OROXYLIN A, AS A POTENTIAL INHIBITOR OF RHEUMATOID ARTHRITIS: IN SILICO EXPERIMENT BASED ON NETWORK PHARMACOLOGY AND MOLECULAR DOCKING

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ABSTRACT

Oroxylin A is a potential inhibitory compound that could be applied to treat rheumatoid arthritis (RA). Rheumatoid arthritis is a chronic, systemic autoimmune disease that can lead to joint damage, deformity, and disability if not effectively treated. Current research utilizes network pharmacology and molecular docking methods to predict the primary mechanism of action of oroxylin A against rheumatoid arthritis. Through screening via protein-protein interaction networks (PPI), 67 potential RA-related targets have been identified, with EGFR, PTGS2, ESR1, MMP9, and GSK3B potentially serving as central targets. KEGG pathway analysis indicates that these 67 potential targets are associated with pathways related to metabolism, pathways in cancer, PI3K-Akt signalling pathway, Ras signalling pathway, and microRNAs in cancer. Molecular docking has been applied to determine the binding mode and affinity of oroxylin A with these five central RA-related targets. These findings offer the potential to inhibit relevant biological targets and provide a basis for further research into the mechanism of oroxylin A against RA.

Keywords: Oroxylin A; rheumatoid arthritis; network pharmacology; molecular docking.

1. Introduction

Rheumatoid arthritis (RA) is a multifactorial autoimmune disease characterized by inflammatory infiltration of the synovial membrane, synovial hyperplasia, joint degradation, and loss of joint function [1]. Globally, rheumatoid arthritis affects an estimated 17.6 million people [2]. The debilitating impact and resulting disability of rheumatoid arthritis impose significant burdens on clinical, economic, and social aspects. Its pathogenic mechanisms are complex, poorly understood, and influenced by various factors. Currently, crucial events in the pathobiology of RA involve the proliferation of synovial membrane cells, including fibroblast-like synoviocytes, macrophages, and lymphocytes. Studies have shown that fibroblast-like synoviocytes play an dominant role in RA progression [3].

In the treatment of rheumatoid arthritis, disease-modifying antirheumatic drugs (DMARDs) have been widely used alongside nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids to assist in reducing inflammation and controlling symptoms [4]. Common DMARDs include hydroxychloroquine, methotrexate, sulfasalazine, and leflunomide, most of which come with frequent side effects, including gastrointestinal reactions, renal damage, and cardiovascular risks [5]. Therefore, there is a pressing need for safe and effective treatment methods from natural active compounds derived from medicinal plants for rheumatoid arthritis.

Oroxylin A, a plant-derived *O*-methylated flavone belongings to the flavonoid group, was first isolated from *Oroxylum indicum* [6]. The chemical structure of oroxylin A is presented in Figure 1. Over the years, oroxylin A has been found to exist widely in various medicinal plants such as *Anchietea pyrifolia, Aster himalaicus, Scutellaria lateriflora*, *Scutellaria barbata*, and *Scutellaria radix* [7]. Oroxylin A has demonstrated diverse pharmacological properties, including anti-inflammatory, anti-cancer, neuroprotective, anticoagulant, anti-viral... In particular, studies on the therapeutic potential of oroxylin A in treating rheumatoid arthritis have shown a significant reduction in serum anti-collagen type II antibodies, IL-1β, IL-6, TNFα, and IL-17. Oroxylin A reduced the secretion of IL-1β and IL-6 from RA FLS stimulated by TNFα in a dose-dependent manner. Oroxylin A also inhibited the TNFα-induced p38 MAPK, ERK1/2, and NF-κB signaling pathways [8]. However, despite extensive research on the pharmacological effects of oroxylin A, the potential targets and fundamental molecular mechanisms of oroxylin A in RA remain limited.

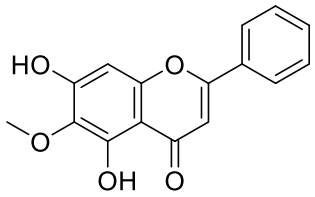


Figure 1: *The chemical structure of oroxylin A*

2. Materials and methods

2.1. Prediction of the targets of oroxylin A and rheumatoid arthritis

The canonical simplified molecular-input line-entry system (SMILES) format of the compound oroxylin A was collected by inputting it into the PubChem database (https://pubchem.ncbi.nlm.nih.gov/compound/5320315). Once this format was obtained, the SwissTargetPrediction database (http://www.swisstargetprediction.ch/) was utilized to predict and select potential targets for oroxylin A.

To identify potential therapeutic targets related to rheumatoid arthritis, the GeneCards database (https://www.genecards.org/) was employed to search and export the recorded results in *.xlsx format (for Excel software). Subsequently, the relevant targets for rheumatoid arthritis and the predicted targets of oroxylin A were input into the online tool Venny 2.1 (https://bioinfogp.cnb.csic.es/tools/venny/) to generate a Venn diagram and extract the intersection of gene combinations between oroxylin A and rheumatoid arthritis.

2.2. Protein-protein interaction (PPI) network construction and screening of core cross targets of AM in the treatment of vitiligo and COVID-19

A PPI network of the ingredient oroxylin A crossover gene for rheumatoid arthritis was created using the STRING database (https://stringdb.org/) to investigate protein-protein interactions at crossover sites. The parameters were left at their default settings, with "Homo sapiens" chosen under the organism parameter and "Medium confidence of 0.400" under the "Minimum required interaction score" option. Then, using the Cytoscape software's Cytohubba plugin, the top 5 key crossover genes were selected for further research [9].

2.3. GO enrichment and KEGG pathway analysis

Crossover genes were imported into the DAVID database to investigate GO and KEGG analysis (https://david.ncifcrf.gov/). Whereas "Homo sapiens" was chosen for GO annotation and KEGG pathway enrichment analysis of the targets at P value < 0.05, and "OFFICIAL_GENE_ SYMBOL" was chosen as the "Select Identifier". The results were visualized and evaluated using the bioinformatics website (http://www.bioinformatics.com.cn/), focusing on the top 10 ranking items.

2.4. Molecular docking

To investigate the relationship between oroxylin A and hub targets, molecular docking analysis was applied using the AutoDock Vina v1.2.5 program [10]. The chemical structure of oroxylin A was drawn using Marvin JS software (https://marvinjs-demo.chemaxon.com/). Subsequently, it was converted into a 3D structure and energy-minimized using the MMFF94s force field with the OpenBabel software. The crystal structures of the five hub targets were downloaded from the RCSB PDB protein database (https://www.rcsb.org/). The grid box parameters for the docking process are presented in Supplementary Figure S1. The exhaustiveness value was set to 400 for the docking process of the studied systems. The binding interaction modes of oroxylin A with the hub targets were visualized using Discovery Studio Visualizer software.

3. Result and discussion

Network pharmacology is recognized as an advanced and comprehensive approach to drug discovery and development due to pharmacology and systems biology integration. In contrast to the traditional single-target pharmacology approach, network pharmacology delves into the intricate interactions among drugs, targets, and biological pathways within living organisms [11]. It allows for identifying key nodes in complex biological networks, providing a more comprehensive understanding of the potential pharmacological effects of drugs or bioactive compounds [12]. Therefore, this study employed network pharmacology techniques to predict multiple interactions between oroxylin A and potential targets that could be key to rheumatoid arthritis.

Based on statistical factors, a total of 100 predicted *Homo sapiens* targets for oroxylin A were obtained from the SwissTargetPrediction database, detailed in Supplementary Table S1. The GeneCards database was used to collect 4,172 proteins related to rheumatoid arthritis. From the collected data, a Venn diagram was applied to calculate the intersection between target genes of oroxylin A and rheumatoid arthritis, as shown in Figure 2. The results revealed 67 common targets extracted from the intersection

of the Venn diagram. Oroxylin A acts on these targets, ultimately achieving its therapeutic effect on rheumatoid arthritis.

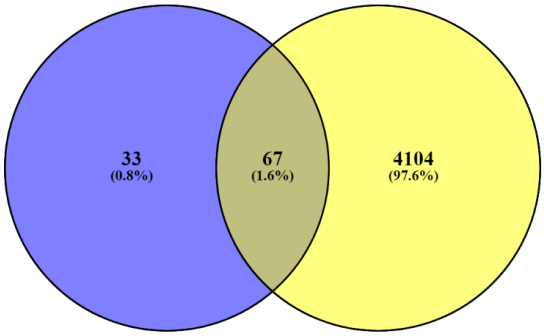


Figure 2: *The intersection of targets of Oroxylin A and Rheumatoid Arthritis*

Next, a protein-protein interaction (PPI) network was constructed from the 67 potential therapeutic targets using the STRING database to elucidate the relationships between targets related to rheumatoid arthritis and oroxylin A. Nodes in the PPI network represent interactions during the development of rheumatoid arthritis. The PPI network comprises 67 nodes and 332 edges, visualized using Cytoscape 3.9.1 (Figure 3). Subnetworks and hub targets were identified using the CytoNCA plug-in with Degree Centralities (DC) analysis. The ranking results by DC are presented in Supplementary Table S2. As shown in Figure 3, a subnetwork consisting of 5 nodes and 10 edges was identified. Furthermore, EGFR, PTGS2, ESR1, MMP9, and GSK3B were identified as hub targets with the highest DC values of 39, 36, 33, 30, and 25, respectively, in oroxylin A's effect on rheumatoid arthritis.

The epidermal growth factor receptor (EGFR) has been demonstrated as a therapeutic target in rheumatoid arthritis, as it induces proliferation and cytokine production in fibroblast-like synoviocytes [13]. In the synovial tissues, the enzyme COX-2 also shows increased expression. MMP, a zinc-dependent endopeptidase belonging to the metzincin superfamily of proteases, is produced by various cells and tissues to participate in the degradation and remodelling of the extracellular matrix (ECM). In rheumatoid arthritis (RA), MMP plays a crucial role, causing a degradation of ECM and significantly impacting the integrity of synovial fluid, cartilage, and bone tissues. MMP can cleave non-matrix components in the extracellular environment, such as cell surface receptors, cytokines, chemokines, and other proteinases, contributing to inflammation and immune response in RA. MMP can also directly activate signalling molecules, such as TNF, contributing to various aspects of immune response in RA. The role of MMP in the development and inflammatory response of immune cells has attracted attention, opening up the potential for targeting MMP as a new treatment strategy in the clinical management of RA [14].

Glycogen synthase kinase three beta (GSK3β), a negative regulator of intracellular glucose balance, is also involved in energy metabolism, inflammation, and cell apoptosis. In RA, the inactivation of GSK3β is identified as an important regulatory factor for the metabolic reprogramming of synoviocytes, particularly in the synovial fluid of RA. GSK3β-Ser9 plays a role in preventing the activation of transcription factors and maintaining calcium transport stability, providing a crucial mechanism to promote destructive tissue effects [15].

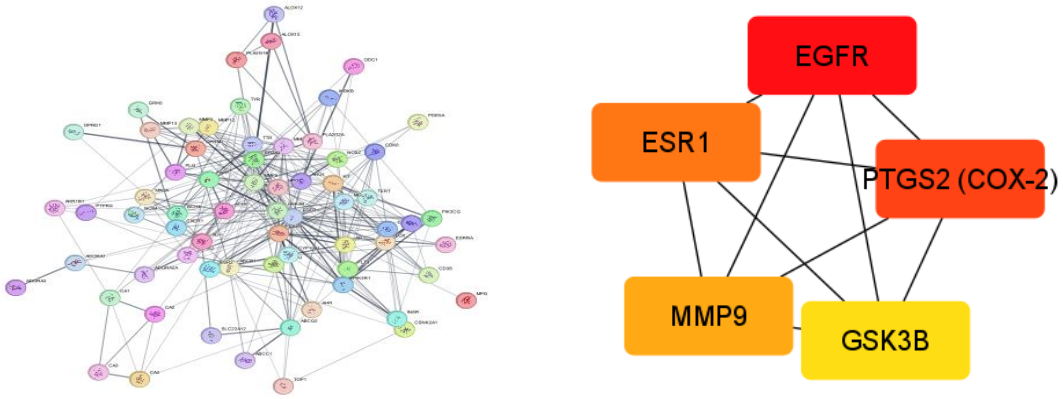


Figure 3: *The PPI network and the identified hub targets*

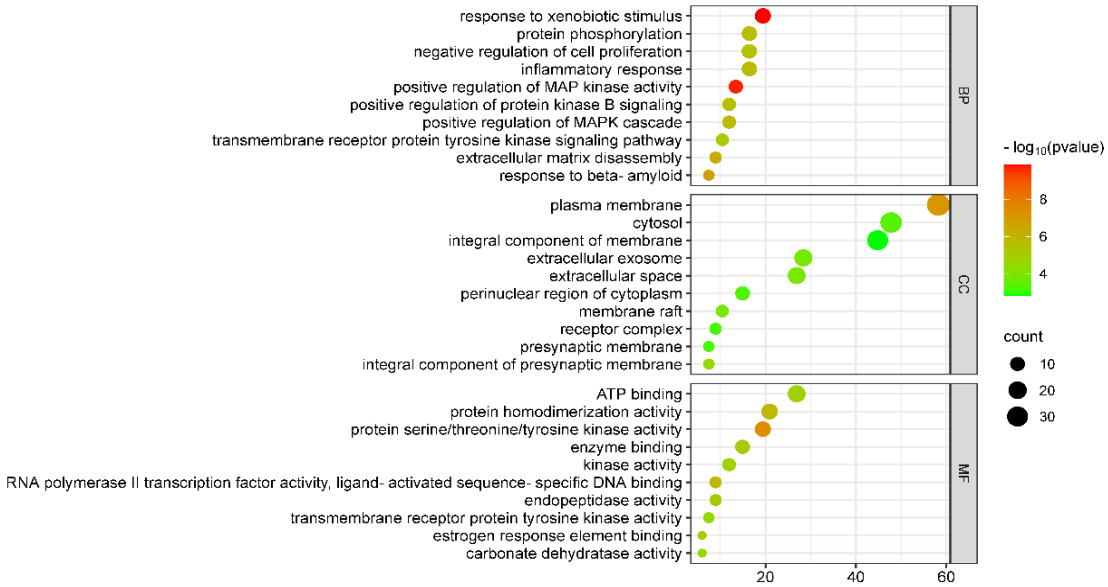


Figure 4: *GO analysis of potential targets*

The DAVID database revealed the molecular functions, cellular components, biological processes, and metabolic pathway annotations of the selected 67 targets (supporting information in Supplementary Table S1). 347 GO terms were identified and represented the top 10 terms for each GO in Figure 4, with 220 terms connected to biological processes, 78 to molecular functions, and 49 to cell components. These terms include responses to xenobiotic stimulus, positive regulation of MAP kinase activity, response to beta-amyloid, protein serine/threonine/tyrosine kinase activity, RNA polymerase II transcription factor activity, ligand-activated sequence-specific DNA binding, and more.

In addition, 75 pathways were found to be associated with the 67 filtered protein targets through KEGG analysis (Figure 5, showing the top 20), including Pathways in cancer, PI3K-Akt signalling pathway, Prostate cancer, Nitrogen metabolism, and Ras signalling pathway. These results suggest that oroxylin A may play a role in treating rheumatoid arthritis by regulating signalling pathways.

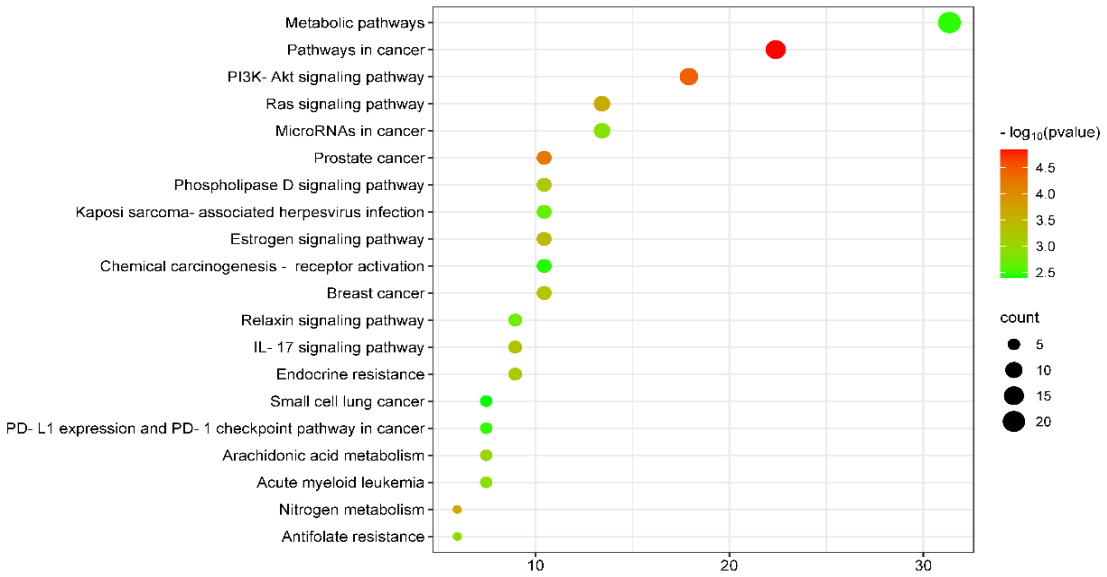


Figure 5: *KEGG analysis of potential targets*

Molecular docking research has been applied to gain insights into the interaction mechanisms and binding affinities of oroxylin A with hub targets, including EGFR (PDB ID: 4HJO), PTGS2 (PDB ID: 5KIR), ESR1 (PDB ID: 3ERT), MMP9 (PDB ID: 4WZV), and GSK3B (PDB ID: 6Y9R), which play a crucial role in combating rheumatoid arthritis. The results of the docking simulations of this compound with the five central targets are described in Figure 6.

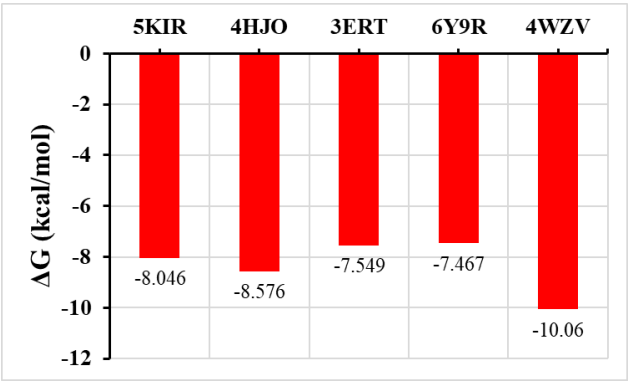
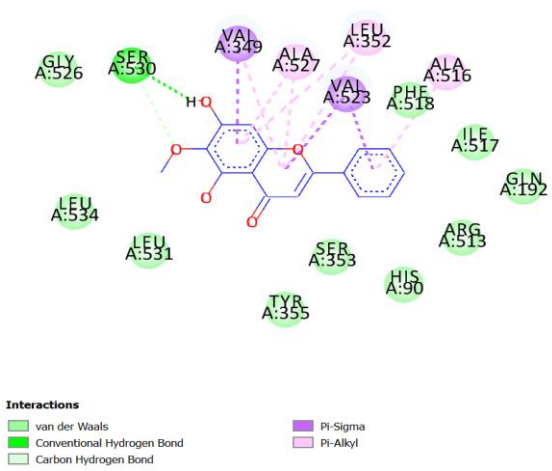


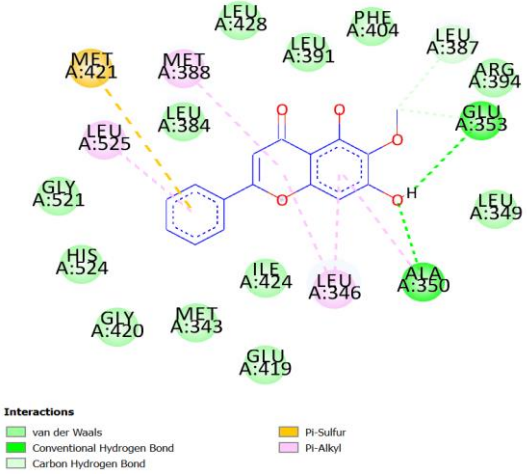
Figure 6: *Binding affinity of oroxylin A with hub targets EGFR (PDB ID: 4HJO), PTGS2 (PDB ID: 5KIR), ESR1 (PDB ID: 3ERT), MMP9 (PDB ID: 4WZV), and GSK3B (PDB ID: 6Y9R)*

Oroxylin A demonstrates strong binding capabilities to all five key targets (PDB IDs: 5KIR, 4HJO, 3ERT, 6Y9R, 4WZV) with binding affinities of -8.576, -8.046, -7.549, -7.467, and -10.06 kcal/mol, respectively. The complex of oroxylin A with MMP9 shows the highest binding energy. Target proteins and small molecules' binding modes are visualized using Discovery Studio Visualizer software, as detailed in Figure 7. In the analysis in Figure 6, oroxylin A forms hydrogen bond interactions with a Ser530 residue.

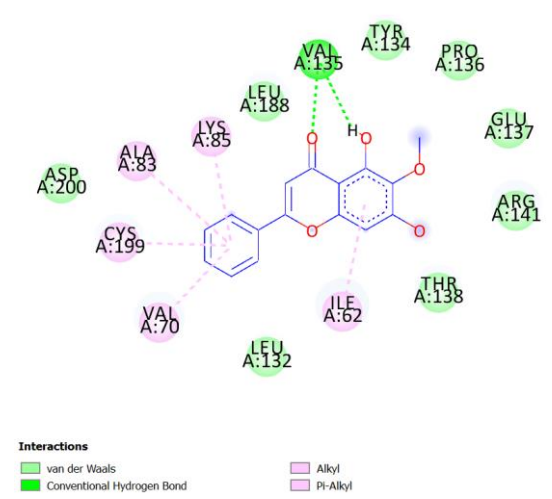
Additionally, pi-sigma interactions at Val349 and Val523, and pi-alkyl interactions at Ala527, Leu352, and Ala516 are formed in the Oroxylin A-COX-2 complex. These interactions at amino acid residues Val349, Leu352, and Val523 are also observed in the active site of the COX-2 enzyme when a known inhibitor like rofecoxib forms binding interactions. Regarding the complex with ESR1, oroxylin A establishes two hydrogen bonds with Ala350 and Glu353, where the interaction with Glu353 residue is also found in the active region of the protein when a known inhibitor, 4-hydroxytamoxifen, forms bonds. In the complex with GSK3B, a hydrogen bond is formed similarly to a derivative of 1H-indazole-3-carboxamide, a known inhibitor interacting with Val135 residue. Oroxylin A forms hydrogen bonds with three amino acid residues of the EGFR protein, including Leu764, Lys721, and Asp831, while it only forms one hydrogen bond with Pro246 of the MMP9 protein. Additionally, hydrophobic interactions in both EGFR and MMP9 complexes with oroxylin A also appear concerning corresponding reference compounds. These results suggest that using oroxylin A may affect all the mentioned key targets, guiding rheumatoid arthritis treatment.



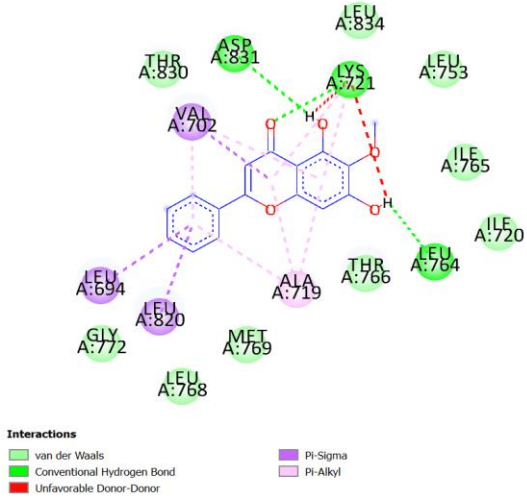
oroxylin A-COX-2



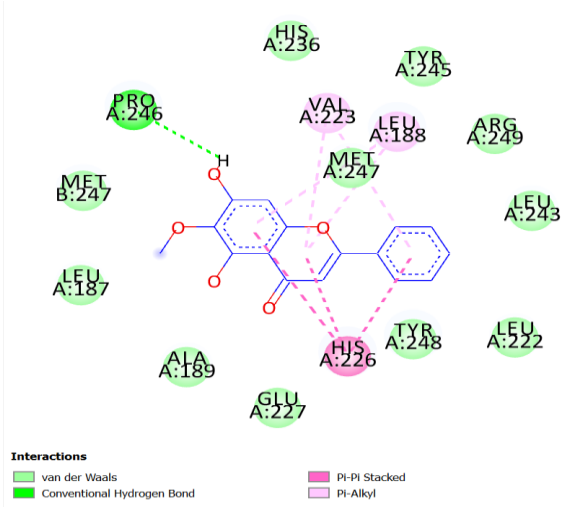
oroxylin A-ESR1



oroxylin A-GSK3β



oroxylin A-EGFR



oroxylin A-MMP9

Figure 7: *Docking complexes of oroxylin A and the studied proteins and their binding residues are shown using Discovery Studio Visualizer software*

4. Conclusion

In this study, the complex mechanism of oroxylin A in treating rheumatoid arthritis (RA) was investigated through network pharmacology and molecular docking approaches. The results revealed that EGFR, PTGS2, ESR1, MMP9, and GSK3B are crucial genes potentially treating RA by disabling signalling pathways related to metabolism, pathways in cancer, and PI3K-Akt signalling. Furthermore, molecular docking simulations showed that oroxylin A has a strong affinity for hub targets, with binding energies ranging from -7.467 to -10.06 kcal/mol. These findings may guide further research to elucidate the molecular targets of oroxylin A related to RA and the applications of pharmacological networks in drug discovery.

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Table. S1: *The potential targets of Oroxylin A*

Targets	UniProt ID	Protein names
FLT3	P36888	Tyrosine-protein kinase receptor FLT3
NOS2	P35228	Nitric oxide synthase, inducible
PTGS2	P35354	Cyclooxygenase-2
ABCB1	P08183	P-glycoprotein 1
KIT	P10721	Stem cell growth factor receptor
OPRD1	P41143	Delta opioid receptor

Targets	UniProt ID	Protein names
KDM4E	B2RXH2	Lysine-specific demethylase 4D-like
XDH	P47989	Xanthine dehydrogenase
ALOX15	P16050	Arachidonate 15-lipoxygenase
CDK1	P06493	Cyclin-dependent kinase 1
ALOX12	P18054	Arachidonate 12-lipoxygenase
GRK6	P43250	G protein-coupled receptor kinase 6
PIM1	P11309	Serine/threonine-protein kinase PIM1
ADORA1	P30542	Adenosine A1 receptor
ADORA2A	P29274	Adenosine A2a receptor
ESR2	Q92731	Estrogen receptor beta
AKR1B1	P15121	Aldose reductase
LCK	P06239	Tyrosine-protein kinase LCK
PTPRS	Q13332	Receptor-type tyrosine-protein phosphatase S
ESR1	P03372	Estrogen receptor alpha
ADORA3	P0DMS8	Adenosine A3 receptor
CYP1B1	Q16678	Cytochrome P450 1B1
HSD17B1	P14061	Estradiol 17-beta-dehydrogenase 1
MAOA	P21397	Monoamine oxidase A
SYK	P43405	Tyrosine-protein kinase SYK
AKR1B10	O60218	Aldo-keto reductase family 1 member B10
ABCG2	Q9UNQ0	ATP-binding cassette sub-family G member 2
AR	P10275	Androgen Receptor
PLG	P00747	Plasminogen
CDK5R1 CDK5	Q15078 Q00535	Cyclin-dependent kinase 5/CDK5 activator 1
CYP19A1	P11511	Cytochrome P450 19A1
CA2	P00918	Carbonic anhydrase II
CCNB3 CDK1 CCNB1 CCNB2	Q8WWL7 P06493 P14635 O95067	Cyclin-dependent kinase 1/cyclin B
CA7	P43166	Carbonic anhydrase VII
CDK6	Q00534	Cyclin-dependent kinase 6
CA1	P00915	Carbonic anhydrase I
CA12	O43570	Carbonic anhydrase XII
CA9	Q16790	Carbonic anhydrase IX
CA4	P22748	Carbonic anhydrase IV
CBR1	P16152	Carbonyl reductase [NADPH] 1
IKBKB	O14920	Inhibitor of nuclear factor kappa B kinase beta subunit

Targets	UniProt ID	Protein names
NTRK2	Q16620	Neurotrophic tyrosine kinase receptor type 2
ODC1	P11926	Ornithine decarboxylase
MMP12	P39900	Matrix metalloproteinase 12
CD38	P28907	Lymphocyte differentiation antigen CD38
TOP1	P11387	DNA topoisomerase I
ARG1	P05089	Arginase-1
MMP9	P14780	Matrix metalloproteinase 9
MMP2	P08253	Matrix metalloproteinase 2
PIK3CG	P48736	PI3-kinase p110-gamma subunit
GSK3B	P49841	Glycogen synthase kinase-3 beta
ABCC1	P33527	Multidrug resistance-associated protein 1
CALM1	P62158	Calmodulin
PLA2G2A	P14555	Phospholipase A2 group IIA
ACHE	P22303	Acetylcholinesterase
SLC22A12	Q96S37	Solute carrier family 22 member 12
TERT	O14746	Telomerase reverse transcriptase
AMY1A	P04745	AMY1C
TNKS	O95271	Tankyrase-1
TTR	P02766	Transthyretin
HSD17B2	P37059	Estradiol 17-beta-dehydrogenase 2
TYR	P14679	Tyrosinase
AHR	P35869	Aryl hydrocarbon receptor
ESRRA	P11474	Estrogen-related receptor alpha
PDE5A	O76074	Phosphodiesterase 5A
APP	P05067	Beta amyloid A4 protein
MCL1	Q07820	Induced myeloid leukemia cell differentiation protein Mcl-1
NAE1	Q13564	NEDD8-activating enzyme E1 regulatory subunit
EGFR	P00533	Epidermal growth factor receptor erbB1
SIGMAR1	Q99720	Sigma opioid receptor
TNKS2	Q9H2K2	Tankyrase-2
NOX4	Q9NPH5	NADPH oxidase 4
CYP1A1	P04798	Cytochrome P450 1A1
OPRM1	P35372	Mu opioid receptor
CXCR1	P25024	Interleukin-8 receptor A
CSNK2A1	P68400	Casein kinase II alpha
MAPT	P10636	Microtubule-associated protein tau
TOP2A	P11388	DNA topoisomerase II alpha
INSR	P06213	Insulin receptor
MYLK	Q15746	Myosin light chain kinase, smooth muscle

Targets	UniProt ID	Protein names
MPO	P05164	Myeloperoxidase
PIK3R1	P27986	PI3-kinase p85-alpha subunit
DAPK1	P53355	Death-associated protein kinase 1
PYGL	P06737	Liver glycogen phosphorylase
MMP13	P45452	Matrix metalloproteinase 13
MMP3	P08254	Matrix metalloproteinase 3
CA3	P07451	Carbonic anhydrase III
CA14	Q9ULX7	Carbonic anhydrase XIV
CA13	Q8N1Q1	Carbonic anhydrase XIII
PLA2G1B	P04054	Phospholipase A2 group 1B
CA5A	P35218	Carbonic anhydrase VA
APEX1	P27695	DNA-(apurinic or apyrimidinic site) lyase
AKR1C2	P52895	Aldo-keto reductase family 1 member C2
AKR1C1	Q04828	Aldo-keto reductase family 1 member C1
AKR1C3	P42330	Aldo-keto-reductase family 1 member C3
AKR1C4	P17516	Aldo-keto reductase family 1 member C4
AKR1A1	P14550	Aldehyde reductase
MPG	P29372	DNA-3-methyladenine glycosylase
GPR35	Q9HC97	G-protein coupled receptor 35
BCHE	P06276	Butyrylcholinesterase

Table S2: *The corresponding degree values of Top 5 targtes*

No.	Uniprot code	Degree	No.	Uniprot code	Degree
1	9606.ENSP00000275493	39.0	35	9606.ENSP00000378488	8.0
2	9606.ENSP00000356438	36.0	36	9606.ENSP00000263317	8.0
3	9606.ENSP00000405330	33.0	37	9606.ENSP00000394624	7.0
4	9606.ENSP00000361405	30.0	38	9606.ENSP00000260302	7.0
5	9606.ENSP00000324806	25.0	39	9606.ENSP00000217244	7.0
6	9606.ENSP00000219070	18.0	40	9606.ENSP00000303830	7.0
7	9606.ENSP00000358022	17.0	41	9606.ENSP00000226279	6.0
8	9606.ENSP00000288135	16.0	42	9606.ENSP00000430656	6.0
9	9606.ENSP00000428056	16.0	43	9606.ENSP00000430684	6.0
10	9606.ENSP00000225275	16.0	44	9606.ENSP00000237014	6.0
11	9606.ENSP00000478255	14.0	45	9606.ENSP00000300900	5.0
12	9606.ENSP00000363822	14.0	46	9606.ENSP00000295683	5.0
13	9606.ENSP00000498246	14.0	47	9606.ENSP00000480012	5.0
14	9606.ENSP00000343925	14.0	48	9606.ENSP00000285379	5.0
15	9606.ENSP00000327251	13.0	49	9606.ENSP00000285930	5.0

No.	Uniprot code	Degree	No.	Uniprot code	Degree
16	9606.ENSP00000284981	13.0	50	9606.ENSP00000383364	5.0
17	9606.ENSP00000368727	13.0	51	9606.ENSP00000312286	4.0
18	9606.ENSP00000340684	12.0	52	9606.ENSP00000354522	4.0
19	9606.ENSP00000299855	12.0	53	9606.ENSP00000242057	4.0
20	9606.ENSP00000378699	12.0	54	9606.ENSP00000356205	4.0
21	9606.ENSP00000364898	12.0	55	9606.ENSP00000251535	4.0
22	9606.ENSP00000477713	11.0	56	9606.ENSP00000293761	4.0
23	9606.ENSP00000309572	11.0	57	9606.ENSP00000347046	3.0
24	9606.ENSP00000349446	11.0	58	9606.ENSP00000234961	3.0
25	9606.ENSP00000379683	10.0	59	9606.ENSP00000382342	3.0
26	9606.ENSP00000308938	10.0	60	9606.ENSP00000234111	3.0
27	9606.ENSP00000277120	10.0	61	9606.ENSP00000285381	3.0
28	9606.ENSP00000303211	10.0	62	9606.ENSP00000384851	3.0
29	9606.ENSP00000458585	9.0	63	9606.ENSP00000347655	2.0
30	9606.ENSP00000241453	9.0	64	9606.ENSP00000366797	2.0
31	9606.ENSP00000263321	9.0	65	9606.ENSP00000467537	2.0
32	9606.ENSP00000419260	9.0	66	9606.ENSP00000241356	1.0
33	9606.ENSP00000264381	9.0	67	9606.ENSP00000219431	1.0
34	9606.ENSP00000265734	9.0			

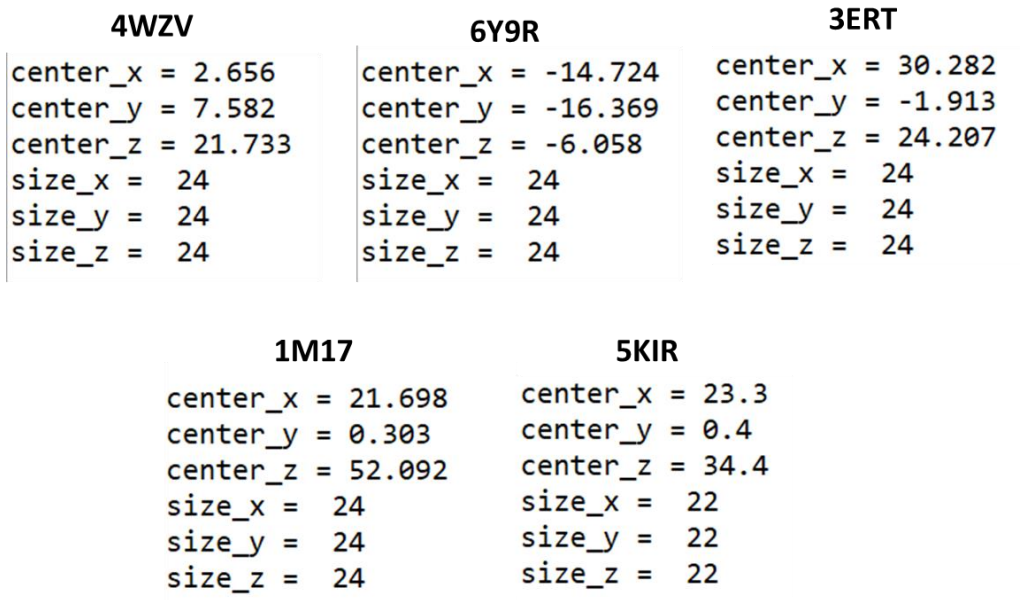

Figure S1: *The grid box parameters for the molecular docking*

TÓM TẮT

OROXYLIN A: CHẤT ỨC CHẾ TIỀM NĂNG CỦA VIÊM KHỚP DẠNG THẤP – NGHIÊN CỨU TRONG *SILICO* DỰA TRÊN DƯỢC LÝ MẠNG VÀ DOCKING PHÂN TỬ

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Oroxylin A là một hợp chất ức chế đầy hứa hẹn có thể được sử dụng để điều trị viêm khớp dạng thấp (RA). RA là một bệnh tự miễn mãn tính, mang tính hệ thống, gây tổn thương khớp, biến dạng và tàn tật nếu không được điều trị đúng cách. Nghiên cứu này sử dụng phương pháp dược lý mạng lưới (network pharmacology) và docking phân tử (molecular docking) để dự đoán cơ chế tác động chính của oroxylin A đối với RA. Tổng cộng 67 mục tiêu tiềm năng liên quan đến RA đã được xác định thông qua phân tích mạng tương tác protein-protein (PPI), trong đó EGFR, PTGS2, ESR1, MMP9 và GSK3B nổi bật là các mục tiêu trung tâm. Phân tích theo cơ sở dữ liệu KEGG cho thấy 67 mục tiêu này có liên quan đến các cơ chế chuyển hóa, cơ chế ung thư, cơ chế tín hiệu PI3K-Akt, cơ chế tín hiệu Ras và các cơ chế microRNA trong ung thư. Phương pháp docking phân tử đã được sử dụng để xác định mô hình và ái lực liên kết của oroxylin A với năm mục tiêu RA trung tâm này. Những phát hiện này nhấn mạnh tiềm năng của oroxylin A trong việc ức chế các mục tiêu sinh học liên quan, mở đường cho các nghiên cứu sâu hơn về cơ chế tác động của nó đối với RA.

Từ khóa: Oroxylin A; viêm khớp dạng thấp; dược lý mạng; docking phân tử.