Pharmacogn. Res., 2026; 18(2):503-510.
https://www.phcogres.com

Original Article

In silico Evaluation of Immuno-Modulatory Lead Molecules from *Elephantopus scaber* Linn. on Pro-Inflammatory Markers TNF-α and IL-1β

Anu Padinhapurath Abhimannue[1,*], Betty Kokkatt Poulose[2]

[1]Department of Biotechnology, St. Mary's College, Thrissur, Kerala, INDIA.
[2]Department of Botany, Sacred Heart College, Chalakudy, Thrissur, Kerala, INDIA.

ABSTRACT

Introduction: Up-regulated expression of TNF-α and IL-1β is a hallmark in chronic inflammation associated pathological conditions. The World Health Organization has identified chronic inflammatory pathological conditions as a leading threat to human health. Statistics point to alarming data where 6 out of every 10 Americans are having chronic inflammatory pathological conditions. Though various therapeutic strategies targeting TNF-α and IL-1β were developed, consistent reporting on side effects was the major hindrance. Hence, there is a need for newer and better therapeutic molecules targeting pro-inflammatory markers. **Objectives:** In the present study, anti-inflammatory property of phyto-constituents identified from *Elephantopus scaber* is analyzed for its inhibitory effect on TNF-α and IL-1β through molecular docking. **Materials and Methods:** The chemical components in the bioactive fraction of *Elephantopus scaber* were identified by UPLC-MS-QTOF and molecular docking was performed with the identified molecules to understand its interaction with pro-inflammatory markers. The 11 ligand molecules were docked with optimized and energy minimized crystal structure of TACE, 2OI0 and IL-1β, 5R8Q**.** Their binding affinities were compared with Rolipram and Indomethacine - the positive controls. **Results:** The binding affinities of the ligands towards 2OI0 and 5R8Q were analyzed and ranked according to their lower energies. Ligand molecules identified in ES1 was found to have better binding efficacy comparing to Ononin and piperine. **Conclusion:** The molecular docking studies have revealed possible bioactive lead molecules which can be further exploited for developing anti-inflammatory drugs.

Keywords: Anti-inflammatory, ADME Prediction, *Elephantopus scaber*, Immunomodulation, Molecular docking,TNF-α and IL-1β Inhibition.

Correspondence:
Dr. Anu Padinhapurath Abhimannue
Department of Biotechnology, St. Mary's College, Thrissur, Kerala, INDIA.
Email: anuabhimannue@gmail.com
ORCID: 0000-0002-3367-8809

Received: 14-08-2025;
Revised: 24-10-2025;
Accepted: 09-12-2025.

INTRODUCTION

Inflammation is the defense mechanism exerted by the immune system against any foreign stimuli including deleterious biological, physical or chemical agents. This mechanism aims to restore cellular homeostasis and resolution of pro-inflammatory conditions. However, a failure in resolving acute state leads to chronic inflammation lasting a prolonged time frame (Chen *et al*., 2017). Chronic inflammation is manifested by the continuous recruitment of pro-inflammatory cells such as macrophages, lymphocytes, and plasma cells releasing inflammatory cytokines, growth factors, Reactive oxygen species, and enzymes, thus contributing to the progression of tissue damage and fibrosis. IL-1β and TNF-α are the key cytokines that orchestrate chronic inflammatory responses (Jacob *et al*., 2018, Pahwa *et al*., 2024).

TNF-α performs a cascade of events leading to the perpetuation of chronic inflammation. TNF-α activates leukocyte adhesion molecules subsequently triggering immune cell infiltration manifested in various pathological conditions (Mohan *et al*., 2021, Megha *et al*., 2021). Up-regulation of TNF-α in COPD patient is reported to alter alveolar structure via pleural thickening, and disfiguring chest and lung cavity volumes (Hipolito *et al*., 2024). Over-expressed TNF-α has been evident in several autoimmune diseases like RA, Psoriatic arthritis and IBD. Over-expressed TNF-α can activate synovial fibroblasts, followed by inducing over-expression of MMP, ultimately resulting in bone and cartilage destruction in RA (Jang *et al*., 2021). IL-1β, mainly secreted by macrophages and mast cells, is tightly associated with immunomodulation leading to disease progression (Ren *et al*., 2009). Increased concentration of IL-1β in plasma and synovial fluids is a characteristic feature of Rheumatoid arthritis (Kay *et al*., 2004). Over-expression of IL-1β is reported to be a hallmark

OPEN ACCESS

Manuscript TECHNOMEDIA

DOI: 10.5530/pres.20260171

in atherosclerosis, where it induces endothelial cells activation, development of atherosclerotic plaque and invasion into blood vessels (Mai *et al*., 2020). IL-1β activates the release of other cytokines resulting in airway inflammation in COPD. Release of IL-8 and IL-6 in bronchial epithelial cells, and IL-6 and IL-17 in bronchoalveolar lavage fluid results in neutrophil recruitment and consequently alveolar dysfunction (Zou *et al*., 2017). Role of IL-1β and TNF-α have been implicated in neuroinflammation resulting in neurodegeneration in Parkinsons Disease (Leal *et al*., 2013).

The World Health Organization has identified chronic inflammatory pathological conditions as a leading threat to human health. Statistics point to alarming data where 6 out of every 10 Americans are having chronic inflammatory pathological conditions (Pahwa *et al*., 2024). Recent evidence points out that chronic inflammation is connected with renal dysfunction, hepatic failure, diabetes, cancer etc. Statistics also point out that 62% of deaths around the globe is due to these diseases alone (Du *et al*., 2015). Hence, therapeutic strategies targeting pro-inflammatory markers become the focus in managing the present scenario.

Though PDE4 inhibitors targeting TNF-α production (Rolipram, Cilomilast and Roflumilast) were developed, FDA prevented its commercialization due to side effects like nausea and gastrointestinal problems. Another class of components like adalimumab, certolizumab, golimumab with a modus operandi of competitive antagonism on the TNF-α receptor was also not successful. It exhibited injection site reactions on short term usage and risks of lymphoma on long term usage (Abhimannue *et al*., 2016). Therapeutic strategies utilizing IL-1 blockers, including IL-1 receptor antagonist (Anakinra), were also developed (Kay *et al*., 2004). However, side effects like fever, injection site reactions, anorexia, hypotension, and opportunistic infections had led to the limited and cautious usage of drugs (Dinarello *et al*., 2013, Abdesselam *et al*., 2010, Imazio *et al*., 2021).

With an increasing prevalence of chronic inflammatory pathological conditions and consistent reporting on side effects of current anti-inflammatory drugs, there is a need for newer and better therapeutic molecules targeting pro-inflammatory markers. Medicinal plants as a whole or its different parts have been reported to possess anti-inflammatory compounds that can target multiple points in inflammatory response pathways. Research elucidating the mechanism of action by these natural anti-inflammatory components also remains a lacuna (Dar *et al*., 2016). In the present study, *in silico* evaluation of immuno-modulatory lead molecules from *Elephantopus Scaber* Linn on pro-inflammatory markers TNF-α and IL-1β is conducted.

MATERIALS AND METHODS

UPLC MS Q-TOF analysis of *E. scaber* bioactive fraction, ES1

Chromatographic separation of components in the crude methanolic extract of *E. scaber* has been already published by Abhimannue *et al*., 2017. Thebioactive fraction of *E. scaber, ES1* was also analyzed as per the same paper. The accurate mass obtained from the UPLC MS Q-TOF was compared with the data from chemspider for the confirmation of the compound and structure.

Ligand preparation

3D structures of all the ligand molecules identified through UPLC MS Q-ToF analysis were built with ChemSketch software developed by Advanced Chemistry Development, Inc. (ACD/Labs). The structure of positive control, Rolipram and Indomethacine were identified from ChemSpider database (http://www.chemspider.com/). All these structures were subsequently converted to pdb format using the Open Babel software (Open Babel, version 2.3.2, http://openbabel.org (accessed 20.03.2015) for virtual screening.

ADME prediction of the ligands

The determination of ADME properties and drug likeness of the ligands is an important parameter to be looked upon and was determined using Molsoft online molecular property calculator (http://molsoft.com/mprop/).The numbers of hydrogen donors and acceptors, rotatable bonds, total polar surface area etc was predicted. The percentage of absorption was calculated using equation: % ABS = 109 – (0.345 × TPSA) (Zhao *et al*., 2002).

Preparation of protein structure

The protein crystal structure of TNF-α Converting Enzyme (TACE) and IL-1β with RCSB PDB ID - 2OI0 and 5R8Q was retrieved from Protein Data Bank (http://www.rcsb.org/pdb/). Prior to docking, the receptors were subjected to protein optimization via removing all heteroatoms and energy minimized with Swiss-Pdb Viewer version 4.1.0 (http://www.expasy.org/spdbv/). The protein optimization and energy minimization brings down the energy of macromolecules to a lower level as seen in the native cellular environment; by reducing the sterric clashes and bringing in more orientations that are similar to the theoretical true binding mode. However, Zn^{2+} - the co-factor of TACE along with its connectors were retained in the structure of the receptor, as they play an important role in its functioning (Rao *et al*., 2007).

Docking

Autodock 4.0 was performed to understand the interaction between pro-inflammatory markers like TNF-α and IL-1β with ligand molecules identified in ES1. A default grid spacing of 0.375

Å with its grid points set to 60 Å each in X, Y and Z coordinates was created with AutoDock 4 to analyze ligand-receptor interaction. For 2OI0, TNF-α Converting Enzyme (TACE) the active site bound to the competitive inhibitor, aryl sulfonamide was chosen for docking and grid box was centered on the X, Y and Z coordinates of amino acid residue VAL 402 (A) at 43.470, 26.765 and 8.236. For IL-1β, 5R8Q the active site bound to the inhibitor, 1-Methyl-N-{[(2s)-Oxolan-2-Yl]Methyl}-1h-Pyrazol e-3-Carboxamide was chosen for docking. The grid box was centered on the X, Y and Z coordinates of amino acid residue TYR (A) at 39.666, 1.048 and 71.207.

For each ligand, a docking experiment consisting of 10 simulations was performed using Cygwin64 Terminal and the outputs were exported to Discovery Studio 4.1 Client for visual inspection of the binding modes and interactions.

RESULTS

UPLC MS Q-TOF analysis of *E. scaber* bioactive fraction, ES1

Eleven molecules were identified from the bioactive fraction of *E. scaber* methanolic extract by UPLC MS QTOF and were selected as ligands for the study. It included Methylumbelliferone, Hydroxydihydrobovolide, Lysine theophylline, Ononin, Alismorientol A, Lotaustralin, 2-amino 4-(4-phenylpiperazino)-1,3,5-triazine, Phytosphingosine, Chamazulene, Ethyl oleate, and Piperine. This data aligns with a previous report where bioactive components of crude extract have been published.

ADME prediction of the ligands

In the present study 11 molecules identified from ES1, the bioactive fraction of *E. scaber* extract were screened with pro-inflammatory molecules like TACE, 2OI0 and IL-1β, 5R8Q taken as specific protein targets. The ligand molecules were analyzed for its molecular properties, drug likeness, percentage of absorption and violation to Lipinski's rule of five, prior to docking (Table 1). The rule states that the Molecular Weight (MW) of the ligand should be ≤ 500, the Hydrogen Bond Acceptor (HBA) and Donor (HBD) groups in the ligand should be ≤ 10 and 5 respectively and mol log P value; which is the partition coefficient of the component in water: octan-1-ol system ≤ 5 (Lipinski et al., 2001).

Other parameters like Topological Polar Surface Area (TPSA), % absorption, No: of stereo-centres and drug likeness score are also considered. TPSA defined as the sum of surfaces of polar atoms in a molecule, predicts the drug transport properties and cell permeation properties. The recommended TPSA values are < 140 A° and 90 A° for cell permeation and blood-brain barrier respectively. The percentage of absorption is calculated from TPSA value using equation: % ABS = 109 – (0.345 × TPSA). It is observed that with increase in TPSA value, the percentage of absorption was found to be decreased. Less No: of Stereo-Centres (N-SC) suggest that upon binding the ligand undergoes only a slight conformational change. The Drug Likeness (DL) is a qualitative concept which predicts the likeness of a molecule to a drug.

All ligands except lysine theophylline (HBD > 5) and ethyl oleate (Mol Log P > 5) were found to follow all parameters of Lipinski's

Table 1: Physico-chemical properties of the ligands.

Sl. No.	Component	MW	HBA	HBD	M LogP	M LogS	MV	N-SC	DL	TPSA $(A^0)^2$	% ABS
1	Methylumbelliferone	176.05	3	1	1.81	-2.60	192.40	0	-0.43	38.26	95.8003
2	Hydroxyl dihydrobovolide	198.13	3	1	2.40	-1.36	246.39	1	-0.61	39.03	95.5347
3	Lysine theophylline	326.17	7	6	-2.80	-1.28	316.45	1	0.73	124.67	65.9889
4	Ononin	430.13	9	4	0.70	-4.54	403.49	5	-0.02	108.26	71.6503
5	Alismorientol A	272.20	4	4	1.61	-0.80	327.66	6	-0.59	62.21	87.5376
6	Lotaustralin	261.12	7	4	-1.94	-0.99	256.22	6	-0.12	96.40	75.742
7	2-amino-4-(4-phenylpiperazino)-1,3,5-triazine	256.14	3	2	1.59	-1.80	228.68	0	-0.22	57.45	89.1798
8	Phytosphingosine	317.29	4	5	3.51	-5.35	353.16	3	-1.59	70.25	84.7638
9	Chamazulene	184.13	0	0	4.76	-5.01	222.28	0	-1.16	0.00	109.00
10	Ethyl oleate	310.29	2	0	7.98	-6.67	388.60	0	-0.78	20.67	101.8689
11	Piperine	285.14	3	0	3.96	-4.88	328.92	0	-0.02	33.47	97.4529
12	Rolipram	275.15	3	1	2.54	-2.96	292.96	1	0.87	47.56	92.592
13	Indomethacine	357.08	4	1	4.00	-4.57	340.58	0	0.91	51.31	91.298

rule of five. The drug likeness score of the ligand molecules were comparable with positive control –Rolipram and Indomethacine.

Molecular docking of bioactive components from ES1 with TACE, 2OI0 and IL-1β, 5R8Q

The 11 ligand molecules identified in ES1 were docked with optimized and energy minimized crystal structure of TACE, 2OI0 and IL-1β, 5R8Q**.** The binding affinities of the molecules with TACE, 2OI0 were compared with Rolipram - the positive control. Ononin was found to have better binding efficiencies than Rolipram. The binding affinities of the molecules with IL-1β, 5R8Q were compared with Indomethacine. However, it was found that piperine from ES1 have better binding efficiency.

The binding affinities of the ligands towards 2OI0 and 5R8Q were analyzed and ranked according to lower energies as shown in the Tables 2 and 3. The docked poses of the positive control and the molecule with the best binding efficiency are presented in the figures (Figures 1 to 4).

DISCUSSION

Monocytes are reported to be critical effectors and regulators of inflammation. These cells respond to a variety of stimuli like pathogens, antigens, tumors etc. and are responsible for the secretion of pro-inflammatory cytokines (Geissmann *et al.*, 2010). Excessive infiltration and accumulation of monocytes are strongly associated with numerous pathological conditions like atherosclerosis (Tabas *et al.*, 2017), bronchial asthma (Tanizaki *et al.*, 1982), ischemic stroke, autoimmune multiple sclerosis and infectious encephalitis (Yang *et al.*, 2014), intraplaque angiogenesis and tissue destruction (Woollard *et al.*, 2010, Pamukcu *et al.*, 2010).

The importance of TNF-α and IL-1β has been demonstrated in the destructive process of chronic inflammation related diseases like rheumatoid arthritis. These pro-inflammatory molecules consecutively activate tissue destroying MMPs and induce osteoclastogenesis through the stimulation of Receptor Activator of Nuclear factor-kB Ligand (RANKL). The synergestic upregulation in IL-1β synthesis by TNF-α has been proposed in chronic inflamed joints of rheumatoid arthritis models (Magyari

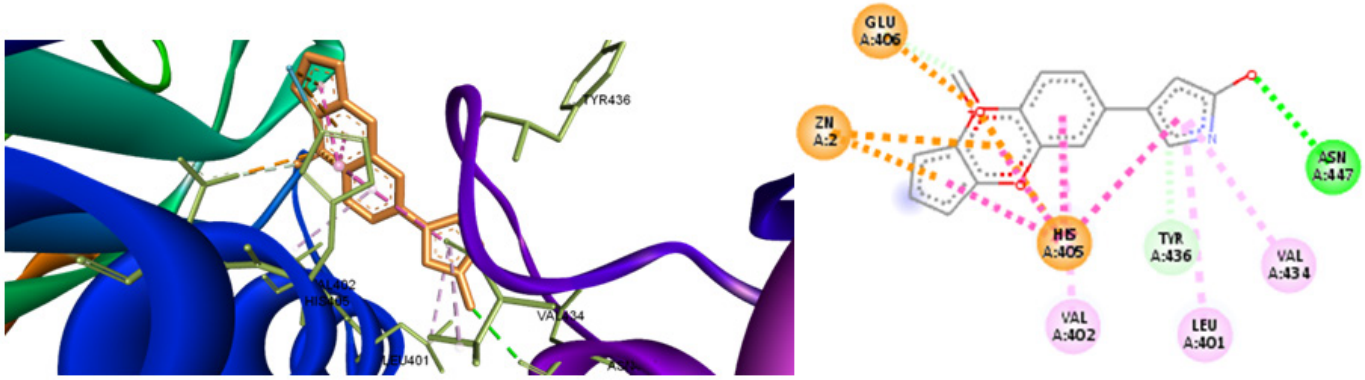

Figure 1: The docked pose of Rolipram, the positive control at the active site of TACE, 2OI0. The key amino acids interacting with the ligand is labeled in the figure and (B) Represents the protein-ligand interactions. Different bindings are shown in various colors. : Conventional hydrogen bond, : Carbon hydrogen bond, Pi- alkyl interaction, Attractive charge, Pi-Cation and : Pi-Pi stacked.

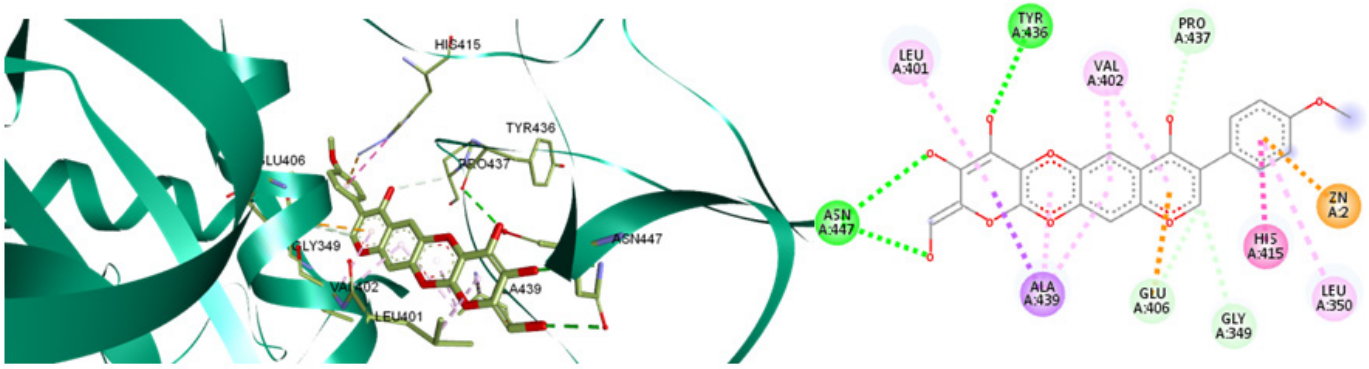

Figure 2: The docked pose of Ononin at the active site of TACE, 2OI0. The key amino acids interacting with the ligand is labeled in the figure and (B): Represents the protein-ligand interactions. Different bindings are shown in various colors. : Conventional hydrogen bond, : Carbon hydrogen bond, Pi- alkyl interaction, Pi-Anion, Pi-cation, : Pi-Pi T-shaped and : Pi-Sigma.

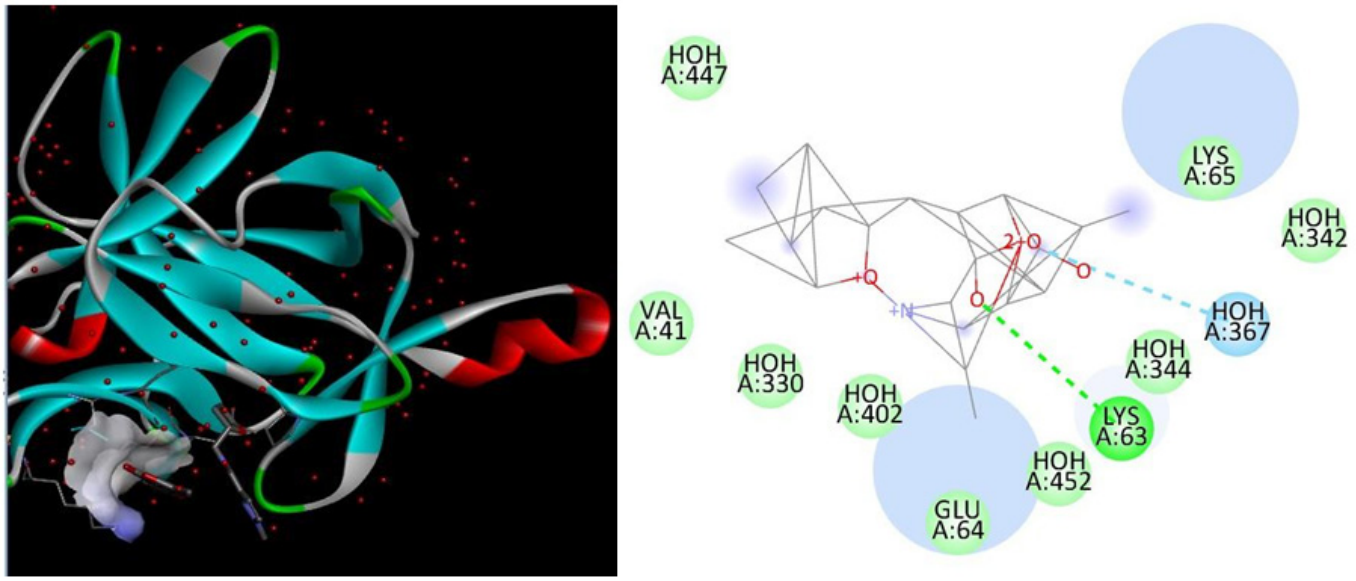

Figure 3: The docked pose of Indomethacin at the active site of IL-1β, 5R8Q. The key aminoacids interacting with the ligand is labeled in the figure and (B): Represents the protein-ligand interactions. Different bindings are shown in various colors. : Conventional hydrogen bond, : Van der Waals interaction, : Water hydrogen bond.

Table 2: The binding energy of the 11 ligands identified in ES1, the bioactive fraction of *E. scaber* towards TACE, 2OI0 along with the list of amino-acids interacting with the protein. # Binding energies are expressed as mean ± S.D., of 10 different docking poses.

Ranking as per binding affinity	Ligand	Min. binding energy (Kcal/mol)	Key protein ligands interaction
Positive control	Rolipram	-9.134 ± 0.0052	GLU A: 406, HIS A: 405, VAL A: 402, 434, LEU A: 401, TYR A: 436, ASN A: 447, Pi- Anion interaction with Zn.
1	Ononin	-10.917 ± 0.038	PRO A:437, VAL A:402, TYR A:436, LEU A:401, 350, ASN A:447, ALA A:439, GLU A: 406, GLY A:349, HIS A:415, Pi- Anion interaction with Zn.
2	Piperine	-10.021 ± 0.2164	LEU A: 401, 348, VAL A: 434, 440, 402, ASN A: 447, TYR A: 433, 436, LYS A: 432, ALA A: 439, ILE A: 438, HIS A: 405, GLU A: 406, GLY A: 349, THR A: 347, PRO A: 437, Pi- Anion interaction with Zn.
3	2-amino-4-(4-phenylpiperazino)-1,3,5-triazine	-9.282 ± 0.0249	LEU A: 348, 401, GLU A: 406, VAL A: 402, 434, TYR A: 436, ALA A: 439.
4	Alismorientol A	-9.21 ± 0.0	GLU A: 398, LEU A: 401, 348, ALA A: 439, VAL A: 440, 434, 402, ASN A: 447, LYS A: 432, TYR A: 433, 436, ILE A: 438, HIS A: 405.
5	Ethyl oleate	-8.967 ± 0.1607	ALA A: 351, 439, GLU A: 406, 398, VAL A: 440, 402, ASP A: 443, LYS A: 397, GLY A: 442, 349, LEU A: 395, 402, 348, 350, SER A: 441, PRO A: 437, PHE A: 347, HIS A: 409, 408, Pi- Anion interaction with Zn.
6	Phytosphingosine	-8.865 ± 0.2393	HIS A: 409, VAL A: 440, 434, TYR A: 433, ALA A: 439, LEU A: 350.
7	Lotaustralin	-8.598 ± 0.0048	GLU A: 406, LEU A: 348, 401, VAL A: 402, HIS A: 405.
8	Chamazulene	-8.048 ± 0.0042	HIS A: 405, TYR A: 436, 433, LYS A: 432, VAL A: 440, 434, LEU A: 401.
5	Hydroxyl dihydrobovolide	-7.568 ± 0.0929	ASN A:447, VAL A:402, HIS A:405
10	Methylumbelliferone	-7.140 ± 0.0031	LEU A:401, VAL A: 434, 402, HIS A:405
11	Lysine theophylline	-4.350 ± 0.0031	LEU A:401, ALA A:439, TYR A:433, 436, HIS A:405

Table 3: The binding energy of the 11 ligands identified in ES1, the bioactive fraction of *E. scaber* towards IL-1β, 5R8Q along with the list of amino-acids interacting with the protein. # Binding energies are expressed as mean ± S.D., of 10 different docking poses.

Ranking according to the binding affinity	Ligand	Min. binding energy (Kcal/mol)	Key protein ligands interaction
Positive Control	Indomethacine	-8.628 ± 0.4413	VAL A: 41, GLU A: 64, LYS A: 63, LYS A: 65.
1	Piperine	-9.826 ± 0.7913	LYS A: 65, GLU A: 38, MET A: 20, VAL A: 19, SER A: 21, LYS A: 27, ASN A: 129, LEU A:29.
1	Ononin	-9.002 ± 0.3817	LEU A: 69, LEU A: 26, MET A: 20, LYS A: 65, VAL A:41.
2	Alismorientol A	-8.972 ± 0.4695	PRO A: 131, LEU A: 69, LEU A: 80, GLN A: 81, LEU A: 82, VAL A:132, TYR A: 24, GLU A: 25, LEU A: 26
3	Ethyl oleate	-8.552 ± 0.1254	LYS A: 63, GLU A: 64, MET A: 20, LYS A: 65, VAL A: 41.
5	Lotaustralin	-8.001 ± 0.0544	SER A:123, MET A:44, GLN A: 141, ALA A:28, LEU A:18, SER A:17
6	2-amino-4-(4-phenylpiperazino)-1,3,5-triazine	-7.595 ± 0.5332	GLU A: 64, LYS A:77, ARG A:98
7	Phytosphingosine	-7.330 ± 0.1824	LYS A:27, MET A: 20, ALA A:28, LEU A:18, SER A: 17.
8	Hydroxyl dihydrobovolide	-6.951 ± 0.1508	SER A: 123, SER A: 43, ASN A:7, GLN A:141, MET A:44
9	Chamazulene	-6.654 ± 0.0870	MET A: 20, LYS A: 65, VAL A:19,, GLN A: 38.
10	Methylumbelliferone	-6.349 ± 0.0870	LYS A:27, MET A:20, ALA A:28, LEU A:18, SER A:17
11	Lysine theophylline	-4.006 ± 0.1203	GLN A: 39, LEU A: 29, GLN A:126, SER A: 17, VAL A:40

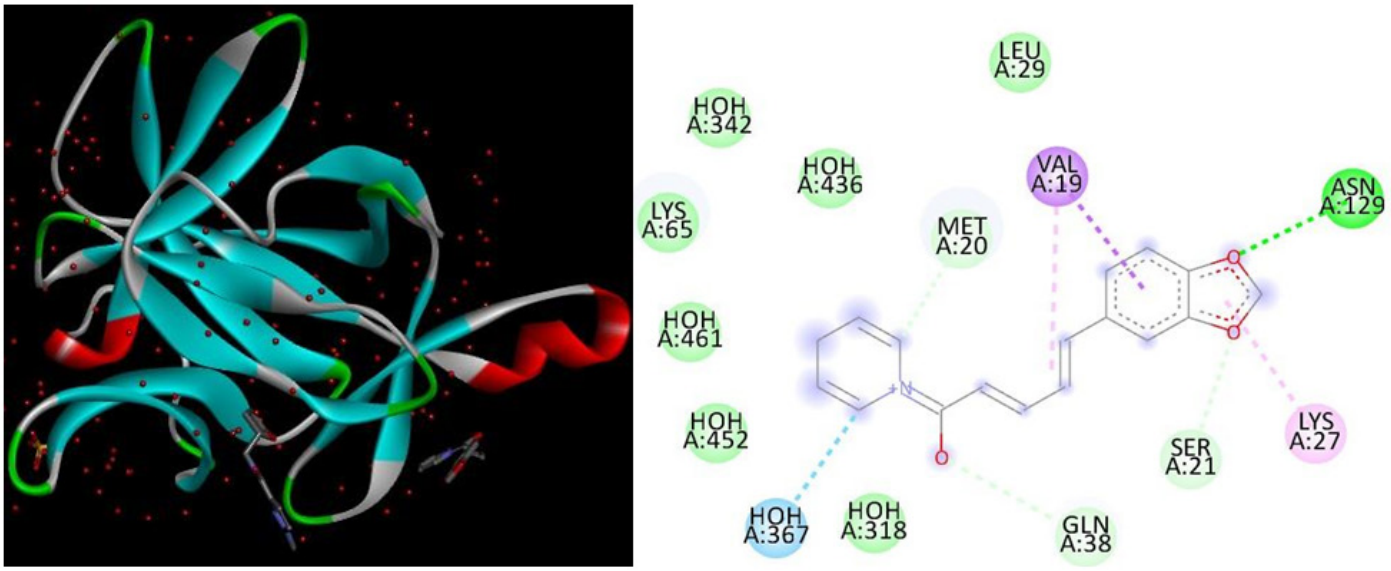

Figure 4: The docked pose of Piperine at the active site of IL-1β, 5R8Q. The key amino acids interacting with the ligand is labeled in the figure and (B): Represents the protein-ligand interactions. Different bindings are shown in various colors. image2: Conventional hydrogen bond, image10: Van der Waals interaction, image10: Water hydrogen bond, image4 Pi- alkyl interaction, image3: Carbon hydrogen bond and image8: Pi-Sigma.

et al., 2014). Hence, TNF-α and IL-1β are considered as effective therapeutic targets in the treatment of chronic inflammation related pathological conditions. Results from Molecular docking studies reveal the potential of bioactive molecule in *E. scaber* in significant inhibition of production of TNF-α and IL-1β.

CONCLUSION

The present study had highlighted the anti-inflammatory potential of *E. scaber* extract with respect to inhibition of pro-inflammatory cytokines production. The bioactive fraction of *E. scaber* methanolic extract had resulted in eleven ligand molecules with druggability features for inhibition of TNF-α and IL-1β production. Molecular docking had lead to some promising agents which can be further exploited for anti-inflammatory therapeutic effect.

ACKNOWLEDGEMENT

The authors thank Mr. Dineep Devadasan (School of Environmental Science, Mahatma Gandhi University, Kottayam, Kerala) for his assistance with the UPLC MS Q-TOF analysis.

ABBREVIATIONS

% ABS: Percentage Absorption; **ACD/Labs:** Advanced Chemistry Development/Labs; **ADME:** Absorption, Distribution, Metabolism, And Excretion; **COPD:** Chronic Obstructive Pulmonary Disease; **DL:** Drug Likeness; **ES1**: *E. Scaber* Bioactive Fraction; **HBA:** Hydrogen Bond Acceptor; **HBD:** Hydrogen Bond Donor; **IBD:** Inflammatory Bowel Disease; **IL-1β:** *Interleukin*-1β; **MMP:** Matrix Metalloproteinase; **MW:** Molecular Weight; **N-SC:** Number of Stereo-Centres; **PDE4 Inhibitors:** Phosphodiesterase 4 Inhibitors; **RA:** Rheumatoid Arthritis; **RANKL:** Receptor Activator of Nuclear Factor-κB Ligand; **RCSB PDB:** Research Collaboratory For Structural Bioinformatics Protein Data Bank; **TACE:** Tumour Necrosis Factor Alpha Converting Enzyme; **TNF-α:** Tumor Necrosis Factor-α; **TPSA:** Topological Polar Surfce Area; **UPLC-MS-QTOF:** Ultra-High Performance Liquid Chromatography (UPLC) With Quadrupole Time-of-Flight (QTOF).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR'S CONTRIBUTION

The experiments were designed and conducted by Anu P. Abhimannue and Betty K.P. Both of them was involved in manuscript designing, writing and reviewing.

SUMMARY

In the study, eleven ligand molecules identified in *E. scaber* bioactive fraction, ES1 through UPLC MS Q-TOF was subjected to molecular docking. Upon docking with the crystal structure of TACE, 2OI0 and IL-1β, 5R8Q the bioactive molecules were found to have significant immuomodulatory effect. The binding affinities of the molecules were compared with respective positive controls and were found to have better binding efficiency. These results reveal the anti-inflammatory potential of bioactive molecule in *E. scaber* in significant inhibition of production of TNF-α and IL-1β.

REFERENCES

Abhimannue, A. P., Mohan, M. C., & B, P. K. (2016). Inhibition of tumor necrosis factor-α and interleukin-1β production in lipopolysaccharide-stimulated monocytes by methanolic extract of *Elephantopus scaber* Linn and identification of bioactive components. Applied Biochemistry and Biotechnology, 179(3), 427–443. https://doi.org/10.1007/s12010-016-2004-0

Aït-Abdesselam, T., Lequerré, T., Legallicier, B., François, A., Le Loët, X. L., & Vittecoq, O. (2010). Anakinra efficacy in a Caucasian patient with renal AA amyloidosis secondary to cryopyrin-associated periodic syndrome. Joint Bone Spine, 77(6), 616–617. https://doi.org/10.1016/j.jbspin.2010.04.018

Chen, L., Deng, H., Cui, H., Fang, J., Zuo, Z., Deng, J., Li, Y., Wang, X., & Zhao, L. (2017). Inflammatory responses and inflammation-associated diseases in organs. Oncotarget, 9(6), 7204–7218. https://doi.org/10.18632/oncotarget.23208

Dar, K. B., Bhat, A. H., Amin, S., Masood, A., Zargar, M. A., & Ganie, S. A. (2016). Inflammation: A multidimensional insight on natural anti-inflammatory therapeutic compounds. Current Medicinal Chemistry, 23(33), 3775–3800. https://doi.org/10.2174/0929867323666160817163531

Dinarello, C. A., & Van Der Meer, J. W. M. (2013). Treating inflammation by blocking interleukin-1 in humans. Seminars in Immunology, 25(6), 469–484. https://doi.org/10.1016/j.smim.2013.10.008

Du, C., Bhatia, M., Tang, S. C. W., Zhang, M., & Steiner, T. (2015). Mediators of inflammation: Inflammation in cancer, chronic diseases, and wound healing. Mediators of Inflammation, 2015(1), Article 570653. https://doi.org/10.1155/2015/570653

Geissmann, F., Manz, M. G., Jung, S., Sieweke, M. H., Merad, M., & Ley, K. (2010). Development of monocytes, macrophages, and dendritic cells. Science, 327(5966), 656–661. https://doi.org/10.1126/science.1178331

Govinda Rao, B. G., Bandarage, U. K., Wang, T., Come, J. H., Perola, E., Wei, Y., Tian, S.-K., & Saunders, J. O. (2007). Novel thiol-based TACE inhibitors: Rational design, synthesis, and SAR of thiol-containing aryl sulfonamides. Bioorganic and Medicinal Chemistry Letters, 17(8), 2250–2253. https://doi.org/10.1016/j.bmcl.2007.01.064

Hipolito, P. M. D., Quilala, P. F., Dimamay, M. P. S., Liles, V. R., Yungca, M. X., & Baclig, M. O. (2024). Tumor necrosis factor-α −308 G/A genetic polymorphism in patients with chronic obstructive pulmonary disease presenting with hyperactive airways. Biomedical Reports, 21(2), Article 113. https://doi.org/10.3892/br.2024.1802

Imazio, M., Lazaros, G., Gattorno, M., Abbate, A., & Brucato, A. (2021). [Anti-interleukin-1 agents: A new class of drugs for recurrent pericarditis. A practical guide for cardiologists]. PubMed. https://doi.org/10.1714/3666.36514

Jacob, J., Babu, B. M., Mohan, M. C., Abhimannue, A. P., & Kumar, B. P. (2017). Inhibition of proinflammatory pathways by bioactive fraction of Tinospora cordifolia. Inflammopharmacology, 26(2), 531–538. https://doi.org/10.1007/s10787-017-0319-2

Jang, D.-I., Lee, A.-H., Shin, H.-Y., Song, H.-R., Park, J.-H., Kang, T.-B., Lee, S.-R., & Yang, S.-H. (2021). The role of tumor necrosis factor alpha (TNF-A) in autoimmune disease and current TNF-A inhibitors in therapeutics. International Journal of Molecular Sciences, 22(5), Article 2719. https://doi.org/10.3390/ijms22052719

Kay, J., & Calabrese, L. (2004). The role of interleukin-1 in the pathogenesis of rheumatoid arthritis. Rheumatology, 43(Suppl. 3), iii2–iii9. https://doi.org/10.1093/rheumatology/keh201

Leal, M. C., Casabona, J. C., Puntel, M., & Pitossi, F. J. (2013). Interleukin-1β and tumor necrosis factor-α: Reliable targets for protective therapies in Parkinson's disease? Frontiers in Cellular Neuroscience, 7, Article 53. https://doi.org/10.3389/fncel.2013.00053

Magyari, L., Varszegi, D., Kovesdi, E., Sarlos, P., Farago, B., Javorhazy, A., Sumegi, K., Banfai, Z., & Melegh, B. (2014). Interleukins and interleukin receptors in rheumatoid arthritis: Research, diagnostics and clinical implications. World Journal of Orthopedics, 5(4), 516–536. https://doi.org/10.5312/wjo.v5.i4.516

Mai, W., & Liao, Y. (2020). Targeting IL-1B in the treatment of atherosclerosis. Frontiers in Immunology, 11, Article 589654. https://doi.org/10.3389/fimmu.2020.589654

Megha, K. B., Joseph, X., Akhil, V., & Mohanan, P. V. (2021). Cascade of immune mechanism and consequences of inflammatory disorders. Phytomedicine, 91, Article 153712. https://doi.org/10.1016/j.phymed.2021.153712

Mohan, M. C., Abhimannue, A. P., & Kumar, B. P. (2019). Modulation of proinflammatory cytokines and enzymes by polyherbal formulation Guggulutiktaka ghritam. Journal of Ayurveda and Integrative Medicine, 12(1), 13–19. https://doi.org/10.1016/j.jaim.2018.05.007

Pahwa, R., Goyal, A., & Jialal, I. (2023). Chronic inflammation. StatPearls – NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK493173/

Pamukcu, B., Lip, G. Y. H., Devitt, A., Griffiths, H., & Shantsila, E. (2010). The role of monocytes in atherosclerotic coronary artery disease. Annals of Medicine, 42(6), 394–403. https://doi.org/10.3109/07853890.2010.497767

Ren, K., & Torres, R. (2009). Role of interleukin-1β during pain and inflammation. Brain Research Reviews, 60(1), 57–64. https://doi.org/10.1016/j.brainresrev.2008.12.020

Tabas, I., & Lichtman, A. H. (2017). Monocyte-Macrophages and T cells in atherosclerosis. Immunity, 47(4), 621–634. https://doi.org/10.1016/j.immuni.2017.09.008

Tanizaki, Y., Hosokawa, M., Goda, Y., Akagi, K., Takeyama, H., & Kimura, I. (1982). Numerical changes in blood monocytes in bronchial asthma. Acta Medica Okayama. PubMed, 36(5), 341–348. https://doi.org/10.18926/amo/30688

Woollard, K. J., & Geissmann, F. (2010). Monocytes in atherosclerosis: Subsets and functions. Nature Reviews. Cardiology, 7(2), 77–86. https://doi.org/10.1038/nrcardio.2009.228

Yang, J., Zhang, L., Yu, C., Yang, X.-F., & Wang, H. (2014). Monocyte and macrophage differentiation: Circulation inflammatory monocyte as biomarker for inflammatory diseases. Biomarker Research, 2(1), 1. https://doi.org/10.1186/2050-7771-2-1

Zhao, Y. H., Abraham, M. H., Le, J., Hersey, A., Luscombe, C. N., Beck, G., Sherborne, B., & Cooper, I. (2002). Rate-limited steps of human oral absorption and QSAR studies. Pharmaceutical Research, 19(10), 1446–1457. https://doi.org/10.1023/a:1020444330011

Zou, Y., Chen, X., Liu, J., Zhou, D. B., Kuang, X., Xiao, J., Yu, Q., Lu, X., Li, W., Xie, B., & Chen, Q. (2017). Serum IL-1 and IL-17 levels in patients with COPD: Associations with clinical parameters. International Journal of Chronic Obstructive Pulmonary Disease, 12, 1247–1254. https://doi.org/10.2147/copd.s131877

Cite this article: Abhimannue AP, Poulose BK. *In silico* Evaluation of Immuno-Modulatory Lead Molecules from *Elephantopus scaber* Linn. on Pro-Inflammatory Markers TNF-α and IL-1β. Pharmacog Res. 2026;18(2):503-10.