INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Research Article

In-Silico Exploration of Natural Plant Derived Compounds in the Management of Arthritis

Manita Demla*, Amit Sharma

Jagannath University, Jaipur 302022, Rajasthan, India.

ARTICLE INFO

Received: 08 July 2024
Accepted: 11 July 2024
Published: 23 July 2024
Keywords:
In Silico, Herbal, Therapies, Management, Arthritis.
DOI:
10.5281/zenodo.12798109

ABSTRACT

This study offers a thorough analysis of arthritis, including information on risk factors, prevalence, and a thorough investigation of both conventional and herbal therapy options. The study highlights the complexity of arthritis and the need for an all-encompassing approach to its treatment. Parallel to this, the essay explores the newly popular area of herbal medicines, going over certain herbs with anti-inflammatory qualities such as Boswellia serrata, ginger, and turmeric. Important aspects of herbal remedies, such as their efficacy and possible interactions, are emphasised, underscoring the need of making well-informed decisions by interacting with medical experts. The study promotes a proactive and customised strategy, acknowledging the variety of individual reactions and the continuous change in the landscape of arthritis treatment options. It provides a basis for enhanced quality of life through integrated and well-informed therapy strategies and acts as a comprehensive guide for both individuals and healthcare providers.

INTRODUCTION

"Arthritis" signifies inflammation and is derived from the Greek words "arthro" meaning joint. The joint inflammations and pains felt by millions of people across the globe are collectively known as arthritis. Inflammation of the joints is a hallmark of many disorders, which can lead to pain, stiffness, and limited mobility [1, 2]. Although it is commonly linked with getting older, arthritis does not discriminate based on age, gender, or demographics and can affect people from all walks of life and at any stage in their lives and one of the most widespread and pervasive problems in public health around the world [3]. Recognizing the complex nature of arthritis is essential for the development of efficient management strategies, the improvement of the quality of life for those who are affected by the condition, and the paving of the way for novel approaches to alleviating the negative effects of this chronic condition on both the body and society. It is estimated that 350 million people, or 4.3 percent of the world's

***Corresponding Author:** Manita Demla
Address: *Jagannath University, Jaipur 302022, Rajasthan, India*
Email : demla.manita@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

population, are afflicted by it; this number is continuing to climb as a result of ageing populations and lifestyle factors [4, 5]. Worldwide, the frequency of this disease varies substantially. People above the age of 60 have a much higher risk of developing osteoarthritis, while those in the middle age range have a higher risk of developing rheumatoid arthritis. Women have a greater risk of developing rheumatoid arthritis and other forms of arthritis compared to men. These gender disparities are plain to see [6-8]. Osteoarthritis (OA) usually impacts the distal interphalangeal joint, whereas proximal interphalangeal (PIP) and metacarpophalangeal (MP) joints are the sites of RA's impact, thereby clinically differentiating the two conditions. Wear and tear, not an inflammatory disorder, is the root cause of OA, the most prevalent form of arthritis. The respiratory, cardiac, and immunological systems are unaffected. Furthermore, unlike RA, which can impact both sides of the body equally, OA usually impacts just one side. The fact that RA patients experience morning stiffness for at least one hour is another distinguishing feature. Morning stiffness is a common symptom of osteoarthritis, although it usually goes away or at least becomes better within 20 to 30 minutes [9, 10]. The objectives of treating rheumatoid arthritis are improvement of joint function, reduction of inflammation and discomfort, and prevention of joint degeneration and deformity. The treatment plan is based on the patient's overall health and any underlying medical issues. Factors such as the rate of disease progression, the joints afflicted, age, overall health, occupation, adherence, and disease education level are relevant here. The primary goals of most first-line treatments are pain relief and inflammatory reduction. Naprosyn, etodolac, ibuprofen (Advil and Motrin), naproxen (Aspirin), and acetylsalicylate are nonsteroidal anti-inflammatory drugs (NSAIDs) that are believed to have a rapid beginning of action (Lodine). When used in high doses, aspirin reduces inflammation associated with RA because it blocks the production of prostaglandins. One of the earliest nonsteroidal anti-inflammatory medications, it eases joint pain (NSAIDs). Overdosing on aspirin could lead to gastrointestinal issues, tinnitus, and hearing loss. There are newer NSAIDs (nonsteroidal anti-inflammatory medicines) that work just as well as aspirin. The daily dosage of these drugs is also reduced. By inhibiting cyclo-oxygenase, nonsteroidal anti-inflammatory medications (NSAIDs) halt the synthesis of prostacyclin, thromboxanes, and prostaglandins. Side effects such as nausea, vomiting, ulceration, and bleeding in the gastrointestinal tract (GI tract) are prevalent [11-15]. As a result of never-ending study and improvements in medical technology, the options for arthritis therapy are always evolving. Because of this, consulting with medical professionals is essential for developing individualised, cutting-edge treatment programmes. The area of arthritis treatment is increasingly focusing on herbal therapies. A wide range of symptom-reduction and, perhaps, disease-progression-altering tactics are available in these treatments. In the context of arthritis, a group of joint-inflammatory diseases, the herbal treatment category of plant-based medicines has shown promise in terms of pain alleviation, inflammation reduction, and overall improvement of joint function [16-19]. Curcumin, found in turmeric, is a well-known active component in many herbal remedies. As an effective anti-inflammatory, curcumin can alleviate some of the aches and pains that come with arthritis. Also, many people are looking to ginger as a natural alternative to painkillers because of its analgesic and anti-inflammatory properties [2, 20-23]. Extensive research has focused on the potential anti-inflammatory properties of Boswellia serrata, sometimes referred to as Indian frankincense, particularly in the treatment of rheumatoid arthritis

and osteoarthritis. These measures may alleviate pain and inflammation by blocking certain enzymes [18, 24-26]. In addition, herbs such as devil's claw and white willow bark have traditionally been used for the management of symptoms associated with arthritis, specifically pain and stiffness. Another herbal option that may help ease the symptoms of arthritis is stinging nettle, which is abundant in a number of different bioactive components [27-30]. Renowned for its antioxidant and anti-inflammatory properties, aloe vera has demonstrated potential in reducing joint pain and improving joint flexibility. Antioxidant-rich herbs—like cat's claw and green tea—are essential for shielding joint tissues from oxidative stress, which keeps overall joint health intact [24]. Numerous variables can influence the efficacy of herbal remedies, such as the specific kind of arthritis being treated, the standard and purity of the herbal product being used, the patient's reaction, and the potential for drug interactions with conventional treatments. For this reason, it is imperative that individuals with arthritis consult with medical professionals before including herbal therapies into their treatment plans. Herbal remedies for arthritis should be viewed as a supplemental element that functions in tandem with traditional medical treatments [8, 14, 31, 32]. It is important to understand that herbal remedies are supposed to provide further relief rather than take the place of conventional treatments, particularly when dealing with the complex nature of arthritis. Furthermore, customised approaches to herbal medicine are necessary to recognise that what benefits one person may not benefit another. It is imperative to seek the counsel of healthcare specialists due to the diverse possibilities about the safety and appropriateness of herbal medicines. They are capable of assessing the remedies' capacity to meet the patient's demands while also considering any possible risks [16, 17, 33, 34]. In general, the use of herbal treatments for arthritis is becoming more prevalent as a result of the ongoing research that is shining light on the advantages and disadvantages of these natural medicines (Table 1). Modifications to one's lifestyle, participation in physical therapy, and the use of prescription medications, when appropriate, should all be included in any comprehensive plan for the management of arthritis, despite the fact that these treatments show promise in terms of relieving symptoms and boosting joint health. People who are living with arthritis have the ability to improve their quality of life and better manage the problems that are presented by this complicated condition if they take advantage of the possible benefits of herbal remedies within the context of a well-informed and integrative framework.

Table 1 Some anti-arthritic plants with their phytopharmacological actions:

Sr no.	Name of the plants		Family	Parts of plants	Phytochemicals	Reported pharmacology	Reference
	Botanical N.	Common name					
1.	Saussurea lappa Clarke.	Kuth root or costus	Compositae		camphene	anticancer, antiulcer, hepatoprotective, anti-viral, anticonvulsant, antiarthritic, Anti-inflammatory activity, antiarthritic	**[35]**
					costol		
					costic acid		
					phellandrene		
					costene		
					aplotaxene		
2.		black- or chebulic myrobalan	Combrataceae		chebulic acid	Anti-inflammatory activity, antiarthritic	**[35]**

	Terminalia chebula Retz.				ellagic acid chebulinic acid chebulagic acid ellagic acid		
3.	Vitex negundo Linn.	Chinese chaste tree	Verbenaceae		Nishindine, casticin	Anti-inflammatory activity, antiarthritic	
4.	Xanthium strumarium Linn	common cocklebur	Compositae		xanthinin xanthatin xanthostrumarin atractyloside carboxyatractylosid e xanthanol isoxanthanol xanthosin 4-oxo-bedfordia acid hydroquinone xanthanolides deacetylxanthumin xanthumin	Anti-inflammatory activity, antiarthritic	
5.	Sida rhombifolia Linn	arrowleaf sida	Malvaceae		β-phenethylamine N-methyl-β-phenethylamine S-(þ) N-β-methyl tryptophan methyl ester vasicinol vasicine vasicinone hypaphorine methyl ester hypaphorine betaine	anti-inflammatory, antipyretic, and anti-arthritic.	
6.	Piper longum Linn	Long pepper, pippali	Piperaceae		piperine piperlongumine piperlonguminine methyl 3,4,5-trimehoxycinnamate	Anti-inflammatory activity, antiarthritic	
7.	Ruta graveolens Linn.	rue	Rutaceae		rutin	antiseptic, anthelminthic, antispasmodic, stimulant, abortificient, expectorant, and anti-rheumatic	
					quercitin rutacridone rutacridone epoxide graveoline gravacridonodiol		
8.	Glycyrrhiza glabra	Liquorice	Fabaceae	Roots	Glycyrrhizin	anti-microbial, hypolipidaemic, antiviral, hypotensive, anti-ulcer, anti-diuretic,	

						anti-inflammatory, anti-mutagenic, expectorant, hepatoprotective, antioxidant, and antipyretic activities	
9.	Coriander sativum Linn.	cilantro or Chinese parsley	Umbelliferae	seeds, fruits and leaves	glycyrrhizic acid coriandrol geraniol boborneol	antirheumatic and anti-arthritic properties	
10.	Cinnammomum zeylicanium Blume.	Ceylon cinnamon	Lauraceae	leaves	Sibinene	analgesic, anti-pyretic, Anti-inflammatory activity, antiarthritic	
					myrcene fenchone nerol bornyl acetate cinnamyl acetate geranial camphene		
11.	Alstonia scholaris Linn	Indian Pulai, White Cheesewood, Devil Tree, Blackboard Tree, Milkwood Pine, Dita Bark	Apocynaceae	bark	echitamine tubotaiwine akaummicine echitamidine picrinine strictamine	Anti-inflammatory activity, antiarthritic	
12.	Ginkgo biloba	maidenhair tree	Ginkgoaceae	Leaves	Ginkgetin	Anti-inflammatory activity	
13.	Pterodon pubescens	sucupira-branca, faveira	Leguminosae	Seeds	Geranylgeraniol	Anti-arthritis activity	
14.	Semecarpus anacardium	bhallatak	Anacardiaceae	Leaves roots and fruits	bhilawanols	Antiarthritic effect by retarding lipid peroxidation and causing a modulation in cellular antioxidant defense system	
15.	Chenopodium album L	Goosefoot	Amaranthaceae	Leaves and roots	ecdysteroids polypodine B ß-ecdysone	Anti-inflammatory activity	
16.	Ginger	jiang (Chinese), adrak (Hindi), jengibre (Spanish), zenzero (Italian), gingembre (French), zanjabeel (Arabic), and ingwer (German)	Zingiber officinale	Essential oils	Nongingerol	Show significant joint-protective effect	
17.	Strychnos potatorum Linn	clearing-nut tree, Nirmali Burmese	Loganiaceae	Seeds	Alsogavebrucine icajine novacine strychnine	Arthritis	
18.	Allium sativum	garlic	Amaryllidaceae	Bulbs and leaves	Ajoene	Anti-inflammatory properties	
19.	*Phyllanthus Emblica*	Indian gooseberry	Rubiaceae		Phyllanthin	Chondroprotective potential, osteoarthritis	

20.	*Rhodophiala bifida*	Oxblood lily, Schoolhouse lily, Hurricane lily	*Amaryllidaceae*	bulb	Montanine	anti-inflammatory	
21.	*Aconitum flavum*	aconite, monkshood, wolfsbane, leopard's bane, devil's helmet	*Ranunculaceae*	root	3-Acetylaconitine	Rheumatoid arthritis	
22.	*Sanguinaria Canadensis*	bloodroot	Papaveraceae		Sanguinarine	anti-inflammatory	
23.	*Berberis aristata*	Indian barberry, Mara manjal	Berberidaceae		Jatrorrhizine	anti-inflammatory	
24.	*Aplidium orthium*		Ascidiacea		Tubastrine	anti-inflammatory	
25.	*Barringtonia racemosa* R oxb.	puff tree	Lecythidaceae	fruits	Bartogenic Acid	Arthritis	
26.	Lindera aggregata	evergreen lindera, Japanese evergreen spicebush	Lauraceae	Dry roots	Norisoboldine	Anti-Arthritic and Anti-Inflammatory	
27.	Salvia miltiorrhiza	red sage or Danshen	Lamiaceae	Inflorescence	Cryptotanshinone	Anti-Arthritic and Anti-Inflammatory	
28.	Siegesbeckia orientalis	Indian weed, St. Paul's wort	Asteraceae		Kirenol	Anti-Arthritic and Anti-Inflammatory	
29.	Withania somnifera	Ashwagandha, Indian Ginseng, or Winter Cherry	Solanaceae	Leaves	Withanolides	Anti-Arthritic and Anti-Inflammatory	
30.	Tanacetum vulgare	Common tansy	Asteraceae	Aerial parts	3,5-O-dicaffeoylquinic acid (3,5-DCQA)	Anti-Arthritic and Anti-Inflammatory	
31.	Centella asiatica	Indian pennywort and Asiatic pennywort	Apiaceae	Leaves	Madecassoside	Anti-Arthritic and Anti-Inflammatory	
32.	Strychnos nux-vomica	nux vomica, poison fruit, semen strychnos, and quaker buttons	Loganiaceae	Seeds	Brucine	Anti-Arthritic and Anti-Inflammatory	
33.	Ananas comosus	pineapple	Bromeliaceae	Fruit	Bromelain	Anti-Arthritic and Anti-Inflammatory	
34.	Tripterygium wilfordii	Mandarin, thunder god vine	Celastraceae	Entire herb	Triptolide	Anti-Arthritic and Anti-Inflammatory	
35.	Cannabis sativa	Jia, Bhang Ganja	Cannabaceae	Leaves	Cannabidiol	Anti-Arthritic and Anti-Inflammatory	
36.	Dysoxylum binectariferum	Akil Karakil	Meliaceae	Seeds	Rohitukine	Anti-Arthritic and Anti-Inflammatory	
37.	Capparis spinosa	Caper bush, Flinders rose	Capparaceae		P-hydroxy benzoic acid	Anti-Arthritic and Anti-Inflammatory	
					5-(hydroxymethyl) furfural		
					Bis (5-formylfurfuryl) ether		
					daucosterol		
					α-Dfructofuranosides		
					Stachydrine		

					Uracil		
38.	Yucca schidigera			Bark	Resveratrol	Anti-Arthritic and Anti-Inflammatory	
					Yuccaols		
					trans-3,3',5,5'-tetrahydroxy -4'-methoxystilbene		
39.	Lasianthus acuminatissimus		Rubiaceae	Roots	Uncargenin A	Anti-Arthritic and Anti-Inflammatory	
40.	Boswellia carteri	luban dhakar	Burseraceae	Resin	Boswellic acids	Anti-Arthritic and Anti-Inflammatory	
41.	Acanthopanax chiisanensis		Araliaceae	Leaves	Chiisanoside Chiisanogenin	Anti-Arthritic and Anti-Inflammatory	
42.	Berberis vulgaris	barberry, European barberry	Berberidaceae	Root extract	Berberine	Anti-Arthritic and Anti-Inflammatory	

MATERIALS AND METHODOLOGY

(i) Computational Analysis

Design of Ligand Library

Greek terms "arthro" (joint) and "itis" (inflammatory) are the origin of the English word "arthritis." A collection of intricate and common chronic illnesses collectively known as arthritis affect millions of people worldwide and are a major source of suffering. Joint inflammation is the defining characteristic of this category of diseases, which manifests itself as discomfort, stiffness, and a reduction in range of motion [40-43]. A ligand library that contains one hundred herbal leads derived from a variety of plant sources was developed through the process of reading the relevant literature. Some of the substances that were discovered to be present in the plants that were the subject of the inquiry were alkaloids, terpenoids, saponins, tannins, steroids, glycosides, carbohydrates, monosaccharides, mixed reducing sugars, and soluble starch [44, 45].

Target Identification

In order to identify the most significant lead molecule responsible for the anti-rheumatoid effect in humans and to identify the mechanism of action that is most likely to be responsible for the anti-rheumatoid activity of that particular plant-based active constituent, one hundred ligands from the various chemical classes of plants were added to the ligand library. The available pharmacological evidence supports the pathophysiological and inflammatory targets' roles in the development of rheumatoid arthritis. Therefore, we can target the factors that cause the disease to proceed, such as Jasus Kinase (JAK), interleukin-1 (IL1), interleukin-6 (IL6), tumour necrosis factor-α (TNFα), and tumour necrosis factor receptor (TNFR1). An inflammatory cytokine called IL1 contributes to the autoimmune reaction that causes cartilage degradation and bone resorption in rheumatoid arthritis [46-48]. The cytokine known as interleukin-6 (IL6) is implicated in the genesis and progression of rheumatoid arthritis. It possesses many phenotypic characteristics. It was discovered that people with rheumatoid arthritis had an excessive amount of IL6 in their serum and synovial fluid. This type of IL6 is responsible for the progression of the disease, which is characterised by the destruction of joints [49]. In addition to promoting the migration of neutrophils and the maturation of osteoclasts, IL6 also promotes the proliferation of pannus cells, which is induced by vascular endothelial growth factor (VEGF) [50, 51]. The Janus kinase–Signal Transducers and Activators of Transcription (JAK-STAT) pathway is implicated in the pathophysiology of immune-mediated inflammatory disorders such as

rheumatoid arthritis. Jasus Kinase (JAK) is an essential component of this system [52, 53] In the case of rheumatoid arthritis, synovia macrophages, B lymphocytes, and natural killer (NK) cells are responsible for the biosynthesis of tumour necrosis factor- α (TNFα), which has a direct role in the modulation of joint inflammation. In arthritic biopsies, it was discovered that TNFα was overexpressed, and the identification of their participation in Rheumatoid arthritis was corroborated through the occurrence of spontaneous inflammation in a variety of arthritic models. It has been discovered that TNFα plays a role in the process of bone resorption, as well as in the process of cartilage degradation [47, 54]. The cytokine tumour necrosis factor (TNF) operates in inflammatory signalling via two distinct receptors, TNFR1 and TNFR2 (TNFR2). While TNFR1 antagonism blocks the inflammatory response, the functional significance of TNFR2 remains unclear [55]. Therefore, targeting TNFR1 can be assumed to interfere with the inflammatory reactions that are involved in the joints and are responsible for the formation of destruction. Additionally, pain can be interrupted by making use of this strategy.

Molecular Docking Studies

Additional molecular docking research will be conducted on the macromolecular therapeutic targets that were chosen because they were actively contributing to the improvement or maintenance of rheumatoid arthritis [56-58]. Molecular docking simulation investigations were carried out with the help of three-dimensional structural models of all of the macromolecular drug targets that were selected for further investigation. These models were obtained from the Protein Databank [59-63]. The complexed ligand was extracted from the macromolecular complexes that were downloaded, and both the emerging target protein and the separated ligand were saved in the default Autodock format. This was done so that they could be redocked in order to verify the docking parameters that were utilised. Following the successful validation of the docking methodology for each therapeutic target, similar parameters were then utilised for the purpose of computationally screening the ligand library against each of the macromolecular targets that were utilised in the present work [64-68].

RESULTS

(i) Computational Analysis

Design of Ligand Library

A ligand library was to be created by selecting ligands from the body of literature that was already accessible. These ligands' two-dimensional structures were created by using ChemDraw8.0 to transform isomeric SMILES that were obtained from PubChem into two-dimensional structures. Every ligand that made the short list had its two-dimensional structure used to create its three-dimensional structure, which was then followed by an energy minimization procedure.

Target Identification

Through mediating the destruction of cartilaginous tissues and bone reabsorption, the inflammatory cytokine IL1 plays a crucial role in the genesis and advancement of the autoimmune response in rheumatoid arthritis [48, 69]. In a crystallised state, IL1 is linked to kinase-4 and a ligand complex known as BSI107591. The X-ray diffraction technique was used to resolve the crystal structure of human IL1 with a resolution of 2.10 Å, employing Trichoplusia ni as an expression system (pdb id: 6mom). Each monomer unit of the IL6 complex contains 303 amino acids, forming a tetrameric structure in its crystal structure. The macromolecular complex consists of four chains: A, B, C, and D. The docking investigation was conducted using chain A, which had the other chains deleted. In order to obtain the nascent receptor and ligand molecules, the complexed ligand BSI107591 was additionally isolated from the macromolecular complex [70, 71]. Synovitis, a systemic symptom of rheumatoid arthritis that

ultimately destroys joints, is heavily influenced by IL6, a proinflammatory cytokine [49, 51]. The X-ray diffraction technique was used to resolve the crystal structure of human IL6 complexed with a nucleotide aptamer at a resolution of 2.40 Å. The expression system used was Escherichia coli (pdb id: 4ni7). An aptamer of 32 nucleotides and a protein chain of 186 amino acids make up a macromolecular complex, which is a monomeric structure. By removing unnecessary water molecules, this macromolecular compound can be utilised as a developing receptor [70, 72]. The activation of apoptotic chondrocytes and elevated levels of matrix metalloproteinases (MMP) in the synovial joints of RA patients is a consequence of the JAK/STAT signalling cascade, of which JAK is a component [73]. The X-ray diffraction technique, in conjunction with the baculovirus expression system, was used to reveal the crystal structure of the human JAK complexed with a polycyclic azaindole inhibitor at a resolution of 2.10 Å. (pdb id: 3jy9). A macromolecular complex consists of a 311-amino-acid protein chain and an inhibitor molecule based on polycyclic azaindole [70, 74]. To prepare for docking analysis, the ligand and nascent receptor were extracted from the macromolecular complex. A drug that inhibits TNFα is used to obtain its crystal structure from the protein databank. The X-ray diffraction technique was used to resolve the three-dimensional structure model of TNFα with a resolution of 2.10 Å, and the expression system used was Escherichia coli (pdb id: 2az5). Each monomer unit of a macromolecular complex contains 148 amino acids, forming a tetrameric structure. Out of the four chains that make up the macromolecular complex—A, B, C, and D—the docking investigation was conducted using chain A, with the other chains being deleted. In order to obtain the nascent receptor and ligand molecules, the complexed ligand 307 was additionally isolated from the macromolecular complex [70, 75]. In order to generate an inflammatory response, TNFα interacts with TNFR1, a type of receptor, to transduce signals. The X-ray diffraction technique was used to resolve the crystal structure of human TNFR1 complexed with a monoclonal antibody and a tiny ligand. The expression system used was Escherichia coli, and the resolution reached 2.30 Å. (pdb id: 7kpa). A 158-amino-acid protein chain and a tiny ligand molecule (D84) form a trimer in a macromolecular complex [70, 74]. It was necessary to remove this complexed ligand from the macromolecular complex in order to obtain a nascent receptor and the ligand that was necessary for docking analysis.

Molecular Docking Studies

All of the three-dimensional structural models of the macromolecular targets that were shortlisted were redocked against the complexed reference ligand, which confirmed that the docking process that was used was effective [76-78]. The molecular ligand library that was developed was subjected to computational screening against each of the macromolecular targets that were proposed to be involved in the treatment and maintenance of rheumatoid arthritis in individuals, once the validation process was deemed to be sufficient. After the conclusion of the virtual screening of the ligand library, the best lead molecule is selected by selecting the one that has the lowest binding energy relative to the range of -5 to -15 kcal/mole that has been established.

Table 1. Binding score obtained for each of the ligand of the designed ligand library against each of the shortlisted macromolecular target involved in the development and progression of rheumatoid arthritis

S. No.	Ligands	IL1	IL6	JK2	TNFα	TNFRA
PDB Id→		6mom	4ni7	3jy9	2az5	7kpa
1	2-Acetylaconitine	-2.18	-4.77	-4.67	-5.81	-3.45

2	3,3',5,5'-Tetrahydromethyl stilbene	-6.15	-7.33	-8.08	-5.41	-8.86
3	3,5-DCQA	-5.94	-5.88	-6.50	-5.04	-8.88
4	4-Oxobedfordiac Acid	-6.37	-5.97	-7.12	-5.93	-7.93
5	5-Formylfurfuryl ether	-6.01	-6.15	-5.90	-5.28	-6.76
6	Ajoene	-5.05	-5.96	-5.27	-4.68	-6.62
7	α-methyl-D-fructofurano	-2.84	-3.37	-2.56	-2.56	-4.32
8	Apigenin	-8.84	-8.58	-8.82	-6.45	-9.85
9	Aplotaxene	-5.53	-6.39	-5.10	-5.11	-6.96
10	Bartogenic Acid	-7.45	-4.01	-6.76	-8.35	-5.39
11	Berberine	-8.40	-8.54	-7.88	-7.65	-9.84
12	β- Phenylethylamine	-6.95	-5.90	-5.37	-3.88	-4.81
13	**Betulin**	**-9.95**	-8.94	**-9.39**	-9.12	-10.82
14	Bornyl acetate	-6.15	-5.83	-5.56	-5.89	-7.20
15	Boswellic Acid	-8.37	-7.27	-7.73	-8.86	-8.76
16	Bromelain	+26.03	+2.10	+4.86	-1.03	+143.85
17	Brucine	-9.33	-9.81	-8.51	-7.87	-11.15
18	Camphene	-5.46	-5.74	-4.87	-5.65	-6.61
19	Cannabidiol	-7.18	-8.82	-6.76	-6.68	-8.84
20	Carboxytetractyloside	-1.95	-3.72	-4.80	-6.02	-3.23
21	Casticin	-8.83	-8.87	-7.89	-6.49	-9.68
22	Chebulagic Acid	+99.40	-3.91	+11.00	-6.30	+153.21
23	Chebulic Acid	-2.65	-2.85	-3.82	-4.17	-4.29
24	Chebulinic Acid	+8.36	-5.22	-0.16	-3.54	+33.09
25	Chiisanogenin	-8.48	-6.65	-8.20	-8.49	-9.65
26	Chiisanoside	+14.63	-7.26	+14.04	-5.64	+80.30
27	Cinnamyl acetate	-6.32	-6.43	-5.47	-5.48	-6.41
28	Coriandrol	-4.81	-5.49	-4.55	-5.07	-6.21
29	Costic Acid	-6.91	-7.30	-6.86	-6.94	-8.39
30	Costol	-6.97	-6.84	-6.90	-6.89	-8.55
31	Cryptotanshinone	-8.92	**-10.80**	-8.02	-8.10	-10.56
32	Daucosterol	-7.51	-6.46	-6.88	-7.16	-10.67
33	**Diosgenin**	**-9.96**	-8.29	**-8.84**	**-9.31**	-10.97
34	Ecdysone	-9.03	-7.30	-8.37	-6.99	**-13.35**
35	Echitamidine	-9.16	-7.96	-7.72	-7.79	-9.87
36	Echitamine	-6.92	-6.44	-5.66	-7.50	-7.75
37	Ellagic Acid	-7.74	-8.86	-6.90	-6.16	-9.08
38	Fenchone	-5.33	-5.81	-5.28	-5.95	-7.19
39	Geranial	-5.46	-5.32	-4.96	-4.76	-6.11
40	Geraniol	-5.54	-5.07	-4.81	-4.55	-5.68
41	Geranyl geraniol	-7.08	-6.65	-5.94	-5.83	-8.58
42	**Ginkgetin**	-8.59	**-10.41**	**-9.08**	-8.22	-11.70
43	Gitogenin	-9.41	-8.58	-8.25	-8.14	-10.71
44	Glycyrrhizic acid	+7.02	-1.22	+5.96	-6.63	+14.07
45	Glycyrrhizin	+47.74	+0.69	+165.01	-4.42	+355.09
46	Graveoline	-8.32	-8.29	-7.48	-7.30	-9.38
47	Hydroquinone	-4.26	-4.46	-4.05	-3.94	-5.74
48	Hypaphorine	-5.32	-6.14	-5.81	-5.48	-6.87
49	Icajine	-9.36	-8.87	-8.16	-8.38	-10.07
50	Isoxanthol	-7.11	-7.83	-7.71	-7.31	-8.92
51	Jatrorrhizine	-7.87	-8.54	-7.80	-6.71	-9.74

52	Karaounidiol	-8.81	-7.17	-7.57	-8.72	-12.83
53	Kirenol	-7.68	-7.03	-6.56	-7.35	-10.86
54	Luteolin	-8.01	-8.12	-8.70	-6.58	-9.81
55	Madecassoside	+34.08	-0.65	+38.93	-4.38	+99.11
56	Montanine	-7.51	-7.78	-7.45	-6.65	-9.35
57	Myrcene	-4.72	-5.29	-4.51	-4.49	-5.33
58	Naringenin	-8.00	-7.58	-8.95	-6.90	-9.67
59	Nerol	-5.16	-5.17	-4.83	-4.58	-5.81
60	Niazirinin	-7.57	-7.63	-7.23	-6.51	-8.48
61	Norisoboldine	-8.40	-8.40	-6.92	-6.75	-8.15
62	**Novacine**	**-10.13**	**-9.25**	-8.31	-7.66	**-10.49**
63	OxyAcetic acid	-7.79	-7.12	-6.45	-6.21	-8.60
64	Phellodendrine	-6.88	-7.26	-6.74	-6.86	-8.88
65	p-Hydroxybenzoic acid	-3.64	-4.48	-4.41	-3.87	-5.12
66	Phyllanthin	-6.31	-7.65	-6.26	-5.48	-8.09
67	Picrinine	-7.46	-8.03	-7.36	-7.37	-9.45
68	Piperine	-8.99	-8.89	-8.59	-6.93	-9.47
69	Piperlongumine	-7.53	-8.98	-7.44	-7.65	-10.05
70	Piperlonguminine	-8.64	-8.03	-8.00	-6.53	-8.46
71	Quercetin	-8.15	-7.51	-7.51	-6.42	-9.14
72	Reserveratrol	-6.85	-7.32	-7.83	-5.72	-8.18
73	Rohitukine	-8.91	-8.54	-7.36	-5.86	-8.14
74	Rutacridone	-9.39	-9.90	-8.59	-7.67	-9.49
75	Rutacridone epoxide	-9.31	-9.86	-8.94	-7.76	-10.23
76	Rutin	-5.98	-5.21	-7.82	-4.97	-7.74
77	Sanguinarine	-9.18	**-9.94**	-8.38	-8.22	-9.75
78	Stachydrine	-3.91	-3.50	-4.12	-3.79	-4.91
79	Strictamine	-7.51	-8.38	-7.21	-7.66	-9.14
80	Strychine	-9.42	-8.79	-8.13	-8.07	-10.46
81	Stearic acid	-4.11	-3.70	-4.48	-3.59	-6.82
82	Taxifolin	-6.39	-6.86	-7.15	-6.10	-8.63
83	Triptolide	-8.05	-9.01	-7.43	-7.44	-9.46
84	Tubastrine	-7.99	-6.42	-6.72	-5.17	-7.06
85	Tubotaiwine	-7.78	-7.74	-7.00	-7.98	-9.06
86	Uncargenin-C	-8.88	-5.11	-7.85	-8.11	-5.03
87	Uracil	-4.03	-4.20	-4.19	-3.70	-5.19
88	Vasicine	-5.89	-7.00	-5.58	-5.62	-7.35
89	Vasicinol	-6.81	-7.03	-5.99	-6.12	-7.52
90	Vasicinone	-6.50	-7.91	-6.32	-5.78	-7.29
91	Vitexin	-7.35	-6.27	-7.87	-5.28	-8.62
92	**Withanolide-A**	**-10.09**	**-10.52**	**-9.02**	-9.09	**-13.14**
93	**Withanolide-B**	**-10.72**	-9.64	**-8.97**	**-10.70**	**-14.60**
94	Xanthanol	-6.94	-7.34	-6.37	-6.12	-8.30
95	Xanthatin	-9.03	-8.29	-7.69	-7.62	-9.07
96	Xanthinin	-6.79	-6.70	-7.28	-7.90	-8.71
97	Xanthosine	-5.61	-5.91	-5.59	-4.86	-7.60
98	Xanthumin	-7.69	-7.10	-7.96	-7.14	-9.66
99	Yuccaol-A	-6.47	-6.92	-8.08	-7.81	-10.00
100	Indomethacin	-7.71	-8.25	-8.06	-7.25	-8.35

By analysing the docking score that was obtained after the computational screening of the designed library, it is evident that the compounds withanolide-A, witrhanolide-B, botulin, ginkgetin, diosgenin, and novacine have the highest binding affinity against all of the macromolecular targets that were utilised in this study. Table 1 contains a tabular representation of the full analysis of the data obtained for the binding score of each of the ligands in the ligand library against each of the macromolecular targets.

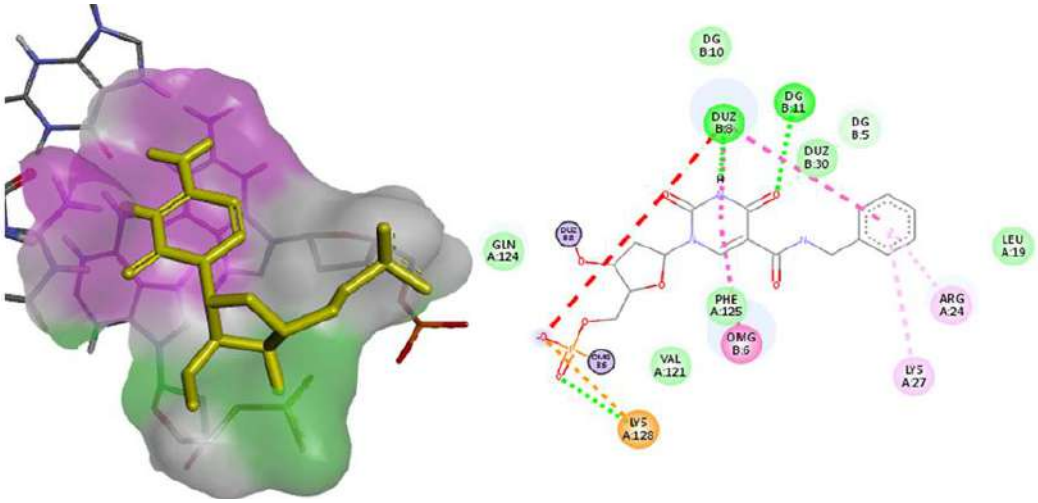

Figure 1. Two-dimensional binding interaction and three-dimensional binding pose of withanolide-A against IL6 receptor.

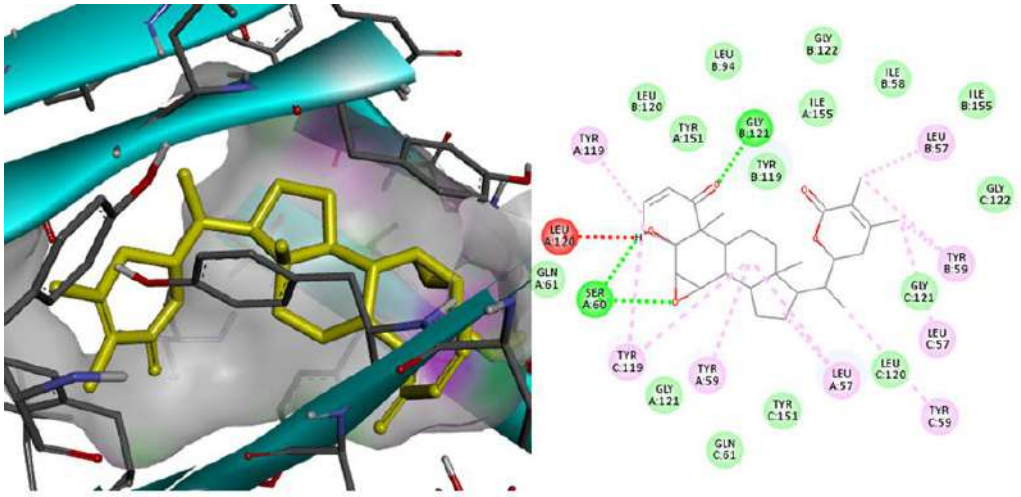

Figure 2. Two-dimensional binding interaction and three-dimensional binding pose of withanolide-B against TNFR1 receptor.

DISCUSSION:

Damage to joints and impairment over time are both outcomes of arthritis, an inflammatory illness that persists over time. If we want to keep major harm and the loss of vital biological processes at bay, we need medical help quickly. The treating physician ought to think about following treat-to-target (T2T) guidelines, which include defining the goals, developing protocols to reach them, and finally evaluating the results. Physical and occupational therapy are also helpful for RA patients. They should exercise frequently to keep

their joints mobile and build up the muscles that surround them. Swimming, yoga, and tai chi are low-impact movement workouts that produce strong muscles without putting too much strain on the joints. You can lessen the severity of exercise-related soreness by using heat or cold packs before and after your workout. At the moment, the treatments that are currently available for arthritis are symptomatic, and there is no evidence that they can either stop or reverse the degradation of cartilage and the loss of joints. As a result of this, there has been a rise in the number of people who are interested in the utilisation of complementary and alternative medicine (CAM) therapies for the treatment of arthritis. On the other hand, the majority of the research that is being conducted at the moment is focused on the identification, isolation, and characterisation of active principle(s) derived from crude extracts of known medicinal plants or herbs. This research frequently ignores the fact that a powerful synergy between several constituents in the crude drug may prove to be more potent and effective than any single purified compound, and this may help to nullify the toxic effects of individual constituents. In doing so, this research may help to eliminate the toxic effects of individual constituents. Not only does this intriguing theory motivate us to conduct additional study, but it also requires us to conduct experiments that are scientifically sound. The health benefits of nutraceuticals may be exploited to develop new and improved modalities for the treatment of degenerative and inflammatory joint diseases once the underlying molecular mechanism(s) for the observed anti-inflammatory and chondroprotective effects of nutraceuticals have been elucidated. This will allow for the possible utilisation of nutraceuticals in the treatment of joint diseases. It is acknowledged in the article that the treatment of arthritis is a process that is both evolving and personalised. This acknowledgement takes into account the variety of individual reactions as well as the particular characteristics of various forms of arthritis. One of the most essential things to keep in mind is that people who suffer from arthritis can significantly improve their quality of life by simultaneously utilising both traditional and alternative treatments.

CONCLUSION:

To summarise, arthritis is one of the most prevalent diseases in the world, and it is prevalent among a large number of people. In today's world, the typical way of life for people is that they do not consume a diet that is balanced, they do not engage in adequate physical activity, and they spend a significant amount of time sitting in front of their laptops. These are the primary factors that contribute to the development of arthritis. Therefore, this disease not only affects older generations but also younger generations. As a result, there are a variety of medicines available for arthritis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, and other similar medications. These treatments help alleviate pain, and the illness can be controlled to some degree, but they come with severe side effects. Enhancements are required to be made to the quality control and standardization processes for the traditional Indian medical system. Due to the fact that this is a review paper, the writers have conducted a comprehensive review of various other studies that discuss the possible applications of plants. More than one hundred publications have been used as references; scholars can use this article as a guide for additional research if they examine it and use it as a reference. The facts pertaining to plants are also strengthened by this article, and it may be of assistance to researchers in the field of phytopharmacology regarding their efforts to advance their research. Therefore, in light of the current state of scientific knowledge, it is recommended that herbal formulations and combination drugs be prepared by making use of

medicinal plant resources. This could lead to the creation of medicines that are effective in treating patients who suffer from rheumatoid arthritis.

REFERENCE

1. Gravallese, E.M. and G.S. Firestein, Rheumatoid Arthritis—Common Origins, Divergent Mechanisms. New England Journal of Medicine, 2023. 388(6): p. 529-542.
2. Samrat Chauhan, L.K., Navpreet Kaur, Randhir Singh, Potential Anti-Arthritic Agents From Indian Medicinal Plants. Research and Reviews: Journal of Pharmacy and Pharmaceutical Sciences, 2015. 4(3): p. 10-22.
3. Turan, N., Ş. Canbulat, and D. Yeler, Examining the Psychological and Spiritual Well-Being of Older Adult Individuals with Rheumatoid Arthritis in Turkey. Journal of Religion and Health, 2023: p. 1-13.
4. Zamani, M., et al., Prevalence of non-alcoholic fatty liver disease in patients with rheumatoid arthritis: A systematic review and meta-analysis. Clinical Gastroenterology and Hepatology, 2023.
5. Matcham, F., et al., The prevalence of depression in rheumatoid arthritis: a systematic review and meta-analysis. Rheumatology, 2013. 52(12): p. 2136-2148.
6. Oliver, J. and A. Silman, Risk factors for the development of rheumatoid arthritis. Scandinavian journal of rheumatology, 2006. 35(3): p. 169-174.
7. Aho, K. and M. Heliövaara, Risk factors for rheumatoid arthritis. Annals of medicine, 2004. 36(4): p. 242-251.
8. Chauhan, S., et al., Current Approaches in Healing of Wounds in Diabetes and Diabetic Foot Ulcers. Current Bioactive Compounds, 2023. 19(3): p. 104-121.
9. Chaudhari, K., S. Rizvi, and B.A. Syed, Rheumatoid arthritis: current and future trends. Nat Rev Drug Discov, 2016. 15(5): p. 305-6.
10. Matteson, E.L. Current treatment strategies for rheumatoid arthritis. in Mayo Clinic Proceedings. 2000. Elsevier.
11. Crofford, L.J., Use of NSAIDs in treating patients with arthritis. Arthritis research & therapy, 2013. 15: p. 1-10.
12. van Laar, M., et al., Pain treatment in arthritis-related pain: beyond NSAIDs. The open rheumatology journal, 2012. 6: p. 320.
13. Simon, L., DMARDs in the treatment of rheumatoid arthritis: current agents and future developments. International journal of clinical practice, 2000. 54(4): p. 243-249.
14. Chauhan, S., et al., Antihyperglycemic and Antioxidant Potential of Plant Extract of Litchi chinensis and Glycine max. International Journal of Nutrition, Pharmacology, Neurological Diseases, 2021. 11(3): p. 225-233.
15. Dhankhar, S., et al., Novel targets for potential therapeutic use in Diabetes mellitus. Diabetology & Metabolic Syndrome, 2023. 15(1): p. 17.
16. Cameron, M., J.J. Gagnier, and S. Chrubasik, Herbal therapy for treating rheumatoid arthritis. Cochrane Database of Systematic Reviews, 2011(2).
17. Little, C. and T. Parsons, Herbal therapy for treating rheumatoid arthritis. The Cochrane Database of Systematic Reviews, 2001(1): p. CD002948-CD002948.
18. Lalit, K., et al., Phyto-pharmacological review of Coccinia indica. World Journal of Pharmacy and Pharmaceutical Sciences (WJPPS), 2014. 3(2): p. 1734-1745.
19. Mittal, P., et al., A Review on Natural Antioxidants for Their Role in the Treatment of Parkinson's Disease. Pharmaceuticals, 2023. 16(7): p. 908.

20. Daily, J.W., M. Yang, and S. Park, Efficacy of turmeric extracts and curcumin for alleviating the symptoms of joint arthritis: a systematic review and meta-analysis of randomized clinical trials. Journal of medicinal food, 2016. 19(8): p. 717-729.
21. Henrotin, Y., F. Priem, and A. Mobasheri, Curcumin: a new paradigm and therapeutic opportunity for the treatment of osteoarthritis: curcumin for osteoarthritis management. Springerplus, 2013. 2: p. 1-9.
22. Rohilla, S., et al., Anabolic Androgenic Steroids: A Review. New Emirates Medical Journal, 2024. 5: p. 1-10.
23. Saharan, R., et al., Hydrogel-based Drug Delivery System in Diabetes Management. Pharmaceutical Nanotechnology, 2024. 12: p. 1-11.
24. Umar, S., et al., Boswellia serrata extract attenuates inflammatory mediators and oxidative stress in collagen induced arthritis. Phytomedicine, 2014. 21(6): p. 847-856.
25. Dhankhar, S., et al., Cognitive Rehabilitation For Early-Stage Dementia: A Review. Current Psychiatry Research and Reviews, 2024. 20: p. 1-14.
26. Kaur, N., et al., ANTI-INFLAMMATORY AND ANALGESIC ACTIVITY OF CURCUMIN WITH DIFFERENT NSAIDS. Indian Drugs, 2018. 55(7).
27. Yarnell, E., Herbs for rheumatoid arthritis. Alternative and Complementary Therapies, 2017. 23(4): p. 149-156.
28. Narwal, S., et al., Current Therapeutic Strategies for Chagas Disease. Anti-Infective Agents, 2023. 21: p. 1-11.
29. Panchal, M., et al., A Comprehensive Review of Alternative Therapeutic Approaches for Nausea and Vomiting Relief in Pregnancy. New Emirates Medical Journal, 2024. 5: p. 1-8.
30. Rohilla, M., et al., Discussing pathologic mechanisms of Diabetic retinopathy & therapeutic potentials of curcumin and β-glucogallin in the management of Diabetic retinopathy. Biomedicine & Pharmacotherapy, 2023. 169: p. 115881.
31. Cameron, M., et al., Evidence of effectiveness of herbal medicinal products in the treatment of arthritis. Phytotherapy Research, 2009. 23(11): p. 1497-1515.
32. Ahmed, M.S., et al., Phytochemical investigations, in-vitro antioxidant, antimicrobial potential, and in-silico computational docking analysis of Euphorbia milii Des Moul. Journal of Experimental Biology and Agricultural Sciences, 2023. 11(2): p. 380-393.
33. Chandrasekar, R. and S. Chandrasekar, Natural herbal treatment for rheumatoid arthritis-a review. International Journal of Pharmaceutical Sciences and Research, 2017. 8(2): p. 368.
34. Dhankar, S., et al., Artificial Intelligence in The Management of Neurodegenerative Disorders. CNS & Neurological Disorders - Drug Targets, 2024. 23: p. 1-10.
35. Choudhary, M., et al., Medicinal plants with potential anti-arthritic activity. Journal of intercultural ethnopharmacology, 2015. 4(2): p. 147.
36. Upadhyay, R.K., Anti-arthritic potential of plant natural products; its use in joint pain medications and anti-inflammatory drug formulations. International Journal of Green Pharmacy (IJGP), 2016. 10(3).
37. Sharma, K., et al., Natural compounds as anti-arthritic agents-A Review. Pharmacognosy Reviews, 2009. 3(5): p. 22.
38. Jain, S., et al., Antiarthritic activities of herbal isolates: A comprehensive review. Coatings, 2021. 11(11): p. 1329.

39. Murugananthan, G. and S. Mohan, Anti-arthritic and anti-inflammatory constituents from medicinal plants. Journal of Applied Pharmaceutical Science, 2013. 3(4): p. 161-164.
40. Rauf, A., et al., Preliminary phytochemical screening and antioxidant profile of Euphorbia prostrate. 2012. 1(1): p. 9-13.
41. Munjal, K., et al., Polyphenol-enriched fraction and the compounds isolated from Garcinia indica fruits ameliorate obesity through suppression of digestive enzymes and oxidative stress. 2020. 16(70): p. 236.
42. Sharma, A., et al., Combination effect of Spirulina fusiformis with rutin or chlorogenic acid in lipopolysaccharide-induced septic cardiac inflammation in experimental diabetic rat model. 2021. 17(6): p. 257.
43. Gupta, S., et al., Unwinding Complexities of Diabetic Alzheimer by Potent Novel Molecules. Am J Alzheimers Dis Other Demen, 2020. 35: p. 1533317520937542.
44. Kumar, S., R. Malhotra, and D.J.P.r. Kumar, Euphorbia hirta: Its chemistry, traditional and medicinal uses, and pharmacological activities. 2010. 4(7): p. 58.
45. Chen, L., R. Chen, and K.J.Z.Z.y.z.z.Z.Z.Z.C.J.o.C.M.M. Wei, Constituents of tannins from Euphorbia prostrata Ait. 1992. 17(4): p. 225-6, 255.
46. Schiff, M.H., Role of interleukin 1 and interleukin 1 receptor antagonist in the mediation of rheumatoid arthritis. 2000. 59(suppl 1): p. i103-i108.
47. Lin, Y.J., M. Anzaghe, and S. Schulke, Update on the Pathomechanism, Diagnosis, and Treatment Options for Rheumatoid Arthritis. Cells, 2020. 9(4).
48. Dayer, J.M., F. Oliviero, and L. Punzi, A Brief History of IL-1 and IL-1 Ra in Rheumatology. Front Pharmacol, 2017. 8: p. 293.
49. Choy, E., Inhibiting interleukin-6 in rheumatoid arthritis. Curr Rheumatol Rep, 2008. 10(5): p. 413-7.
50. Srirangan, S. and E.H. Choy, The role of interleukin 6 in the pathophysiology of rheumatoid arthritis. Ther Adv Musculoskelet Dis, 2010. 2(5): p. 247-56.
51. Pandolfi, F., et al., Interleukin-6 in Rheumatoid Arthritis. Int J Mol Sci, 2020. 21(15).
52. Angelini, J., et al., JAK-Inhibitors for the Treatment of Rheumatoid Arthritis: A Focus on the Present and an Outlook on the Future. Biomolecules, 2020. 10(7).
53. A, T.V., et al., Selective JAKinibs: Prospects in Inflammatory and Autoimmune Diseases. BioDrugs, 2019. 33(1): p. 15-32.
54. Davis, J.S., et al., Infectious Complications of Biological and Small Molecule Targeted Immunomodulatory Therapies. Clin Microbiol Rev, 2020. 33(3).
55. Bluml, S., et al., Targeting TNF receptors in rheumatoid arthritis. Int Immunol, 2012. 24(5): p. 275-81.
56. Kaur, A., S. Mujwar, and N. Adlakha, In-silico analysis of riboswitch of Nocardia farcinica for design of its inhibitors and pharmacophores. International Journal of Computational Biology Drug Design, 2016. 9(3): p. 261-276.
57. Kaushal, S.K., et al., Molecular Docking based analysis to elucidate the DNA Topoisomerase IIbeta as the potential target for the Ganoderic acid, A natural therapeutic agent in cancer therapy. Curr Comput Aided Drug Des, 2019.
58. Minaz, N., et al., Impact of diabetes on male sexual function in streptozotocin-induced diabetic rats: Protective role of soluble epoxide hydrolase inhibitor. Biomedecine & pharmacotherapie, 2019. 115: p. 108897.

59. Mujwar, S., Computational repurposing of tamibarotene against triple mutant variant of SARS-CoV-2. Comput Biol Med, 2021. 136: p. 104748.
60. Mujwar, S., et al., Drug Repurposing Approach for Developing Novel Therapy Against Mupirocin-Resistant Staphylococcus aureus. Assay Drug Dev Technol, 2019. 17(7): p. 298-309.
61. Mujwar, S. and V. Kumar, Computational Drug Repurposing Approach to Identify Potential Fatty Acid-Binding Protein-4 Inhibitors to Develop Novel Antiobesity Therapy. Assay drug development technologies, 2020. 18(7): p. 318-327.
62. Mujwar, S., et al., Docking based screening of curcumin derivatives: a novel approach in the inhibition of tubercular DHFR. International Journal of Computational Biology and Drug Design, 2021. 14(4): p. 297-314.
63. Mujwar, S. and A. Tripathi, Repurposing Benzbromarone as Antifolate to Develop Novel Antifungal Therapy for Candida Albicans. 2021.
64. Mujwar S, P.K., Prediction of riboswitch as a potential drug target and design of its optimal inhibitors for Mycobacterium tuberculosis. International Journal of Computational Biology and Drug Design, 2015. 8(4): p. 326-347.
65. Mujwar S, P.K., Prediction of Riboswitch as a potential drug target for infectious diseases: An Insilico case study of anthrax. Journal of Medical Imaging and Health Informatics, 2015. 5(1): p. 7-16.
66. Mujwar, S., Computational bioprospecting of andrographolide derivatives as potent cyclooxygenase-2 inhibitors. Biomedical Biotechnology Research Journal, 2021. 5(4): p. 446.
67. Shah, K., et al., Molecular Docking and In Silico Cogitation Validate Mefenamic Acid Prodrugs as Human Cyclooxygenase-2 Inhibitor. Assay Drug Dev Technol, 2019. 17(6): p. 285-291.
68. Shah, K., et al., Computational Design and Biological Depiction of Novel Naproxen Derivative. ASSAY Drug Development Technologies, 2020. 18(7): p. 308-317.
69. Schiff, M.H., Role of interleukin 1 and interleukin 1 receptor antagonist in the mediation of rheumatoid arthritis. Ann Rheum Dis, 2000. 59 Suppl 1: p. i103-8.
70. Berman, H.M., et al., The protein data bank. 2000. 28(1): p. 235-242.
71. Melgar, K., et al., Overcoming adaptive therapy resistance in AML by targeting immune response pathways. Sci Transl Med, 2019. 11(508).
72. Gelinas, A.D., et al., Crystal structure of interleukin-6 in complex with a modified nucleic acid ligand. J Biol Chem, 2014. 289(12): p. 8720-34.
73. Huang, J., et al., Promising Therapeutic Targets for Treatment of Rheumatoid Arthritis. Front Immunol, 2021. 12: p. 686155.
74. Wang, T., et al., Janus kinase 2 inhibitors. Synthesis and characterization of a novel polycyclic azaindole. J Med Chem, 2009. 52(24): p. 7938-41.
75. He, M.M., et al., Small-molecule inhibition of TNF-alpha. Science, 2005. 310(5750): p. 1022-5.
76. Agrawal N, U.P., Mujwar S, Mishra P,, Analgesic, anti-inflammatory activity and docking study of 2-(substituted phenyl)-3-(naphthalen1-yl)thiazolidin-4-ones. Journal of Indian Chemical Society, 2020. 97: p. 39-46.
77. Jain, R. and S. Mujwar, Repurposing metocurine as main protease inhibitor to develop novel antiviral therapy for COVID-

19. J Structural Chemistry, 2020. 31(6): p. 2487-2499.
78. Soni, N., K.R. Pardasani, and S. Mujwar, Insilico analysis of dietary agents as anticancer inhibitors of insulin like growth factor 1 receptor (IGF1R). J Pharm Pharm Sci, 2015. 7(9): p. 191-196.

HOW TO CITE: Manita Demla*, Amit Sharma, In-Silico Exploration of Natural Plant Derived Compounds in the Management of Arthritis, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 7, 1636-1653. https://doi.org/10.5281/zenodo.12798109