- 5. Rutu Gruhitam:** Time and method of collection
- 6. Nihit:** Method of preservation
- 7. Upaskrit:** Sanskar, Pharmaceutical processing for its preparations
- 8. Matra:** Dosage
- 9. Vyadhi:** Various diseases in which drug can be therapeutically used
- 10. Evam Vidham Purushasya:** Clinical trials or in which person it is probably useful.

Ethno-medicine is a study of traditional medicine practiced by various ethnic groups. Charaka clearly states that information about unknown drugs should be collected from forest dwellers, shepherds tribes etc. This will expand the knowledge of herbs.[4]

To find new molecule in the plant.

Explore the floras in the world.

अनेन उपदेशेन नानौषधिभूतं जगधत धिधित्त्रव्यं उपलभ्यते तां तां युक्तिमर्थं च तं तं अधमप्रेत्य! (च.सु.26/12)

There is no single drug in the universe, which is not Aushadha or which is useless.

Network Pharmacology Following On Methodology

Research in drug discovery has an efficacy crises which is efficient in proving mainly single-target. Currently one drug-one disease-one disease approaches in drug discovery have become increasingly inefficient. Still single-target strategies might prove a useful approach for single gene disorders, however, for complicated diseases that are caused by the interaction of multiple genes, such one single-target approaches are not fruitful [10]. The concept of developing multi-target drugs against complex diseases such as diabetes and cancer is fast growing in drug discovery. Regarding this, network pharmacology defines disease mechanisms as networks best targeted by multiple, synergistic drugs.

Following drug research on Maricha as single drug for treatment lining in following disease.

References Of Maricha From Bruhatraye

REF. NO.	KALPA/ KALPANA	SINGLE/ COMBINATION	KALPA	KARMA	OTHER
C.S.S.2/3	chuma as, 'Maricha'	combination	-	Used with different medicines	-
C.S.S.2/23	Kwath as 'Maricha'	combination	Siddha yavagu	Krumighn a	-
C.S.S.3/12	Churna as 'Maricha'	combination	-	Kustha pradeh	-
C.S.S.4/9.6	Churna as 'Maricha'	combination	-	Dipaniya gana	-
C.S.S.4/11	Churna as 'Maricha'	combination	-	Krumighn a gana	-
C.S.S.4/13	Churna as 'Maricha'	combination	-	Shirovirec hanopag	-
C.S.S.4/17	Churna as 'Maricha'	combination	-	Shoolpras haman	-
C.S.S.27/297	Churna as 'Maricha'	single	-	Maricha gunas	-
C.S.V.8/142	Churna as 'Maricha'	combination	-	Katukskan da	-
C.S.V.8/151	Churna as 'Maricha'	combination	-	Shirovirec han	Virec han
C.S.Chi, 2-1/30	Churna as 'Maricha'	combination	Bmhani gutika	Bruhan	-
C.S.Chi, 2-2/24	Churna as 'Maricha'	combination	Vrushya dadhisar	Vajikaran	-
C.S.Chi, 2-4/11	Churna as 'Maricha'	combination	Manasa gutika	Vajikaran	-
C.S.Chi, 2-4/21	Churna as 'Maricha'	combination	Pupilika yog	Vajikaran	-
C.S.Chi, 7/48	kwath as 'Maricha'	combination	-	Kushta	Nasa ya
C.S.Chi, 7/74	kwath as 'Maricha'	combination	Madhava sava	Kushta	-
C.S.Chi, 14/203	churna as 'Maricha'	single	-	Arsha, aahar with maricha	-
C.S.Chi, 15/102	churna as 'Maricha'	combination	-	Grahani	-
C.S.Chi, 15/120	kwath as 'Maricha'	combination	Takraris hata	Deepan	-
C.S.Chi, 15/164	kwath as 'Maricha'	combination	Madhava rishta	Grahani	-
C.S.Chi, 15/168	churna as 'Maricha'	combination	-	Kaphaj grahani	-
C.S.Chi, 16/129	churna as 'Maricha'	combination	-	Atisaar	-
C.S.Chi, 17/98	yush as 'Maricha'	combination	-	Hikka , Shwas	-
C.S.Chi, 17/110	kalka as 'Maricha'	combination	-	Hikka, Shwas	-

C.S.Chi, 18/71	churna as 'Maricha'	combination	dhoomv arti	Kasa	varti
C.S.Chi, 18/73	churna as 'Maricha'	combination	dhoomv arti	Kasa	varti
C.S.Chi, 18/90	churna as 'Maricha'	combination	-	Pittaj Kasa	
C.S.Chi, 18/104	churna as 'Maricha'	combination	-	Kasa	Gud a
C.S.Chi, 18/180	churna as 'Maricha'	combination	-	Swarbhed, kaas	Leh
C.S.Chi, 19/107	churna as 'Maricha'	combination	-	Kaphatisaa r	-
C.S.Chi, 19/111	churna as 'Maricha'	combination	Siddha takra	Kaphatisaa r	-
C.S.Chi, 20/39	churna as 'Maricha'	combination	-	Kaphaj chardi	Leh
C.S.Chi, 20/50	churna as 'Maricha'	combination	-	Vishachiki tsa	Agad
C.S.Chi, 23/183	avaleh as 'Maricha'	combination	-	Akshigatvi sha	Anja n
C.S.Chi, 24/23	kwath as 'Maricha'	combination	-	Vatik madatyaya	Mad ya
C.S.Chi, 24/127	kwath as 'Maricha'	combination	-	Vatik madatyaya	Mad ya
C.S.Chi, 24/128	churna as 'Maricha'	combination	Asthang lavanyog	Kaphaj madatyaya	-
C.S.Chi, 24/177	kwath as 'Maricha'	combination	-	Kaphaj madatyaya	-
C.S.Chi, 24/181	kwath as 'Maricha'	combination	-	Kaphaj madatyaya	Raga /shadav
C.S.Chi, 24/183	kwath as 'Maricha'	combination	-	Kaphaj madatyaya	Raga
C.S.Chi, 26/138	churna as 'Maricha'	combination	-	Shirorog	Nasy a
C.S.Chi, 26/192	churna as 'Maricha'	combination	Kolaka churna	Shirorog	-
C.S.Chi, 26/216	churna as 'Maricha'	combination	-	Arochak	-
S.S.Su.3 8/22	churna as 'Maricha'	Single	-	Pippalliya di gan	-
S.S.Chi, 9/10	kwath as 'Maricha'	combination	-	Prameha (pathya dravya)	-
S.S.U.39/189	kwath as 'Maricha'	combination	-	Kaphaj jwara	-
S.S.U.40/149	churna as 'Maricha'	with masha+g hrit	-	Nisarak - pravahika	-
S.S.U.42/60	churna as 'Maricha'	combination	-	gulama-maiavarod h	Varti
S.S.U.42/71	churna as 'Maricha'	combination	-	gulma-kaphaj shool	Gud avart i
S.S.U.52/18	churna as 'Maricha'	combination	-	Kasa	-
S.S.U.52/21	churna as 'Maricha'	maricha+ madhu	-	Kasa	-
S.S.U.52/53	churna as 'Maricha'	maricha+ sidhu pan	-	Kasa	-
S.S.U.53/37	churna as 'Maricha'	Maricha+ gudodak	-	Kasa	-
A.H.S.6/159	churna as 'Maricha'	single	-	Maricha guna	-
A.H.S.6/163	churna as 'Maricha'	single	-	chavika & pippali mool gunas	-

				similar to maricha	
A.H.S.10/130	churna as'Maricha'	single	-	Katuvara	-
A.H.S.15/33	churna as'Maricha'	single	-	vatsakadi gana	-
A.H.Chi.3/29	churna as'Maricha'	combinati on	-	Pittaj kasa,leh	-
A.H.Chi.3/48	churna as'Maricha'	maricha+ madhu	-	Kaphaj kasa	-
A.H.Chi.3/97	churna as'Maricha'	combinati on	Ammtpr ash leh	Kaas	As Prak shep
A.H.Chi.3/115	churna as'Maricha'	combinati on	Kushman dak rasayan	Kasa	-
A.H.Chi.3/142	churna as'Maricha'	combinati on	-	Kaas	-
A.H.Chi.3/173	Avaleh as'Maricha'	single	kaas parama- aushadh a	Kasa	Mari cha in leh form
A.H.Chi.4/32	churna as'Maricha'	maricha+ yavasksha	-	Shwas, Hikka	-
A.H.Chi.6/20	churna as'Maricha'	maricha+ pippali	-	Kaphaj vanti	-
A.H.Chi.6/21	churna as'Maricha'	combinati on	-	Kaphaj vanti	-
A.H.Chi.8/76	Kalka as'Maricha'	combinati on	-	arsha	-
A.H.Chi.8/83	churna as'Maricha'	combinati on	Siddha Shaka/o dan	Arsha	-
A.H.Chi.8/157	churna as'Maricha'	combinati on	-	arsha	guda
A.H.Chi.8/158	churna as'Maricha'	combinati on	-	arsha	guda
A.H.U.20/21	kwath	combinati on	-	Nasa rog	Nasy a
A.H.U.22/49	churna	combinati on	-	Mukha rog	-
A.H.U.36/71	churna	combinati on	Tvantar vish	Pan/nasya	Nasy a
A.H.U.40/19	Avaleh	combinati on	-	Vajikaran	-
A.H.U.3/52	Churna as'ushana'	combinati on	-	Hikka, shwas	-
A.H.U.15/127	Churna as'ushana'	combinati on	Siddha takra	Pittodar	-
A.H.U.21/10	kwath	combinati on	-	Vatadushta ksha stanya	ya

DISCUSSION :

Above methodology studied provides references and conclusions that single drug **maricha(Piper nigrum)** has been used since ancient times in various preparations and medicinal purposed basically for Kapha and Kasa oriented vyadis .

Many one drug single preparattions highlighted has been used for one single diseases.

निजवीर्येण यद् द्रव्यं स्रोतोभ्यो दोषसंचयम् / निरस्यति प्रमाथि स्यत् तद्वा मरिचं वचा // (शा.पू. ४/२३)

A dravya by virtue of its potency , removes the accumulates doshas from srotas are called pramathi.

Two drugs combinations to be studied for network pharmacology provides result orientation using Anupan

concept in ayurveda which helps drug to reach to the site of diseases in easier and faster way.

Maricha itself has pramathi karma as its individual guna are also highlighted for the cause of target medications.

The above aspects to relate with modern network phamacology concept are enough to provide evidences for one drug one target methodology has been taught upon and researched upon with various other drugs and diseases prognosis with references have been existed in Ayurveda practise since ancieint times.

To make things more benefical combinations has been added which means adding more than one drug for single preparation but used in one single diseases.

Conclusion And Scope:

Network pharmacology deals with this following principal of one drug one disease concept or one drug one target strategy which is correlated and studied for ayurvedic drugs just like Maricha many references can be found and studied for future scope on network pharmacology for successful preparations and result oriented work for one drug one target concept the textual reference can be revised and restudied for further chemical combination of the drug can also be focused upon for the study.

As per Bhavprakash nighantu the details of maricha has been mentioned in following quotes.Which also explains the connection to network pharmacology concept, briefed above.

मरिचं वेल्लजं कृष्णमूर्णं धर्मपतनम् |
मरिचं कटुकं तीक्ष्णं दीपनं कफवातजित् |
उष्णं पित्तकरं रुक्षं श्वासशूलकुम्भीन्द्रेत् | ५५ |
तदाद्रं मधुरं पाके नात्युष्णं कटुकं गुरु |
किञ्चित्तीक्ष्णगुणं श्लेष्मप्रसेकि स्यादपित्तलम् | ५६ |

REFERENCES:

- Noor, F.; Ashfaq, U.A.; Javed, M.R.; Saleem, M.H.; Ahmad, A.; Aslam, M.F.; Aslam, S. Comprehensive computational analysis reveals human respiratory syncytial virus encoded microRNA and host specific target genes associated with antiviral immune responses and protein binding. J. King Saud Univ. Sci. 2021, 33, 101562. [CrossRef]
- Xin, W.; Zi-Yi, W.; Zheng, J.-H.; Shao, L. TCM network pharmacology: A new trend towards combining computational, experimental and clinical approaches. Chin. J. Nat. Med. 2021, 19, 1–11.
- Gertsch, J. Botanical drugs, synergy, and network pharmacology: Forth and back to intelligent mixtures. Planta Med. 2011, 77, 1086–1098. [CrossRef] [PubMed]
- Zuo, H.-L.; Lin, Y.-C.-D.; Huang, H.-Y.; Wang, X.; Tang, Y.; Hu, Y.-j.; Kong, X.-j.; Chen, Q.-j.; Zhang, Y.-z.; Hong, H.-C. The challenges and opportunities of traditional Chinese medicines against COVID-19: A way out from a network perspective. Acta Pharmacol. Sin. 2021, 42, 845–847. [CrossRef]
- Noor, F.; Saleem, M.H.; Aslam, M.F.; Ahmad, A.; Aslam, S. Construction of miRNA-mRNA network for the identification of key biological markers and their associated pathways in IgA nephropathy by employing the integrated bioinformatics analysis. Saudi J. Biol. Sci. 2021, 28, 4938–4945. [CrossRef]
- Pal, S.K.; Shukla, Y. Herbal medicine: Current status and the future. Asian Pac J. Cancer Prev. 2003, 4, 281–288.
- Rehman, A.; Ashfaq, U.A.; Shahid, F.; Noor, F.; Aslam, S. The Screening of phytochemicals against NS5 Polymerase to treat Zika Virus infection: Integrated computational based approach. Comb. Chem. High Through. Screen. 2021, 25, 738–751. [CrossRef]
- Tan, N.; Gwee, K.A.; Tack, J.; Zhang, M.; Li, Y.; Chen, M.; Xiao, Y. Herbal medicine in the treatment of functional gastrointestinal disorders: A systematic review with meta-analysis. J. Gastroenterol Hepatol. 2020, 35, 544–556. [CrossRef]
- Shao, L.; Zhang, B. Traditional Chinese medicine network pharmacology: Theory, methodology and application. Chin. J. Nat. Med. 2013, 11, 110–120.
- Casas, A.I.; Hassan, A.A.; Larsen, S.J.; Gomez-Rangel, V.; Elbatreek, M.; Kleikers, P.W.; Guney, E.; Egea, J.; López, M.G.; Baumbach, J.J. From single drug targets to synergistic network pharmacology in ischemic stroke. Proc. Natl. Acad. Sci. USA 2019, 116, 7129–7136. [CrossRef]
- Zhang, R.; Zhu, X.; Bai, H.; Ning, K. Network pharmacology databases for traditional Chinese medicine: Review and assessment. Front. Pharmacol. 2019, 10, 123. [CrossRef] [PubMed]
- Zhang, G.-B.; Li, Q.-Y.; Chen, Q.-I.; Su, S.-B. Network pharmacology: A new approach for Chinese herbal medicine research. Evid.-Based Complement. Altern. Med. 2013, 2013, 621423. [CrossRef]
- Hopkins, A.L. Network pharmacology: The next paradigm in drug discovery. Nature chemical biology 2008, 4, 682–690. [CrossRef] [PubMed]
- Dong, Y.; Hao, L.; Fang, K.; Han, X.-x.; Yu, H.; Zhang, J.-j.; Cai, L.-j.; Pan, T.; Zhang,

- W.-d.; Pang, K. A network pharmacology perspective for deciphering potential mechanisms of action of *Solanum nigrum* L. in bladder cancer. *BMC Complement. Med. Ther.* 2021, 21, 1–14. [CrossRef] [PubMed]
15. Li, W.; Yuan, G.; Pan, Y.; Wang, C.; Chen, H. Network pharmacology studies on the bioactive compounds and action mechanisms of natural products for the treatment of diabetes mellitus: A review. *Front. Pharmacol.* 2017, 8, 74. [CrossRef]
16. Li, J.-X.; Li, R.-Z.; Sun, A.; Zhou, H.; Neher, E.; Yang, J.-S.; Huang, J.-M.; Zhang, Y.-Z.; Jiang, Z.-B.; Liang, T.-L. Metabolomics and integrated network pharmacology analysis reveal Tricin as the active anti-cancer component of Weijing decoction by suppression of PRKCA and sphingolipid signaling. *Pharmacol. Res.* 2021, 171, 105574. [CrossRef]
17. Qu, F.; Xu, Q.; Pelkonen, O. Chapter Network Pharmacology and Traditional Chinese Medicine. In *Alternative Medicine*; Sakagami, H., Ed.; IntechOpen: London, UK, 2012; Chapter 12. [CrossRef]
18. Chandran, U.; Mehendale, N.; Patil, S.; Chaguturu, R.; Patwardhan, B. Network pharmacology. *Innov. Approaches Drug Dis.* 2017, 127–164.
19. Pan, S.Y.; Pan, S.; Yu, Z.-L.; Ma, D.-L.; Chen, S.-B.; Fong, W.-F.; Han, Y.-F.; Ko, K.-M. New perspectives on innovative drug discovery: An overview. *J. Pharm. Pharm. Sci.* 2010, 13, 450–471. [CrossRef]
20. Malas, T.B.; Kudrin, R.; Starikov, S.; 't Hoen, P.A.; Peters, D.J.; Roos, M.; Hettne, K.M. Drug repurposing using a semantic knowledge graph. *Data Driven Knowl. Discov. Polycyst. Kidney* 2021, 75.