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Anti-psoriatic and Anti-inflammatory Potentials of Phytochemicals from *Curcuma longa* against Interleukin-17A and Inducible Nitric Oxide Synthase: An *In Silico* Study

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ABSTRACT

Psoriasis is a chronic autoimmune cell-mediated inflammatory skin disease that affects approximately 125 million people worldwide. Turmeric has been long known for its potent anti-inflammatory activities. In this study, in silico studies were used to evaluate the efficacy of isolated phytochemicals from turmeric in the treatment of psoriasis. One hundred and fifteen phytochemicals from this plant and two standard medications (Flurandrenolide and Triamcinolone), active ingredients used in some topical steroid creams were evaluated for their inhibitory properties against Interleukin-17A (IL-17A) and Inducible NOS (iNOS) receptor using a computer-aided drug design approach. The binding scores and inhibitory efficiencies were obtained via virtual screening. ADMET SAR-2 website was used to conduct the Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) analysis, the Molinspiration and SwissADME tools were used to investigate the drug-likeness characteristics and oral bioavailability of the selected compounds respectively. Other analyses of the selected compounds include bioactivity, activity spectra for substances (PASS) prediction, binding mode, and molecular interaction. The results revealed that Bisabolone (−9.3 kcal/mol), Curcumanolide B (−8.6 kcal/mol), (E)-sesquisabinene hydrate (−8.5 kcal/mol), and procurcumadiol (−8.3 kcal/mol) are potential inhibitors of iNOS receptor, while hop-17(21)-en-3-ol (7.6 kcal/mol) is a potential inhibitor of IL-17A receptor. These compounds have better ADMET properties, binding affinities, drug-likeness, PASS properties, bioactivities, oral bioavailability, good binding mechanism, and interactions with the active site of the target receptor when compared with Flurandrenolide and Triamcinolone. As a result, this preliminary investigation suggests that these phytochemicals should be studied further to design novel psoriasis therapeutics.

Keywords: Anti-inflammatory; Molecular docking; Psoriasis; Skin disorder; Turmeric.

INTRODUCTION

Psoriasis is a chronic autoimmune skin disease affecting 2 – 3 % of the population worldwide (Baliwag et al., 2015). It is characterized by dilated dermal capillaries and accelerated epidermal proliferation that can grow up to ten times more quickly than usual. The death of the underlying cells at the surface of the skin causes their sheer volume to produce red plaques shielded with white scales that cause scaly and itchy skin, discomfort, swelling, and mutilating skin lesions (MacDonald and Burden, 2007). There is no age limit on the onset of psoriasis, as it affects both men and women equally. Although, the disease is more common in adults than children. The estimates in children vary between 0.7 % (Augustin et al., 2010) in Europe to almost none in Asia (Bø et al., 2008; Chen et al., 2008). Several factors that cause psoriasis include bacterial infection, autoimmune disorders, genetic and environmental factors. Also, chronic interactions between hyper-proliferative keratinocytes and invading activated immune cells cause it to occur. Numerous co-morbidities, such as severe depression, cancer, and cardiovascular disease (CVD) are associated with psoriasis (Ni and Chiu, 2014; Takeshita et al., 2017). Currently, there is no cure for psoriasis. All the presently available treatments such as topical treatments, light therapy, and systemic medications are only used to manage the disease (Winterfield et al., 2005; Gisondi et al., 2017; Golbari et al., 2018). Topical treatments include the use of topical corticosteroids, vitamin D analogs, anthralin, retinoids, and calcineurin inhibitors, which are used to treat mild to moderate psoriasis. The most common side effects of these treatments include

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skin irritation and thinning of the skin (Choi et al., 2017). In Light therapy, natural or artificial ultraviolet (UV) light is used to treat mild psoriasis by exposing skin to controlled amounts of natural sunlight. Skin cell turnover is reduced by UV exposure, which also reduces scaling and irritation. Systemic treatments involve the use of retinoids, methotrexate, and cyclosporine to treat patients with severe psoriasis, but are associated with severe side effects. Retinoids may result in hair loss and lip inflammation. Methotrexate treats psoriasis by reducing the growth of skin cells and reducing inflammation, but it can cause fatigue, loss of appetite, and stomach upset. Hoffman et al., (2016) suggest that cyclosporine should not be used long-term or at high doses due to the risks of infection, cancer, kidney problems, and high blood pressure. Thus, all of the available treatments are only used to control the disease as soon as it emerges (Tollefson et al., 2018), and do not have a permanent cure for psoriasis.

Research on phytochemicals from medicinal plants is highly on the rise due to its little or no adverse effects as an alternative therapeutic and pharmacological agent in the discovery and development of new drugs. Turmeric (*Curcuma longa L.*) is a rhizomatous herbaceous perennial plant of the ginger family, *Zingiberaceae*. The plant originates from tropical South Asia, but it is now widely planted throughout the world's tropical and subtropical climates. The plant's rhizomes are cooked and dried to create the bright orange-yellow powder known as turmeric powder. *Curcuma Longa* has long been used as a spice and for medicinal purposes, especially in Asia. Phytochemicals obtained from turmeric include monoterpenoids, phenolics, sesquiterpene, bisabolene, diarylheptanoid, and steroids have been discovered to possess anti-psoriatic and anti-inflammatory actions (Li et al., 2011). In addition to its numerous uses are its biological activities against various health challenges such as antidiabetic effects (Kuroda et al., 2005), anti-inflammatory effects (Abe et al., 1999), anti-oxidant effect (Gupta and Ghosh, 1999), lipid-lowering effect (Ramirez-Tortosa et al., 1999) among others. Previous researchers have reported the potency of *Curcuma longa* in several In silico studies against cancer (Rahman et al., 2022) and COVID-19 (Rajagopal et al., 2020).

This study investigated the anti-psoriatic and anti-inflammatory potentials of previously isolated phytochemicals from turmeric plant against two psoriasis-targeted receptors; IL-17A (PDB ID: 5HI5) and iNOS (PDB ID: 3E7G) through molecular docking and series of chemoinformatic studies.

MATERIALS AND METHODS

Materials

The software used for this study are BIOVIA discovery studio, Spartan'14 software, PyRx virtual screening tool, CASTp (http://sts.bioe.uic.edu/castp/index.html?2011), and ADMEsar2 (http://lmmd.ecust.edu.cn/admetsar2), molinspiration (http://molinspiration.com/), swissADME (http://www.swissadme.ch/), PASS online web servers (http://www.way2drug.com/passonline).

Methods

Preparation of the ligands

One hundred and fifteen (115) isolated phytochemicals from *Curcuma longa* were sourced from literature. These phytochemicals belong to different classes such as monoterpenoid, aristolene, bisabolene, caryophyllene, cedrane, diterpenoid, elemane, fatty acid, germacrene, guanine, phenolic, phenylpropene, selinane, sesquiterpene, and triterpenoid. Flurandrenolide and triamcinolone were both used as standard drugs against IL-17A and iNOS receptors. The 2D/3D structures of these compounds were obtained from the PubChem database (https://pubchem.ncbi.nlm.nhi.gov). All 2D structures were then converted to 3D using Spartan'14 software, and the most stable conformed structures were chosen and optimized using density functional theory (DFT) with B3LYP function and 6-31+G* as a basis.

Preparation of the target receptors

To prepare the target receptor, the X-ray structures of interleukin-17A (IL-17A) (PDB ID: 5HI5) and inducible Nitric oxide synthase (iNOS) (PDB ID: 3E7G) were downloaded in protein data bank (PDB) file format from the protein data bank with a resolution of 1.80Å and 2.20Å respectively. The receptors were then prepared by removing impurities and water molecules to escape interferences, using the BIOVIA discovery studio software. The binding pocket of the initial inhibitors present in 5HI5 and 3E7G was used to determine the binding parameters as preferences.

Determination of the receptors' active sites

The binding pockets, ligand interactions, and all amino acids in the active site of IL-17A (PDB ID: 5HI5) and iNOS (PDB ID: 3E7G) receptors were established using CASTp (http://sts.bioe.uic.edu/castp/index.html?2011) (Tian et al., 2018) and Biovia Discovery Studio. The data obtained were compared and validated with previously published experimental studies as

reported by Liu et al., (2016) and Garcin et al., (2008).

ADMET profiling and Drug-likeness analysis

Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) of the ligands were evaluated using the ADMET SAR-2 database (http://1mmd.ecust.edeu.cn/admetar2/) (www.admetexp.org) (Cheng et al., 2012), which is a free web tool for evaluating ADMET properties, while the drug-likeness (Lipinski rule of 5) were done using Molinspiration online tool (http://molinspiration.com/) (Daina et al., 2017).

Oral bioavailability assessments of the ligands

Oral bioavailability assessments of the ligands were achieved using the Swiss-ADME web server (http://www.swissadme.ch/) (Daina et al., 2017)

Prediction of activity spectra for substances (PASS) analysis

The biological activities of the ligands and the standard drugs were carried out using PASS online web server (Filimonov et al., 2014).

Molecular Docking Protocol

Molecular docking and scoring of the optimized ligands and the standard drugs against IL-17A (5HI5) and iNOS (3E7G) were obtained using PyRx software. The inhibition constants (Ki) in μM of the ligands and the standards were obtained using their binding affinities (ΔG) in kcal/mol as shown in (equation i) below.

$$K_i = \exp(\Delta G / RT) \quad \text{i}$$

Where R = Gas constant (1.987×10^{-3} kcal/K/mol); T = 298.15 K (absolute temperature); K_i= Inhibition constant and ΔG = Binding energy

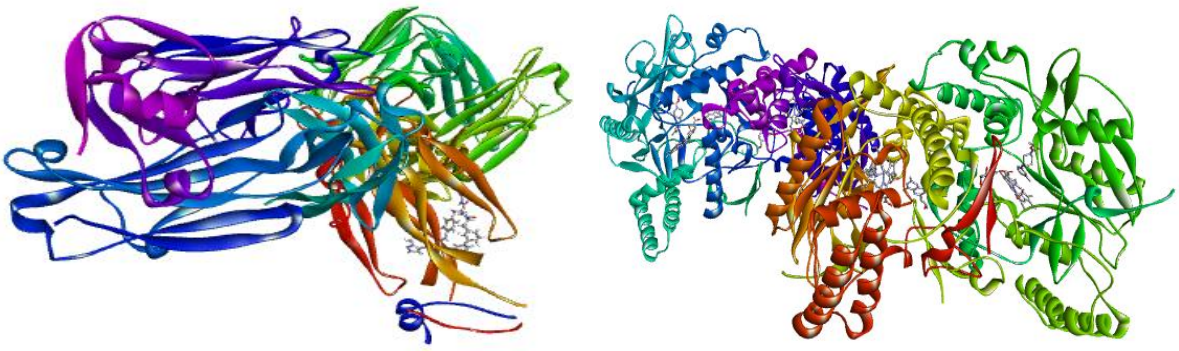
RESULTS

Structural and active site analysis of IL-17A target receptor

Interluekin-17A (IL-17A) receptor (PDB ID: 5HI5) (Figure 1) is an X–ray crystallographic structure containing 132 amino acid residues in a complex with polyamide compound inhibitors (Liu *et al*., 2016). As shown by the X–ray diffraction study, the enzyme has a resolution of 1.80 Å. The crystal structure of the complex of the inhibitors with IL-17A reveals dynamic changes in the protein's binding site. Compound 1 binds at the dimer interface within the central pocket formed by residues from both IL-17A monomers, inducing a significant reconfiguration of the dimer and widening of the central pocket. Ligand binding causes separation of the entire N-terminal β-strands of the two IL-17A polypeptides, with residues Leu120 moving away from each other. Upon binding of compound 1, both the solvent-accessible surface and the volume of the binding pocket are more than doubled. Compound 1 covers 564Å^2 of the hydrophobic surface area of the IL-17A dimer, forming hydrogen bonds with Leu120 of the cytokine dimer. Amino acids such as Leu120 and residues in the hydrophobic side pocket, including Glu118, Ile119, Leu122, Leu135, and Lys137, play crucial roles in forming interactions with compound 1. The 2-fluorophenylalanine side chain makes hydrophobic contacts with Leu120, Leu122, and Leu135 of one monomer. The structural changes in the IL-17A dimer interface area from 1666Å^2 in the apo structure to 1127Å^2 in the complex, along with the reduction in interchain hydrogen bonds from 22 to 15, indicate the impact of ligand binding on the protein's structure and stability (Liu *et al*., 2016). The structural analysis provides valuable insights into the druggability of the IL-17A binding site, offering a foundation for the design and optimization of small-molecule ligands targeting IL-17A for therapeutic purposes.

Structural and active site analysis of iNOS target receptors

The X-ray crystallographic structure of iNOS (PDB ID: 3E7G) (Figure 1) has a resolution of 2.20 Å, and contains 424 amino acid residues complexed with an AR-C95791 inhibitor. It is characterized by crystal dimensions of a = 90.206Å, b = 158.671Å, and c = 191.141Å. Nitric oxide synthase (NOS) enzymes synthesize nitric oxide (NO), an intermediate molecule generated from the amino acid L-arginine by three NOS enzymes. The neuronal (nNOS) and endothelial (eNOS) NOS isozymes are expressed constitutively and regulated by Ca^{2+} to generate NO for neuroprotection, vasodilatation, and function of the endocrine. The Ca^{2+} insensitive inducible NOS (iNOS) isozyme is expressed in response to pathogens or cytokines and produces NO at an increased rate to kill bacteria, viruses, and tumour cells. Limited bioavailability of NO from nNOS and eNOS may result in hypertension, atherosclerosis, impotence, and cardiovascular diseases. However, excess production of NO from iNOS is associated with inflammatory bowel disease, inflammation, stroke, cancer, and so on. Even the aberrant induction of iNOS is related to the pathophysiology of human diseases such as tumour development, colitis, psoriasis, multiple sclerosis arthritis, and so on (Kroncke et al., 1998). The amino acid residues at the active site of the iNOS receptor are Gln263, Arg266, Phe286, Asp280, Asn283, Gln377, Tyr347, Arg388, Val305, Tyr372, Ala351, Tyr373, Asp382,



(A) **(B)**

Figure 1: The Crystal Structures of (A) IL-17A (PDB ID:5HI5) and (B) iNOS (PDB ID: 3E7G) receptors in complex with ligands.

Pro350, Val352, Trp463 and Tyr491 (Garcin et al., 2008).

Pharmacokinetic analysis of the selected compounds

An important assay in the early stage of drug development is the Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) profile of a chemical compound. ADMET data helps in the selection and identification of molecules with the best safety profile at the earlier stage of drug discovery. It helps to prevent wasting time and valuable resources on pharmacological compounds that may ultimately be eliminated. A drug molecule with a good ADMET profile must meet the following requirements; excellent human intestinal absorption (HIA), solubility (Log S) that is between -1 and -5, non-inhibitor of cytochrome P450 enzymes, non-Ames toxic (AM), non-carcinogenic (C), non-inhibitor of HERG (HI), and no or very low degree of toxicity (Tsaioun and Kates, 2010). One hundred and eighty-five (185) compounds isolated from *Curcuma longa* were screened using ADMET SAR-2 web-server, 115 compounds which include 51 monoterpenoids, 1 Aristolene, 22 Bisabolene, 2 Caryophyllene, 1 Cedrane, 2 Diterpenoid, 1 Elemane, 5 Fatty acid, 1 Germacrane, 5 Guanine, 2 Phenolic, 2 Phenylpropene, 5 Selinane, 13 Sesquiterpene, and 2 Triterpenoid passed the screening, and were selected as shown in Supplementary Table I.

The potential of a drug molecule to cause mutation in DNA is related to Ames toxicity value, which could be a major reason for excluding a drug molecule during the discovery process (Mccarren et al., 2011). As shown in Supplementary Table I, all the selected lead compounds are non-carcinogenic. Most of the ligands as well as the standards possess non-toxic type IV acute oral toxicity, some possess type III (slightly toxic) which could easily be converted to type IV (nontoxic) during hit-lead optimization (Onawole et al., 2017). The blood-brain barrier (BBB+) is a parameter associated with drugs in connection with the central nervous system. Some of the compounds and SD-2 can cross the BBB. Also, all the selected compounds and the standards have excellent chances of being absorbed in the human intestine (HIA) due to their positive HIA values. They all have outstanding aqueous solubility (Log S) values that are within the recommended range of -1 to -5. This shows that both the standards and the selected compounds have strong absorption and distribution potential. The metabolic activities of the selected drug compounds were predicted using microsomal enzymes (Cytochrome P450 inhibitors). Some of the selected drugs and standards are non-inhibitors of all the cytochrome P450 isoforms, which improves their metabolism as potential therapeutic medications. The ability of a drug molecule to inhibit human ether a-go-go (hERG) is extremely hazardous since it may result in blocking the potassium ion channel of the myocardium, which would interfere with the electrical activity of the heart and possibly cause untimely death (Sanguinetti & Tristani-Firouzi 2006). All of the selected compounds and standards are also non-inhibitors of hERG. In conclusion, all of the selected lead compounds and standards exhibit excellent ADMET properties. Hence subjected to further analyses.

Drug-likeness analysis of the selected ligands

Another essential phase in the drug discovery process is the evaluation of the physicochemical and drug-like properties of a potential drug compound. According to Lipinski, an oral therapeutic drug must abide by the "rule of five" with no more than one violation, this is because an orally bioavailable drug must possess

Table I. The docking scoring, binding affinities, and inhibition constant (K_i) values of the interaction of passed ligands and the standards with IL-17A and iNOS receptors.

Ligands	Binding Affinity (ΔG), kcal/mol	Inhibition constant (K_i), μM
IL-17A receptor (PDB ID: 5HI5)		
TRITERPENOIDS		
Hop-17(21)-en-3-ol	-7.6±0.0	2.7
Hopenone	-1.0±0.0	184750
GUANINE		
Curcumenol	-6.2±0.0	28.4
Procurcumenol	-5.8±0.0	55.7
Procurcumadiol	-5.9±0.0	47.1
Isoprocurcumenol	-5.6±0.0	78.1
Epiprocurcumenol	-5.6±0.0	78.1
MONOTERPENOIDS		
2-norpinanone	-4.5±0.0	500
BISABOLENE		
(E)-gamma-atlantone	-6.0±0.0	40.5
(Z)-gamma-atlantone	-4.9±0.0	254.8
alpha-bisabolol	-5.8±0.0	55.7
beta-Bisabolene	-5.1±0.0	181.8
Bisacumol	-5.7±0.0	66.0
curculonone_D	-5.9±0.0	47.1
beta-atlantone	-4.9±0.1	254.8
curculonone_A	-5.9±0.1	47.1
Bisabolone	-6.0-±0.0	40.5
curculonone_B	-5.7±0.0	66.0
Dehydrocurcumene	-5.6±0.0	78.1
gamma-Bisabolene	-5.9±0.0	47.1
bisacurone_A	-6.1±0.0	33.6
curculonone_C	-5.5±0.1	92.5
curlone_	-5.8±0.1	55.1
SESQUITERPENE		
Curcumanolide_B	-6.6±0.0	14.4
1-epi-cubenol	-5.5±0.1	92.5
alpha-Cubebene	-5.6±0.1	78.1
alpha-Humulene	-5.6±0.0	78.1
(E)-sesquisabinene_hydrate	-5.3±0.0	129.7
Caryophyllene	-5.6±0.2	78.1
2,6,10-dodecatrien-1-ol,3,7,11-trimethyl	-5.5±0.1	92.5
bicyclo[7.2.0]undecane,10,10-dimethyl-2,6-bis(methylene)	-5.9±0.1	47.1
Curcumanolide_A	-6.3±0.0	123.9
GERMACRANE		
(4S,5S)-germacrone-4,5-epoxide	-5.8±0.0	55.7
SELINANE		
Corymbolone	-5.3±0.0	129.7
Juniper camphor	-5.8±0.0	55.1
CARYOPHYLLANE		
(E)-caryophyllene	-5.7±0.0	65.9
Caryophyllene_oxide	-5.6±0.1	78.1
STANDARDS		
Flurandrenolide	-6.9 ±0.0	8.8
Triamcinolone	-7.0 ±0.0	7.3
Inhibitor ligand	-8.0±0.1	1.4

Table I. (Continued)

Ligands	Binding Affinity (ΔG), kcal/mol	Inhibition constant (K_i), µM
iNOS receptor (PDB ID: 3E7G)		
TRITERPENOIDS		
Hopenone	-9.9 ± 0.0	0.1
Hop-17(21)-en-3-ol	-9.7 ± 0.0	0.1
GUANINE		
Procurcumenol	-8.7 ± 0.0	0.4
Curcumenol	-8.4 ± 0.0	0.7
Procurcumadiol	-8.3 ± 0.0	0.8
Epiprocurcumenol	-7.9 ± 0.0	1.6
Isoprocurcumenol	-7.8 ± 0.0	1.9
MONOTERPENOIDS		
m-cymene	-7.9 ± 0.0	1.6
Menthofuran	-7.9 ± 0.0	1.6
benzene, 1-methyl-4-(1-methylpropyl)	-7.8 ± 0.0	1.9
Carvacrol	-7.7 ± 0.0	2.3
-terpinene	-7.7 ± 0.0	2.3
o-cymene	-7.6 ± 0.0	2.7
p-methylacetophenone	-7.6 ± 0.0	2.7
Thymol	-7.6 ± 0.0	2.7
Carvone	-7.5 ± 0.0	3.2
geranyl acetate	-7.5 ± 0.0	3.2
Neryl acetate	-7.5 ± 0.0	3.2
p-cymen-8-ol	-7.5 ± 0.0	3.2
Citronellyl pentanoate	-7.5± 0.1	3.5
Sylvestrene	-7.4 ± 0.0	3.8
(Z)-cinerone	-7.3 ± 0.0	4.5
Limonene	-7.3 ± 0.0	4.5
Phellandrene	-7.3 ± 0.0	4.5
Terpineol	-7.3 ± 0.0	4.5
4,8-dimethyl-3,7-nonadien-2-ol	-7.1 ± 0.0	6.3
Menthol	-7.1 ± 0.0	6.3
Geraniol	-7.0± 0.0	7.3
2-norpinanone	-6.9 ± 0.0	8.8
Geranial	-6.9 ± 0.0	8.8
Geranic acid	-6.9 ±0.0	8.8
Neral	-6.9 ± 0.0	8.8
terpinen-4-ol	-6.9 ± 0.0	8.8
(E)-carveol	-6.8 ± 0.0	10.4
3,4,5,6-tetramethyl-2,5-octadiene	-6.8 ± 0.0	10.4
BISABOLENE		
Bisabolone	-9.3 ± 0.0	0.2
Bisacumol	-9.0 ± 0.0	0.3
dehydrocurcumene	-9.0 ± 0.0	0.3
Curlone	-8.8 ± 0.0	0.4
beta-Bisabolene	-8.6 ± 0.0	0.5
(E)-gamma-atlantone	-8.5 ± 0.0	0.6
alpha-bisabolol	-8.5 ± 0.0	0.6
beta-atlantone	-8.5 ± 0.0	0.6
Bisacurone C	-8.4 ± 0.0	0.7
Curculonone A	-8.4 ± 0.0	0.7
Curculonone C	-8.4 ± 0.0	0.7
gamma-atlantone	-8.2 ± 0.0	1.0
(Z)-gamma-Bisabolene	-8.2 ± 0.0	1.0

Table I. (Continued)

Ligands	Binding Affinity (ΔG), kcal/mol	Inhibition constant (K_i), µM
Bisacurone A	-8.2 ± 0.0	1.0
Bisacurone B	-8.1±0.1	1.3
Curculonone B	-8.0± 0.1	1.5
Bisacurone	-7.9 ± 0.0	1.6
Zingerone	-7.7 ± 0.0	2.3
Dehydrozingerone	-7.5 ± 0.0	3.2
Curculonone D	-7.3 ± 0.0	4.5
	SESQUITERPENE	
Curcumanolide_B	-8.6 ± 0.0	0.5
(E)-sesquisabinene_hydrate	-8.5 ± 0.0	0.6
2,6,10-dodecatrien-1-ol, 3,7,11-trimethyl	-8.2 ± 0.0	1.0
1-epi-cubenol	-7.5 ± 0.0	3.2
alpha-Cubebene	-7.4 ± 0.0	3.8
5,9-undecadien-2-one, 6,10-dimethyl-, (Z)	-7.4 ± 0.1	4.1
Curcumanolide A	-7.3 ± 0.0	4.5
alpha-Humulene	-7.2 ± 0.0	5.3
Caryophyllene	-7.1 ± 0.0	6.3
cis-Nerolidal	-7.2 ± 0.1	5.8
bicyclo[7.2.0]undecane, 10,10-dimethyl-2,6-bis(methylene)	-7.0 ± 0.0	7.4
Adoxal	-6.9 ± 0.0	8.8
	GERMACRANE	
(4S,5S)-germacrone-4,5-epoxide	-8.3 ± 0.0	0.8
	SELINANE	
alpha-Santalene	-7.8 ± 0.0	1.9
beta-Santalene	-7.8 ± 0.0	1.9
Juniper camphor	-7.6 ± 0.0	2.7
Corymbolone	-7.3 ± 0.0	4.5
	CARYOPHYLLANE	
Caryophyllene oxide	-7.1 ± 0.0	6.3
	FATTY ACID	
8,11-Octadecadienoic acid, methyl ester	-7.2± 0.1	5.8
Oleic acid	-7.0± 0.0	7.4
Linoleic acid	-6.9 ± 0.0	8.8
	CEDRANE	
di-epi-cedrene	-7.3 ± 0.0	4.5
	PHENYLPROPENE	
(E)-4-(4-hydroxy-3-methoxyphenyl)but-3-en-2-one	-7.5 ± 0.0	3.2
(E)-ferulic_acid	-7.2 ± 0.0	5.3
	DITERPENOID	
Geranyllinalool	-8.0± 0.0	1.4
Phytol	-7.5± 0.1	3.5
	ELEMANE	
beta-Elemene	-7.3 ± 0.0	4.5
	STANDARDS	
Flurandrenolide	-8.3±0.0	0.8
Triamcinolone	-8.2 ±0.0	1.0
Inhibitor ligand	-10.9±0.0	0.01

molecular weight (MW) ≤ 500 Da, hydrogen bond donors (HBDs) ≤ 5, hydrogen bond acceptors (HBAs) ≤ 10, and log *P* (octanol-water partition coefficient) ≤ 5 (Lipinski, 2004). All the 115 ligands that passed the ADMET screening also obey the Lipinski rule and falls within all the accepted range. The drug-likeness of the selected lead compounds and standards were evaluated with Molinspiration online software (http://www.molinspiration.com/). As shown in Supplementary Table II, none of the selected compounds and the standards had more than one violation of the 'rule of five' which is an indication that the compounds have excellent oral bioavailability profiles.

Molecular docking analysis

The traditional method of discovery and development of a new drug is tedious, costly, time-consuming, and has a low success rate. Computer-Aided Drug Design (CADD) has drawn renewed interest in recent developments in drug discovery/design because it is easier, faster, and cheaper with outstanding success rates in the screening of molecules for biological and chemical interactions compared to the traditional methods. Molecular docking is an important process in computational chemistry. It is a structure-based drug design approach that predicts the binding interactions between ligands and target receptors at the binding site (Ferreira et al., 2015). A potential active drug is expected to have inhibitory values from 0.1 μM and 1.0μM and it should not be greater than 10nM (Schultes et al., 2015). The inhibition constant was calculated using Ki = exp [-ΔG/RT], where Ki = Inhibition constant, ΔG = Binding energy, R = Gas constant (1.987×10^{-3} kcal/K/mol); T = 298.15 K (absolute temperature). The standards and ligands that passed both ADMET and drug-likeness parameters were docked separately with the IL-17A and iNOS receptors to obtain the values of the binding energy. The docking results of the ligands and standards with inhibition constant values between the range of 0.1 μM to 10 μM were reported according to their classes in Table I. The docking scores (binding affinities) of the passed ligand from *Curcuma longa* ranged between -7.6 to -1.0 kcal/mol for the IL-17A receptor and -9.9 to -6.8 kcal/mol with the iNOS receptor. Notably, the inhibitor ligand that attaches to IL-17A receptor has binding energy value of -8.0 kcal/mol, while one of the inhibitor ligands that attaches to iNOS receptor has binding energy value of -10.9 kcal/mol. This indicates that the inhibitors' ligands have higher inhibitory efficiencies towards the receptors.

As shown in Table I, for the IL-17A, Triterpenoid; Hop-17(21)-en-3-ol, and Hopenone have binding affinities of -7.6 and -1.0 kcal/mol respectively. Guanine ranged between -6.2 to -5.6 kcal/mol with curcumenol being the best among others. Bisabolene ranged between -6.1 to -4.9 kcal/mol. Sesquiterpene ranged between -6.6 to -5.3 kcal/mol with Curcumanolide B having the best binding energy of -6.6 kcal/mol. Germacrane; (4S,5S)-germacrone-4,5-epoxide has a binding affinity of -5.8 kcal/mol. Selinane; Corymbolone and Juniper camphor have a binding energy of 5.3 and 5.8 kcal/mol respectively. The Standards (flurandrenolide and triamcinolone) have binding energies of -6.9 and -7.0 kcal/mol respectively (Table I). However, it is noteworthy to state that Hop-17(21)-en-3-ol has significant binding energy of -7.6 kcal/mol against IL-17A receptor among all the investigated ligands.

Similarly, on Table I is the docking result of the iNOS receptor, Triterpenoids; Hop-17(21)-en-3-ol, and Hopenone have the binding affinities of -9.7 and -9.9 kcal/mol respectively. Bisabolene ranged between -9.0 to -7.3 kcal/mol with bisacumol and dehydrocurcumene having the best binding affinity of -9.0 kcal/mol each. Sesquiterpene ranged from -8.6 to -6.9 kcal/mol with (E)-sesquisabinene_hydrate and Curcumanolide_B having the best binding affinities of -8.5 and -8.6kcal/mol respectively. Monoterpenoids ranged between -7.9 to -6.8 kcal/mol with menthofuran and m-cymene having the best binding affinity of -7.9 kcal/mol each. Fatty acid ranged between -7.15 to -6.9 kcal/mol with oleic acid and 8,11-Octadecadienoic acid methyl ester with the best binding affinities of -7.0 and -7.15 kcal/mol respectively. Di-epi-cedrene of Cedrane has a binding affinity of -7.3 kcal/mol. For the Phenylpropene; (E)-ferulic_acid and (E)-4-(4-hydroxy-3-methoxyphenyl) but-3-en-2-one have the binding affinities of -7.2 and -7.5 kcal/mol respectively. Diterpenoid; Phytol and Geranyllinalool have binding affinities of -7.45 and -8.0 kcal/mol respectively. Germacrane; (4S,5S)-germacrone-4,5-epoxide have a binding affinity of -8.3 kcal/mol. Guanine ranged between -8.7 to -7.8 kcal/mol with curcumenol and procurcumenol having the best binding affinities of -8.4 and -8.7 kcal/mol respectively. Selinane ranged between -7.8 to -7.3 kcal/mol with alpha-santalene and beta santalene having a binding affinity of -7.8 kcal/mol each. Caryophyllane; Caryophyllene_oxide have a binding affinity of -7.1 kcal/mol. Elemane; beta-Elemene have a binding affinity of -7.3 kcal/mol, and the standards (flurandrenolide and triamcinolone) have binding affinity values of -8.2 and -8.3 kcal/mol respectively (Table I).

Table II. Oral bioavailability analysis of the selected compounds and the standards with IL-17A receptor and iNOS receptors

Ligands	Formular	VINA Score	Mass	TPSA(Å)²	#Rotatable bonds	XLOGP3	WLOGP	ESOL Log S	Lipinski #violations	BA Score	PAIN# alerts	Fraction Csp3	Synthetic Accessibility
IL-17A (PDB ID: 5HI5)													
TRITERPENOID													
Hop-17(21)-en-3-ol	$C_{30}H_{50}O$	7.6	426.7	20.2	1	8.56	8.17	-7.81	1	0.55	0	0.93	6.26
BISABOLENE													
(E)-gamma-atlantone	$C_{15}H_{22}O$	-6.0	218.3	17.1	3	5.17	4.36	-4.25	0	0.55	0	0.53	3.47
(Z)-gamma-atlantone	$C_{15}H_{22}O$	-4.9	218.3	17.1	3	5.17	4.36	-4.25	0	0.55	0	0.53	3.47
GUANINE													
Curcumenol	$C_{15}H_{22}O_2$	-6.2	234.3	29.5	0	2.24	3.18	-2.70	0	0.55	0	0.73	5.73
Procurcumenol	$C_{15}H_{22}O_2$	-5.8	234.3	37.3	0	2.34	3.02	-2.77	0	0.55	0	0.67	4.04
MONOTERPENOID													
2-norpinanone	$C_{18}H_{26}N_2O_3$	-4.5	318.4	75.3	4	1.39	3.10	-2.43	0	0.55	1	0.89	6.11
SESQUITERPENE													
Curcumanolide B	$C_{15}H_{22}O_2$	-6.6	234.3	26.3	1	4.29	3.63	-3.93	0	0.55	0	0.67	4.36
STANDARDS													
Flurandrenolide	$C_{24}H_{33}FO_6$	-6.9	436.5	93.1	2	1.38	2.92	-3.28	0	0.55	0	0.83	5.91
Triamcinolone	$C_{21}H_{27}FO_6$	-7.0	394.4	98.3	2	1.16	1.04	-2.88	0	0.55	0	0.71	5.46
iNOS (PDB ID: 3E7G)													
BISABOLENE													
Bisabolone	$C_{15}H_{26}O_2$	-9.3	238.4	29.5	1	2.50	3.44	-2.83	0	0.55	0	0.87	4.38
Bisacumol	$C_{15}H_{22}O$	-9.0	218.3	20.2	4	4.08	3.82	-3.78	0	0.55	0	0.47	2.63
Dehydrocurcumene	$C_{15}H_{20}$	-9.0	200.3	0.00	4	5.25	4.62	-4.42	1	0.55	1	0.33	2.74
Curlone	$C_{15}H_{22}O$	-8.8	218.3	17.1	4	4.01	4.07	-3.46	0	0.55	0	0.53	4.17
Beta-bisabolene	$C_{15}H_{24}$	-8.6	204.4	0.00	4	6.43	5.04	-4.89	1	0.55	0	0.60	3.90
(E)-gamma-atlantone	$C_{15}H_{22}O$	-8.5	218.3	17.1	3	5.17	4.36	-4.25	0	0.55	0	0.53	3.47

Table II. Oral bioavailability analysis of the selected compounds and the standards with IL-17A receptor and iNOS receptors

Ligands	Formular	VINA Score	Mass	TPSA(Å)²	#Rotatable bonds	XLOGP3	WLOGP	ESOL Log S	Lipinski #violations	BA Score	PAIN# alerts	Fraction Csp3	Synthetic Accessibility
alpha-bisabolol	$C_{15}H_{26}O$	-8.5	222.4	20.2	4	3.79	4.23	-3.34	0	0.55	0	0.73	3.95
beta-atlantone	$C_{15}H_{22}O$	-8.5	218.3	17.1	4	5.27	4.21	-4.25	0	0.55	0	0.53	3.73
curculonone C	$C_{14}H_{22}O_2$	-8.4	222.3	29.6	4	2.75	3.12	-2.69	0	0.55	0	0.79	3.82
bisacurone C	$C_{15}H_{24}O_3$	-8.4	252.4	57.5	4	1.88	2.24	-2.32	0	0.55	0	0.67	4.39
curculonone A	$C_{14}H_{22}O_2$	-8.4	222.3	37.3	4	2.40	2.88	-2.47	0	0.55	0	0.64	3.77
bisacurone A	$C_{15}H_{24}O_3$	-8.2	252.4	57.5	4	1.88	2.24	-2.32	0	0.55	0	0.67	4.39
(Z)- *gamma*-bisabolene	$C_{15}H_{24}$	-8.2	204.4	0.00	3	6.33	5.18	-4.90	1	0.55	0	0.60	3.46
GUANINE													
Curcumenol	$C_{15}H_{22}O_2$	-8.4	234.3	29.5	0	2.24	3.18	-2.70	0	0.55	0	0.73	5.73
procurcumadiol	$C_{15}H_{22}O_3$	-8.3	250.3	57.5	0	1.28	2.13	-2.20	0	0.55	0	0.67	4.30
SESQUITERPENE													
Curcumanolide B	$C_{15}H_{22}O_2$	-8.6	234.3	26.3	1	4.29	3.63	-3.93	0	0.55	0	0.67	4.36
(E)-sesquisabinene hydrate	$C_{15}H_{26}O$	-8.5	222.4	20.2	4	4.08	3.92	-3.53	0	0.55	0	0.87	3.82
TRITERPENOID													
Hopenone 1	$C_{30}H_{48}O$	-9.9	424.7	17.1	1	8.25	8.38	-7.60	1	0.55	0	0.90	6.12
Hop-17(21)-en-3-ol	$C_{30}H_{50}O$	-9.7	426.7	20.2	1	8.56	8.17	-7.81	1	0.55	0	0.93	6.26
STANDARDS													
Flurandrenolide	$C_{24}H_{33}FO_6$	-8.3	436.5	93.1	2	1.38	2.92	-3.28	0	0.55	0	0.83	5.91
Triamcinolone	$C_{21}H_{27}FO_6$	-8.2	394.4	98.3	2	1.16	1.04	-2.88	0	0.55	0	0.71	5.46

BA score = Bioavailability score

Oral bioavailability analysis of the selected ligands and standard

The oral bioavailability analysis of the compounds with excellent binding energy values were obtained through the SwissADME web tool (http://www.swissadme.ch/) (Diana et al., 2017). The recommended ranges for the properties are molecular weight (SIZE) of 500 g/mol, Total Polar Surface Area (TPSA) (POLAR) of 20 – 130 $Å^2$, lipophilicity (LIPO) (XLOGP3) value of -0.7 and +5.0, solubility (INSOLU) ≤ 6, rotatable bond (FLEX) of ≤ 9, and fraction of carbon in the Sp^3 (Csp3) hybridization (INSATU) value of 0.25 – 1.0 for an effective drug candidate (Lipinski, 2004). As shown in Table II, for the IL-17A receptor, all classes of compounds fall within the recommended ranges, with the exception of *(E)-gamma*-atlantone, and *(Z)-gamma*-atlantone (Bisabolenes) which both have poor permeability as a result of XLOGP3 values of 5.17 each. Flurandrenolide and triamcinolone fell out of the value of the rotatable bonds.

Similarly, for the iNOS receptor, all the classes fall within the recommended range except some Bisabolene (Dehydrocurcumene, *Beta*-bisabolene, *(E)-gamma*-atlantone, *beta*-atlantone, and (Z)- *gamma*-bisabolene), and triterpenoid (Hopenone 1 and Hop-17(21)-en-3-ol) that may possess poor permeability due to higher values of the XLOGP3 values. Although, this can be optimized at the lead-optimization stage of drug discovery process. The standards (flurandrenolide and triamcinolone), also fell out of value for the rotatable bonds, which is a function of flexibility (Table II). Summarily, most of the ligands passed the oral bioavailability tests more than the standards. Therefore, all those ligands were subjected to further analysis.

Bioactivity test of the selected ligands and standard drug

Supplementary Table III displays the bioactivity potentials of the selected lead compounds and standards. For a compound to qualify as a lead, its inhibition constant value should fall within the micro-molar range of 0.1–1.0 μM, while for it to be considered a drug, it should not exceed 10 nM. The recommended values for bioactivity parameters such as Ligand Efficiency (LE), Fit Quality (FQ), and Ligand-efficiency-dependent lipophilicity (LELP) (Eq. 2–5) for a lead are ≥ 0.3, ≥ 0.8, and -10 to 10, respectively (Hopkins, et al., 2014).

$$Ligand\ Efficiency\ (LE) = -(B.E) \div Heavy\ atoms\ (H.A) \quad (1)$$

$$L.E\ scale = 0.873e^{-0.026 \times H.A} - 0.064 \quad (2)$$

$$FQ = LE \div LE\ scale \quad (3)$$

$$LELP = LogP \div LE \quad (4)$$

Regarding the IL-17A receptor, all classes conform to the recommended ranges of the bioactivity parameters. Among the standards, flurandrenolide did not meet the criteria for LE (0.25), FQ (0.77), and LELP (10.37). Similarly, for the iNOS receptor, all the classes satisfy the recommended range. However, both standards (flurandrenolide and triamcinolone) did not meet the LE criteria with values of 0.27 and 0.29 respectively. Therefore, all the selected lead compounds were analysed further.

Prediction of activity spectra for substances (PASS) of the selected compounds and standards.

In other to validate the biological activities of the selected compounds, the PASS online web server (http://pharmexpert.ru/passonline/) was used to predict the activity. All the selected leads and the standards show excellent biological activities such as Anti-inflammatory, Immunosuppressant, Anti-psoriatic, and Anti-eczematic properties. The antimicrobial properties and other biological functions of *Curcuma longa* have been reported (Gupta & Ravishankar, 2005; Jiang et al., 2017). In addition, Anand et al., (2007) reported that curcuminiods in commercial turmeric extracts consists of 77 % curcumin, 17 % demethoxycurcumin and 6 % bisdemethoxycurcumin. Its activities involve wound healing and anti-inflammatory properties (Kocaadam and Şanlier, 2017; Dai et al., 2018), and anti-cancer potentials (Astinfeshan et al., 2019).

Binding mode and molecular interactions of the best lead compounds and the standards

Another important in silico drug design process is the identification of the binding site and assessment of the binding interactions of the ligands in the active pocket of the target receptor. This eases the improvement of ligand affinity to the pocket during the lead optimization stage of drug discovery. As shown in Table III and Figure 2, for the IL-17A receptor, Hop-17(21)-en-3-ol interacts with Pro63, Ile66, Ile96, Val117, and Val119 via Alkyl and Pi-alkyl interactions with the active site of the receptor. The standard drug (flurandrenolide) interacts with Trp67 and Ser118 via conventional hydrogen bond, Pro63 via carbon hydrogen bond, Ile66, Ile96, and Val117 via alkyl interactions with the active site of the receptor. On the other hand, triamcinolone interacts with Leu97 residue via conventional hydrogen bond, Val119 via carbon hydrogen bond, Ile66 and Ile96 via alkyl

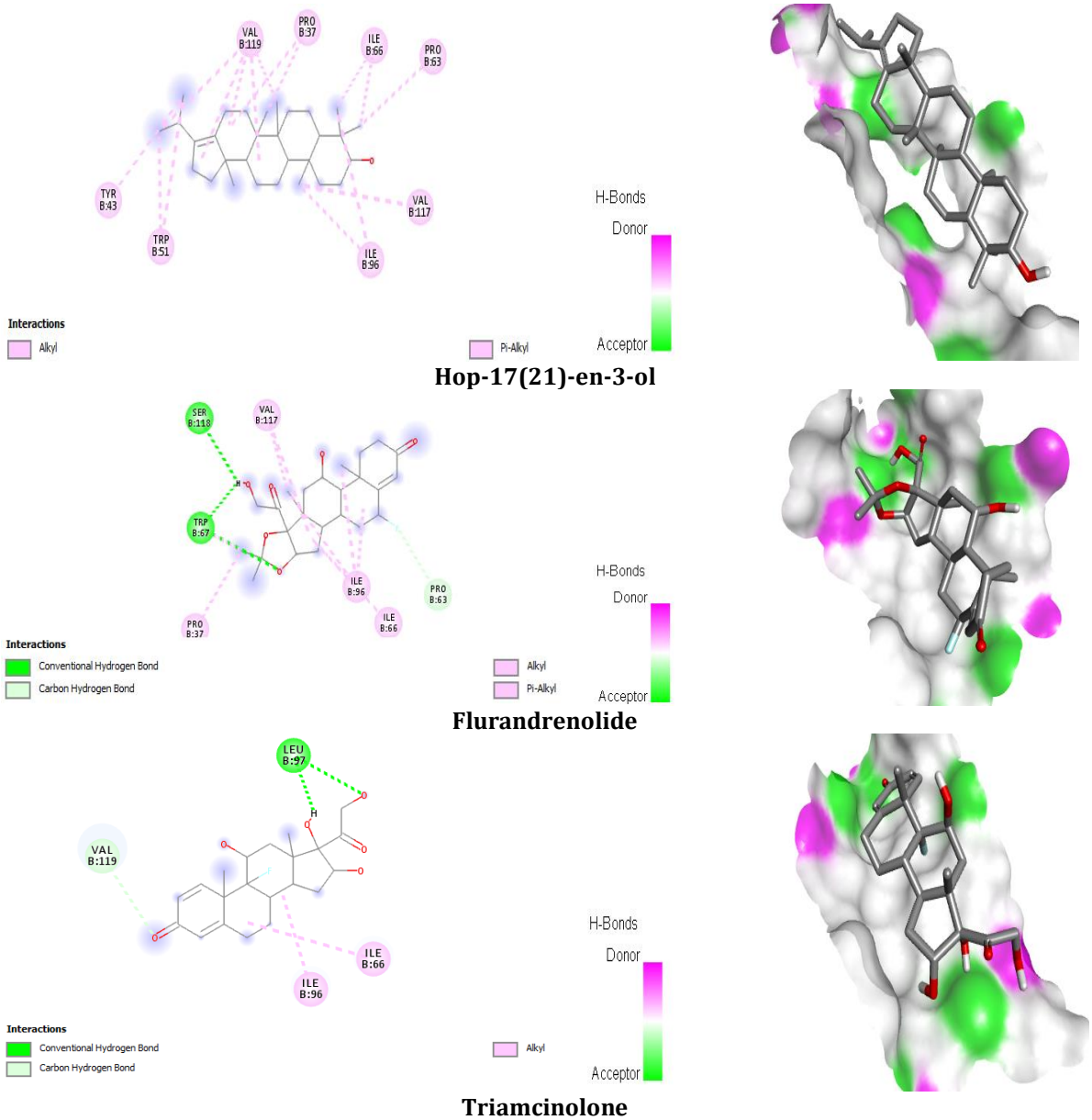


Figure 2. Binding mode and interaction of the lead compound with IL-17Areceptor (PDB ID: 5HI5)

interactions with the active site of the receptor. All these amino acid residues were confirmed to be present at the active site of the receptor. However, Hop-17(21)-en-3-ol was selected among others based on its outstanding binding energy value of -7.6 kcal/mol compared to the standard drugs flurandrenolide and Triamcinolone with binding energy values of -6.9 kcal/mol and -7.0 kcal/mol respectively.

In the case of the iNOS receptor, Curcumanolide B interacts with Phe369, Val352, Trp194, Leu209, Pro350, and Tyr489 through hydrophobic/electrostatic interactions and with Cys200 through a conventional hydrogen bond (Table III and Figure 3). Procurcumadiol interacts with Cys200, Trp194, and Glu377 through conventional hydrogen bonds and with Phe369, Pro350, Trp372, and Met434 through hydrophobic/electrostatic interactions. Bisabolone interacts with Phe369, Trp194, Leu209, Val352, Pro350, Cys200, Ile244, and Tyr489 through hydrophobic/electrostatic interactions (Table III and Figure 3). (E)-sesquisabinene hydrate interacts with Arg199 through a conventional bond and with Phe369, Trp194, Leu209, Val352, Ala197, Cys200, Ile244, Met355, and Tyr489 through

hydrophobic/electrostatic interactions (Table III and Figure 3). Val352 amino

pocket of one of the standards (flurandrenolide), showing that they share similar binding pockets

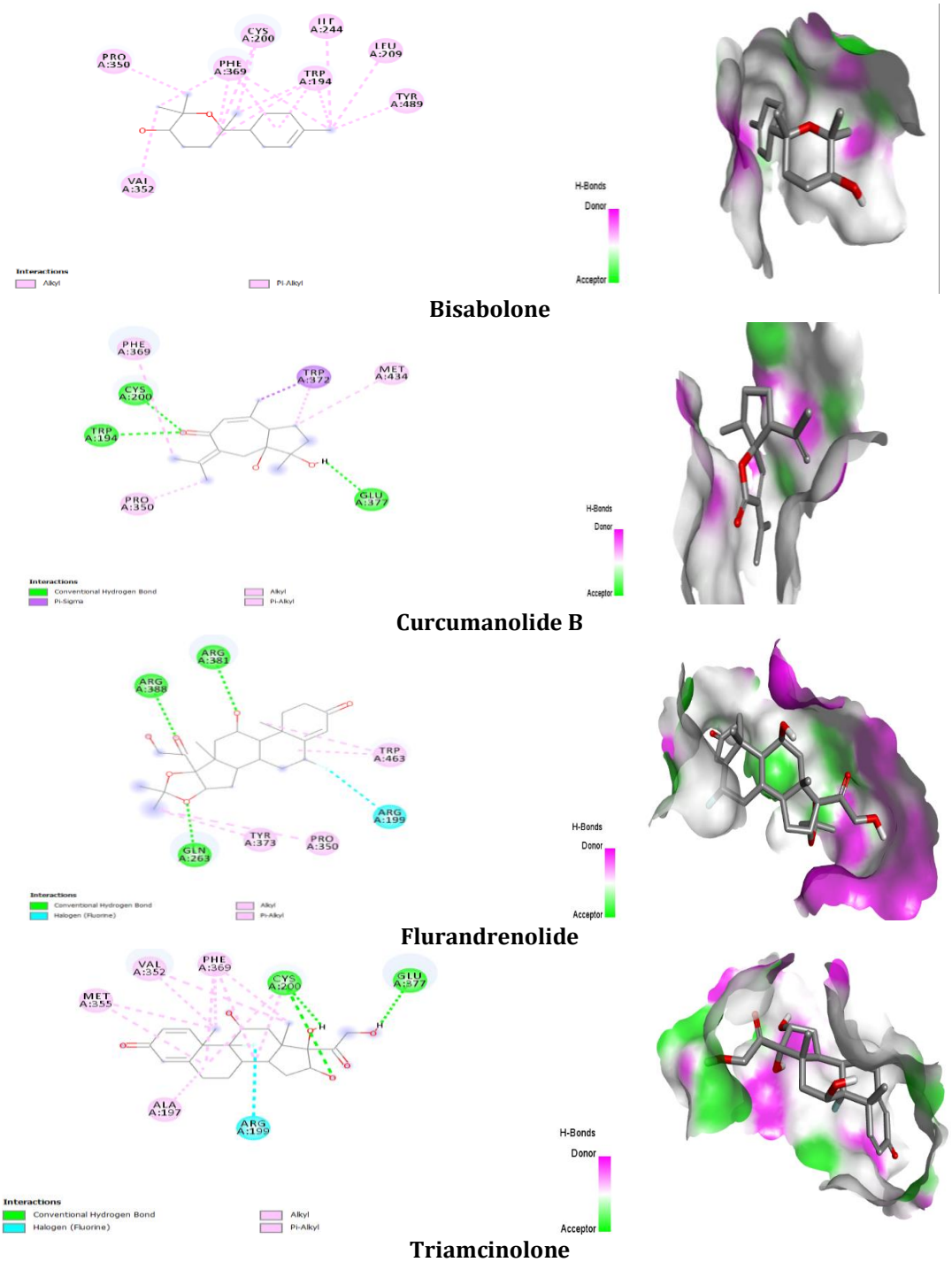


Figure 3. Binding mode and interaction of the lead compounds with the iNOS receptor (PDB ID: 3E7G)

acid residue is commonly found in the binding interaction of bisabolene, curcumanolide B, (E)-sesquisabinene hydrate, and Triamcinolone. Also, Pro350 amino acid residue is found in the binding interaction of bisabolene, curcumanolide B, and procurcumadiol, it is also found in the binding and interactions with the active site of the iNOS receptor. Evidence from several reports show that *Curcuma longa* is effective in the treatments of diseases associated with inflammatory pathways. Thus, the therapeutic benefits are related to the regulation of several enzymatic pathways,

transcriptional factors and cytokines (Lee et al., 2013).

Table III. Receptor amino acids forming Hydrogen-bond and other Electrostatic/Hydrophobic interactions for passed ligands with IL-17A and iNOS receptors.

Compounds	Binding affinity (ΔG), kcal/mol	5HI5 Receptor amino acids forming H-bond ligands	Electrostatic/Hydrophobic Interactions involved	Inhibition constant
		IL-17A (PDB ID: 5HI5)		
Hop-17(21)-en-3-ol	-7.6±0.0	Nil	Pro37, Tyr43, Trp51, Pro63, Ile66, Ile96, Val117, Val119	**2.7**
Flurandrenolide	--6.9 ±0.0	Trp67, Ser118	Pro37, Pro63, Ile66, Ile96, Val117	**8.8**
Triamcinolone	-7.0 ±0.0	Leu97	Ile66, Ile96, Val119	**7.3**
		iNOS (PDB ID: 3E7G)		
Bisabolone	-9.3±0.0	Nil	Pro350, Val352, Cys200, Phe369, Ile244, Trp194, Leu209, Tyr489	0.2
Curcumanolide B	-8.6±0.0	Nil	Cys200, Trp194, Phe369, Tyr489, Leu209, Val352, Pro350	0.5
(E)-sesquisabinene hydrate	-8.5±0.0	Arg199	Arg199, Phe369, Trp, 194, Tyr489, Ala197, Val352, Met355, Cys200, Leu209, Ile244,	0.6
Procurcumadiol	-8.3±0.0	Gly202, Trp194, Trp372, Glu377	Phe369, Cys200, Trp194, Pro350, Trp372, Met434, Glu377	0.8
Flurandrenolide	-8.3±0.0	GLN263, Arg388, Asp382	Arg388, Arg381, Trp463, Arg199, Pro350, Tyr373, Gln263	0.8
Triamcinilone	-8.2 ±0.0	Glu377, Trp372	Met355, Val352, Phe369, Cys200, Glu377, Arg199, Ala197	1.0

DISCUSSION

Curcuma longa has been reported in the prevention, treatment and management of various diseases including psoriasis (Iweala *et al*., 2023). Targeting the signaling pathway of disease pathology is crucial in seeking therapeutic intervention against any disease (Adelusi et al., 2021). This study explored the potentials of reported phytochemicals from *Curcuma longa* as anti-psoriatic and anti-inflammatory against IL-17A and iNOS receptors using an In silico approach. The IL-17A and iNOS receptors are vital proteins that play crucial roles in immune response and inflammatory processes. The IL-17A protein was reported to be a clinically efficacious pathway modulator in psoriasis (Ruiz de Morales et al., 2020). In silico predictions have generated a series of opportunities to accelerate the detection of novel potent compounds as new therapeutics (Al-Mazaideh et al., 2021). The pharmacokinetic investigation was carried out to filter phytochemicals (ligands) that could serve as therapeutic agents in the treatment of psoriasis. The ADMET profiles were first conducted to identify ligands with no toxicity. Some selected ligands were identified due to their ability to cause no toxicity related to the liver, non-mutagenic, non-carcinogenic, and non-inhibitor of hERG, among others (Supplementary Table I). The selected phytochemicals also exhibit excellent drug-likeness profiles due to their no more than one violation of the Lipinski rule of five (Supplementary Table II). The molecular docking results of the selected compounds and standard anti-psoriatic medications (flurandrenolide and triamcinolone) with the target receptors (IL-17A and iNOS) are depicted in Table I. Phytochemicals with more negative values are assumed to exhibit strong interactions with their receptors, which may significantly affect enzyme activities. In the case of the IL-17A receptor, the docking scores of selected ligands from *Curcuma longa* ranged

between -7.6 to -1.0 kcal/mol. The Standards (flurandrenolide and triamcinolone) have binding energies of -6.9 and -7.0 kcal/mol respectively (Table I). Among all the investigated ligands against the IL-17A receptor, only Hop-17(21)-en-3-ol has a better binding energy of -7.6 kcal/mol against IL-17A than the two standard medications. This selected compound interacts with the active site of the receptor via some amino acid residues at the active site Although no hydrogen bond, only electrostatic interaction is present with Pro63, Ile66, Ile96, Val117, and Val119 (Figure 2). Some of these residues such as Pro63, Ile66, Val117 and Val119 are also found in the interactions of the standard drugs, though characterized by hydrogen bond, carbon hydrogen bond and alkyl interaction (Table III). It is therefore suggested that Hop-17(21)-en-3-ol could be a probable inhibitor of the IL-17A receptor due to its better inhibitory efficiency and could also serve as an anti-psoriatic therapeutic coupled with its outstanding biological activities than the two standard medications.

For the iNOS receptor, the docking scores ranged from -9.9 to -6.8 kcal/mol. Several ligands with different classes of phytochemicals have more binding energy values than the standard medications against the iNOS receptor. Hop-17(21)-en-3-ol and Hopenone have the best binding affinities of -9.7 and -9.9 kcal/mol respectively, and both bisacumol and dehydrocurcumene have -9.0 kcal/mol. (E)-sesquisabinene hydrate (-8.5 kcal/mol), curcumanolide B (-8.6 kcal/mol), curcumenol (-8.4 kcal/mol) and procurcumenol (8.7 kcal/mol), while the standards (Flurandrenolide and triamcinolone) have -8.2 kcal/mol and -8.3 kcal/mol respectively. The amino acid residues such as Trp194, Cys200, Leu209, Val352, Pro350, Phe369, and Tyr489, Met434 among others (Table III). Pro350, Val352 residues that are commonly found in the bisabolene, curcumanolide B, and procurcumadiol, (E)-sesquisabinene hydrate, Triamcinolone, and flurandrenolide characterized by hydrogen bond and other electrostatic interactions were reported on the iNOS receptor by Garcin et al., 2008. The pharmacological activities of *Curcuma longa* are attributed to the presence of curcuminoids, which are potential therapeutics to cure metabolic diseases and cancer with no side effects (Siviero et al., 2015). Alici et al., (2022) reported that curcumin derivatives could serve as potent inhibitors of SARS-COV-2 due to their reliable ADME profile and molecular binding potency. Notably, the native ligand inhibitor of the IL-17A receptor has a binding energy value of -8.0 kcal/mol, and one of the inhibitor ligands that attach to the iNOS receptor has a binding energy value of -10.9 kcal/mol. This is an indication of higher inhibitory efficiencies of the inhibitors' ligands towards the receptors.

Other health benefits and anti-inflammatory potential of *Curcuma longa* have been reported by Iweala et al., (2023). In addition, several studies have specifically reported the activity potentials of curcumins from *Curcuma longa* in various diseases (Alici et al., 2022; Saeed et al., 2022). Targeting a specific pathway concerning disease pathology could be an effective way to address the prevention, treatment and management of several diseases. This study suggested Hop-17(21)-en-3-ol (7.6 kcal/mol) as a probable inhibitor of the IL-17A receptor and could act as an anti-psoriatic agent. Also, Bisabolone (−9.3 kcal/mol), Curcumanolide B (−8.6 kcal/mol), (E)-sesquisabinene hydrate (−8.5 kcal/mol), and procurcumadiol (−8.3 kcal/mol) were identified as probable inhibitors of iNOS and could be effective anti-inflammatory agents. It is important to validate the selected compounds from *Curcuma longa* on animal models to ascertain the claim of their potential. However, comprehensive studies on clinical trials as well as quality control are needed to be established in other to have a safe dosage of the identified compound in the treatment of psoriasis and inflammation.

CONCLUSION

This study explored the potential of *Curcuma longa* as anti-psoriatic and anti-inflammatory agents. Molecular docking simulation, ADMET profiling, Lipinski Rule of 5 (RO5), and other analyses were employed to explore 115 phytochemicals isolated from *Curcuma longa* against two possible psoriasis targets; interleukin-17A (IL-17A) and inducible Nitric oxide synthase (iNOS) receptors. The results obtained revealed that Hop-17(21)-en-3-ol (7.6 kcal/mol) is a probable inhibitor of IL-17A receptor which drives autoimmune and multiple inflammatory disorders, while Bisabolone (−9.3 kcal/mol), Curcumanolide B (−8.6 kcal/mol), (E)-sesquisabinene hydrate (−8.5 kcal/mol), and Pocurcumadiol (−8.3 kcal/mol) were identified as probable inhibitors of iNOS due to their excellent binding energies, ADMET profiles, drug-likeness, oral-bioavailability properties, PASS properties, bioactivity, outstanding binding mode, and molecular interactions with the target receptor. The computational analysis revealed that *Curcuma longa* has the potential to serve as excellent anti-psoriatic and anti-inflammatory agents due to its excellent inhibitory efficiency, physicochemical properties, and biological activities compared to the standard medications of synthetic nature.

These natural products can act as promising agents for the development and improvement of useful inhibitors in the treatment of psoriasis.

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