

A Review on Therapeutic Activities of *Coriandrum sativum L* for Rheumatoid Arthritis Remedy

Abstract

Rheumatoid Arthritis (RA) is an immune-mediated inflammatory condition. It occurs when the immune system attacks the tissue surrounding joints due to the release of specific chemicals and enzymes that start consuming away the cartilage and bones. The ant-arthritis of *Coriandrum sativum* (CS) has not been summarized before, so this review aims to assess further and explore its efficacy in RA disorders. The online literature search was performed using databases such as ScienceDirect, PubMed, Google Scholar, Wiley Online, Library, Springer, and Taylor& Francis for review. Articles published from January 2010 to January 2024 were composed. Additionally, the molecular docking of the eight selected CS phytochemicals was carried out against the AR protein target (PDB ID: 2AXJ) to support the review. Different parameters such as docking score, oral bioavailability, drug-likeness, absorption, distribution, metabolism, excretion, and toxicity (ADMET) were examined. Docking scores depicted that, anethole, beta-pinene, camphor, and geraniol phytochemicals demonstrated a commendable potential as inhibitors of 2AXJ molecule. The score hierarchy is camphor (-6.9 kcal/mol), beta-pinene (5.9 kcal/mol), geraniol (-5.3 kcal/mol), and anethole (-5.2 kcal/mol). The four phytochemicals also appear to have good drug-likeness properties and oral bioavailability. Therefore the in vitro and in vivo studies have demonstrated that CS has strong potential as anti-arthritis and anti-inflammatory. However, clinical trials for both fresh and extracted CS are also necessary to validate the findings.

Key words: Rheumatoid Arthritis, inflammatory, docking scores, phytochemicals, bioavailability.

1. Introduction

Rheumatoid Arthritis (RA) is a prevalent autoimmune disease affecting humans, with a global predominance of approximately 1%. [1]. It is an inflammatory disease in which the immune system of the body attacks healthy cells by mistake causing painful swelling in the affected body parts [2]. The disease is best described by the development of pannus which results in the hyperplastic synovium and subsequent erosion of bone and cartilage [3,72,73,74]. Even though its etiology and pathogenesis have been better defined, the molecular mechanism underlying its pathology is still not fully understood [4].

RA, septic arthritis, osteoarthritis (OA), mechanical back pain, and recurrent tendonitis are a few chronic joint disorders that show musculoskeletal symptoms of stiffness pain and joint dysfunction. Although many forms of arthritis have been reported AO and RA are the most prevalent type [5]. RA can occur in all ages but it is more likely in middle ages. Women are reportedly affected with RA more regularly than men [6]. Environmental factors are considered to play a significant role in the disease process, in addition to genetic factors, family history,

hormones, age, and smoking habits. Similarly, it has long been believed that microorganisms cause autoimmune disease by residing on target organs with self-peptide-like epitopes [7]. According to the WHO statistics, at least 50% of RA patients in developed nations are unable to work a full-time job. This is most likely because the disability manifests within ten years of the disease's onset [8]. In African and Middle Eastern countries, the estimated incidence of RA varied from 0.14% in the western sub-Sahara Africa to 0.54% in the urban areas of other African cities [9].



(a) (b)
Figure 1: (a) coriander leaves and (b) coriander seeds

Many conventional anti-arthritic medications have been used to treat arthritis conditions, but their efficiency and tolerability can be outweighed by the documented adverse effects on human health [10]. Therefore, the demanding priority is to search for complementary and alternative treatment options such as traditional medicine, medical plants, and their Phytoconstituents which demonstrate substantial anti-inflammatory activities with minimal harmful effects on human health [11].

Coriandrum sativum L (CS) plants (Figure 1) comprising bioactive compounds such as terpenoids, terpene, camphor, limonene, and geraniol to mention a few, have anti-inflammatory, analgesic, and antioxidant activities that reduce the development of arthritis which inhibit symptoms like pain, swelling, and inflammations [10,11]. CS also contains high nutritional values such as proteins, oils, carbohydrates, fibers, trace elements, vitamins, and a wide variety of minerals [12]. This review therefore provides the updated summary of the therapeutic actions of coriandrum sativum L towards rheumatoid arthritis disease, supported by a molecular docking study of the selected bioactive compounds of the same plant against the AR protein target.

2. Material and Method

2.1. Review of Therapeutic Activities

The plant's name was verified first using www.theplantlist.org, the review was based on the data search carried out in the scientific literature database that served as the foundation including ScienceDirect, PubMed, Google Scholar, Wiley Online, Library, Springer and Taylor& Francis using articles published from January 2010 to January 2024. The search used the following keywords: Rheumatoid Arthritis, *Coriandrum sativum* L, anti-inflammatory, inflammatory, and therapeutic activities. The same was used as a guide to search for articles in another database. A full text and abstract articles were gathered, reviewed, and summarized and conclusions were drawn.

2.2. Selection of Bioactive Compounds for Computational

The structures of bioactive compounds: linalool, limonene, camphor, geraniol, pinene, linalyl-acetate, citronellal, anethole, and methotrexate were selected and then downloaded from the PubChem library as 3D conformers and saved as a structure data file (sdf) [13].

2.3. Protein Selection and Preparation

The Protein target of AR crystal structures of T cell receptor beta chains related to rheumatoid arthritis was retrieved from the Protein Data Bank (PDB ID: 2AXJ) [14]. The targeted macromolecule was obtained using the X-ray diffraction method with a resolution of 2.65 Å, R-free value of 0.286, R-work value of 0.233 and R-observed value of 0.233 which gives the molecule good quality with high resolution [15]. The standard structure from the Protein Data Bank is not optimized for instant use, and it often includes only heavy atoms; therefore, water molecules, heteroatoms, actosite, and co-factors were deleted [16]. Since hydrogen atoms are typically absent from crystallographic structures, polar hydrogen atoms were added to the prepared protein [17]. The protein receptor was then saved in the Protein Data Bank, Partial Charge (Q), & Atom Type (T) (PDBQT) format for further analysis. The protein target was created via BIOVIA Studio visualization software [18].

2.4. Ligand Preparations

The natural compounds of *coriandrum sativum* L were retrieved from an accessible commercial PubChem library. Then, the bioactive compounds were screened using Swiss ADME and pkCSM software to identify the safe compounds that have drug-like properties [19]. The 2D and 3D structures were optimized to avoid unnatural overlapping of any two nonbonding atom in protein structure and to find the best position of the ligand against protein target. These natural substances were then subjected to virtual screening using PyRx software for identification of substances with high binding affinities [20].

2.5. Molecular docking

Molecular docking is the crucial tools in computer aided drug design and structural molecular biology [21]. The Autodock Vina tool was used to illuminate the binding conformations of the hit

chemical with the protein (PDB ID: 2AXJ) [22]. Energy for all ligands was minimized to allow the molecular arrangement at the favorable energetic space followed by conversion of all ligands in Pdbqt format [23]. The following values are the recorded on Vina Wizard and the Vina search: center X: 36.3838 Y: 118.1348, Z: 3.-17.983, for a box of dimension X: 173.2050, Y: 130.7446, Z: 122.4656, and exhaustiveness was set as eight (8). Other AutoDock parameters were set to be the defaults. The binding affinities results were saved in Comma Separate Value (CSV) format after the wizard had been executed. A PDB file including the ligands with different affinities was prepared for the receptor-ligand interaction. Conformations with high affinities were taken for further study in BIOVIA Discovery Studio for examination of docking poses.

2.6. Bioavailability radar

Six physiochemical traits are taken into account when evaluating drug-likeness quickly using bioavailability radar. Lipophilicity, size polarity, solubility, flexibility, and saturation are a few of these. For a molecule to be categorized as drug-like, its radar plot must entirely fall inside the pink areas on each axis, which represent physicochemical ranges [24].

3. Results and Discussions

3.1. Review of Therapeutic Activities

Coriandrum sativum L (CS) has long been utilized in traditional medical systems to treat rheumatoid arthritis [25]. Researcher reported that CS leaves considerably influence all parameters without negatively affecting arthritis patients [26]. The leaves have therapeutic effects due to numerous phytochemicals, including vitamins and minerals. The combined effects of the phytochemicals present give rise to the antioxidant and anti-arthritic properties exhibited by the CS leaves.

The investigation of molecular alterations in the rat gastrocnemius muscle following five days of RA induction and the possible outcome of CS treatment using a proteomic method was performed [27]. The research shed light on the potential uses of CS as a supplemental treatment to prevent and delay RA pathogenesis. They finally revealed that CS therapy could partially restore the molecular abnormalities induced by RA such as reduced mitochondria function, impaired carbon metabolism, and myofiber-type alteration. Another research reported a series of publications dealing with the anti-inflammatory activities of different food extracts and clinical studies of RA patients. CS is among the nutraceuticals studied. The results of their research publicized that the majority of the nutraceuticals studied possess beneficial effects towards chronic inflammatory disease and therefore, concluded that anti-inflammatory and antioxidant nutraceuticals may serve as complementary medicine for the treatment of RA [28].

CS seeds' efficiency in fighting RA patients' oxidative stress was also studied. The results of this study showed that treatment with CS significantly increases the level of enzymatic and non-enzymatic antioxidants. It further discovered that the subjects' liver, kidney, and hematological profiles remained unchanged, indicating that CS supplementation was a safe and efficient way to

help RA patients combat oxidative stress [29]. The preclinical studies conducted over the past 20 years have demonstrated the beneficial effects of commonly used Indian spices including CS and their phytochemicals, which are beneficial in the treatment of RA. It was further reported that, due to their abundance, low cost, and safety in consumption they still have a great deal of potential to be developed into a non-toxic broad spectrum of RA dietary agents [30].

The *in vivo* and *in vitro* studies of CS have demonstrated strong evidence of its anti-inflammatory activity. The study concluded that both *in vivo* and *in vitro* have shown that CS modifies and regulates several signaling pathways and inflammatory mediators [12, 30]. Other researchers conducted a study that evaluated the anti-inflammatory activities of CS hydroalcoholic extract in experimental models. The results of this study indicated that the anti-inflammatory activities of CS hydroalcoholic validate the traditional use of CS in the treatment of chronic inflammatory disorders [31].

Studies reported that CS seeds are traditionally consumed to relieve pain, RA, and inflammation. Further reported that the same has been used and prescribed to treat gastrointestinal disorders such as diarrhea, nausea, flatulence, and indigestion. It is believed that CS works by inducing the liver to secrete more bile or other digestive enzymes which intensifies the digestive system [32]. Many biological activities attributed to the bioactive phytochemicals found in CS were reported. The major compound linalool widely presented in seeds is notable for its capacity to alter numerous important diseases. The compound is well known for its antioxidant, anticancer, neuroprotective, anxiolytic, anticonvulsant anti-inflammatory, analgesic, hypotensive, and antimicrobial capacities [33]. Numerous biological activities of CS such as antioxidant, anticancer, neuroprotective, anxiolytic, hypnotic, anticonvulsant, anti-inflammatory, and anti-diabetic, have also been reported [34].

Another study reported that all parts of the CS plant are used as traditional therapy for the treatment of different disorders in the traditional medical practices of various societies. Different bioactive components of this herb have been linked to a broad range of pharmacological effects including anti-inflammatory, anti-microbial, anti-oxidant, and anti-diabetic, anxiolytic, anti-epileptic, anti-depression, and anti-mutagenic [35]. CS has various phenolic compounds primarily flavonoids, coumarins, and phenol carboxylic acids, found in dried CS seeds, and believed to play a crucial role in herbs' therapeutic qualities. The research has demonstrated the CS hypoglycemic, hypolipidemic, anti-hypertensive, anti-microbial, anti-helminthic, and anti-mutagenic properties. Additionally, it has been demonstrated to alleviate RA symptoms and joint pain [36].

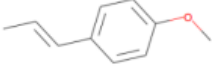

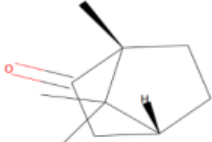

Researchers examined anti-inflammatory activities in the ethanolic extract of CS using carrageenan-induced paw oedema in albino rats. The study demonstrated a significant antioedematogenic effect of the ethanolic extract of CS leaves on carrageenan-induced paw oedema. The results of this study suggest that CS may be useful in treating acute inflammatory disorder because the carrageenan-induced inflammatory mode is a significant predictive test for anti-inflammatory agents. Additionally, the CS seed extracts have been used as stimulants,

carminatives, antispasmodics, diuretics, and anti-rheumatic in the traditional system of medicine [37].

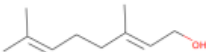
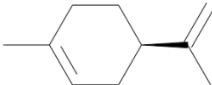
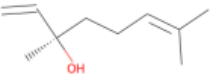
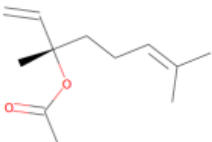
CS oil is beneficial for the treatment of rheumatism. CS which belongs to the Apiaceae family contains borneol, geraniol, and linalool which are very helpful for RA remedies [38]. One of the conducted preclinical studies concluded the therapeutic value of CS which has cineole as its main active ingredient exhibits anti-arthritis properties using hydroalcoholic extract from seed, stem, and leaves against formaldehyde and Freund's adjuvant inducing swelling in rats and exhibited an effective therapy for RA [39]. The review of therapeutic activities of some of the independent phytochemicals of CS was also conducted to examine its inhibition potential for rheumatoid arthritis as shown in Table 1

UNDER PEER REVIEW

Table 1: Therapeutic activities of the selected independent phytochemicals of CS

Name	Molecular structure	Therapeutic activities of CS	
		Selected phytochemicals	References
Anethole		Anethole a prominent CS compound has a variety of medical uses such as anti-inflammatory, anti-arthritic, antioxidant, and tumor-suppressive effects. Due to its antioxidant, gastroprotective, and hepatoprotective properties, this compound has long been utilized in pharmaceutical formulation.	[40, 41]
Beta Pinene		Research indicates a strong correlation between pinene's anti-inflammatory properties and its ability to reduce pain. In addition, pinene is well known for its anti-septic, antioxidant, and anti-depression properties. They are used to treat ailments like fibromyalgia and arthritis.	[42, 43]
Camphor		Historically, camphor has been used as a cold remedy to treat inflammation-related illnesses like rheumatism sprains bronchitis, asthma, and muscle soreness and to relieve chest congestion. Typically, camphor is prepared as a cream, oil, or balm to reduce pain and inflammation in the muscles and joints, it is easily absorbed through the skin and has a strong test and odor.	[44, 45]
Citronellal		Citronellal is a monoterpene alcohol, found in the essential oils of numerous aromatic plants. It has various pharmacological characteristics including antioxidant activity and possible anti-inflammatory and antinociceptive effects. Rheumatism in pre-elderly patients was found to be more effectively managed with citronella oil to reduce the intensity of rheumatic pain.	[46, 47]

Therapeutic activities of CS

Name	Molecular structure	Selected phytochemicals	References
Geraniol		<p>Plant-derived acyclic isoprenoid monoterpene geraniol has demonstrated anti-inflammatory properties in a variety of in vivo and in vitro models. Furthermore, geraniol maintains the activity of antioxidant enzymes and scavenges free radicals. Geraniol triggers cell cycle arrest and apoptosis modifies several molecular targets and regulates transcription to control inflammation.</p>	<p>[48, 49]</p>
Limonene		<p>Limonene is a monoterpene found in various plants, it offers a therapeutic alternative for the management of various diseases. Numerous studies have been conducted on the therapeutic effect of limonene and the compound has demonstrated an array of health benefits, including anti-inflammatory, antioxidant, antinociceptive, anticancer, antidiabetic, antihyperalgesic, antiviral, and gastroprotective properties.</p>	<p>[50, 51]</p>
Linalool		<p>Linalool is a natural compound with anti-inflammatory properties that can be used to treat a variety of disorders. Recent research shows that linalool suppresses arthritic development, pro-inflammatory mediators, and spleen and thymus indices to reduce adjuvant arthritics. Therefore, linalool may be used medicinally to treat human arthritis.</p>	<p>[52, 53]</p>
Linalyl-acetate		<p>Linalyl-acetate, the major ingredient in lavender and clary sage essential oils, has exhibited a wide range of pharmacological effects such as antioxidants, anti-inflammatory, anti-hypertensive, and neuroprotective qualities. These findings imply that linalyl-acetate and lavender oil may help to prevent rheumatoid arthritis.</p>	<p>[54, 55]</p>

3.2. Docking Scores

Molecular docking scores for anethole, beta-pinene, camphor, citronellal, geraniol, limonene, linalool, and linalyl-acetate are shown in Table 2. The scores revealed that the camphor ligand has the lowest binding affinity toward the 2AXJ target. A lower docking score indicates that ligand and target binding are more stable [56]. The different structures bound to the target caused variations in ligand-target interactions which led to different docking scores [57].

Table 2. Docking score for ligand-protein target

Name	PubChem ID	Molecular Formula	Binding Affinity/Docking Score (kcal/mol)
Anethole	CID:637563	C ₁₀ H ₁₂ O	-5.2
Beta Pinene	CID:14896	C ₁₀ H ₁₆	-5.9
Camphor	CID:2537	C ₁₀ H ₁₆ O	-6.9
Citronellal	CID:7794	C ₁₀ H ₁₈ O	-3.9
Geraniol	CID:637566	C ₁₀ H ₁₈ O	-5.3
Limonene	CID:22311	C ₁₀ H ₁₆	-4.6
Linalool	CID:6549	C ₁₀ H ₁₈ O	-3.5
Linalyl-acetate	CID:8294	C ₁₂ H ₂₀ O ₂	-4.8

Anethole with a docking score of (-5.2 kcal/mol), is the primary aroma and bioactive ingredient found in more than 20 plant species including CS, star anise, and fennel [58]. Previous research has shown that anethole possesses a wide range of pharmacological effects in the treatment of diseases, including anti-inflammatory, neuroprotective, anti-diabetic, immunomodulatory, and antithrombotic effects [59]. A well-known member of monoterpenes families, beta-pinene has a docking score of (-5.9 kcal/mol) and is found in essential oils of many different plants. Numerous pharmacological activities of the bioactive compound have been reported, including anticoagulant, antitumor, antimicrobial, and antimalarial, antioxidant, anti-inflammatory, anti-leishmania, and analgesic effects [60].

Camphor with a docking score of (-6.9 kcal/mol) is a natural compound extracted from the *C. camphora* plant and is extensively employed in the environment, industries, and pharmaceutical sector. It has long been recommended in traditional medicine for treating inflammation-related disorders including rheumatism. In addition, the compound is used to treat fever, convulsion, stroke, sputum fainting, sputum coma, laryngeal pain, mouth pain, anthrax, and bloodshot eyes. It is also capable of resuscitation and heat clearance [61].

Geraniol with a docking score of (-5.3 kcal/mol) exhibits antitumor activities against melanoma, hepatoma, and murine leukemia cells both in vitro and in vivo. Similarly, geraniol has antioxidant and anti-inflammatory properties. Therefore, it is believed that this bioactive compound has strong preventive potential which can protect against oxidative and inflammatory change [62]

The top four lead compounds (camphor, beta-pinene, geraniol, anethole) demonstrated to have a strong affinity with rheumatoid arthritis protein. The amino acid residues of Pro-204, Pro-77, and

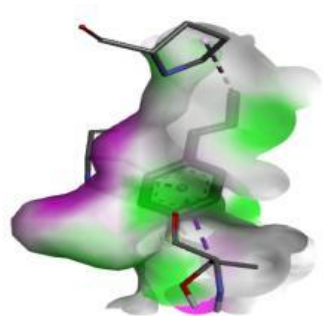
Thr-199 of 2AXJ protein were found to interact with anethole (CID 637563) (Figure 2). Two amino acid residues Pro-204 and Pro-77 interacted via a pi-alkyl non-covalent bond while the Thr-199 residue interacted via a pi-sigma bond which is a lateral overlap of the two atomic orbitals.

Four amino acid residues of 2AXJ protein (Phe-200, Val-196, Val-166, and Val-161) were found to interact with beta-pinene (CID 14896) (Figure 3). The amino acid residues Val-196, Val-166, and Val-161 have interacted via a pi-alkyl non-covalent bond while the Phe-200 residue interacted via the pi-sigma bond.

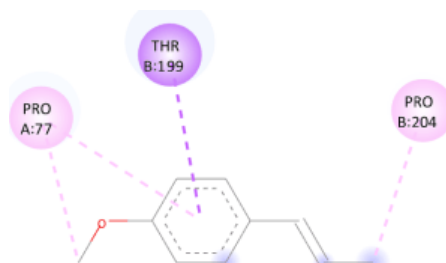
Camphor (CID 2537) was found to bind with Ser-197, Val-196, Val-166, and Val-161 residues of 2AXJ protein (Figure 4). Ser-197 residue was involved in hydrogen bond interaction with the protein target while Val-196, Val-166, and Val-161 residues were involved in a p-alkyl covalent bond. Hydrogen bond interaction determines the strength of the protein-ligand complex and is used to assess the molecular recognition, directionality, and specificity of contacts [63].

Geraniol (CID 637566) residue Val-196 was involved in a pi-alkyl noncovalent bond while Phe-200 was involved in a pi-sigma bond (Figure 5). Sigma bonds are created when atomic orbitals overlap head to head while pi-bonds are created by lateral overlapping of two atomic orbitals [64]. From the top four compounds, camphor had better binding with the 2AXJ protein compared with the other three compounds. It is the only compound that displays hydrogen bond interaction, the bonding that determines the strength of molecular docking

Figure 2

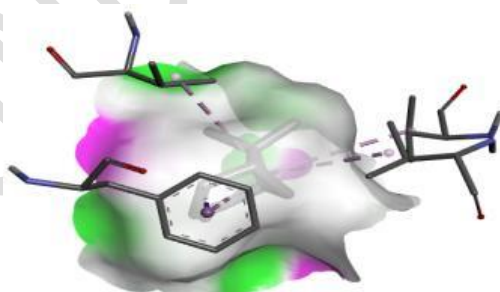


Anethole 3D

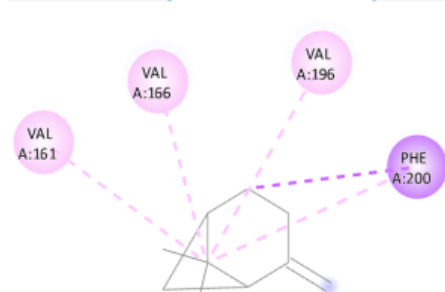


Anethole 2D

Figure 3



Beta Pinene 3D



Beta Pinene 2D

Figure 4

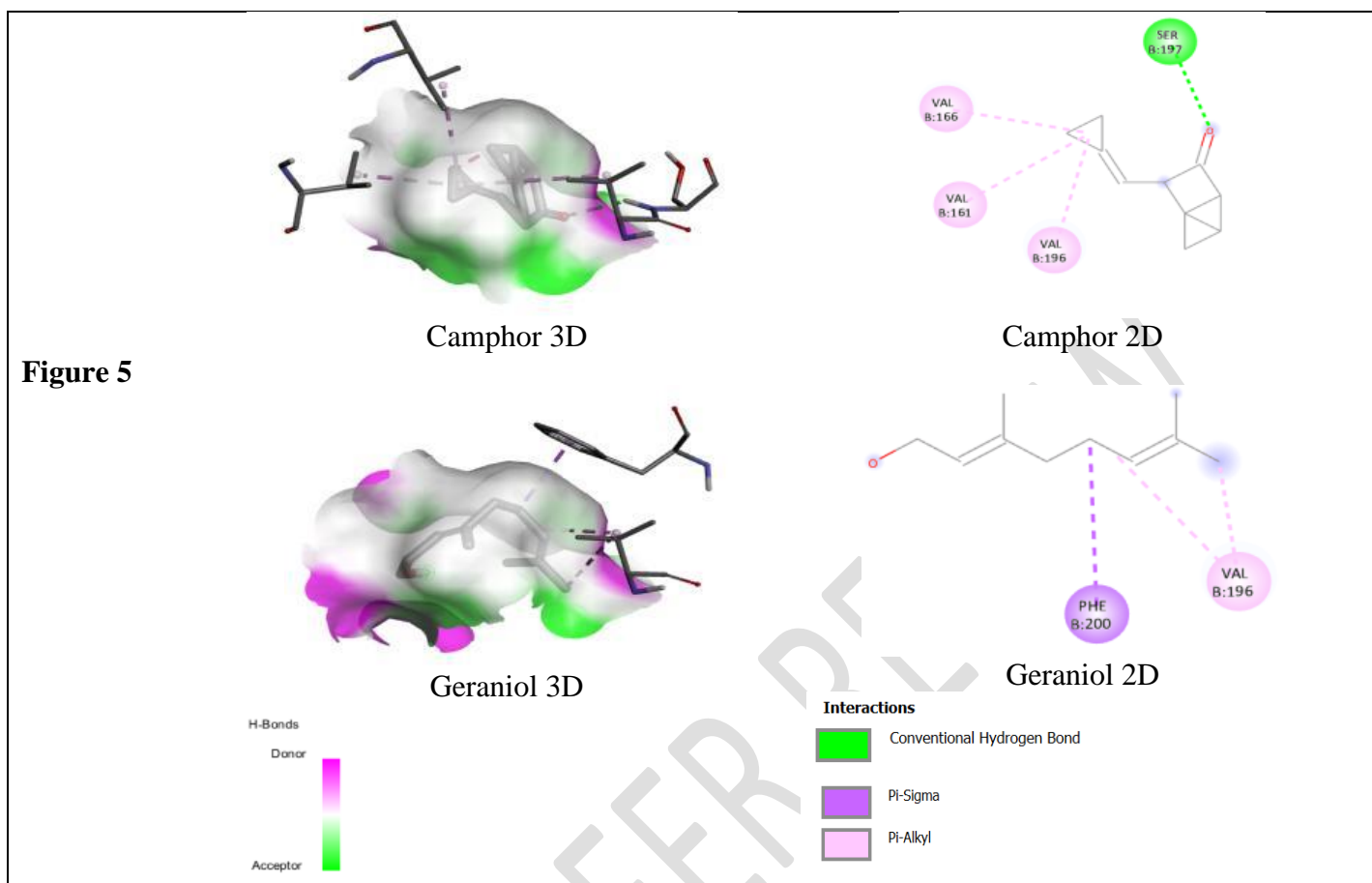


Fig. 2-5. Docking study of molecules

Bioavailability Radar

A molecule's radar plot should fall inside the colored zone to be considered drug-like (Figure 5). The pink zone represents the appropriate range for each variable, such as lipophilicity: XLOGP3 ranges from -0.7 to 5.0, the molecular weight (Mw) ranges from 150 to 500 g/mol, the topological polar surface area (TPSA) ranges from 20 to 130 Å², the solubility is less than logS, the saturation (INSATU) is greater than 0.25, and the flexibility is less than 9 rotatable bonds. Thus, according to the bioavailability radar shown in Figure 6, all four compounds appear to be oral bioavailability.

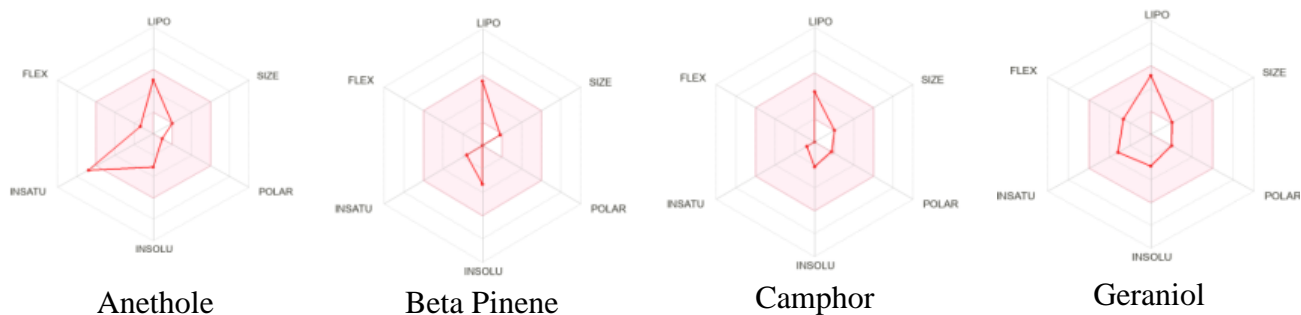


Figure 6: Bioavailability radar of the top four compounds

Pharmacokinetic and physicochemical analysis

Poor pharmacokinetic properties are one of the primary factors for the termination of drug development. Key criteria for the development of anti-arthritis medication include minimal or nonexistent toxicity, optimal value of physicochemical properties, and good oral bioavailability [65]. Therefore, researchers must select drug candidates with the correct balance of potency, absorption, distribution, metabolism, excretion, and toxicity (ADMET) [66]. In this study, the four best-scoring phytochemicals of CS were evaluated: physicochemical, pharmacokinetic (PK), Drug-Likeness, and ADMET Prediction using pkCSM and SwissADME web tools [67].

The ability of gastrointestinal (GI) absorption and blood-brain barrier penetration were projected using the BOILED-Egg model of molecules. [68]. The cutoff value for the physicochemical properties was determined using several rules, including the bioavailability score, Veber's, Ghose's, and Lipinski's rule of five (Ro5) [69]. The Swiss vector machine algorithm was used to evaluate the molecular features of drug-likeness such as molecular weight (MW), hydrogen bond donor (HBD), hydrogen bond acceptor (HBA), lipophilicity log (log P), aqueous solubility (log S), topological polar surface area (TPSA), number of rotatable bonds (nRA), and molar reactivity (MR) (Table 3).

Table 3: Physicochemical and drug-like properties analysis

Descriptor/Properties	Value				Units
	CID:637563	CID:14896	CID:2537	CID:637566	
Molecular Weight	148.20	136.23	152.23	154.25	g/mol
Monoisotopic Mass	148.0888	136.1252	152.1201	154.1357	Da
Rotatable Bonds	2	0	0	4	-
H. Acceptors	1	0	1	1	-
H. Donors	0	0	0	1	-
LogP	2.7	2.9987	2.4017	2.6714	-
Num. arom. heavy atoms	2	0	0	0	-
Fraction Csp3	0.2	0.80	0.9	0.60	-
Num. of heavy atoms	11	10	11	11	-
Topological Polar Surface Area	9.2	0	17.1	20.2	Å ²
Molar Refractivity	47.83	45.2	45.64	50.4	-

Additionally, in silico data were generated for the main human cytochrome P450 (CYP) isoforms CYP1A2, CYP3A4, CYP2D6, CYP2C9, and CYP2C19 which are involved in drug metabolism. The total clearance and renal OCT2 substrate were quantitatively predicted to ascertain the CS phytochemicals' excretion route. The safety profile of the phytochemicals is one of the key factors in drug development [70]. All phytochemicals' main toxicity endpoint was evaluated according to pharmacokinetic analysis. In addition, several safety factors were assessed including LD50, hepatotoxicity, skin sensitization, cellular toxicity, and hERG liability (Table 4).

Table 4: ADMET prediction of the top-scored natural compounds

Properties	Model name	Predicted Value				Unit
		CID:637563	CID:14896	CID:2537	CID:637566	
Absorption	Water solubility	-2.936	-4.191	-2.895	-2.866	mol/L
	P-gp substrate	No	No	No	No	-
	P-glycoprotein	No	No	No	No	-
	Gastrointestinal absorption	High	Low	High	High	-
	Caco-2 permeability	1.669	1.385	1.499	1.49	cm/s
	Intestinal absorption %	95.592	95.525	95.965	92.788	-
Distribution	BBB permeability	0.529	0.818	0.612	-0.606	Log BB
	VDss (human)	0.343	0.685	0.331	0.17	Log L/kg
	Fraction unbound	0.226	0.35	0.459	0.447	Fu
	CNS permeability	-1.659	-1.857	-2.158	-2.159	Log Ps
	Leadlikeness	No	No	No	No	-
Metabolism	Inhibitor					
	CYP2C19	No	No	No	No	-
	CYP2C9	No	No	No	No	-
	CYP2D6	No	No	No	No	-
	CYP3A4	No	No	No	No	-
	CYP1A2	Yes	No	No	No	-
Excretion	Total Clearance	0.268	0.03	0.109	0.437	ml/min/kg
	Renal OCT2 substrate	No	No	No	No	-
Toxicity	Skin sensitization	Yes	No	Yes	Yes	-
	Hepatotoxicity	No	No	No	No	-
	AMES toxicity	No	No	No	No	-
	hERG I inhibitor	No	No	No	No	-
	hERG II inhibitor	No	No	No	No	-
	Minnow toxicity	0.869	1.012	1.458	1.213	log mM
	T.Pyiformis toxicity	0.807	0.628	0.233	0.595	log ug/L
LD50	1.798	1.673	1.653	1.636	mol/kg	

4. Conclusion

Coriandrum sativum L has been used extensively for both culinary and traditional purposes. While linalool is the primary constituent of CS extract, other major groups of phytochemicals such as anethole, beta-pinene, camphor, and geraniol are also seen to be responsible for the treatment of different disorders including AR [71]. In this review, the effectiveness of CS in the treatment of RA has been discussed and assessed based on earlier research and publications, where CS exhibited anti-arthritis potential. A computational study was also conducted to support the review. Potential parameters such as docking score, drug-likeness, ADMET predictions, and oral bioavailability were examined. Docking scores showed that, anethole, beta-pinene, camphor, and geraniol phytochemicals have a creditable latent as inhibitors of 2AXJ molecule. The score hierarchy is camphor (-6.9 kcal/mol), beta-pinene (5.9 kcal/mol), geraniol (-5.3 kcal/mol), and anethole (-5.2 kcal/mol). The selected phytochemicals also seem to have good drug-likeness properties and oral bioavailability. However, further study on the clinical trial of both fresh and extracted CS to validate RA treatments is still recommended.

5. Acknowledgement

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6. Conflict of Interest

The authors declare that there have been no conflicts of interest apprehended in this study.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

Option 2:

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc have been used during writing or editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology

Details of the AI usage are given below:

- 1.
- 2.
- 3.

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