Pharmacogn. Res., 2025; 17(4):1274-1280.
https://www.phcogres.com

Original Article

Network Pharmacology Approach to Determine the Molecular Mechanism of *Chitraka* (*Plumbago zeylanica* L.) in the Treatment of Obesity

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ABSTRACT

Background: The state of excessive bodily fat buildup is known as obesity (Sthoulya). Anti-obesity drugs in the market might cause adverse effects, for safer and more effective anti-obesity medications from plant-based sources becomes a top focus. In Ayurveda, Chitraka moola (*Plumbago zeylanica* L.) is a commonly used herb, because of its therapeutic effect. Network pharmacology is an area of drug discovery and development research by creating an opportunity for the methodical study of conventional treatments. This study highlights key phytochemicals, targets and signalling pathways of Chitraka for the treatment of obesity. **Materials and Methods:** This study assessed through biological databases, GeneCard, HPA databases, PPI Network Construction, KEGG pathway enrichment analysis, target-Compound-Pathway' Network Construction and Molecular Docking Analysis. **Results:** Using the BindingDB and Uniprot databases, pinpointed 155 target genes with respect to these 28 active phytochemicals, Curated gene-disease data were extracted from the GeneCard and HPA databases based on the term obesity it was found that 26 out of the 28 drugs target exactly 137 disease targets linked to obesity, Using the String database, a PPI network was built. KEGG functional enrichment analysis to investigate the signalling pathways was carried out using SHINYGO database, Cytoscape was used to build the interaction relationship between 15 significantly enriched KEGG pathways, 137 intersecting targets and 26 core active ingredients, Molecular Docking visualises the binding pose with the highest docking score. **Conclusion:** This study emphasizes crucial mechanism, target and bioactive of *Chitraka* against obesity, indicating a strong pharmacological foundation for additional clinical research.

Keywords: Obesity, Chitraka moola, *Plambago zeylanica*, Network Pharmacology, Sthoulya, Lupeol, β-sitosterol.

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Received: 16-05-2025;
Revised: 09-07-2025;
Accepted: 22-09-2025.

INTRODUCTION

Obesity is a medical illness marked by the dysfunction of the body's weight regulation mechanisms, resulting in an excessive buildup of fat tissue and presenting considerable health hazards.[1] All ages can be affected by obesity; in 2016, about 13% of people worldwide were overweight.[2] As a major and growing public health concern, obesity poses an increasing risk of developing into a chronic illness in the future. The anti-obesity drugs that are now in the market include orlistat, rimonabant and sibutramine; these drugs might cause adverse effects, including dyspepsia, flatulence, diarrhoea, and fecal incontinence.[3] Weight-loss surgery is performed on individuals who are extremely obese when pharmacological approaches fail to manage their weight. Postoperative fatalities, wound infection, ulceration, intestinal blockage, vitamin deficiencies, and other problems are possible outcomes of weight loss surgery.[4] As a result, creating new, safer, and more effective anti-obesity medications from plant-based sources becomes a top focus.

In Ayurveda, *Chitraka moola* (*Plumbago zeylanica* L.) is a commonly used herb, particularly because of its *lekhaniya karma, ushna tikshna guna*, and *katu rasa*.[5] Additionally, it is a key component of *Trimad*, a polyherbal Ayurvedic preparation that is advised for the treatment of obesity.[6] According to research updates, *Chitraka* has a broad range of pharmacological properties, such as anti-inflammatory, antioxidant, anti-obesity, and antihyperlipidemic effects.[7] Research on *Chitraka* has so far concentrated on a wide variety of metabolic problems without pinpointing the precise mechanism of action for any one of those conditions. Thus, research on *Chitraka's* active ingredients and mechanisms of action against obesity ought to establish

DOI: 10.5530/pres.20252331

its pharmacological relevance in reducing obesity. Network pharmacology is an approach for incorporating bioinformatics with pharmacology. Data integration and computer analysis can comprehensively elucidate the association between medications and diseases and examine the mechanism of pharmacological action.[8] Using computational pharmacology and molecular docking techniques, this study aims to assess and estimate the key phytochemicals, targets and signalling pathways of *Chitraka* for the treatment of obesity. It also provides a scientific foundation for future drug development and clinical use.

MATERIALS AND METHODS

Collection of *Chitraka* phytochemicals and associated disease targets from biological databases

Using the terms "*Plumbago zeylanica*" and part use root, two databases - Dr Duke's Phytochemical and Ethnobotanical Databases[9] and IMPPAT 2.0 (Indian Medicinal Plants, Phytochemistry, and Therapeutics 2.0)[10] were searched for phytochemicals in *Chitraka*. The two main criteria for screening the phytochemicals that were obtained were oral bioavailability and drug likeness. Initially, information on the canonical smiles of each phytochemical using the PubChem database[11] was availed. Next, the prediction of several ADME variables using the SwissADME database[12] was performed. BindingDB,[13] a similarity-based online service, was used to determine the target of *Chitraka* phytochemicals with a similarity score of ≥0.85. After obtaining the disease targets linked to each phytochemical pertaining to Chitraka root, the UniProtKB database[14] was utilised to standardise the target names.

Collection of Obesity-Related Target Genes from GeneCard and the Human

Protein Atlas (HPA) databases

The Human Protein Atlas[15] and GeneCards[16] database portals were used to gather information regarding therapeutic targets linked to obesity. To find targets, the word "obesity" was employed. The Venny 2.1.0 tool[17] was chosen for filtering the overlapping disease targets from Chitraka and Obesity.

Protein-Protein Interaction (PPI) Network Construction

Using STRING version 11.0,[18] a PPI network was constructed in order to comprehend an association comprising interconnecting target genes for key phytochemicals in *Chitraka*. In order to validate reliability, the species we chose was "Homo sapiens," and medium confidence was set up at 0.50 FDR.

KEGG pathway enrichment analysis

Following the selection of Homo sapiens as the species, the potential targets of *Chitraka's* action on obesity were entered into the ShinyGO database,[19] and KEGG analysis was carried out. After that, the results were filtered based on FDR. A list of the top fifteen pathways was selected and outlined.

'Target-Compound-Pathway' Network Construction

Following the export and processing of data related to active phytochemicals, enriched pathways, and intersected targets, the Target-Compound-Pathway network of *Chitraka* was constructed using Cytoscape 3.7.2.[20] The network analyser was used to perform the topological assessment. To ascertain the function and connection between the active phytochemicals and the overlapped targets of obesity, the network was analysed in terms of degree strength.

Molecular Docking Analysis

The RSCB PDB[21] and Pubchem databases were used to obtain the crystal structures of the top five compounds and the three most prominent target proteins, respectively. To fix the protein structures, polar linkages were inserted and water molecules were removed using the Biovia DS program. PyRx software[22] was used to automatically identify binding sites, and the docking approach was used to predict the binding relationship of top target proteins and ligands. The program Biovia Discovery Studio has been used to illustrate the interaction with the best docking scores in both two and three dimensions.

RESULTS

Collection of *Chitraka* phytochemicals and associated disease targets from biological databases

158 phytochemicals were compiled in *Chitraka* as a result of a phytochemical search throughout the databases (IMMPAT and Dr Duke's Phytochemical and Ethnobotanical Databases). After screening the phytochemicals for toxicity and ADME using the SwissADME and PubChem databases, 28 phytochemicals were chosen based on their oral absorption, bioavailability and Lipinski violation. Using the BindingDB and Uniprot databases, we gathered and pinpointed 155 target genes in total with respect to these 28 active phytochemicals.

Collection of Obesity-Related Target Genes from Gene Card and The Human Protein Atlas (HPA) databases

Curated gene-disease data were extracted from the GeneCard and HPA databases based on the term "obesity." After thorough screening and removal of duplicate genes, 11468 genes associated with obesity were found. To further obtain the overlapping gene, the genes of obesity and the phytochemical-related genes in Chitraka (155) were intersected with the aid of the Venny 2.1.0 tool. The final result was 137 intersection genes. It was found that 26 out of the 28 drugs target exactly 137 disease targets linked to obesity.

Protein-Protein Interaction (PPI) Network Construction

Using the String database, a PPI network was built. After importing 137 common targets related to *Chitraka* and obesity into the String platform. The PPI network shown in Figure 1 was developed with a medium level of confidence set at 0.50.

KEGG pathway enrichment analysis.

KEGG functional enrichment analysis to investigate the signalling pathways was carried out using SHINYGO database. The involved possible KEGG pathways are displayed in Figure 2.

'Target- Compound-Pathway' Network Construction

Cytoscape 3.7.2 software was used to build the interaction relationship between 15 significantly enriched KEGG pathways, 137 intersecting targets, and 26 core active ingredients which is shown in Figure 3.

Molecular Docking analysis

Molecular docking was used to investigate putative binding mechanisms and the validity of the networks between the three hub targets and the six bioactive phytochemicals. Six key phytochemicals - Altechromone A, beta-Sitosterol, beta-Asarone, Vanillic Acid, Isozeylanone, and Lupeol - according to binding energies ≥ 5, most likely showed a strong interaction with the three major targets that were identified which is enlisted in Table 1. Figure 4 visualises the binding pose with the highest docking score.

DISCUSSION

Plumbago zeylanica, also known as *Chitraka*, is a pharmacologically significant plant that has *Ushna, Tikshna, Katu*, and *Srotoshodhaka* properties that disrupt pathogenesis and help manage *Santarpanottha Vikara* like *Sthoulya* by clearing *Ama, Kapha,* and *Meda.*[23,24]

Patients on a low-calorie diet regimen were given capsules containing 500 mg of *Plumbago zeylanica* L. and 1 g of haridra powder four times a day, respectively, as part of an earlier clinical investigation. When compared to haridra, the patient's weight may have decreased with the indicated intervention of *Plumbago zeylanica* L. and haridra powder.[25] Even though Chitraka is frequently used in clinical settings, little is known about how it functions molecularly to treat obesity. Therefore, network pharmacology and molecular docking experiments were conducted to gain a better understanding of the molecular processes of Chitraka in obesity. The network analysis indicates that isozeylanone, luteol, vanillic acid, beta-sitosterol, beta-asarone and altechromone a are among the active phytochemicals in Chitraka that may help reduce obesity.

Docking simulation, which showed binding energies below -5.0 kcal/mol, further supported this finding. Previous studies have shown the significance of these bioactives for the treatment of

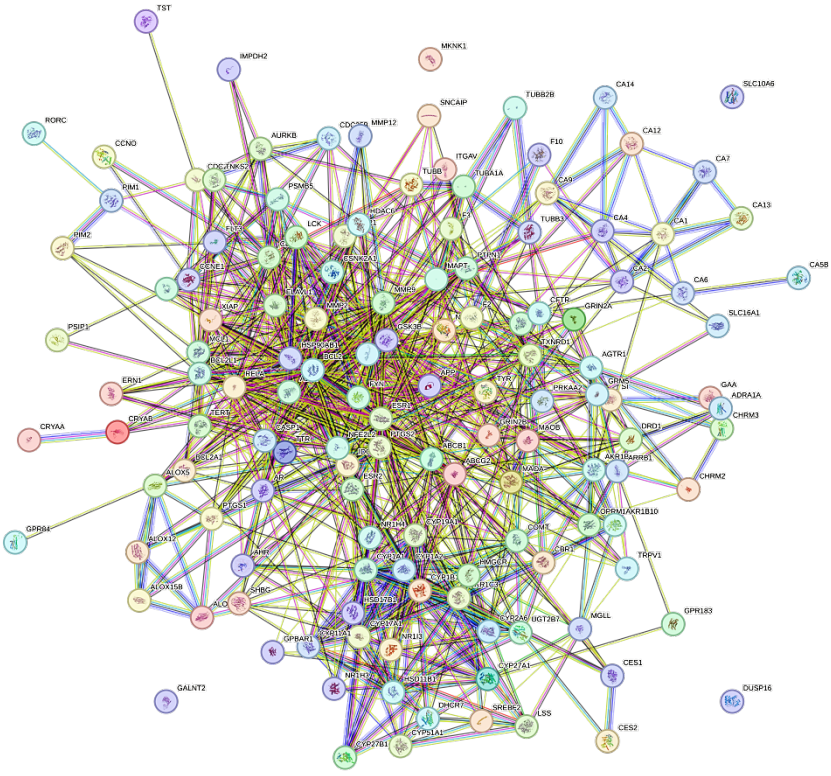

Figure 1: PPI network obtained from STRING database.

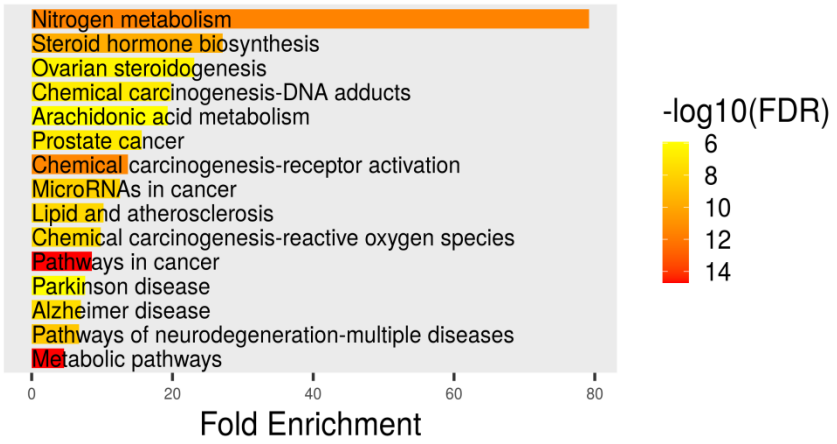

Figure 2: KEGG enrichment analysis.

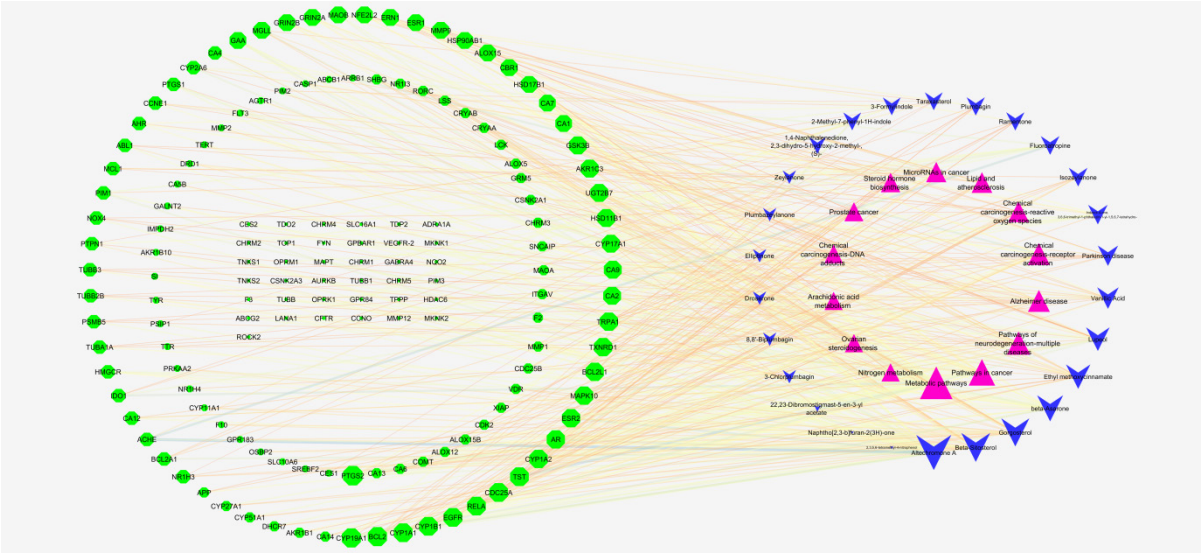

Figure 3: 'Target- Compound-Pathway' Network of *Chitraka* against obesity.

obesity. According to a prior study, ERK phosphorylation is inhibited by lupeol, interfering with inflammatory signaling and hypertrophy of adipocytes. When ERK activity is reduced, lipid droplet size and inflammatory cytokine production are reduced. Lupeol reduces adipocyte hypertrophy and associated inflammation, providing a promising approach to the prevention and treatment of obesity.[26] β-sitosterol may have antiobesogenic effects by encouraging fatty acid β-oxidation and lipolysis in adipose tissues, which are mediated by peroxisome Proliferator-Activated Receptor α (PPAR-α). β-sitosterol may help reduce inflammation associated with obesity and insulin resistance by blocking inflammatory pathways.[27] The phosphorylation of ERK1/2, which has been found to regulate the early stages of adipogenesis, was decreased by β-asarone treatment.

These results suggest that β-asarone possesses anti-adipogenic qualities, in part via suppressing the expression of adipogenic transcription factors.[28] Therefore, these phytochemicals might be the main substances that Chitraka uses to prevent obesity. Research indicates that an increase in body fat mass is linked to alterations in adipose tissue BCL2 expression, including a decrease in BCL2 levels. This implies that BCL2 might have a role in the processes of cell death that take place alongside obesity and the emergence of insulin resistance.[29] The CYP19A1 gene, which produces the aromatase enzyme, is essential for the manufacture of oestrogen and can affect the distribution and control of body fat, which may affect the risk of obesity, particularly in women.[30] According to a different study, there is a substantial relationship between CYP19A1 gene polymorphisms and plasma barium and both are linked to central obesity.[31]

TST, a crucial enzyme with a possible function in metabolic regulation, especially in adipocytes, has been connected with elevated adiposity and insulin resistance in the context of obesity along with metabolic health.[32] Research indicates that TST regulates the mitochondrial function of adipocytes and that its expression is negatively connected with fat mass and positively with

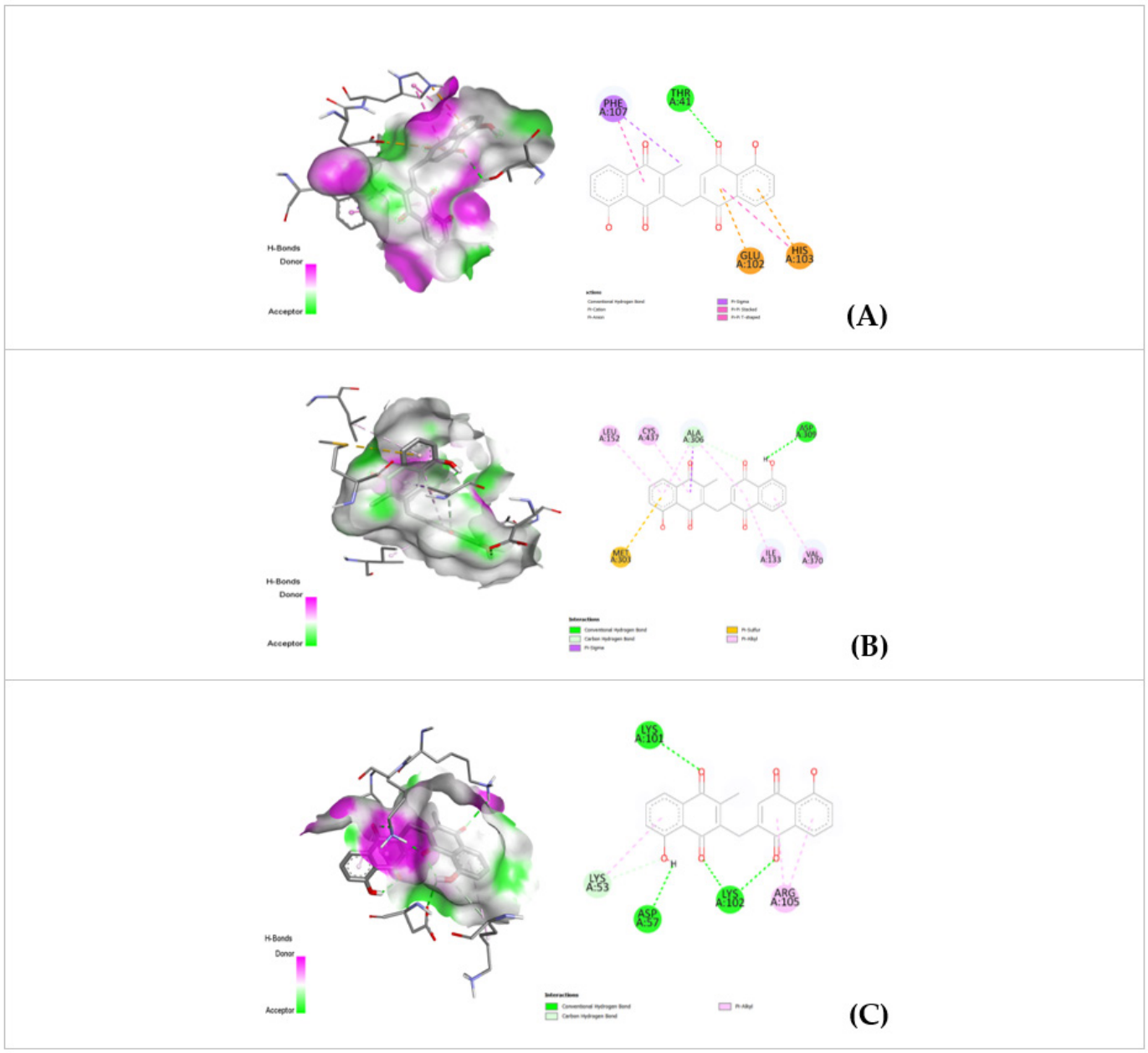

Figure 4: Binding interaction's visual depiction with the most significant docking scores (A: TST-Isozeylanone, B: CYP19A1-Isozeylanone, C: BCL2-Isozeylanone).

Table 1: Key Chitraka bioactive compounds' docking score against important obesity targets.

Bioactives	Binding Affinity		
	TST (8agf)	CYP19A1 (3s79)	BCL2 (2vm6)
Isozeylanone	-8	-10.3	-7.9
Lupeol	-7.5	-7.8	-8
Vanillic Acid	-5.5	-6	-5.7
Beta-Sitosterol	-7.6	-8.1	-7.5
Beta-Asarone	-5.4	-5.9	-5.5
Altechromone A	-6.4	-6.4	-6.1

adipose insulin sensitivity.[33] In obesity, Arachidonic Acid (AA), a polyunsaturated fatty acid, is metabolized by the Cyclooxygenase (COX), Lipoxygenase (LOX) and Cytochrome P450 (CYP) pathways. This results in the production of eicosanoids that affect inflammation and other processes, potentially making obesity related disorders worse.[34] Nitrogen metabolism, which deals with how the body processes nitrogen-containing substances like amino acids, is disturbed in obesity.

This can result in problems like elevated ammonia production and decreased urea cycle activity, which can aggravate metabolic problems and fatty liver disease.[35] Given the role that nitrogen metabolism plays in obesity and associated disorders such as fatty liver disease, restoring nitrogen balance and focusing on the gut-liver axis may be effective treatment strategies.[36] The findings of this investigation offer a solid theoretical foundation for the investigation of anti- by identifying particular signaling pathways and associated target proteins. Additionally, using molecular docking, the mechanism of action of Chitraka's main phytochemicals against obesity was further investigated. However, there are many drowbacks with this study. First, the quality of the currently available databases limited the reliability of our similarity-based approach to investigating probable targets of bioactive compounds and target prediction methods only cover a few hundred to thousands of targets, which could introduce biases into the enrichment analysis. Furthermore, pre-clinical and clinical trials are the sole ways to determine safety and efficacy evaluations, which are still required.

CONCLUSION

Through 'Targets-compounds-Pathway' network, the study found that the *Chitraka* phytochemicals contributed to synergistic impacts (multi-pathway, multi-target) to reduce obesity. Key molecules of *Chitraka* acting on obesity were confirmed by a molecular docking test that demonstrated strong binding affinity of numerous important compounds, such as isozeyalanone, luteol and β-sitosterol, on important targets TST, CYP19A1 and BCL2. Overall, we clarified a crucial mechanism, target, and bioactive of *Chitraka* against obesity, indicating a strong pharmacological foundation for additional clinical research.

ACKNOWLEDGEMENT

Dr. Suhas Kumar Shetty, Principal, KAHER'S Shri BM Kankanawadi Ayurveda Mahavidhyalaya Shahapur, Belagavi, Karnataka.

ABBREVIATIONS

IMMPAT 2.0: Indian Medicinal Plants, Phytochemistry and Therapeutics 2.0; **ADME:** Absorption-distributio n-metabolism-excretion; **HPA:** Human Protein Atlas; **FDR:** False Discovery Rate; **RSCB PDB:** RCSB Protein Data Bank; **ERK1/2:** Extracellular signal-regulated kinases; **BCL2:** B-cell lymphoma/leukemia 2; **CYP19A1:** Cytochrome P450 family 19 subfamily A member 1; **TST:** Thiosulfate Sulfurtransferase

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

In Ayurveda, *Chitraka moola* (*Plumbago zeylanica* L.) is a commonly used herb in Obesity (Sthoulya) particularly because of its *lekhaniya karma, ushna tikshna guna* and *katu rasa*. Additionally, it is a key component of *Trimad*, a polyherbal Ayurvedic preparation that is advised for the treatment of obesity. Research on *Chitraka's* active ingredients and mechanisms of action against obesity ought to establish its pharmacological relevance in reducing obesity. Network pharmacology is an approach for incorporating bioinformatics with pharmacology. Through 'Targets-compounds-Pathway' network, the study found that the *Chitraka* phytochemicals contributed to synergistic impacts (multi-pathway, multi-target) to reduce obesity. Overall, we clarified a crucial mechanism, target, and bioactive of *Chitraka* against obesity, indicating a strong pharmacological foundation for additional clinical research.

REFERENCES

1. Panuganti KK, Nguyen M, Kshirsagar RK. Obesity. StatPearls – NCBI bookshelf; 2023. A vailable from: https://www.ncbi.nlm.nih.gov/books/NBK459357/.
2. Hryhorczuk C, Sharma S, Fulton SE. Metabolic disturbances connecting obesity and depression. Front Neurosci. 2013; 7: 177. doi: 10.3389/fnins.2013.00177, PMID 24109426.
3. Rodgers RJ, Tschöp MH, Wilding JP. Anti-obesity drugs: past, present and future. Dis Model Mech. 2012; 5(5): 621-6. doi: 10.1242/dmm.009621, PMID 22915024.
4. Wolfe BM, Kvach E, Eckel RH. Treatment of obesity: weight loss and bariatric surgery. Circ Res. 2016; 118(11): 1844-55. doi: 10.1161/CIRCRESAHA.116.307591, PMID 27230645.
5. Singh S, Priyadarshi A, Sharma P. A brief review on medicinal property of Chitraka (*Plumbago zeylanica* Linn.) from Kosha and Nighantus. IJSRR. 2018; 7(2): 25-31.
6. Salunke M, Deshpande M, Bhalerao S. Experiential documentation of Trimad for its anti-obesity potential: A survey of Ayurvedic physicians from Pune city. J Ayurveda Integr Med. 2017; 8(3): 190-3. doi: 10.1016/j.jaim.2017.03.004, PMID 28822619.
7. Shukla B, Saxena S, Usmani S, Kushwaha P. Phytochemistry and pharmacological studies of *Plumbago zeylanica* L.: a medicinal plant review. Clin Phytosci. 2021; 7(1): 34. doi: 10.1186/s40816-021-00271-7.
8. Boezio B, Audouze K, Ducrot P, Taboureau O. Network-based approaches in pharmacology. Mol Inform. 2017; 36(10): 1700048. doi: 10.1002/minf.201700048, PMID 28692140.
9. Lans C, Van Asseldonk T. Dr. Duke's phytochemical and ethnobotanical databases, a cornerstone in the validation of ethnoveterinary medicinal plants, as demonstrated by data on pets in British Columbia. In: Máthé Á, editor. Medicinal and aromatic plants of North America. 1st ed. Switzerland: Springer; 2020. p. 219-46. doi: 10.100 7/978-3-030-44930-8_10.
10. Mohanraj K, Karthikeyan BS, Vivek-Ananth RP, Chand RP, Aparna SR, Mangalapandi P, *et al.* IMPPAT: A curated database of Indian Medicinal Plants, Phytochemistry and Therapeutics. Sci Rep. 2018; 8(1): 4329. doi: 10.1038/s41598-018-22631-z, PMID 29531263.
11. Mohanraj K, Karthikeyan BS, Vivek-Ananth RP, Chand RP, Aparna SR, Mangalapandi P, *et al.* IMPPAT: A curated database of Indian Medicinal Plants, Phytochemistry and Therapeutics. Sci Rep. 2018; 8(1): 4329. doi: 10.1038/s41598-018-22631-z, PMID 29531263.
12. Daina A, Michielin O, Zoete V. SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci Rep. 2017; 7: 42717. doi: 10.1038/srep42717, PMID 28256516.
13. Liu T, Lin Y, Wen X, Jorissen RN, Gilson MK. BindingDB: A web-accessible database of experimentally determined protein-ligand binding affinities. Nucleic Acids Res. 2007; 35((Database issue)):D198-201. doi: 10.1093/nar/gkl999, PMID 17145705.

14. Apweiler R, Bairoch A, Wu CH, Barker WC, Boeckmann B, Ferro S, *et al.* UniProt: the universal protein knowledgebase. Nucleic Acids Res. 2004; 32((Database issue)):D115-9. doi: 10.1093/nar/gkh131, PMID 14681372.
15. Thul PJ, Lindskog C. The human protein atlas: A spatial map of the human proteome. Protein Sci. 2018; 27(1): 233-44. doi: 10.1002/pro.3307, PMID 28940711.
16. Stelzer G, Rosen N, Plaschkes I, Zimmerman S, Twik M, Fishilevich S, *et al.* The GeneCards suite: from gene data mining to disease genome sequence analyses. Curr Protoc Bioinformatics. 2016; 54: 1.30.1-1.30.33. doi: 10.1002/cpbi.5, PMID 27322403.
17. Collazos JC. Venny 2.1.0 [Internet]. Available from: https://bioinfogp.cnb.csic.es/tools/venny/.
18. Szklarczyk D, Kirsch R, Koutrouli M, Nastou K, Mehryary F, Hachilif R, *et al.* The STRING database in 2023: protein-protein association networks and functional enrichment analyses for any sequenced genome of interest. Nucleic Acids Res. 2023; 51(D1):D638-46. doi: 10.1093/nar/gkac1000, PMID 36370105.
19. Ge SX, Jung D, Yao R. ShinyGO: A graphical gene-set enrichment tool for animals and plants. Bioinformatics. 2020; 36(8): 2628-9. doi: 10.1093/bioinformatics/btz931, PMID 31882993.
20. Shannon P, Markiel A, Ozier O, Baliga NS, Wang JT, Ramage D, *et al.* Cytoscape: A software environment for integrated models of biomolecular interaction networks. Genome Res. 2003; 13(11): 2498-504. doi: 10.1101/gr.1239303, PMID 14597658.
21. Berman HM, Battistuz T, Bhat TN, Bluhm WF, Bourne PE, Burkhardt K, *et al.* The Protein Data Bank. Acta Crystallogr D Biol Crystallogr. 2002; 58(6 No 1):899-907. doi: 10.1107/s0907444902003451, PMID 12037327.
22. Dallakyan S, Olson AJ. Small-molecule library screening by docking with PyRx. Methods Mol Biol. 2015; 1263: 243-50. doi: 10.1007/978-1-4939-2269-7_19, PMID 25618350.
23. Arya N, Sharma A. The therapeutic and toxicological effect of Chitraka (*Plumbago zeylanica* L.) – a review. Ayushdhara. 2015; 2(4).
24. Kumari H, Pushpan R, Nishteswar K. Medohara and Lekhaniya dravyas (anti-obesity and hypolipidemic drugs) in Ayurvedic classics: A critical review. Ayu. 2013; 34(1): 11-6. doi: 10.4103/0974-8520.115437, PMID 24049399.
25. Gupta P, Sharma S. Clinical study to assess the efficacy of Haridra and Chitraka in management of Medoroga (Obesity). WJPLS. 2020; 6(12): 187-9.
26. Selvaraju V, Babu SR, Judd RL, Geetha T. Lupeol attenuates palmitate-induced hypertrophy in 3T3-L1 adipocytes. Biomolecules. 2025; 15(1): 129. doi: 10.3390/biom15010129, PMID 39858523.
27. Jayaraman S, Devarajan N, Rajagopal P, Babu S, Ganesan SK, Veeraraghavan VP, *et al.* β-sitosterol circumvents obesity-induced inflammation and insulin resistance by down-regulating IKKβ/NF-κB and JNK signaling pathway in adipocytes of type 2 diabetic rats. Molecules. 2021; 26(7): 2101. doi: 10.3390/molecules26072101, PMID 33917607.
28. Lee MH, Chen YY, Tsai JW, Wang SC, Watanabe T, Tsai YC. Inhibitory effect of β-asarone, a component of Acorus calamus essential oil, on inhibition of adipogenesis in 3T3-L1 cells. Food Chem. 2011; 126(1): 1-7. doi: 10.1016/j.foodchem.2010.08.052.
29. Tinahones FJ, Coín Aragüez L, Murri M, Oliva Olivera W, Mayas Torres MD, Barbarroja N, *et al.* Caspase induction and BCL2 inhibition in human adipose tissue: a potential relationship with insulin signaling alteration. Diabetes Care. 2013; 36(3): 513-21. doi: 10.2337/dc12-0194, PMID 23193206.
30. Tinahones FJ, Coín Aragüez L, Murri M, Oliva Olivera W, Mayas Torres MD, Barbarroja N, *et al.* Caspase induction and BCL2 inhibition in human adipose tissue: a potential relationship with insulin signaling alteration. Diabetes Care. 2013; 36(3): 513-21. doi: 10.2337/dc12-0194, PMID 23193206.
31. Lu Y, Qin L, Wei Y, Mo X, Tang X, Liu Q, *et al.* Association between barium exposure, CYP19A1 and central obesity: A cross-sectional study in rural China. J Trace Elem Med Biol. 2023; 78: 127170. doi: 10.1016/j.jtemb.2023.127170, PMID 37075568.
32. Kruithof PD, Lunev S, Aguilar Lozano SP, De Assis Batista F, Al-Dahmani ZM, Joles JA, *et al.* Unraveling the role of thiosulfate sulfurtransferase in metabolic diseases. Biochim Biophys Acta Mol Basis Dis. 2020; 1866(6): 165716. doi: 10.1016/j.bbadis.2020.165716, PMID 32061776.
33. Morton NM, Beltram J, Carter RN, Michailidou Z, Gorjanc G, McFadden C, *et al.* Corrigendum: genetic identification of thiosulfate sulfurtransferase as an adipocyte-expressed antidiabetic target in mice selected for leanness. Nat Med. 2018; 24(4): 525. doi: 10.1038/nm0418-525e, PMID 29634685.
34. Zhang Y, Liu Y, Sun J, Zhang W, Guo Z, Ma Q. Arachidonic acid metabolism in health and disease. Med. 2023; 4(5): e363. doi: 10.1002/mco2.363, PMID 37746665.
35. Bistrian BR, Blackburn GL, Flatt JP, Sizer J, Scrimshaw NS, Sherman M. Nitrogen metabolism and insulin requirements in obese diabetic adults on a protein-sparing modified fast. Diabetes. 1976; 25(6): 494-504. doi: 10.2337/diab.25.6.494, PMID 1278601.
36. Delgado TC, De Las Heras J, Martínez-Chantar ML. Understanding gut-liver axis nitrogen metabolism in fatty liver disease. Front Endocrinol (Lausanne). 2022; 13: 1058101. doi: 10.3389/fendo.2022.1058101, PMID 36589817.

Cite this article: Hegade PB, Bhirdi PNB, Lingayat A. Network Pharmacology Approach to Determine the Molecular Mechanism of *Chitraka* (*Plumbago zeylanica* L.) in the Treatment of Obesity. Pharmacog Res. 2025;17(4):1274-80.