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Computational Approaches in Drug Repurposing for Rheumatoid Arthritis: From Network Pharmacology to Molecular Docking

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Abstract:

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease characterised by persistent synovial inflammation, progressive joint destruction, and systemic complications that significantly affect patient quality of life. Although several therapeutic options, including conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biologics, and targeted synthetic DMARDs, have improved disease management, limitations such as adverse effects, treatment resistance, and inability to regenerate damaged tissue remain major challenges. Drug repurposing has emerged as a promising strategy to accelerate the identification of novel therapeutic agents by utilizing approved drugs with established safety profiles. Computational approaches have revolutionized this process through the integration of network pharmacology, molecular docking, and molecular dynamics simulations. Network pharmacology enables the identification of complex interactions among genes, proteins, and signalling pathways involved in RA pathogenesis, facilitating multi-target therapeutic discovery. Molecular docking and molecular dynamics simulations further provide insights into ligand-target interactions, binding affinity, and structural stability at the atomic level. Recent advances involving Artificial Intelligence (AI), Machine Learning (ML), protein–protein interaction networks, and multi-omics integration have significantly enhanced predictive capabilities and drug candidate prioritisation. Computational studies have identified promising repurposed compounds such as rifampicin as potential therapeutic candidates for RA. Future research should focus on integrating deep learning and graph-based approaches with experimental validation through *in-vitro, ex-vivo*, and clinical investigations to bridge translational gaps. Overall, computational drug repurposing presents a cost-effective, time-efficient, and

precision-driven strategy for discovering novel therapies for RA and other complex autoimmune diseases.

Keywords: Rheumatoid Arthritis; Drug Repurposing; Network Pharmacology; Molecular Docking; Molecular Dynamics; Artificial Intelligence; Computational Drug Discovery

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Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disease causing continuous inflammation of the synovial tissue (the lining of the joints). Over time, this ongoing inflammation destroys the joints by damaging the surrounding bone and cartilage, which can lead to severe disabilities and reduced life expectancy. Globally, RA affects approximately 0.5% to 1.0% of the population, with higher prevalence rates reported in industrialized regions like North America and Northern Europe (around 0.5% to 1.1%) compared to developing regions, where rates typically range between 0.1% and 0.5%.[2-6] The prevalence of RA in women is three times higher than that in men. The incidence rate is about 1 percent. RA can occur in anyone regardless of age, although it tends to affect people who are 30 to 50 years old[7,8] . The exact pathology and etiology of RA remain unknown, but there are certain factors such as genetic, environmental, and immunological, among others, that have increased the prevalence rate of onset RA. The environmental factors include smoking and alcohol consumption which increase the chances of acquiring RA by 40 times than non-exposure. Innate immunity and adaptive immunity both play a critical role in RA development, making them immune factors. There are other factors that may increase the chances of acquiring RA, including excessive intake of sugar, salt, red meat, protein, and iron; deficiency in vitamin D and antioxidant uptake; low birth weight; breastfeeding, and geographical location. Many genetic studies have found that about 30% to 60% of RA cases involve genetic causes. Genes that cause RA are mainly cytokine promoter genes and T-cell signalling genes. They have RA-related data. The most important genetic factor

involved in RA is the *HLA-DRB1* locus.[9] People who smoke and possess HLA-DRB1 genes tend to develop increased levels of Anti-citrullinated Protein Antibodies (ACPA). Ultimately, this may lead to the development of RA.[10]. As such, ACPA plays a critical role in the physiopathology of RA.

In the past few decades, great progress has been made in gaining insight into the physiopathology of RA, which eventually gave rise to the development of a number of drugs that could help in treating RA. But till date, the drugs available currently for RA therapy have been unable to promote the regeneration of damaged tissue. Moreover, the drugs currently available interfere with the immune response, which can cause severe side effects on the patient[11]. In this regard, drug repurposing has emerged as a promising approach for identifying new therapy options for RA. There are many advantages to drug repurposing compared to traditional drug development, such as the capacity to find new therapeutic applications for drugs that are already approved. Drug repurposing takes advantage of the vast amount of information about the efficacy and safety of approved medicines[12-16]. This method is gaining popularity within the realm of medicine, including RA.

The pharmacological treatment of Rheumatoid Arthritis follows a tier-based system. The initial level of treatment is comprised of conventional synthetic DMARDs such as methotrexate, leflunomide, and sulfasalazine. Methotrexate functions as an antifolate agent and an immunosuppressant whereas leflunomide works by blocking the formation of pyrimidine in activated lymphocytes. Symptomatic relief from the disease is offered by NSAIDs such as naproxen and ibuprofen through the inhibition of COX enzymes while glucocorticoids such as prednisone offer a generalized anti-inflammatory effect and are used for immunosuppression. If the treatment proves to be ineffective, then the next step is the use of bDMARDs[17,18]. This group includes the following: TNF-α inhibitors (such as etanercept, adalimumab, infliximab), which block tumour necrosis factor alpha. IL-6 receptor antagonists (such as tocilizumab, sarilumab), which block interleukin-6 signalling. IL-1 receptor antagonists (such as anakinra) which block interleukin-1. Costimulators of T cell activation inhibition agents (such as abatacept), which block full T-cell activation by blocking CD80/CD86 binding. B-cell depletion therapy (such as rituximab) – anti-CD20 monoclonal antibody. One of the newest groups of drugs approved for use is tsDMARDs (targeted synthetic DMARDs). This group primarily comprises JAK inhibitors such as tofacitinib, baricitinib, and upadacitinib. These oral drugs act through intracellular inhibition of Janus kinase-signal transducer and activator of transcription (JAK-STAT) signaling pathway and thus inhibit several inflammatory cytokines. There are other promising drugs in the development pipeline. These include Bruton's Tyrosine Kinase (BTK) inhibitors, which inhibit B-cell receptor signalling, such as fenebrutinib; next generation Janus kinase (JAK) inhibitors, which inhibit the JAK1 pathway through ivarmacitinib SHR0302, and decernotinib (VX-509), which inhibits the JAK3 pathway; and various inhibitors of p38 mitogen-activated protein kinase (MAPK), such as VX-702 and SCIO-469, even though this class has shown little efficacy thus far. In terms of preclinical research, other target areas for inhibition

include inhibitors of phosphatidylinositol 3-kinase (PI3K) pathways (such as GS9901), mammalian target of rapamycin (mTOR) inhibitors (such as rapamycin), Notch inhibitors (such as LY411575), and signal transducer and activator of transcription[20, 21]. Finally, advanced technological treatments have been considered, such as PROTAC technology used to degrade proteins, like JAK; nanoparticles for the specific delivery of medication to the inflammation site; and CRISPR-Cas9 for engineering smart cells that can produce anti-inflammatory medicine on their own[22].

Even with this wide range of options, RA is an incurable condition, and the approach taken towards treatment is hierarchical, involving the pyramid concept of escalating treatment. The current medications pose a possibility of causing adverse effects, ranging from immunosuppression to cytopenia, to liver injury. The problem of ensuring effective treatment without causing toxic effects is why it would be important to explore drug repurposing to discover better treatments for RA.

The main drive behind carrying out this study is the pressing need for the identification of novel compounds that could help overcome some limitations posed by the current treatments of RA. One of the most promising approaches towards this goal is the drug repurposing approach, where the safety and efficiency of already available FDA approved drugs are harnessed to reveal additional uses for these molecules. This approach has potential to greatly shorten the process of drug development thus allowing patients to benefit from new drugs faster than ever before. Considering that this research will focus on the molecular processes responsible for RA and especially the proteins that are responsible for its development, one can expect to find drugs that could potentially be used for modulation of these proteins using the drug repurposing method. In addition, the use of Molecular Dynamics (MD) simulations will aid us in attaining better results by giving us detailed information regarding the stability and flexibility as well as the manner of binding in the drug-target complexes at an atomic level. Molecular dynamics can give us dynamic information about protein-ligand interaction, thus giving us additional insights into the interaction compared to the conventional docking technique. By doing this, we ensure that the drug candidates we have chosen are stable and behave in a positive way.[23-24] This study has attempted to provide new treatment choices for RA and has highlighted the effectiveness of a particular computing process that can be used to repurpose drugs, which can be employed as an approach to treat various other diseases in the future.

Application of Artificial Intelligence in RA

The idea of drug repurposing along with AI for discovering through legacy data has been increasingly gaining popularity among pharmaceutical industries and research firms; in fact, there have been multiple RA-focussed studies advocating the application of computational approach in drug discovery. In one particular study, drug and disease data were combined in order to create a genetic disease network for designing a drug ranking algorithm. It is this algorithm that helped discover new drugs that could be repurposed for treating RA due to their

genetic relation to RA[24]. In a pre-clinical experiment, the repositioning of the drug known as pirfenidone which is used for the treatment of anti-pulmonary fibrosis was shown to have the capacity to block inflammation and angiogenesis through various mechanisms in collagen-induced arthritic rats. Such findings provide evidence on the literature suggesting the possible use of pirfenidone in treating RA; although, more research is needed in humans[24]. In another investigation, a bioinformatics approach was adopted to develop a transcriptional regulatory network for finding tissue-specific drugs that could be repurposed as treatment for rheumatoid arthritis. The drugs under consideration were evaluated and prioritized using evidence available from extensive literature review conducted through text mining analysis. It was recommended that momelotinib, ibrutinib, and sodium butyrate may serve as potential drug candidates for rheumatoid arthritis; however, more research is needed[26]. While medical imaging data is traditionally used to assess rheumatoid arthritis (RA) severity, AI-driven drug discovery relies heavily on structural and molecular informatics. Utilizing 3D macromolecular structures and chemical networks allows for the precise computational modeling and quantification of target-ligand interactions essential for identifying new therapeutic candidates.[27-29]. Many researches on RA treatment regimens demonstrate that the combination of two or three therapies is associated with better results compared to the use of DMARDs alone. The early use of combination therapy is associated with significantly lower levels of disease activity[29]. This result is in accordance with the logic behind the idea of drug sensitisation, which suggests that administration of several drugs in combination activates multiple pathways in order to elicit a greater response from the body. Still, there are very few data concerning combination therapy currently available, and there is still much room for more studies. The above examples prove the efficiency of employing the *in-silico* drug discovery approach for finding new therapeutic candidates; at the same time, the process requires validation of the findings in order to choose the drug to be investigated further.

Computational approaches

Network pharmacology

Multi-target mechanism of *Commiphora wightii*

Commiphora wightii, belonging to the family Burseraceae and class Magnoliopsida, is commonly named a Guggul plant.[31] It is a short-height plant that is 2 to 3m in length or a branching shrub, occurring in Pakistan and Indian states. The plant's exudates serve antibacterial, anti-inflammatory, and antioxidant properties.[31] It is thought to be an effective drug for orthopaedic disorders, arteriosclerosis, obesity, hypolipidemia, [31] inflammation, gout, and rheumatism. [33] *Commiphora wightii* is a well-known antihyperlipidemic drug. Guggulsterones (GSs) are active components of this drug which are responsible for this effect.[35] Beta-Sitosterol (BS) is one of the phytochemicals found in the plant species *C wightii*; it is regarded as a safe and effective natural supplement that has been demonstrated to *offer* several advantages. Beta-Sitosterol has been found to possess antioxidants, antimicrobials, angiogens, antioxidants, immunomodulation, antidiabetic, anti-inflammatory, anticancer, and

antinociception properties with no known side effects.[36] From the previous research, it is found out that guggul taken orally helps in curing tumors inside, cancerous wounds, obesity, malfunctioning liver, parasites in the intestine, white patches on skin, sinus, and swelling. Moreover, this natural medicine is also useful for the prevention and curing of other diseases like IBD, ulcers, arthritics, cardiovascular diseases, and diabetes, etc.[37] GS and boswellic acid are the two key constituents of guggul. GS is extracted from *Commiphora* while BA is isolated from Boswellia. Guggul possesses a high number of lignans and keto sterols, which make it one of the most healthy substances[38] .The efficacy of *C wightii* on various types of inflammatory diseases including RA has been clearly established due to its anti-inflammatory activity by inhibiting the formation of osteoclasts in RANKL-mediated inflammation and blocking the IL-1beta-induced expression of chemokines (ENA-78) as well as MMP-1, MMP-3 through NF-κB, p50, and p65 subunit inhibition in RA patients.[39]

Network pharmacology is an innovative, scientific, potential, and most utilized technique helpful in the area of designing drugs by analyzing the interaction of these drugs with particular diseases, genes, and target proteins[40] The “one target” and “one protein” model is transformed into a more elaborate model of “drugs-targets-pathways-diseases” through the integration of several genes, drugs, pathways, and targets due to its efficiency and comprehensiveness. The complicated interactions between genes and diseases can be decoded using molecular biology, bioinformatics, and databases in NP to understand therapies and their efficient targets. This trait of NP is beneficial and has been widely established for identifying potential active targets and mechanisms in traditional herbal medicine concerning a specific disease. In addition, the integration of NP and docking with traditional herbal medicine has opened doors for RA treatment in a highly effective manner. Thus, NP has been proven an immensely advantageous technique for solving problems related to traditional herbal medicine.[41]

We are employing novel techniques like NP and molecular docking technique to study the mode of action of *C wightii* as a potential remedy for RA. It is anticipated that the results of this project will lay the groundwork for future research and provide essential guidelines for the development of a specific treatment for RA.

Currently, research has shown that the utilization of TCM either in isolation or combined with DMARDS has improved the conditions of RA patients with little to no adverse side effects.[42-43] Therefore, TCMs have great advantages and prospects in RA treatment.

Juanbi recipe is an ancient prescription of TCM. Studies showed that Juanbi recipe relieved RA in both animal experiments[43-46] and clinical trial[47]. However, the pharmacological mechanism of Juanbi recipe in RA treatment is still unclear. This study intended to explore the core target genes and mechanisms of Juanbi recipe in RA treatment.

There are numerous types of compounds present within the ingredient of the TCMs, and therefore, the strategy of one molecule binding with one target is inefficient for finding new medications. However, network pharmacology offers a network approach that consists of

multiple molecules, targets, and pathways, providing a completely new approach to explore the mechanism of drug function. Network pharmacology has played a significant role in drug discovery and target identification[48.] The combination of molecular docking technology and network pharmacology is applied to the design of new Chinese medicine, to reveal the multi-target and multi-pathway therapeutic potential of Chinese medicine[49]. Network pharmacology has become a strategy and application for TCM development and biomarkers[50.]

Molecular docking

Molecular docking becomes a vital component of drug discovery in the contemporary world by providing an insight into the interactions of small molecules with target proteins. This technique is of great importance in our study concerning drug repurposing methods for RA based on our previous findings on the network analysis of protein-protein and protein-drug interactions.

Preparation of Proteins

The proteins that had been selected as targets for molecular docking studies were prepared for docking *via* SPDBV or Swiss Protein Data Bank Viewer which was an offline program used for acquiring and analyzing protein data obtained from the Protein Data Bank. Preparation of the proteins included ligand removal, energy minimization, and Ramachandran plot validation of the proteins' structure[51.]

Identification of Binding Sites

Active binding sites in the pockets of the catalytic sites of the proteins were determined through an online software called Protein-Ligand Interaction Profiler (PLIP). This procedure was very important for identifying the areas of the protein where small molecules may interact [.51-53]

Preparation of Ligands

To evaluate the therapeutic potential of *Commiphora wightii* (Guggul) against Rheumatoid Arthritis, a sequential virtual screening and network pharmacology workflow was employed.

First, a reference drug-target interaction network was constructed using a library of 2,637 FDA-approved drugs. By analyzing this network in Cytoscape, the specific target proteins heavily involved in RA pathogenesis were identified and mapped.

Second, a separate dataset of 2,299 herbal bioactive molecules unique to *Commiphora wightii* was retrieved. Rather than screening both libraries simultaneously, the network pharmacology step served as a filter: the Guggul bioactive molecules were docked exclusively against the specific target proteins validated by the FDA reference network. The 3D structures of these ligands were generated using the PubChem database and optimized via MarvinSketch for molecular docking simulations.[54].

Molecular Docking

Molecular docking studies were done with the help of PyRx 0.8, a friendly virtual screening software designed for molecular docking experiments. PyRx, written in Python language, has an easy-to-use GUI and uses Autodock Vina (PyRx 0.8) for effective docking of ligands. The process of molecular docking was performed by creating a model of the target protein as a macromolecule, optimizing energy levels of the ligands, building up grids for defining binding sites, and performing the docking simulation for every combination of ligand and protein. Molecular docking data were used to determine the binding affinity and possible interaction mechanisms between the chosen drugs and corresponding protein targets. Scores of docking and conformations were carefully examined and documented in CSV file format for later analysis. This method combines computer-based technologies with molecular biology and may result in discovering potential drugs to combat RA [55-,57]

Case study

Structure-Based drug design using virtual screening The wild types of human *CD20, TYK2, and IL-6* have been selected with 210, 317, and 299 amino acid lengths, and the crystal structures (PDB ID: 6VJA, 6NZP, and 1P9M, respectively) and retrieved from the Protein Data Bank (PDB) [58-60]. AutoDock FR software was applied to prepare proteins for virtual screening and molecular docking[58]. The ligands (herbal bioactive compounds) were processed by the OpenBabel program to add hydrogen (H) and generate of 3D structure in PDB format. The AutoDock Vina tool [59]was employed to carry out docking studies using the PDBQT files of *CD20, TYK2, and IL-6* structures and ligand library (a total of 2299 molecules). The evaluation of herbal bioactive compounds' properties about Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) and Lipinski's Rules was conducted using the OSIRIS Property Explorer and pkCSM websites [60]. Each docked complex 3D structure was analyzed by applying the PyMOL visualization tool [61].

Physicochemical characteristics and ADMET properties

The OSIRIS Property Explorer and pkCSM were used in this study to evaluate the properties of selected candidates. These properties include several physicochemical properties, among which the following can be mentioned: rotatable bonds, octanol-water partition coefficient, molecular weight, solubility in water, hydrogen bond donors and acceptors, and topological polar surface area. Also, pharmacokinetic properties, such as Caco-2 permeability, P-glycoprotein inhibition, and human intestinal absorption; distribution properties including central nervous system permeability, volume of distribution, and penetration through blood-brain barrier were evaluated in this project. Moreover, the metabolic properties of the candidate molecules have been assessed by considering their inhibitory effects on cytochrome P450 subfamilies. Regarding excretion properties, total clearance and renal OCT2 substrate property have been studied, while toxicity properties such as Ames toxicity, human ether-related gene channels inhibitors, oral rat acute and chronic toxicity, and skin sensitizers have

been considered. Molecular Dynamics (MD) simulations MD simulation of potentially docked complexes were carried out *via* GROMACS-2022 in order to examine the interaction of ligands and receptors under physiological conditions[63,54]. The protein's topology was generated with the OPLS-AA force field54. Ligand molecular topology files were generated using the LigParGen server All systems were solubilized in a cubic box using the TIP3P water model [63], and the systems were neutralized by adding counter ions (Na^+ and Cl^-) at a concentration of 0.15 M. Minimization of energy of the neutralized systems was done by using the techniques of steepest descent and conjugate gradient algorithms. For both of these techniques, 50,000 iterations were used for each one. Equilibration was achieved via carrying out volume and pressure equilibration. Initially, temperature was incrementally increased up to 310 K in NVT ensemble, followed by pressure and density equilibration in NPT ensemble. The simulation times of main runs were conducted for 150 ns for each system. For constraining hydrogen atoms at equilibrium distances, the shake technique was used. Periodic boundary conditions were applied in all of the MD simulations. Electrostatic interactions were calculated by PME technique[64]. Coulombic and van der Waals interactions were cut off at 1.2 nm, and bond lengths and angles were constrained with the LINC algorithm [68]. The data of the MD trajectory was collected at an interval of 10 ps. In order to construct the model of the membrane protein CD20, the CHARMM-GUI server was used, where a membrane bilayer structure was first created, and subsequently, the protein ion channel was embedded in the membrane bilayer by a substitution technique. The CHARMM36 force field was used in this simulation. Analysis of the resulting trajectory data showed that the top candidate complexes achieved equilibrium within the lipid bilayer, maintaining structural stability throughout the simulation run, as evidenced by stable Root Mean Square Deviation (RMSD) profiles, minimal local fluctuations (RMSF), consistent compactness (R_g), and a robust network of intermolecular hydrogen bonds. A total of 512 molecules of POPC (1-Palmitoyl-2-Oleoyl-sn-Glycero-3-Phosphocholine) were used to form the bilayer structure, and thickness of water layers on either side of the membrane bilayer structure was set as 2.2 nm. Equilibration runs were performed by application of positional restraints on protein, lipid, and drug molecules in an NVT-NPT ensemble for 1 ns with standard coupling techniques. Finally, simulation run was performed in a production run for 150 ns without any restraints on the molecules. Analysis of hydrogen bonds (H-bonds), RMSF, RMSD, Radius of gyration (Rg), and RDF was done by using commands in GROMACS gmx h-bond, gmx rmsf, gmx rms, gmx gyrate, and gmx rdf, respectively.

Future Directions

In order to advance computational drug repurposing, combine ML and AI techniques with network pharmacology to improve multi-target prediction capabilities, as seen in recent RA literature where drugs such as Rifampicin have been discovered through PPI networks and MD simulation techniques. Emphasis should be placed on validating the results obtained in experiments, either *in vitro* or *ex vivo* models (e.g. fibroblast synoviocyte models) and clinical trials to validate top hits such as guggulsterones, to overcome the translational challenge in

computational techniques. Future directions include fusing multi-omics datasets (genomics, proteomics) and utilizing deep graph networks to generate analogs *de novo.*

Conclusion

To conclude, the application of computational methods such as network pharmacology, molecular docking, and molecular dynamic simulations provides a promising avenue in the search for new therapeutic targets for drug repurposing in RA treatment. The advantage of this methodology is in its ability to find a multi-target drug with proven safety in a matter of time without going through laborious and lengthy processes of drug development from scratch. In addition to addressing the multifactorial nature and complexity of RA, computational methods allow for a cheaper, yet more precise, way of finding effective drugs to treat autoimmune conditions such as RA.

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AUTHOR CONTRIBUTIONS

JE Rachel Nivedita: Conceptualization, literature search, manuscript drafting, data compilation, and overall coordination of the study.

K. Revathi Sushma: Literature review, content development, data interpretation, and manuscript editing.

Yashi Gangil: Collection and analysis of scientific literature, preparation of figures/tables, and manuscript review.

Safa Hussain: Literature survey, reference management, formatting, and proofreading of the manuscript.

Dr. Likilesha: Study supervision, critical review of the manuscript, scientific validation of the content, and final approval of the manuscript.

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The authors declare that there is no conflict of interest regarding the publication of this manuscript.

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Reference :

(1) Brown P, Pratt AG, Hyrich KL. Therapeutic advances in rheumatoid arthritis. BMJ. 2024:e070856.

(2) Li KH, Kaker M, Lau J, Noonan K, Zhang S, McDermott CL, Lockhart CM. The landscape of real-world evidence of rituximab utilization and clinical outcomes in patients with cancer, rheumatoid arthritis, and multiple sclerosis: A scoping review. *J Manag Care Spec Pharm*. 2024;30(5):480–489.

(3) Jahid M, Khan KU, Rehan-Ul-Haq, Ahmed RS. Overview of rheumatoid arthritis and scientific understanding of the disease. *Mediterr J Rheumatol*. 2023;34(3):284–291.

(4) Cross M, Smith E, Hoy D, Carmona L, Wolfe F, Vos T, Williams B, Gabriel S, Lassere M, Johns N, Buchbinder R, Woolf A, March L. The global burden of rheumatoid arthritis: Estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis*. 2014;73(7):1316–1322.

(5) Hunter TM, Boytsov NN, Zhang X, Schroeder K, Michaud K, Araujo AB. Prevalence of rheumatoid arthritis in the United States adult population in healthcare claims databases, 2004–2014. *Rheumatol Int*. 2017;37(9):1551–1557.

(6) Vellingiri B, V A, I A, B V, V D, C S. AB0206 expression of inflammatory genes and the IL1B gene association with the severity of rheumatoid arthritis in Tamil Nadu population. *Ann Rheum Dis*. 2018;77:1288.

(7) Spinel-Bejarano N, Quintana G, Heredia R, Yunis JJ, Caminos JE, Garcés MF, Rondon F, Iglesias-Gamarra A. Comparative study of elderly-onset rheumatoid arthritis and young-onset rheumatoid arthritis in a Colombian population: Clinical, laboratory and HLA-DRB1 findings. *Clin Exp Rheumatol*. 2013;31:40–46.

(8) Almutairi K, Nossent J, Preen D, Keen H, Inderjeeth C. The global prevalence of rheumatoid arthritis: A meta-analysis based on a systematic review. *Rheumatol Int*. 2021;41(5):863–877.

(9) Van Drongelen V, Holoshitz J. Human leukocyte antigen–disease associations in rheumatoid arthritis. *Rheum Dis Clin*. 2017;43:363–376.

(10) Dedmon LE. The genetics of rheumatoid arthritis. *Rheumatology*. 2020;59(10):2661–2670.

(11) Buch MH, Eyre S, McGonagle D. Persistent inflammatory and non-inflammatory mechanisms in refractory rheumatoid arthritis. *Nat Rev Rheumatol*. 2021;17(1):17–33.

(12) Kingsmore KM, Grammer AC, Lipsky PE. Drug repurposing to improve treatment of rheumatic autoimmune inflammatory diseases. *Nat Rev Rheumatol*. 2020;16:32–52.

(13) Petitdemange A, Blaess J, Sibilia J, Felten R, Arnaud L. Shared development of targeted therapies among autoimmune and inflammatory diseases: A systematic repurposing analysis. *Ther Adv Musculoskelet Dis*. 2020;12:1759720X20969261.

(14) Grammer AC, Lipsky PE. Drug repositioning strategies for the identification of novel therapies for rheumatic autoimmune inflammatory diseases. *Rheum Dis Clin N Am*. 2017;43(3):467–480.

(15) Unal U, Comertpay B, Demirtas TY, Gov E. Drug repurposing for rheumatoid arthritis: Identification of new drug candidates via bioinformatics and text mining analysis. *Autoimmunity*. 2022;55(3):147–156.

(16) Favalli EG, Ingegnoli F, De Lucia O, Cincinelli G, Cimaz R, Caporali R. Repurposing of biologic and targeted synthetic anti-rheumatic drugs in COVID-19 and hyper-inflammation: A comprehensive review of available and emerging evidence at the peak of the pandemic. *Front Pharmacol*. 2020;11:598308.

(17) Ding Q, Hu W, Wang R, Yang Q, Zhu M, Li M, Cai J, Rose P, Mao J, Zhu YZ. Signaling pathways in rheumatoid arthritis: Implications for targeted therapy. *Signal Transduct Target Ther*. 2023;8:68.

(18) Huang J, Fu X, Chen X, Li Z, Huang Y, Liang C. Promising therapeutic targets for treatment of rheumatoid arthritis. *Front Immunol*. 2021;12:686155.

(19) Jouybari MT, Mojtahedi F, Babaahmadi M, Faeed M, Eslaminejad MB, Taghiyar L. Advancements in extracellular vesicle targeted therapies for rheumatoid arthritis: Insights into cellular origins, current perspectives, and emerging challenges. *Stem Cell Res Ther*. 2024;15(1):276.

(20) Gao Y, Zhang Y, Liu X. Rheumatoid arthritis: Pathogenesis and therapeutic advances. *MedComm*. 2024;5:e509.

(21) Selvaraj N, Swaroop AK, Kumar RR, Natarajan J, Selvaraj J. Network-based drug repurposing: A critical review. *Curr Drug Res Rev*. 2022;14:116–131.

(22) Sundar P, Girija K, Pradheesh SJ, Shanthoshivan AG, Akashwaran S, Swaroop AK. Drug repurposing of daclatasvir and famciclovir as antivirals against dengue virus infection by in silico and in vitro techniques. *Indian J Biochem Biophys*. 2021;58:557–564.

(23) Xu R, Wang Q. A genomics-based systems approach towards drug repositioning for rheumatoid arthritis. *BMC Genomics*. 2016;17(S7):518.

(24) Unal U, Comertpay B, Demirtas TY, Gov E. Drug repurposing for rheumatoid arthritis: Identification of new drug candidates *via* bioinformatics and text mining analysis. *Autoimmunity*. 2022;55(3):147–156.

(25) Liu C, Fan F, Zhong L, Su J, Zhang Y, Tu Y. Repurposing of pirfenidone (anti-pulmonary fibrosis drug) for treatment of rheumatoid arthritis. *Front Pharmacol*. 2021;12:631891.

(26) Wu M, Wu H, Wu L, Cui C, Shi S, Xu J, Liu Y, Dong F. A deep learning classification of metacarpophalangeal joints synovial proliferation in rheumatoid arthritis by ultrasound images. *J Clin Ultrasound*. 2022;50(2):296–301.

(27) Wu M, Wu H, Wu L, Cui C, Shi S, Xu J, Liu Y, Dong F. A deep learning classification of metacarpophalangeal joints synovial proliferation in rheumatoid arthritis by ultrasound images. *J Clin Ultrasound*. 2022;50(2):296–301.

(28) Steunebrink LMM, Versteeg GA, Vonkeman HE, Ten Klooster PM, Kuper HH, Zijlstra TR, van Riel PLCM, van de Laar MAFJ. Initial combination therapy *versus* step-up therapy in treatment to the target of remission in daily clinical practice in early rheumatoid arthritis patients: Results from the DREAM registry. *Arthritis Res Ther*. 2016;18:60.

(29) Jain S, Gupta S, Sahu N. Formulation and evaluation of TDDS of Indian medicinal plant. *Int J Drug Discov Herb Res*. 2021;11:1003–1010.

(30) Sharma R, Bhat ZF, Kumar A, Kumar S, Bekhit AEDA. Characterization of *Commiphora wightii*-based bioactive edible film and its efficacy for improving the storage quality of meat products. *J Food Saf*. 2021;41.

(31) Zhu N, Rafi MM, DiPaola RS, Xin J, Chin CK, Badmaev V, Ghai G, Rosen RT, Ho CT. Bioactive constituents from gum guggul (*Commiphora wightii*). *Phytochemistry*. 2001;56(7):723–727.

(32) Chandran H, Meena M, Barupal T, Sharma K. Plant tissue culture as a perpetual source for production of industrially important bioactive compounds. *Biotechnol Rep*. 2020;26:e00450.

(33) Vyas KY, Bedarkar P, Galib R, Prajapati PK. Comparative anti-hyperlipidaemic activity of Navīna (fresh) and Purāṇa (old) Guggulu. *Anc Sci Life*. 2015;35(2):101–109.

(34) Bin Sayeed MS, Karim SMR, Sharmin T, Morshed MM. Critical analysis on characterization, systemic effect, and therapeutic potential of beta-sitosterol: A plant-derived orphan phytosterol. *Medicines*. 2016;3(4):29.

(35) Shishodia S, Aggarwal BB. Guggulsterone inhibits NF-kappaB and IkappaBalpha kinase activation, suppresses expression of anti-apoptotic gene products, and enhances apoptosis. *J Biol Chem*. 2004;279(45):47148–47158.

(36) Francis JA, Raja SN, Nair MG. Bioactive terpenoids and guggulusteroids from *Commiphora mukul* gum resin of potential anti-inflammatory interest. *Chem Biodivers*. 2004;1(11):1842–1853.

(37) Kunnumakkara AB, Banik K, Bordoloi D, Harsha C, Sailo BL, Padmavathi G, Roy NK, Gupta SC, Aggarwal BB. Googling the Guggul (*Commiphora* and *Boswellia*) for prevention of chronic diseases. *Front Pharmacol*. 2018;9:686.

(38) Jiang Y, Zhong M, Long F, Yang R, Zhang Y, Liu T. Network pharmacology-based prediction of active ingredients and mechanisms of *Lamiophlomis rotata* against rheumatoid arthritis. *Front Pharmacol*. 2019;10:1435.

(39) Liu C, Fan F, Zhong L, Su J, Zhang Y, Tu Y. Elucidating the material basis and potential mechanisms of Ershiwuwei Lvxue Pill acting on rheumatoid arthritis by UPLC-Q-TOF/MS and network pharmacology. *PLoS One*. 2022;17(2):e0262469.

(40) Zhang L, Cao Z, Yang Y, Tan X, Mao J, Su L. Traditional Chinese medicine on treating active rheumatoid arthritis: A protocol for systematic review and meta-analysis. *Medicine (Baltimore)*. 2020;99(24):e20642.

(41) Sun Y, Huang Y, Chen T, Li X, Chen J, Wang Z, Lin K, Gao Y, He L. Effect of downregulation of serum MMP-3 levels by traditional Chinese medicine ingredients combined with methotrexate on the progression of bone injury in patients with rheumatoid arthritis: A protocol for a systematic review and meta-analysis. *Medicine (Baltimore)*. 2020;99(43):e22841.

(42) Wang T, Jia Q, Chen T, Yin H, Tian X, Lin X, Liu Y, Zhao Y, Wang Y, Shi Q, Huang C, Xu H, Liang Q. Alleviation of synovial inflammation of Juanbi-Tang on collagen-induced arthritis and TNF-Tg mice model. *Front Pharmacol*. 2020;11:45.

(43) Li J, Li L, Wang Y, Zhao Y, Hu P, Xu Z, Liu F, Liang Q, Tian X, Huang C. Systematic investigation on the anti-rheumatoid arthritis material basis and mechanism of Juan Bi Tang. Part 1: Integrating metabolic profiles and network pharmacology. *J Pharm Biomed Anal*. 2021;202:114133.

(44) Liu X, Wang YQ, Cai L, Ye LH, Wang F, Feng YY. Effect of Wenhua Juanbi Recipe on expression of receptor activator of nuclear factor kappa B ligand, osteoprotegerin, and tumor necrosis factor receptor superfamily member 14 in rats with collagen-induced arthritis. *Chin J Integr Med*. 2017;23(3):208–214.

(45) Zhao L, Zhang H, Li N, Chen J, Xu H, Wang Y, Liang Q. Network pharmacology, a promising approach to reveal the pharmacology mechanism of Chinese medicine formula. *J Ethnopharmacol*. 2023;309:116306.

(46) Zhao L, Zhang H, Li N, Chen J, Xu H, Wang Y, Liang Q. Network pharmacology, a promising approach to reveal the pharmacology mechanism of Chinese medicine formula. *J Ethnopharmacol*. 2023;309:116306.

(47) Zhang M, Lou H, Ma J, Xiong K, Hou X. Network pharmacology and molecular docking approaches predict the mechanisms of *Coridiidius chinensis* in treating manganese-induced nervous system diseases: A review. *Medicine (Baltimore)*. 2023;102(43):e35669.

(48) Wang Y, Cui T, Li Y, Liao M, Zhang H, Hou W, Zhang T, Liu L, Huang H, Liu C. Prediction of quality markers of traditional Chinese medicines based on network pharmacology. *Chin Herb Med*. 2019;11(4):349–356.

(49) Krishna Swaroop AK, Krishnan Namboori PK, Esakkimuthukumar M, Praveen TK, Nagarjuna P, Patnaik SK, Selvaraj J. Leveraging decagonal *in-silico* strategies for uncovering IL-6 inhibitors with precision. *Comput Biol Med*. 2023;163:107231.

(50) Elangovan S, et al. Vitamin D analog calcitriol for breast cancer therapy: An integrated drug discovery approach. *J Biomol Struct Dyn*. 2023;41(20).

(51) Dharmaraj S, Swaroop AK, Esakkimuthukumar M, Negi P, Jubie S. *In-silico* design and development of novel hydroxyurea lipid drug conjugates for breast cancer therapy targeting PI3K/AKT/mTOR pathway. *Drug Res*. 2024;74(1):32–41.

(52) Mariappan E, Swaroop AK, Negi P, RajanBabu S, Murugesan DK, Varma NP, Selvaraj J. Identification of effective natural compounds as HIF-1Alpha mimetics for diabetic wound healing: A systematic *in-silico* study. *J Appl Pharm Sci*. 2023;13(1):041–050.

(53) Kar A, Paramasivam B, Jayakumar D, Swaroop AK, Selvaraj J. Drug repurposing for thioredoxin interacting protein through molecular networking, pharmacophore modelling, and molecular docking approaches.

(54) Patnaik SK, Swaroop AK, Naik MR, Selvaraj J, Chandrasekar MJN. Repurposing of FDA-approved drugs and neuropep peptides as anticancer agents against ErbB1 and ErbB2. *Drug Res*. 2023;73(6):341–348.

(55) Esakkimuthukumar M, Swaroop AK, Patnaik SK, Kumar R, Praveen TK, Naik MR, Jubie S. A novel family of small molecule HIF-1 alpha stabilizers for the treatment of diabetic wounds: An integrated *in silico, in vitro,* and *in vivo* strategy. *RSC Adv*. 2022;12:31293–31302.

(56) Boulanger MJ, Chow D, Brevnova EE, Garcia KC. Hexameric structure and assembly of the interleukin-6/IL-6 alpha-receptor/Gp130 complex. *Science*. 2003;300(5628):2101–2104.

(57) Rougé L, Chiang N, Steffek M, Kugel C, Croll TI, Tam C, Estevez A, Arthur CP, Koth CM, Ciferri C, Kraft E, Payandeh J, Nakamura G, Koerber JT, Rohou A. Structure of CD20 in complex with the therapeutic monoclonal antibody rituximab. *Science*. 2020;367(6483):1224–1230.

(58) Wrobleski ST, Moslin R, Lin S, Zhang Y, Spergel S, Kempson J, Tokarski JS, Strnad J, Zupa-Fernandez A, Cheng L, Shuster D, Gillooly K, Yang X, Heimrich E, McIntyre KW, Chaudhry C, Khan J, Ruzanov M, Tredup J, Mulligan D, Xie D, Sun H, Huang C, D'Arienzo C, Aranibar N, Chiney M, Chimalakonda A, Pitts WJ, Lombardo L, Carter PH, Burke JR, Weinstein DS. Highly selective inhibition of Tyrosine Kinase 2 (TYK2) for the treatment of autoimmune diseases: Discovery of the allosteric inhibitor BMS-986165. *J Med Chem*. 2019;62(20):8973–8995.

(59) Ravindranath PA, Forli S, Goodsell DS, Olson AJ, Sanner MF. AutoDockFR: Advances in protein-ligand docking with explicitly specified binding site flexibility. *PLoS Comput Biol*. 2015;11(12):e1004586.

(60) Trott O, Olson AJ. AutoDock Vina: Improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. *J Comput Chem*. 2010;31(2):455–461.

(61) Pires DEV, Blundell TL, Ascher DB. pkCSM: Predicting small-molecule pharmacokinetic and toxicity properties using graph-based signatures. *J Med Chem*. 2015;58(9):4066–4072.

(62) Behmard E, Ghasemian A, Barzegari E, Farjadfar A, Kouhpayeh A, Najafipour S. Advanced simulations and screening to repurposing a 3C protease inhibitor against the rupintrivir-resistant human norovirus-induced gastroenteritis. *J Mol Graph Model*. 2023;118:108345.

(63) Abraham MJ, Murtola T, Schulz R, Páll S, Smith JC, Hess B, Lindahl E. GROMACS: High performance molecular simulations through multi-level parallelism from laptops to supercomputers. *SoftwareX*. 2015;1:19–25.

(64) Mark P, Nilsson L. Structure and dynamics of the TIP3P, SPC, and SPC/E water models at 298 K. *J Phys Chem A*. 2001;105(43):9954–9960.

(65) Essmann U, Perera L, Berkowitz ML, Darden T, Lee H, Pedersen LG. A smooth particle mesh Ewald method. *J Chem Phys*. 1995;103(19):8577–8593.

(66) Hess B, Bekker H, Berendsen HJC, Fraaije JGEM. LINCS: A linear constraint solver for molecular simulations. *J Comput Chem*. 1997;18(12):1463–1472.

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