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Systematic Study of Multitarget Molecular Docking: from Polypharmacology to Tissue Pharmacology

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Abstract

Purpose: This study describes the shift in modern drug discovery toward a computational systems-based paradigm, emphasizing multi-target molecular docking as a key strategy to unravel complex molecular interactions in biological systems.

Methods: A systematic literature review was conducted using publications from 2020 to 2025 retrieved from the PubMed, Scopus, ScienceDirect, and MDPI databases.

Results/findings: The analysis demonstrates that integrating molecular docking, Molecular Dynamics (MD) simulations, and network pharmacology enhances polypharmacology and drug repurposing strategies for complex diseases, such as diabetes, Alzheimer's, and viral infections. Bioactive compounds, including quercetin, luteolin, kaempferol, diosgenin, β-amyrenone, and copper (II) complexes, target critical biological pathways (AGE–RAGE, NF-κB, STAT3–CASP3–HIF1A) and essential viral proteins.

Conclusions: The integration of multi-target molecular docking, network pharmacology, and AI-based drug design forms a new paradigm in modern drug discovery. This approach enables a systemic analysis of ligand–protein interactions, accelerates the identification of therapeutic targets, and improves the accuracy and efficiency of virtual screening. The combination of these three approaches strengthens the direction towards computational systems pharmacology, which supports data-driven and sustainable drug design.

Limitations: This study is based solely on existing computational data, without experimental validation to confirm the predicted interactions.

Contributions: This study highlights the integrative potential of multi-target molecular docking and network pharmacology as a bridge between computational prediction and experimental pharmacology. It offers a conceptual foundation for AI-assisted drug design and encourages future research on experimental validation and predictive modeling to optimize multitarget therapies.

Keywords: *AI in Drug Discovery, Drug Design, Multi-target Molecular Docking, Network Pharmacology, Polypharmacology.*

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1. Introduction

Drug discovery has undergone significant paradigm shifts in the past two decades (Chakraborty, Bhattacharya, Lee, Wen, & Lo, 2024; Neelam, 2025). Advances in bioinformatics and molecular biology technologies have led to major changes in the paradigm of modern drug discovery. Currently, various complex diseases, including Alzheimer's disease, are major focuses. Alzheimer's Disease (AD) poses significant public health challenges because of progressive neurodegeneration, degradation of

cognitive function, and memory loss (Kazemeini et al., 2024). A rapidly developing approach to address these challenges is multi-target molecular docking. This computational (in silico) method allows the simultaneous analysis of interactions between a single ligand molecule and multiple target receptors (Abdelsayed, 2025). Unlike traditional methods that focus on a single target, multi-target strategies offer a comprehensive understanding of the mechanisms of action of compounds. The integration of this method with network pharmacology enables the construction of complex maps that link drugs, targets, and disease pathways. This network-based approach helps identify new therapeutic targets and improve treatment effectiveness while reducing side effects (Qi et al., 2025; Zhang, Zhu, Bai, & Ning, 2019).

Molecular docking is one of the most frequently applied techniques for screening bioactive compounds. This technique models the interactions between ligands (active molecules) and target receptors (proteins) to evaluate the binding affinity, molecular orientation, and possible mechanisms of compound action against enzyme targets (Hidayah & Amin, 2025). Commonly evaluated target proteins include spike proteins, Main Protease (MPro), and envelope proteins (Ahmad & Amin, 2025).

Through a deep understanding of these interactions, researchers can identify candidate compounds with the potential to selectively inhibit viral activity (Ahmad & Amin, 2025). Multi-target–oriented drug development strategies have now become essential approaches in managing complex diseases such as cancer and neurodegenerative diseases (Bi, Wang, Wang, & Liu, 2025; Doostmohammadi, Jooya, Ghorbanian, Gohari, & Dadashpour, 2024).

However, most previous studies have been partial or have focused on a single type of target. The comprehensive integration of multi-target docking, molecular dynamics, and network pharmacology is still relatively limited. Several previous studies, such as those conducted by Syahputra et al. (2024) and Zhai et al. (2025), have highlighted the great potential of this integration; however, they have not systematically discussed the shift from polypharmacology to network pharmacology. This indicates the need for a systematic review to identify development trends, methodologies used, and the scientific contributions of applying various computational approaches in drug discovery (Amin, Azijah, & Gunawan, 2025).

This study has scientific novelty in the integration of three main conceptual approaches: multi-target molecular docking, network pharmacology, and AI-based drug design. This integration represents a paradigm transformation in drug discovery that is holistic, efficient, and sustainability-oriented, in line with the evolution of computational pharmacology toward the era of data-driven medicine.

The objective of this study is to systematically examine the development of multi-target molecular docking in modern drug design, with an emphasis on the paradigm shift from polypharmacology to network pharmacology and its integration with artificial intelligence technologies to strengthen system-based drug design innovation.

2. Literature Review and Hypothesis Development

2.1 Literature Review

Molecular docking is a computational technique designed to predict interactions between receptors and ligands through simulation approaches, with a primary focus on determining molecular conformations and binding free energy (Amin & Tsani, 2025). Molecular docking methods have three interrelated main objectives: estimating the position or orientation of a ligand within a receptor (pose prediction), performing virtual screening of candidate compounds, and determining the level of binding affinity between the ligand and receptor.

An effective docking approach is required to generate ligand position predictions that resemble experimental conformations within the binding site, with acceptable deviations, and to explain the physicochemical interactions occurring between the two (Syaqila, Pebralia, & Restianingsih, 2024).

The main objective of molecular docking is to support the drug discovery process through computational modeling of complex interactions between two molecules in a three-dimensional form. This approach enables the identification of the most suitable binding orientations and molecular conformations, as well as the estimation of the resulting binding free energy (Amin, Mustafidah, Nabila, & Maharani, 2025). Molecular complexes formed are considered increasingly stable as their free energy values decrease; therefore, this information plays an important role in determining the affinity and potential biological activity of candidate drug compounds (Amin, Wihdatunnisa, Aisyah, & Kurniawan, 2024).

The multi-target docking approach has emerged as a solution to the limitations of the one drug–one target model. This concept acknowledges that most chronic and degenerative diseases (such as cancer, Alzheimer's disease, and diabetes) have multifactorial mechanisms involving multiple proteins and signaling pathways (Hossain & Hussain, 2025).

Therefore, multi-target docking provides a scientific basis for understanding the synergistic effects of complex compounds on multiple receptors. Meanwhile, the integration of network pharmacology combines the principles of systems biology, bioinformatics analysis, and computational pharmacology methods to comprehensively explain the dynamic relationships between drug compounds, molecular targets, and various biological pathways involved in their pharmacological activities (Zhai et al., 2025).

Over the past decade, this integrative approach has shown exponential growth. For example, Tarkaa et al. (2023) investigated the molecular mechanisms of *Curcuma longa* in breast cancer treatment through an integrated approach combining network pharmacology, molecular docking, and molecular dynamics. Of the 156 identified phytochemical compounds, 54 interacted with key proteins involved in breast cancer pathogenesis. GO and KEGG analyses showed the regulation of several major molecular pathways, whereas molecular docking and molecular dynamics simulation results confirmed the stability of the ligand protein complexes.

These findings confirm the potential of *C. longa* as a multi-target therapeutic candidate based on modern computational approaches (*Frontiers in Pharmacology*). Recent studies have also highlighted the role of Artificial Intelligence (AI) in accelerating drug design. According to Meli, Morris, and Biggin (2022), the development of structure-based deep learning models enables the in silico prediction of protein ligand binding affinity. This approach is considered capable of accelerating and improving the accuracy of the drug discovery process compared to classical scoring functions. The review discusses various network architectures, feature extraction strategies, training databases, and the role of explainable AI in building more transparent and applicable predictive models for modern drug design.

Based on these considerations, the conceptual framework of this study was built upon three main components that interact interactively: multi-target molecular docking, network pharmacology, and AI-based drug design. First, multi-target molecular docking evaluates the affinity and stability of the interactions between ligands and target proteins. Through this analysis, quantitative information was obtained regarding the binding strength and potential interactions of compounds with multiple biological receptors simultaneously.

Second, network pharmacology identifies the relationships among molecular targets, biological pathways, and the resulting pharmacological effects. This approach provides a systemic perspective on how compounds function in complex biological networks. Third, AI-based drug design optimizes the prediction and virtual screening processes through the application of AI algorithms.

This AI-based approach enables a more accurate analysis of interaction patterns and structure–activity relationships, thereby accelerating the drug discovery process. These three concepts are cyclically interconnected. Affinity and ligand protein orientation data generated from molecular docking serve as important inputs for network pharmacology analysis, whereas AI-based drug design learns patterns from both approaches to improve the accuracy and efficiency of drug design in subsequent stages.

Thus, network pharmacology has emerged as a system-oriented scientific discipline that integrates principles of biology, bioinformatics analysis, and computational pharmacology methods to comprehensively explain the dynamic relationships between drug compounds, molecular targets, and various biological pathways involved in their pharmacological activities (Zhai et al., 2025).

2.2 Development of Conceptual Propositions

The conceptual propositions used in this study are as follows:

H_0: There is no significant relationship between the application of multi-target molecular docking strategies and the effectiveness of identifying critical biological targets in new drug development.

H_1: There is a significant relationship between the application of multi-target molecular docking strategies and the effectiveness of identifying critical biological targets in new drug development.

3. Research Methodology

This study was developed using a Systematic Literature Review (SLR) approach to identify, evaluate, and synthesize research findings relevant to multi-target molecular docking in modern drug design. The review process was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines to ensure methodological transparency and reproducibility.

Literature searches were conducted in internationally reputable scientific databases, namely, PubMed, Scopus, ScienceDirect, and MDPI, with a publication time range of 2020–2025. The keywords used included combinations of the following terms: “multi-target molecular docking,” “network pharmacology,” “polypharmacology,” “AI in drug discovery,” and “computational drug design.” The search strategy was formulated using logical operators (AND, OR) to maximize the relevance of the results.

a. Inclusion Criteria
   1. Articles in English or Indonesian published between 2020 and 2025.
   2. Studies on original research that use molecular docking, network pharmacology, molecular dynamics, or AI integration in drug discovery.
   3. Articles available in full-text and indexed in reputable databases (Scopus, PubMed, and MDPI).
   4. Studies reporting predictive results or validation of multi-target mechanisms of action in pharmacology or bioinformatics.

b. Exclusion Criteria
   1. ” Non-peer-reviewed articles, conference abstracts, editorials, or book chapters.
   2. Studies with incomplete data or without clear docking methodology
   3. Inclusion of duplicate articles from the same database.
   4. Reviews that are not relevant to the focus of multi-target drug design or do not include a systemic analysis.

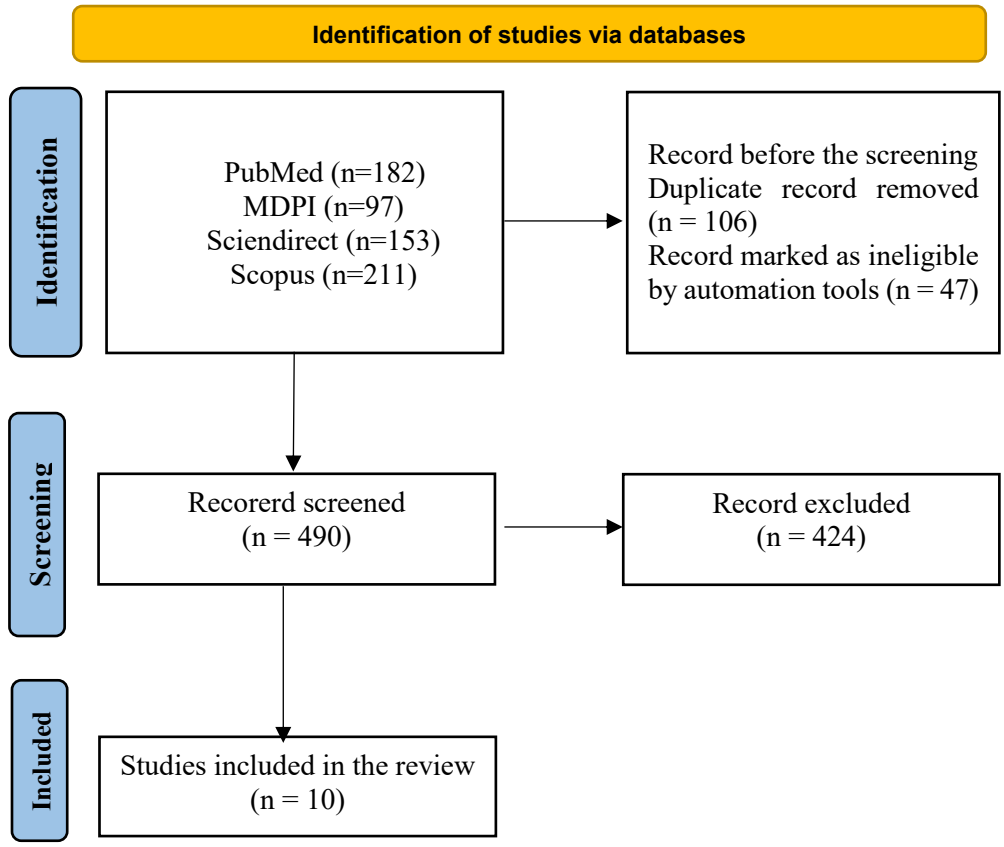

Figure 1. PRISMA (2020) identification flow diagram

4. Results and Discussion

This review presents an in-depth and comprehensive understanding of the evolution and application of the multi-target molecular docking approach in modern drug development. The discussion focuses on the paradigm shift from polypharmacology, which emphasizes the ability of a single drug molecule to interact with multiple biological targets, to network pharmacology, which highlights a systemic view of drug mechanisms of action through complex interactions among proteins, signaling pathways, and molecular networks within biological systems.

Table 1. Literature results

Researcher	Title	Software	Results
Luo et al. (2023)	Integration Of Molecular Docking, Molecular Dynamics and Network Pharmacology to Explore the Multi-Target Pharmacology of Fenugreek Against Diabetes	Molecular Docking (MD) dan Network Pharmacology (NP)	Multi-target molecular docking verified the polypharmacology of fenugreek. Its main compounds (quercetin and luteolin) showed superior binding affinity to multiple diabetes targets (AKT1 and IL6) compared to metformin, confirming the role of docking in modern multi-target drug design.

Mun, Hui, Sing, Karunakaran, and Ravichandran (2022)	Multi-Targeted Molecular Docking, Pharmacokinetics, And Drug-Likeness Evaluation of Coumarin Based Compounds Targeting Proteins Involved in Development Of COVID-19	Chem Office-16, Discovery Studio Visualizer 3.0, Swiss Protein Data Base Viewer, Open Babel, Pyrx, and AutoDock Vina.	Multi-target molecular docking effectively demonstrated the effectiveness of coumarin-derived compounds. The new derivatives (PHE1, HYM1) were proven to be superior and capable of binding multiple SARS-CoV-2 targets (Mpro, RdRp, etc.). This confirms the effectiveness of docking in achieving polypharmacology for the treatment of complex diseases.
Yang et al. (2025)	The Multi-Target Intervention Reveals the Mechanism by Which Finerenone Alleviates Polymyxin B-Induced Kidney Injury: An Integrated Study of Network Pharmacology, Transcriptomics, And Molecular Docking		Multi-target molecular docking validated the role of finerenone. Based on network pharmacology and transcriptomic data, docking confirmed the superior binding affinity of finerenone to critical kidney disease nodes (STAT3, CASP3, and HIF1A), proving a multi-target intervention at the structural level.
Reza et al. (2022)	Repurposing Of Anti-Lung Cancer Drugs as Multi-Target Inhibitors Of SARS-Cov-2 Proteins: An Insight from Molecular Docking And MD-Simulation Study	AutoDock Vina, UCSF Chimera, and Discovery Studio Visualizer	Multi-target molecular docking effectively identified capmatinib. This repurposed drug was proven to be stable and superior in binding to three key SARS-CoV-2 targets (Mpro, PLpro, and spike), strengthening the role of docking in polypharmacology.
Kini et al. (2025)	Multitarget Insights into Traditional Chinese Phytoconstituents Against Tuberculosis Via Network Pharmacology, Molecular Docking, And MD Simulation	eFP server and mycoCSM	Multi-target molecular docking strengthens network pharmacology findings for tuberculosis. The Traditional Chinese Medicine (TCM) compound glabroisoflavanone A was proven superior and stable (confirmed by Molecular Dynamics (MD) simulation) in binding three key TB targets simultaneously, emphasizing the role of docking in the polypharmacology of natural compounds.

Guo et al. (2025)	Investigating The Neuroprotective Effects and The Potential Mechanisms Of B-Amyrenone in Cerebral Ischemic/Reperfusion Injury Based on Pharmacology Network, Bioinformatics, And Molecular Docking Simulation	Database for Annotation, Visualization, and Integrated Discovery (DAVID)	Multi-target molecular docking strengthens network pharmacology findings for neuroprotection. The compound β-amyrenone showed superior binding to four key inflammatory targets of CIRI (IL-1β, PTGS2, MAPK3, and ESR1), supported by in vitro validation of neuronal protection. This demonstrates the effectiveness of polypharmacology at the functional level
Thapa et al. (2025)	LC-MS Profiling and Multi-Target Mechanistic Insights of Hibiscus Rosa-Sinensis in Diabetes: Network Pharmacology, Molecular Docking, MD Simulation, PCA, And In-Vitro A-Amylase Inhibition	AutoDock Vina v1.2.0	The multi-target molecular docking approach successfully strengthened network pharmacology results for diabetes therapy. Quercetin was proven to be the most stable and effective compound binding three main targets (PTK2, SRC, and α-amylase). Structural validation consistent with in vitro α-amylase inhibitory activity confirms the importance of docking methods in discovering polypharmacology-based solutions from natural products.
Dong et al. (2021)	Molecular Mechanism of Epicedium Treatment for Depression Based on Network Pharmacology and Molecular Docking Technology	Autodock tools 1.5.6, ChemBioDraw 3D	This study demonstrated that the active compounds in Epimedium exert antidepressant effects through multicomponent, multitarget, and multi-pathway mechanisms. The combined approach of network pharmacology and molecular docking proved to be a rational and feasible method to elucidate complex herbal drug mechanisms and provide a scientific basis for new drug development from natural products.

Luo et al. (2023)	Integration Of Molecular Docking, Molecular Dynamics and Network Pharmacology to Explore the Multi-Target Pharmacology of Fenugreek Against Diabetes	BindingDB. DrugBank, STITCH, SwissTargetPrediction databases	The multi-target molecular docking and network pharmacology approach successfully explained the mechanism of action of fenugreek against diabetes. Its main active compounds, quercetin and luteolin, showed stronger binding affinity to AKT1 and IL6 targets than metformin. These results reinforce the concept of polypharmacology of natural compounds in targeting complex disease pathways, such as AGE-RAGE and NF-κB.
Arthi, Dharmasivam, Kaya, and Rahiman (2023)	Multi-Target Activity of Copper Complexes: Antibacterial, DNA Binding, And Molecular Docking With SARS-Cov-2 Receptor		This study successfully synthesized new copper (II) complexes that showed promising multi-target activity against bacteria, DNA, and the SARS-CoV-2 receptor. The combination of in vitro testing and multi-target molecular docking validation represents a strong strategy for identifying new drug candidates with a broad spectrum of action.

Modern approaches in drug discovery, especially those derived from natural products, are increasingly relying on the synergy between computational modeling and experimental validation to uncover complex mechanisms of action, while opening new opportunities to address human health challenges more effectively. Most studies highlight the role of natural compounds, such as flavonoids (quercetin, luteolin, and kaempferol) and terpenoids (β-amyrin and diosgenin), in targeting key proteins in diseases. Luo et al. (2023) provided a complex illustration of an integrative strategy through the combination of network pharmacology, molecular docking, Molecular Dynamics (MD) simulations, and in vitro testing, and successfully dissected the antidiabetic mechanism of fenugreek.

The results of this study indicate that this efficacy is mediated by bioactive compounds, such as diosgenin, luteolin, and quercetin, which target inflammatory signaling pathways and oxidative stress, including Advanced Glycation End Products (AGE)-RAGE and nuclear factor-κB, which was then confirmed by increased glucose absorption in IR-HepG2 cells, making it a promising contributor to the management of diabetes mellitus. The findings related to the antidiabetic mechanism of this herbal product are further reinforced by the research of Thapa et al. (2025), who applied a similar integrative approach. However, this study focused on a different plant species, *Hibiscus rosa-sinensis*, thus broadening our understanding of the natural potential in managing metabolic disorders that affect millions of people worldwide.

This research started with an innovative step through phytochemical profiling using LC-MS, which allows for the direct identification of bioactive compounds from plant extracts, providing a stronger empirical foundation for further exploration, not only validating α-amylase inhibition mechanisms through computational modeling but also confirming it experimentally in vitro, where the *Hibiscus* extract exhibited superior inhibition activity (IC50 = 107.75 µg/mL) compared to the standard acarbose (IC50 = 129.413 µg/mL). This finding further emphasizes the pivotal role of flavonoid compounds, especially quercetin, in mediating antidiabetic effects across species.

The role of flavonoid compounds, such as quercetin, luteolin, and kaempferol, is not limited to metabolic diseases. This was illustrated by the research of Dong et al. (2021), who investigated the antidepressant mechanism of the herbal plant *Epimedium* and showed how natural resources can contribute to addressing the increasingly urgent mental health challenges of the modern era. Through an in-silico approach integrating network pharmacology and molecular docking, the researchers revealed that luteolin, quercetin, and kaempferol belong to a class of compounds that are identical and predictive and act as hypothesis generators, effectively demonstrating the strategic value of computational modeling as an initial, cost-effective stage, allowing acceleration of research towards more inclusive and sustainable therapies to support human quality of life.

In addition to exploring natural resources, this integrated computational approach has also proven highly valuable in drug repurposing strategies, enabling rapid responses to global health threats, such as pandemics, that disrupt the lives of millions worldwide. This is consistent with the research conducted by Reza et al. (2022), who screened 17 anticancer drugs to identify potential inhibitors against SARS-CoV-2, paving the way for repurposing existing therapies to save lives more efficiently. By utilizing molecular docking validated through Molecular Dynamics (MD) simulations, researchers successfully identified capmatinib as a promising candidate, showing superior binding affinity to three essential viral targets: Mpro, PLpro, and the spike protein, promising a more comprehensive therapeutic strategy. A similar multi-target approach for combating SARS-CoV-2 was also explored by Mun et al. (2022) although with a focus on natural coumarin derivatives, reflecting a continued commitment to natural resource-based treatments.

This study introduces rational design principles through structural modification of the parent coumarin compound, aiming to optimize binding affinity to viral targets, although with a relatively simpler methodology. Overall, these authors highlight the flexibility of computational methods in screening a wide variety of molecular classes, both synthetic and natural, to address emergency situations, such as the COVID-19 pandemic. A higher level of methodological integration combining in silico approaches with experimental genomic data is shown in the research of Yang et al. (2025), which not only advances our understanding of drug toxicity but also paves the way for safer therapeutic interventions for patients vulnerable to kidney complications in the modern era of medicine.

In the context of drug repurposing, this study explores the potential of finerenone as a protective agent against kidney damage induced by polymyxin B, an antibiotic often used as a last resort for drug-resistant infections but associated with significant nephrotoxicity risks. The key innovation in this research lies in the application of transcriptomic analysis based on RNA-seq, which produces authentic gene expression data from kidney cells exposed to toxins, providing deep empirical evidence to support the exploration of molecular mechanisms. This data was then used to validate and enrich predictions from the network pharmacology approach, convincingly revealing the STAT3-CASP3-HIF1A signaling axis as the central pathway underlying polymyxin B toxicity and the main intervention point for protection by finerenone.

Guo et al. (2025) focused on compound β-amyrin as the main candidate, in which network pharmacology and molecular docking analysis initially predicted its interactions with inflammatory protein targets, such as IL-1β and PTGS2. This hypothesis was directly tested in the laboratory, generating strong empirical evidence. In vitro testing confirmed the overall neuroprotective effects through increased cell viability and reduced apoptosis and precisely normalized the expression of IL-1β and PTGS2, which aligned with the in-silico projections. A comprehensive computational approach,

including network pharmacology and Molecular Dynamics (MD) the potential of phytoconstituents from traditional Chinese medicine in combating tuberculosis. This study reflects an extraordinary level of computational precision, exemplified by the execution of 200 ns MD simulations on the leading candidate, glabroisoflavanone A, which was shown to form highly stable binding interactions with the bacterial target (5XGI/DNA gyrase B).

Additionally, the free-binding energy strength obtained using the MM-GBSA method (approximately 75 kcal/mol) provides strong evidence for its potential as a new antituberculosis drug candidate. In contrast to previous studies that have primarily focused on organic compounds, the research by Arthi et al. (2023) opens a new perspective from the realm of inorganic medicinal chemistry, which could revolutionize multi-target drug strategies to address global health challenges, such as bacterial and viral infections. These researchers successfully synthesized six copper (II) complexes and conducted a comprehensive evaluation of their multifunctional activities, paving the way for the development of more adaptive and effective therapeutic agents for human welfare.

This study presents a detailed Structure-Activity Relationship (SAR) analysis in which structural modifications through the addition of the ligand 1,10-phenanthroline and the nitro group consistently improved antibacterial efficacy, DNA-binding capability, and potential interactions with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) receptors, highlighting how simple molecular changes can have significant clinical impacts. This study serves not only as an exploratory tool but also as a strong validation mechanism for elaborating the reasons behind the superior activity of several synthetic compounds.

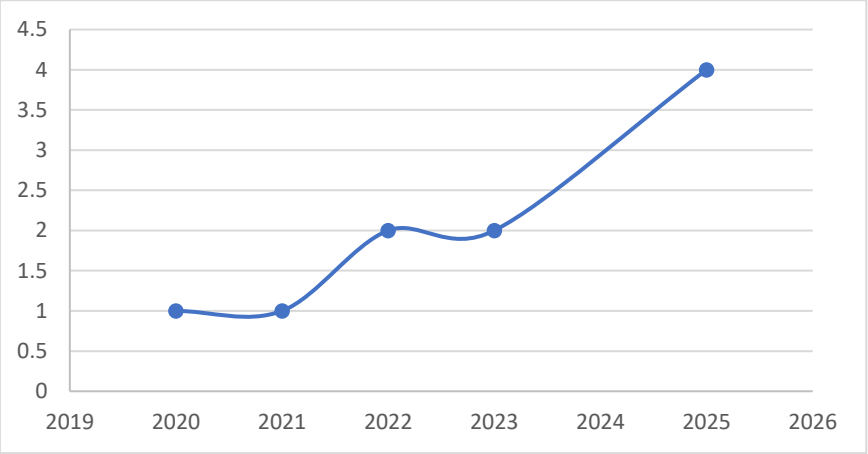

Figure 2. Graph of the development in the number of publications that met the inclusion criteria

From these articles, it can be seen that the synergy between computational and experimental approaches has become a cornerstone of contemporary pharmacology, enabling a deep understanding of the complex mechanisms of various bioactive molecules for multiple disease targets (multi-target).

5. Conclusions

5.1 Conclusion

This study highlights the integration of multi-target molecular docking, network pharmacology, and AI-based drug design as a transformative approach in modern drug discovery. By combining these methods, the study provides a comprehensive analysis of protein-ligand interactions, speeding up the identification of therapeutic targets for complex diseases. AI significantly enhances the accuracy of binding affinity predictions and virtual screening, pushing the boundaries of computational systems pharmacology and enabling more sustainable drug design.

5.2 Research Limitations

The study's limitations include its reliance on in silico simulations, which depend on the accuracy of docking algorithms, scoring functions, and system validation parameters. Variability in prediction

results can arise from differences in software and protein databases, requiring careful interpretation. Additionally, the lack of experimental validation (in vitro and in vivo) means that the biological effectiveness of the compounds analyzed still needs further laboratory confirmation. Furthermore, the limitations in omics data and the absence of cross-species network pharmacology models may impact the accuracy of systemic analysis.

5.3 Suggestions and Directions for Future Research

Future studies should focus on developing more integrative computational models by combining multi-target molecular docking, molecular dynamics simulations, and machine learning-based predictive modeling. This would improve the precision of ligand-receptor interaction predictions and binding energy estimations. Additionally, in silico findings should be validated through biological experiments to confirm the clinical relevance of identified bioactive compounds. Integrating omics data and expanding cross-species network pharmacology models will also enhance the accuracy and robustness of the analysis.

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Author Contributions

SA conceptualized the study, contributed to the study design, and participated in manuscript drafting. RPC was responsible for data collection, analysis, and manuscript revision. AR supervised the research process, provided critical revisions to the manuscript, and approved the final version. All authors have read and approved the final manuscript for submission.

References

Abdelsayed, M. (2025). AI-driven polypharmacology in small-molecule drug discovery. *International journal of molecular sciences, 26*(14), 6996. doi:https://doi.org/10.3390/ijms26146996

Ahmad, Z., & Amin, S. (2025). Literatur Penggunaan Molecular Docking Dalam Identifikasi Senyawa Potensial Sebagai Agen Anti-Sars-Cov-2. *Journal of Public Health Science, 2*(2), 230-238. doi:https://doi.org/10.70248/jophs.v2i2.2208

Amin, S., Azijah, R. N., & Gunawan, F. R. (2025). Eksplorasi Senyawa Alami sebagai Lead Antikanker Payudara dengan Pendekatan In Silico. *Jurnal Ilmu Medis Indonesia, 5*(1), 63-74. doi:https://doi.org/10.35912/jimi.v5i1.4560

Amin, S., Mustafidah, S., Nabila, N. S., & Maharani, C. (2025). Review Artikel: Pendekatan in Silico dalam Kimia Medisinal tentang Resistensi Antibiotik. *Jurnal Ilmu Medis Indonesia, 5*(1), 31-39. doi:https://doi.org/10.35912/jimi.v5i1.4561

Amin, S., & Tsani, G. A. (2025). Tinjauan Literatur: Molecular Docking Fitokimia Indonesia Terhadap Target Terapeutik Empat Jenis Kanker. *Journal of Public Health Science, 2*(2), 183-190. doi:https://doi.org/10.70248/jophs.v2i2.2191

Amin, S., Wihdatunnisa, I., Aisyah, R., & Kurniawan, Y. S. (2024). Potensi Senyawa Kuersetin sebagai Antikanker Payudara melalui Pendekatan Molecular Docking. *Jurnal Ilmu Medis Indonesia, 4*(1), 41-51. doi:https://doi.org/10.35912/jimi.v4i1.4565

Arthi, P., Dharmasivam, M., Kaya, B., & Rahiman, A. K. (2023). Multi-target activity of copper complexes: Antibacterial, DNA binding, and molecular docking with SARS-CoV-2 receptor. *Chemico-Biological Interactions, 373*, 110349. doi:https://doi.org/10.1016/j.cbi.2023.110349

Bi, X., Wang, Y., Wang, J., & Liu, C. (2025). Machine learning for multi-target drug discovery: Challenges and Opportunities in Systems Pharmacology. *Pharmaceutics, 17*(9), 1186. doi:https://doi.org/10.3390/pharmaceutics17091186

Chakraborty, C., Bhattacharya, M., Lee, S.-S., Wen, Z.-H., & Lo, Y.-H. (2024). The changing scenario of drug discovery using AI to deep learning: Recent advancement, success stories, collaborations, and challenges. *Molecular Therapy Nucleic Acids, 35*(3), 1-21. doi:https://doi.org/10.1016/j.omtn.2024.102295

Dong, Y., Tao, B., Xue, X., Feng, C., Ren, Y., Ma, H., Liu, S. (2021). Molecular mechanism of Epicedium treatment for depression based on network pharmacology and molecular docking technology. *BMC Complementary Medicine and Therapies, 21*(1), 222. doi:https://doi.org/10.1186/s12906-021-03389-w

Doostmohammadi, A., Jooya, H., Ghorbanian, K., Gohari, S., & Dadashpour, M. (2024). Potentials and future perspectives of multi-target drugs in cancer treatment: the next generation anti-cancer agents. *Cell Communication and Signaling, 22*(1), 228. doi:https://doi.org/10.1186/s12964-024-01607-9

Guo, L., Li, J., Wang, C., Wei, J., Qin, Z., Teng, H., & Mei, X. (2025). Investigating the neuroprotective effects and the potential mechanisms of β-amyrenone in cerebral ischemic/reperfusion injury based on pharmacology network, bioinformatics, and molecular docking simulation. *Letters in Drug Design & Discovery, 22*(8), 100135. doi:https://doi.org/10.1016/j.lddd.2025.100135

Hidayah, N. A., & Amin, S. (2025). Tinjauan Literatur: Penggunaan Molecular Docking Dalam Identifikasi Senyawa Potensial Sebagai Agen Antidiabetes. *Journal of Public Health Science, 2*(2), 128-135. doi:https://doi.org/10.70248/jophs.v2i2.2231

Hossain, M. S., & Hussain, M. H. (2025). Multi-Target Drug Design in Alzheimer's Disease Treatment: Emerging Technologies, Advantages, Challenges, and Limitations. *Pharmacology Research & Perspectives, 13*(4), e70131. doi:https://doi.org/10.1002/prp2.70131

Kazemeini, S., Nadeem-Tariq, A., Shih, R., Rafanan, J., Ghani, N., & Vida, T. A. (2024). From plaques to pathways in Alzheimer's disease: the mitochondrial-neurovascular-metabolic hypothesis. *International Journal of Molecular Sciences, 25*(21), 11720. doi:https://doi.org/10.3390/ijms252111720

Kini, D. D., Dey, T., Theja, G. D., Shalini, S., Ruthicshaw, R., & SG, K. M. (2025). Multitarget Insights into Traditional Chinese Phytoconstituents against Tuberculosis via Network Pharmacology, Molecular Docking, and MD Simulation. *Pharmacological Research-Modern Chinese Medicine, 17*, 100695. doi:https://doi.org/10.1016/j.prmcm.2025.100695

Luo, W., Deng, J., He, J., Yin, L., You, R., Zhang, L., He, J. (2023). Integration of molecular docking, molecular dynamics and network pharmacology to explore the multi-target pharmacology of fenugreek against diabetes. *Journal of Cellular and Molecular Medicine, 27*(14), 1959-1974. doi:https://doi.org/10.1111/jcmm.17787

Meli, R., Morris, G. M., & Biggin, P. C. (2022). Scoring functions for protein-ligand binding affinity prediction using structure-based deep learning: a review. *Frontiers in Bioinformatics, 2*, 885983. doi:https://doi.org/10.3389/fbinf.2022.885983

Mun, C. S., Hui, L. Y., Sing, L. C., Karunakaran, R., & Ravichandran, V. (2022). Multi-targeted molecular docking, pharmacokinetics, and drug-likeness evaluation of coumarin based compounds targeting proteins involved in development of COVID-19. *Saudi Journal of Biological Sciences, 29*(12), 103458. doi:https://doi.org/10.1016/j.sjbs.2022.103458

Neelam, A. k. N. (2025). Advancing drug discovery: the role of computer-aided design and development in modern pharmaceuticals. *Discover Pharmaceutical Sciences, 1*(1), 8. doi:https://doi.org/10.1007/s44395-025-00008-2

Qi, W., Shi, B., Tang, W., Zeng, J., Zhuo, M., & Ma, H. (2025). Integrating network pharmacology, molecular docking, and molecular dynamics simulations to explore potential compounds and mechanisms of Coptis Chinensis in Treating Streptococcal Infections. *PeerJ, 13*, e19960. doi:https://doi.org/10.7717/peerj.19960

Reza, R., Dutta, T., Baildya, N., Ghosh, N. N., Khan, A. A., & Das, R. K. (2022). Repurposing of anti-lung cancer drugs as multi-target inhibitors of SARS-CoV-2 proteins: An insight from molecular docking and MD-simulation study. *Microbial pathogenesis, 169*, 105615. doi:https://doi.org/10.1016/j.micpath.2022.105615

Syahputra, D., Ysrafil, Y., Alexandra, F. D., Praja, R. K., Fatmaria, F., & Pratika, R. A. (2024). Network pharmacology combined with molecular docking and molecular dynamics to verify the therapeutic potential of mung beans (Vigna radiata) against prostate cancer. *Beni-Suef University Journal of Basic and Applied Sciences, 13*(1), 100. doi:https://doi.org/10.1186/s43088-024-00552-3

Syaqila, C. N., Pebralia, J., & Restianingsih, T. (2024). Molecular Docking Senyawa (8)-Shogaol Sebagai Obat Antikanker. *Journal Online of Physics, 9*(3), 72-76. doi:https://doi.org/10.22437/jop.v9i3.36116

Tarkaa, C., Oyaniyi, D., Salaam, R., Ebuh, R., Akangbe, O., Oladokun, S., Ajayi, O. (2023). Elucidating the molecular targets of Curcuma longa for breast cancer treatment using network pharmacology, molecular docking, and molecular dynamics simulation. *Precis. Med. Res, 5*(2), 8. doi:https://doi.org/10.53388/pmr20230008

Thapa, S., Maurya, S. N., Manjunath, K., Devi, K., Varghese, S. A., Lamsal, A., Biradar, M. S. (2025). LC-MS profiling and multi-target mechanistic insights of Hibiscus rosa-sinensis in diabetes: network pharmacology, molecular docking, MD simulation, PCA, and in-vitro α-amylase inhibition. *Pharmacological Research-Modern Chinese Medicine, 16*, 100636. doi:https://doi.org/10.1016/j.prmcm.2025.100636

Yang, G., Yao, P., Shang, S., Yang, J., Li, W., Chen, Y., & Zhang, H. (2025). The multi-target intervention reveals the mechanism by which Finerenone alleviates Polymyxin B-induced kidney injury: an integrated study of network pharmacology, transcriptomics, and molecular docking. *European Journal of Pharmacology, 1005*, 177968. doi:https://doi.org/10.1016/j.ejphar.2025.177968

Zhai, Y., Liu, L., Zhang, F., Chen, X., Wang, H., Zhou, J., Lu, P. (2025). Network pharmacology: a crucial approach in traditional Chinese medicine research. *Chinese Medicine, 20*(1), 8. doi:https://doi.org/10.1186/s13020-024-01056-z

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:https://doi.org/10.3389/fphar.2019.00123