IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

Network Pharmacology: A Detailed and Systematic Review

Ansari Vikhar Danish Ahmad[1], Dr Subur W Khan[2], Saher Chaus[3], Quadri Mohammed Soheb Abdul Khalique[4]
Department of Pharmacology, YB Chavan College of Pharmacy, Dr Rafiq Zakaria Campus Aurangabad[1,2]
Department of Quality Assurance, YB Chavan College of Pharmacy, Dr Rafiq Zakaria Campus Aurangabad[3]
Department of Pharmaceutics Mangaldeep Institute of Pharmacy Nipani, Aurangabad[4]

Abstract: *The advancement of network pharmacological medicine has spread out new avenues for understanding the complicated bioactive elements found in numerous medicative plants. The dominant paradigm in drug discovery is that the conception of planning maximally selective ligands to act on individual drug targets. However, several effective medication act via modulation of multiple proteins instead of single targets. Systems and network medication and their therapeutic arm, network pharmacological medicine, revolutionize however we tend to outline, diagnose, treat, and, ideally, cure diseases. However, the rational style of polypharmacology faces right smart challenges within the would like for brand spanking new strategies to validate target combos and optimize multiple structure-activity relationships whereas maintaining drug-like properties. Advances in these areas are making the muse of future paradigm in drug discovery: network pharmacological medicine.*

I. Introduction

Drug discovery, the process by which new candidate medications are discovered, initially began with random searching of therapeutic agents from plants, animals, and naturally occurring minerals [1]. For this, they depended on the materia medica that was established by medicine men and priests from that era. This was followed by the origin of classical pharmacology in which the desirable therapeutic effects of small molecules were tested on intact cells or whole organisms. Later, the advent of human genome sequencing revolutionized the drug discovery process that developed into targetbased drug discovery, also known as reverse pharmacology. This relies on the hypothesis that the modulation of the activity of a specific protein will have therapeutic effects. The protein that the drug binds to or interacts with is also referred to as a "target." In this reductionist approach, small molecules from a chemical library are screened for their effect on the target's known or predicted function [2]

Network pharmacology aims to understand diseases at the systematic level, and to know the interaction between the drug and the body on the basis of equilibrium theory of biological networks. It is substantially bringing the significant changes of theory and methodology in drug design. [3-5]

II. Network Ethnopharmacology

During the progression period of network biology, natural products were gaining importance in the chemical space of drug discovery, as these have been economically designed and synthesized by nature for the benefit of evolution [6] . Researchers began analyzing the logic behind traditional medicine systems and devised computational ways to ease the analysis. A comprehensive herbal medicine information system that was developed integrates information of more than 200 anticancer herbal recipes that have been used for the treatment of different types of cancer in the clinic, 900 individual ingredients, and 8500 small organic molecules isolated from herbal medicines.[7]

This system, which was developed using an Oracle database and Internet technology, facilitates and promotes scientific research in herbal medicine. This was followed by the development of many databases that serve as a source of botanical information and a powerful tool that provides a bridge between traditional medicines and modern molecular biology. These kinds of databases and tools made the researchers conceive the idea of NP of botanicals and their formulations to understand the underlying mechanisms of traditional medicines. We refer to such networks as "ethnopharmacological networks" and the technique as "Network Ethnopharmacology (NEP)". [8]

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

Another database, TCMGeneDIT, provides information about TCMs, genes, diseases, TCM effects, and TCM ingredients mined from a vast amount of biomedical literature. This would facilitate clinical research and elucidate the possible therapeutic mechanisms of TCMs and gene regulations [9]. To study the combination rule of TCM formulae, an herb network was created using 3865 collaterals-related formulae [10]. They developed a distance-based, mutual-information model (DMIM) to uncover the combination rule. DMIM uses mutual-information entropy and "between herb distance" to measure the tendency of two herbs to form an herb pair. They experimentally evaluated the combination of a few herbs for angiogenesis. Understanding the combination rule of herbs in formulae will help the modernization of traditional medicine and also help to develop a new formula based on the current requirement. A network target-based paradigm was proposed for the first time to understand the synergistic combinations [11], and an algorithm termed "NIMS" (network target-based identification of a multicomponent synergy) was also developed. This was a step that facilitated the development of multicomponent therapeutics using traditional wisdom. An innovative way to study the molecular mechanism of TCM was proposed during this time by integrating the TCM experimental data with microarray gene expression data [12].

As a demonstrative example, Si-Wu-Tang's formula was studied. Rather than uncovering the molecular mechanism of action, this method would help to identify new health benefits of TCMs. The initial years of the second decade of the 21st century witnessed the network ethnopharmacological exploration of TCM formulations. The scope of this new area attracted scientists, and they hoped NEP could provide insight into multi-compound drug discoveries that could help overcome the current impasse in drug discovery.[12]

NEP was used to study the anti-inflammatory mechanism of Qingfei Xiaoyan, a TCM (Cheng et al., 2013). [13] The predicted results were used to design experiments and analyze the data. Experimental confirmation of the predicted results provides an effective strategy for the study of traditional medicines. The potential of TCM formulations as multiple compound drug candidates has been studied using TCM formulations-based NP. TCM formulations studied in this way are listed in Table 5.1. Construction of a database containing 19,7201 natural product structures, followed by their docking to 332 target proteins of FDA-approved drugs, shows the amount of space shared in the chemical space between natural products and FDA drugs. Molecular-docking technique plays a major role in NP. The interaction of bio actives with molecular targets can be analyzed by this technique. Molecular docking-based NEP can be a useful tool to computationally elucidate the combinatorial effects of traditional medicine to intervene disease networks. An approach that combines NP and pharmacokinetics has been proposed to study the material basis of TCM formulations [14]. This can be extrapolated to study other traditional medicine formulations as well.

Table 5.1: TCM Formulations That Were Explored Using Network Pharmacology

Formulation Name	Observations About Bioactive Compounds	References
QiShenYiQi	Shows antiapoptosis, antiinflammation, antioxidant, anticoagulation, energy utilization facilitation and angiogenesis promotion against myocardial infarction	15
	Shows antiapoptosis, antiinflammation, antioxidant, anticoagulation, energy utilization facilitation and angiogenesis promotion against myocardial infarction	16
Fufang xueshuantong	Ameliorate the activation of coagulation system in thrombosis	17
Gansui banxia tang	Modulates Hsp90α, ATP1A1, and STAT3 and combats hepatocellular carcinoma, intestinal tuberculosis, and gastrointestinal inflammation	18
Bushenhuoxue	formula Useful in chronic kidney disease, as it regulates the coagulation and fibrinolytic balance, expression of inflammatory factors, and inhibits abnormal ECM accumulation	19
Ge-genqin-lian	decoction Useful in Type 2 diabetes, as it increases the insulin secretion in RIN-5F cells and improves insulin resistance	15
Liu-Wei-Di-Huang	pill Deals with Yin deficiency of chen through PPAR signaling, progesteronemediated oocyte maturation, adipocytokine signaling, and aldosterone-regulated sodium reabsorption	20

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

Si-Wu-Tang	Useful in primary dysmenorrhea of gynecology blood stasis syndrome, as it regulates lipid metabolism (Shaofu Zhuyu decoction), amino acid metabolism (Xiangfu SWT), carbohydrate metabolism (THSWT), ErbB, and VEGF signal transduction pathway (Qinlian SWT)	21
	Useful in climacteric syndrome, blood deficiency, as it regulates TGFβ signaling, pathway, oxidative stressinduced gene expression via Nrf2, and upregulates VEGFα expression	22
	Useful in women's diseases through regulation of Nrf2-mediated oxidative stress response pathways, upregulation of Nrf2-regulated genes, increases an antioxidant-response element activity, phytoestrogenic effect	23
Taohong Siwu decoction)	Useful in osteoarthritis, as it inhibits MMP expression, reduces local ILs, ADAMTS-4, TNFα, iNOS, COX, VDR, PPARγ, CDK2, HO-1 pathways	24
Qingfei-Xiaoyan Wan	Useful in inflammation of respiratory system, asthma through reduction in the infiltration of cytokines through ERK1, and five inflammatory pathways	25
Buchang Naoxintong	Deals with coronary heart disease and stroke by targeting APOB, APOE, APOA1, LPL, LDLR	26
Bushen Zhuanggu	formula Used against metastatic breast cancer, as it regulates OPG/RANKL/ RANK system, TGFβ, COX-2, EGFR pathway	27
Qing-Luo-Yin	Used against rheumatoid arthritis, as it regulates angiogenesis, inflammatory responses, and immune response pathways	28
	Used against rheumatoid arthritis with cold patterns, as it regulates nitrogen metabolism, PXR/RXR activation, linoleic acid metabolism, and metabolism of xenobiotics by CYP	29
Zhike Chuanbei Pipa	Dropping Pill Useful in airway inflammation and asthma, as it regulates the Toll-like receptor, TGFβ, MAPK, HSP 90-α pathways, and inhibits NF-κB	30
Fufang Danshen	formula Useful in cardiovascular diseases, as it regulates PPARγ, ACE, KCNJ11, KCNQ1, ABCC8 pathways	31
Realgar-Indigo	naturalis formula Used against acute promyelocytic leukemia, as it regulates ubiquitination/degradation of promyelocytic leukemiaretinoic acid receptor α oncoprotein, stronger reprogramming of myeloid differentiation regulators, and enhanced G1/G0 arrest in APL cells	32
Panax notoginseng	Useful in cardiovascular disease, as it targets various receptors and transcriptional factors that influence various types of cells in their proliferation, differentiation, migration and secretion, and prevents or inhibits early events of CVDs	33
Xuesaitong injection	Used against myocardial infarction, as it modulates ErbB, MAPK, VEGF, and Wnt pathways	34
Buyang Huanwu	decoction Qi deficiency and blood-stasis diseases targeted through COX-2 and PPAR-gamma; potentially useful in cancer treatment	35
Buyang Huanwu	decoction Qi deficiency and blood-stasis diseases targeted through COX-2 and PPAR-gamma; potentially useful in cancer treatment	35

III. Traditional Medicine Inspired Ethnopharmacological Networks

Dragon's blood (DB) tablets, which are made of resins from Dracaena spp., Daemonorops spp., Croton spp., and Pterocarpus spp., is an effective TCM for the treatment of colitis. In a study, an NP-based approach was adopted to provide new insights relating to the active constituents and molecular mechanisms underlying the effects of DB (Xu et al., 2014a). The constituent chemicals of the formulation were identified using an ultra-performance liquid chromatography-electrospray ionization-tandem mass spectrometry method. The known targets of those identified 48 compounds were mined from literature and putative targets that were predicted with the help of computational tools. The compounds were further screened for bioavailability followed by the systematic analysis of the known and putative targets for colitis. The network evaluation revealed the mechanism of action of DB bio actives for colitis through the modulation of the proteins of the NOD-like receptor signalling pathway [figure 1]

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

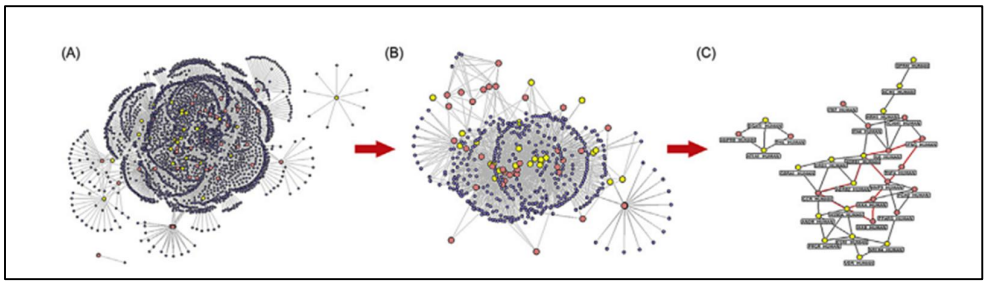

Figure 1: Putative DB targets-known colitis therapeutic targets protein interaction (PPI) network

a) The network between all targets and other human proteins.
b) The network of hub proteins in network (A).
c) The network of the major putative DB targets and the major known colitis therapeutic targets in network (B). Yellow spherical nodes indicate the putative targets; pink spherical nodes indicate the known therapeutic targets; purple spherical nodes indicate other human proteins that interact with putative targets or known therapeutic targets. Red edges in (C) indicate the PPIs of targets involved in the NODlike receptor signaling pathway. [36]

NP was used to explain the addition and subtraction theory of TCM. Two decoctions: Xiao Chaihu and Da Chaihu were studied using NP approach to investigate this theory. According to the addition and subtraction theory, the addition or removal of one or more ingredients from a traditional formulation resulted in a modified formula that plays a vital role in individualized medicine. Compounds from additive herbs were observed to be more efficient on disease associated targets (Figure 2).

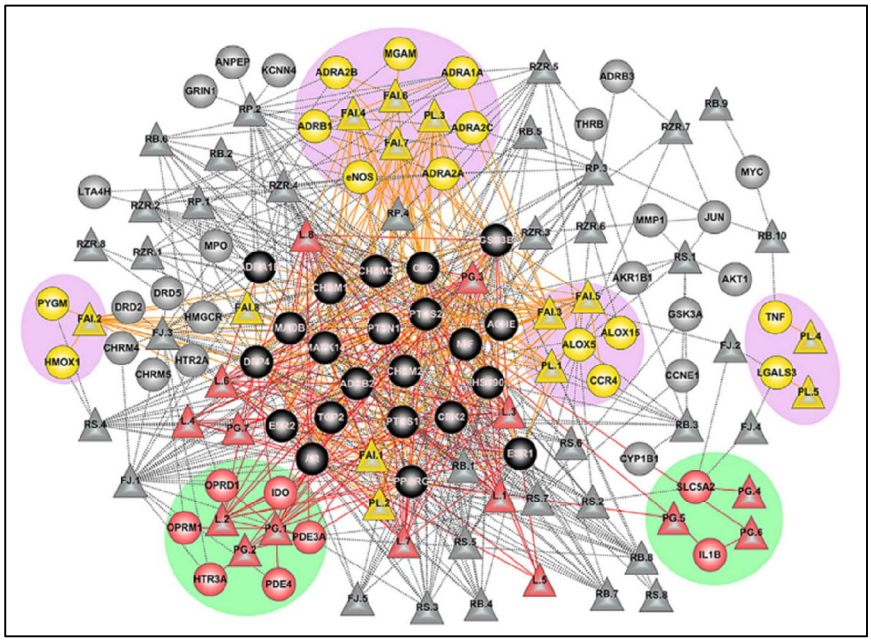

Figure 2: Drug-target network depicting the addition and subtraction theory of TCM.
Drug target interactions are shown as connecting lines between drugs (compounds, triangles) and targets (circles). The black nodes (circles) represent targets that are targeted by all the herbs of the formulation. Drugs belonging to individual herbs are highlighted in purple and green backgrounds. [37]

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

NP is a valuable method to study the synergistic effects of bioactives of traditional medicine formulation. This was experimentally shown on the Sendeng-4 formulation for rheumatoid arthritis. Data and network analysis have shown that the formulation acts synergistically through nine categories of targets [38]. Another network that studied three botanicals, Salviae miltiorrhizae, Ligusticum chuanxiong, and Panax notoginseng for coronary artery disease (CAD), displayed their mode of action through 67 targets, out of which 13 are common among the botanicals (Fig. 5.4). These common targets are associated with thrombosis, dyslipidemia, vasoconstriction, and inflammation [39]. This gives insight to how these botanicals are managing CAD.

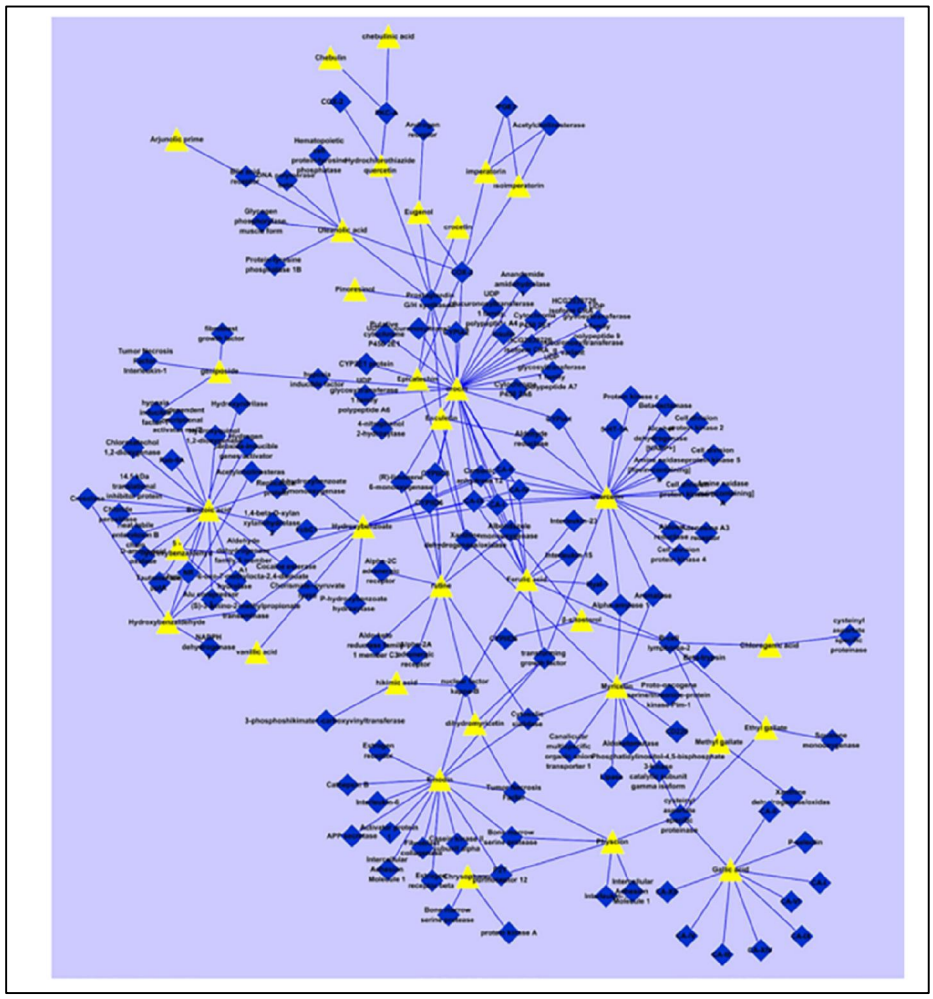

Figure 3: The chemical composition-target interaction network of Sendeng-4.
The yellow nodes represent chemical components and the blue nodes represent targets. The edges represent interactions. [40]

IV. KNOWLEDGE BASES FOR NETWORK ETHNOPHARMACOLOGY

In order to develop an ethno-pharmacological network, exploring the existing databases to gather information regarding bioactives and targets is the first step. Further information such as target-related diseases, tissue distribution and pathways are also to be collected depending on the type of study that is going to be undertaken. The Universal Natural Products Database (UNPD)

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

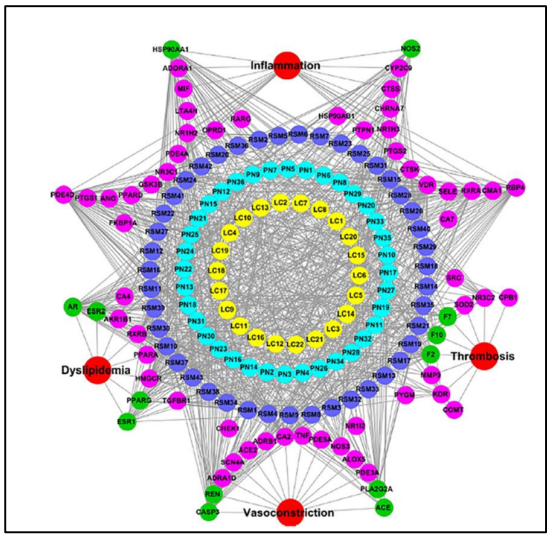

Figure 4: Network of three botanicals for coronary artery disease (CAD). [41]

(Gu et al., 2013a) [42] is one of the major databases that provides bioactives information. Other databases that provide information regarding bioactives include CVDHD [42], TCMSP [43] (Ru et al., 2014), TCM@Taiwan [44] (Sanderson, 2011), Supernatural (Banerjee et al., 2015) [45], and Dr. Dukes's phytochemical and ethnobotanical database (Duke and Backstrom-Sternberg, 1994).[46]

V. NETWORK CONSTRUCTION

A network is the schematic representation of the interaction among various entities called nodes. In pharmacological networks, the nodes include bioactives, targets, tissue, tissue types, disease, disease types, and pathways. These nodes are connected by lines termed edges, which represent the relationship between them (Morris et al., 2012). Building a network involves two opposite approaches: a bottom-up approach on the basis of established biological knowledge and a top-down approach starting with the statistical analysis of available data.

At a more detailed level, there are several ways to build and illustrate a biological network. Perhaps the most versatile and general way is the de novo assembly of a network from direct experimental or computational interactions, e.g., chemical/gene/protein screens. Networks encompassing biologically relevant nodes (genes, proteins, metabolites), their connections (biochemical and regulatory), and modules (pathways and functional units) give an authentic idea of the real biological phenomena (Xu and Qu, 2011).

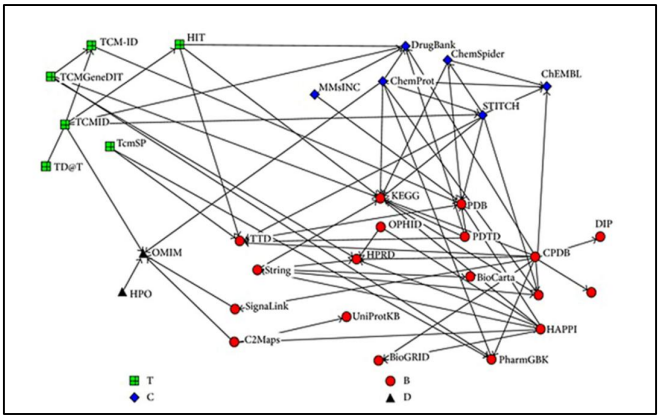

Figure 5: Database relationship network. [47]

The Connectivity Map, or the CMap tool, allows the user to compare gene-expression profiles. The similarities or differences in the signature transcriptional expression profile and the small molecule transcriptional response profile may

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

lead to the discovery of the mode of action of the small molecule. The response profile is also compared to response profiles of drugs in the CMap database with respect to the similarity of transcriptional responses. A network is constructed and the drugs that appear closest to the small molecule are selected to have better insight into the mode of action. Other software, such as Gephi, an exploration platform for networks and complex systems, and Cell Illustrator, a Java-based tool specialized in biological processes and systems, can also be used for building networks [48]

VI. Ayurveda and Network Ethnopharmacology

Ayurveda, the Indian traditional medicine, offers many sophisticated formulations that have been used for hundreds of years. The Traditional Knowledge Digital Library (TKDL, http://www.tkdl.res.in) contains more than 36,000 classical Ayurveda formulations. Approximately 100 of these are popularly used at the community level and also as over-the-counter products. Some of these drugs continue to be used as home remedies for preventive and primary health care in India. Until recently, no research was carried out to explore Ayurvedic wisdom using NP despite Ayurveda holding a rich knowledge of traditional medicine equal to or greater than TCM. Our group examined the use of NP to study Ayurvedic formulations with the well-known Ayurvedic formulation Triphala as a demonstrable example [48]

VII. Network Ethnopharmacology of Triphala

1) Triphala Bioactives

The botanicals of Triphala—EO, TB, and TC—contain 114, 25, and 63 bioactives, respectively, according to UNPD data collected during June 2015. Of these, a few bioactives are common among the three botanicals. Thus, Triphala formulation as a whole contains 177 bioactives. Out of these, 36 bioactives were Score-1, based on Binding DB search carried out during June 2015. EO, TB, and TC contain 20, 4, and 20 Score-1 bioactives, respectively (Fig. 5.6). The Score-1 bioactives that are common among three plants are chebulanin, ellagic acid, gallussaeure, 1,6-digalloyl-beta-D-glucopiranoside, methyl gallate, and tannic acid. This bioactive information is the basic step toward constructing human proteome and microbial proteome targeting networks

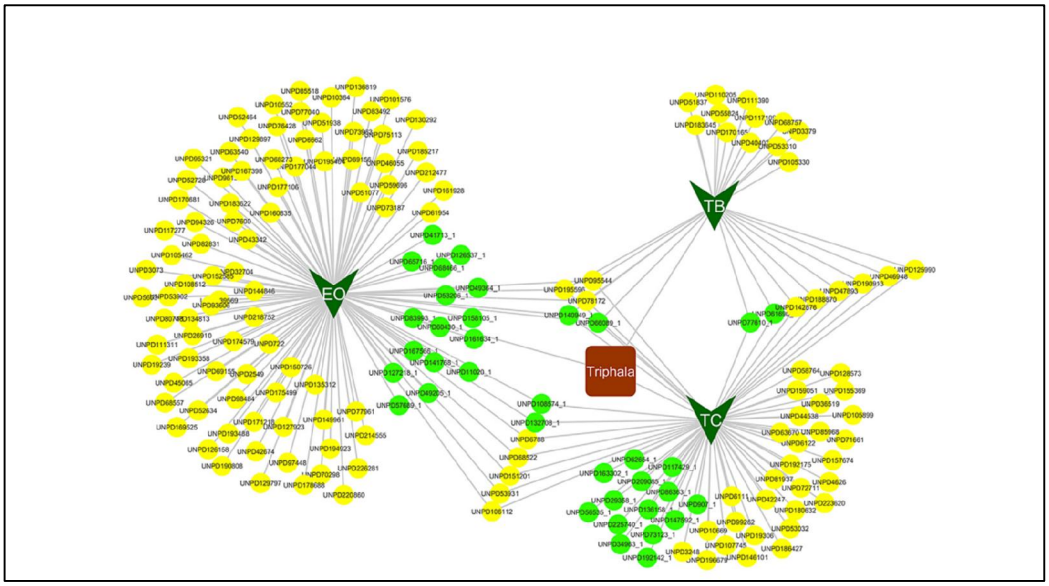

Figure 6: Bioactive network of Triphala.

Dark green versus are the botanicals of Triphala and oval nodes are the bioactives where green represents Score 1 bioactives.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

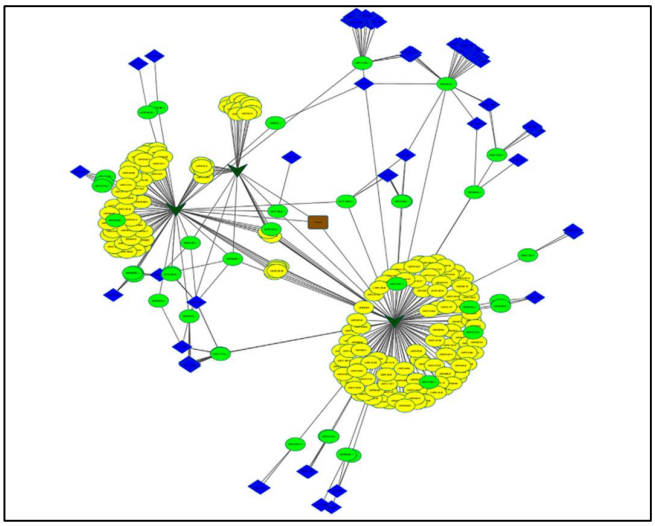

Figure 7: Bioactivetarget network of Triphala.
Dark green versus are the botanicals of Triphala and oval nodes are the bioactives where green represents score 1 bioactives. Blue diamond's denote targets

2) Human Proteome and Diseasome Targeting Network of Triphala

The proteome-targeting network of Triphala, thus, shows its ability to synergistically modulate 60 targets that are associated with 130 disease indications. This data is generated with the available information that included only one-fifth of the total number of bioactives. Further logical analysis and experimental studies based on the network result are needed to explore the in-depth mechanism of action of Triphala. For researchers in this area, these kinds of networks can give an immense amount of information that can be developed further to reveal the real mystery behind the actions of traditional medicine.

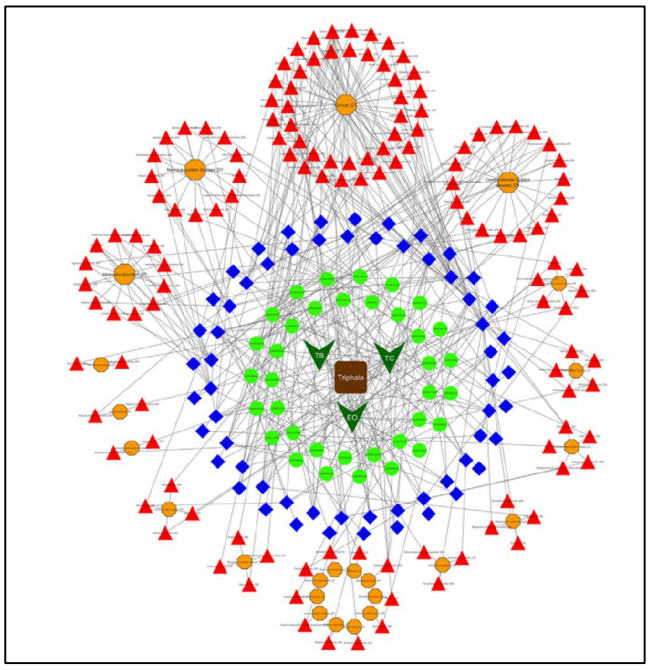

Figure 8: The human proteome and diseasome targeting network of Triphala.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

Dark green versus are the botanicals of Triphala and oval green nodes are the score1 bioactives. Targets are represented by blue diamond nodes, red triangle nodes depict diseases, and orange octagons indicate disease types

VIII. Applications of Network Pharmacology

1. Traditional medicine
   - Scientific evidence for use of Ayurvedic medicine
   - Understanding the rationale of traditional formulations
   - Understanding the mechanism of action of Ayurvedic medicines
   - Safety and efficacy of Ayurvedic medicines
   - Possible substitutes for endangered botanicals
   - Network-based designing and prescribing of plant formulations
   - Analysis of multiple bioactives, studying synergistic action
   - Botanical biomarkers for quality control
2. Pharmacology
   - To develop new leads from natural products
   - Understanding the mechanism of action of drugs
   - Determining the possible side effects of drugs
   - Predicting new indications
   - Predicting toxicity
   - Predicting possible drug-drug interactions
   - Rational design of drugs based on group of interacting proteins
   - Drug repurposing
3. Drug research
   - Identifying novel drug targets
   - Reduced cost and time through in silico evaluation
   - Understanding the signaling pathway of disease types
   - Designing experiments based on drugs and targets
   - Therapeutics for multigene-dependent diseases
   - Discovery of disease-causing genes
   - Diagnostic biomarkers
   - Studying drug resistance or antibiotic resistance

IX. Conclusion

Network medicine presents a scope for exploring traditional knowledge to search out solutions for the present issues difficult the drug discovery business. NEP also can play a key role in new drug discovery, drug repurposing, and rational formulation discovery. Several of the bioactivetarget combos are through an experiment studied. The data synthesis exploitation NP provides data relating to the mode of action of traditional medication formulations supported their constituent bioactive.

References

[1] Bag, A., Bhattacharyya, S.K., Pal, N.K., 2013. Antibacterial potential of hydroalcoholic extracts of Triphala components against multidrug-resistant uropathogenic bacteria--a preliminary report. Ind. J. Exp. Biol. 51, 709-714.
[2] Hacker, M., Messer II, W.S., Bachmann, K.A., 2009. Pharmacology: Principles and Practice. Elsevier/Academic Press.
[3] Gertsch J. 2011. Botanical drugs, synergy, and network pharmacology: forth and back to intelligent mixtures. Planta Medica, 77(11): 1086-1098.
[4] Zhang WJ, Li X. 2016. A cluster method for finding node sets / sub-networks based on between- node similarity

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

in sets of adjacency nodes: with application in finding sub-networks in tumor pathways. Proceedings of the International Academy of Ecology and Environmental Sciences, 6(1): 13-23.

[5] Hao DC, Xiao PG. 2014. Network Pharmacology: A Rosetta Stone for Traditional Chinese Medicine. Drug Development Research, 75(5): 299-312.

[6] Wetzel, S., Bon, R.S., Kumar, K., Waldmann, H., 2011. Biology-oriented synthesis. Angew. Chemie-Int. Ed. 50, 1080010826.

[7] Fang, X., Shao, L., Zhang, H., Wang, S., 2005. CHMIS-C: a comprehensive herbal medicine information system for cancer. J. Med. Chem. 48, 14811488.

[8] Chandran, U., Mehendale, N., Tillu, G., Patwardhan, B., 2015a. Network pharmacology: an emerging technique for natural product drug discovery and scientific research on ayurveda. Proc. Ind. Natl. Acad. Sci. 81, 561568

[9] Fang, Y.-C., Huang, H.-C., Chen, H.-H., Juan, H.-F., 2008. TC;MGeneDIT: a database for associated traditional Chinese medicine, gene and disease information using text mining. BMC Compl. Altern. Med. 8, 58.

[10] Li, S., Zhang, B., Jiang, D., Wei, Y., Zhang, N., 2010. Herb network construction and comodule analysis for uncovering the combination rule of traditional Chinese herbal formulae. BMC Bioinformatics 11, BioMed Central Ltd.

[11] Li, S., Zhang, B., Zhang, N., 2011. Network target for screening synergistic drug combinations with application to traditional Chinese medicine. BMC Syst. Biol. 5, BioMed Central Ltd.

[12] Wen, Z., Wang, Z., Wang, S., Ravula, R., Yang, L., Xu, J., et al., 2011. Discovery of molecular mechanisms of traditional Chinese medicinal formula Si-Wu-Tang using gene expression microarray and connectivity map. PLoS One 6.

[13] Cheng, B.F., Hou, Y.Y., Jiang, M., Zhao, Z.Y., Dong, L.Y., Bai, G., 2013. Anti-inflammatory mechanism of qingfei xiaoyan wan studied with network pharmacology. Yao Xue Xue Bao 48, 686693

[14] Gu, S., Yin, N., Pei, J., Lai, L., 2013c. Understanding traditional Chinese medicine antiinflammatory herbal formulae by simulating their regulatory functions in the human arachidonic acid metabolic network. Mol. Biosyst. 9, 19311938.

[15] Li, X., Wu, L., Liu, W., Jin, Y., Chen, Q., Wang, L., et al., 2014c. A network pharmacology study of Chinese medicine QiShenYiQi to reveal its underlying multi-compound, multitarget, multi-pathway mode of action. PLoS One 9, 111. Li, Y., Li, R., Ouyang, Z., Li, S., 2015.

[16] Wu, L., Wang, Y., Li, Z., Zhang, B., Cheng, Y., Fan, X., 2014. Identifying roles of "Jun-ChenZuo-Shi" component herbs of QiShenYiQi formula in treating acute myocardial ischemia by network pharmacology. Chin. Med. 9, 24.

[17] Sheng, S., Wang, J., Wang, L., Liu, H., Li, P., Liu, M., et al., 2014. Network pharmacology analyses of the antithrombotic pharmacological mechanism of Fufang Xueshuantong Capsule with experimental support using disseminated intravascular coagulation rats. J. Ethnopharmacol. 154, 735744.

[18] Sheng, S., Wang, J., Wang, L., Liu, H., Li, P., Liu, M., et al., 2014. Network pharmacology analyses of the antithrombotic pharmacological mechanism of Fufang Xueshuantong Capsule with experimental support using disseminated intravascular coagulation rats. J. Ethnopharmacol. 154, 735744.

[19] Shi, S.H., Cai, Y.P., Cai, X.J., Zheng, X.Y., Cao, D.S., Ye, F.Q., et al., 2014. A network pharmacology approach to understanding the mechanisms of action of traditional medicine: bushenhuoxue formula for treatment of chronic kidney disease. PLoS One 9.

[20] Liang, X., Li, H., Li, S., 2014. A novel network pharmacology approach to analyse traditional herbal formulae: the Liu-Wei-Di-Huang pill as a case study. Mol. Biosyst. 10, 10141022

[21] Liu, P., Duan, J.-A., Bai, G., Su, S.-L., 2014. Network pharmacology study on major active compounds of siwu decoction analogous formulae for treating primary dysmenorrhea of gynecology blood stasis syndrome. Zhongguo Zhong Yao Za Zhi 39, 113120.

[22] Luo, F., Gu, J., Zhang, X., Chen, L., Cao, L., Li, N., et al., 2015. Multiscale modeling of druginduced effects of ReDuNing injection on human disease: from drug molecules to clinical symptoms of disease. Sci. Rep. 5, 10064.

[23] Ma, Y., Stern, R.J., Scherman, M.S., Vissa, V.D., Yan, W., Jones, V.C., et al., 2001. Drug targeting mycobacterium tuberculosis cell wall synthesis: genetics of dTDP-rhamnose synthetic enzymes and development of a microtiter plate-based screen for inhibitors of conversion of dTDP-glucose to dTDP-rhamnose. Antimicrob.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

Agents Chemother. 45, 14071416.

[24] Ma, T., Tan, C., Zhang, H., Wang, M., Ding, W., Li, S., 2010. Bridging the gap between traditional Chinese medicine and systems biology: the connection of cold syndrome and NEI network. Mol. Biosyst. 6, 613619.

[25] Morris, J.S., Ph, D., Kuchinsky, A., Pico, A., Institutes, G., 2012. Analysis and Visualization of Biological Networks with Cytoscape. UCSF, p. 65. Nicola, G., Smith, C.A., Lucumi, E., Kuo, M.R., Karagyozov, L., Fidock, D.A., et al., 2007. Discovery of novel inhibitors targeting enoyl-acyl carrier protein reductase in plasmodium falciparum by structure-based virtual screening. Biochem. Biophys. Res. Commun. 358, 686691.

[26] Ogata, H., Goto, S., Sato, K., Fujibuchi, W., Bono, H., Kanehisa, M., 1999. KEGG: kyoto encyclopedia of genes and genomes. Nucl. Acids Res. 27, 2934. Paolini, G.V., Shapland, R.H.B., van Hoorn, W.P., Mason, J.S., Hopkins, A.L., 2006. Global mapping of pharmacological space. Nat. Biotechnol. 24, 805815. Patwardhan, B., 2014a. Rediscovering drug discovery. Comb. Chem. High Throughput Screen 17, 819.

[27] Patwardhan, B., 2014b. The new pharmacognosy. Comb. Chem. High Throughput Screen 17, 97. Patwardhan, B., Chandran, U., 2015. Network ethnopharmacology approaches for formulation discovery. Ind. J. Tradit. Knowl. 14, 574580. Patwardhan, B., Mutalik, G., Tillu, G., 2015. Integrative Approaches For Health: Biomedical Research, Ayurveda and Yoga. Academic Press, Elsevier Inc. Pei, L., Bao, Y., Liu, S., Zheng, J., Chen, X., 2013. Material basis of Chinese herbal formulas explored by combining pharmacokinetics with network pharmacology. PLoS One 8, e57414.

[28] Peng, K., Xu, W., Zheng, J., Huang, K., Wang, H., Tong, J., et al., 2013. The disease and gene annotations (DGA): an annotation resource for human disease. Nucl. Acids Res. 41, 553560

[29] Wu, L., Wang, Y., Nie, J., Fan, X., Cheng, Y., 2013. A network pharmacology approach to evaluating the efficacy of Chinese medicine using genome-wide transcriptional expression data. Evid. Based Complement. Alternat. Med. 2013, 915343.

[30] Wu, L., Wang, Y., Li, Z., Zhang, B., Cheng, Y., Fan, X., 2014. Identifying roles of "Jun-ChenZuo-Shi" component herbs of QiShenYiQi formula in treating acute myocardial ischemia by network pharmacology. Chin. Med. 9, 24.

[31] Wu, X., Jiang, R., Zhang, M.Q., Li, S., 2008. Network-based global inference of human disease genes. Mol. Syst. Biol. 4, 189.

[32] Xiang, Z., Sun, H., Cai, X., Chen, D., Zheng, X., 2015. The study on the material basis and the mechanism for anti-renal interstitial fibrosis efficacy of rhubarb through integration of metabonomics and network pharmacology. Mol. Biosyst. 11, 10671078.

[33] Xu, H., Zhang, Y., Lei, Y., Gao, X., Zhai, H., Lin, N., et al., 2014a. A systems biology-based approach to uncovering the molecular mechanisms underlying the effects of dragon's blood tablet in colitis, involving the integration of chemical analysis, ADME prediction, and network pharmacology. PLoS One 9, e101432.

[34] Xu, H.-Y., Wang, S.-S., Yang, H.-J., Bian, B.-L., Tian, S.-S., Wang, D.-L., et al., 2014b. Study on action mechanism of adjuvant therapeutic effect compound Ejiao slurry in treating cancers based on network pharmacology. Zhongguo Zhong Yao Za Zhi 39, 31483151.

[35] Xu, Q., Qu, F., Pelkonen, O., 2011. Network Pharmacology and Traditional Chinese Medicine. In: Hiroshi, Sakagami (Ed.), Alternative medicine. InTech, pp. 277297. Yang, H., Xing, L., Zhou, M.-G., et al., 2012. Network pharmacological research of volatile oil from Zhike Chuanbei Pipa Dropping Pills in treatment of airway inflammation. Chinese Traditional and Herbal Drugs 43, 11291135.

[36] Xu H, Zhang Y, Lei Y, Gao X, Zhai H, Lin N, et al. A systems biology-based approach to uncovering the molecular mechanisms underlying the effects of dragon's blood tablet in colitis, involving the integration of chemical analysis, ADME prediction, and network pharmacology. PLoS One. 2014;9:e101432.

[37] Li B, Tao W, Zheng C, Shar PA, Huang C, Fu Y, et al. Systems pharmacology-based approach for dissecting the addition and subtraction theory of traditional Chinese medicine: An example using Xiao-Chaihu-Decoction and Da-Chaihu Decoction. Comput. Biol. Med. Elsevier; 2014;53C:1929.

[38] Zi, T., Yu, D., 2015. A network pharmacology study of Sendeng-4, a Mongolian medicine. Chin. J. Nat. Med. 13, 108118.

[39] Zhou, W., Wang, Y., 2014. A network-based analysis of the types of coronary artery disease from traditional Chinese medicine perspective: potential for therapeutics and drug discovery. J. Ethnopharmacol. 151, 66-77.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 8, May 2022
Impact Factor: 6.252

[40] From Zi, T., Yu, D., 2015. A network pharmacology study of Sendeng-4, a Mongolian medicine. Chin. J. Nat. Med. 13, 108118.
[41] Zhou, W., Wang, Y., 2014. A network-based analysis of the types of coronary artery disease from traditional Chinese medicine perspective: potential for therapeutics and drug discovery. J. Ethnopharmacol. 151, 6677.
[42] Gu, S., Yin, N., Pei, J., Lai, L., 2013c. Understanding traditional Chinese medicine antiinflammatory herbal formulae by simulating their regulatory functions in the human arachidonic acid metabolic network. Mol. Biosyst. 9, 19311938.
[43] Ru, J., Li, P., Wang, J., Zhou, W., Li, B., Huang, C., et al., 2014. TCMSP: a database of systems pharmacology for drug discovery from herbal medicines. J. Cheminform 6, 13.
[44] Sanderson, K., 2011. Databases aim to bridge the East-West divide of drug discovery. Nat. Med. 17, 1531, Nature Publishing Group, a division of Macmillan Publishers Limited. All Rights Reserved.
[45] Banerjee, P., Erehman, J., Gohlke, B.-O., Wilhelm, T., Preissner, R., Dunkel, M., 2015. Super natural II--a database of natural products. Nucl. Acids Res. 43, D935D939.