Journal of Applied Life Sciences International

25(2): 15-25, 2022; Article no.JALSI.85408
ISSN: 2394-1103

A Preliminary *In-silico* Analysis and Molecular Docking of Active Compounds in *Coriandrum sativum* as Potential Drug Targets Against SARS-COV-2 Infection

T. Arvind Prabhu [a*], N.M Hariharan [a], K.E Premalatha [a], P. L. Sujatha [b] and H. Kalifathulla [c]

[a] Sree Sastha Institute of Engineering and Technology, Chennai-600 123, India.
[b] College of Food and Dairy Technology, Koduvalli, Chennai – 600 052, India.
[c] Tamil Nadu Sports and Physical Education University, Chennai-600 127, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JALSI/2022/v25i230284

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/85408

Original Research Article

Received 03 March 2022
Accepted 05 April 2022
Published 21 April 2022

ABSTRACT

A novel strain of coronavirus, namely, SARS-CoV-2 has already taken the lives of more than 2 million people worldwide, causing several socio-economic and political disturbances, affecting our daily life. There are no definite therapies available and research is still being conducted to identify and develop an effective antiviral drug leads against SARS-CoV-2. Therefore, there is an immediate need to identify and develop new or repurposed antiviral (anti-coronavirus) drug leads. The virus requires the main protease (Pdb ID:6WTT), a multifunctional protein involved in the processing and replication of the viral RNAs. This paper aims to screen potential phytochemical compounds of *Coriandrum sativum* against the viral main protease. In order to identify a novel potent inhibitor, we have performed docking studies on the SARS-CoV-2 main protease with the phytochemical compounds of *Coriandrum sativum*. Among studied compounds, Cosomosiin, Erucic acid, Rosemarinic, and Pimentel appear to be potential inhibitors of the SARS-CoV-2 main protease. When docked against the crystal structure of the main protease, these four compounds revealed Libdock scores of 141.40, 133.89, 143.89, and 148.60 respectively. However, all these identified phytochemical compounds need to be further validated by molecular dynamics and invitro lab experiments for clinical use only after appropriate trials.

**Corresponding author: E-mail: arvindprabhu24@gmail.com;*

Keywords: Coriandrum sativum; SARS-CoV-2 main protease; molecular dynamic simulation; molecular docking; libdock score.

1. INTRODUCTION

The latest category of coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [initially recognized as 2019 novel coronavirus (2019-nCoV)], is responsible for this pandemic condition in the world [1]. At present, the newly mutated SARS-CoV-2 has caused millions of deaths around the world, representing a severe threat to general well-being. The most characteristic feature shared by SARS-2 coronaviruses is the single-strand, positive-sense RNA genomes with a total structural weight of 105.02 kDa. Coronavirus polyproteins encode two proteases, namely, the main protease called 3C-like protease (Mpro) and papain-like protease (Plpro), which correlate while releasing and processing the translated nonstructural proteins. Both Plpro and Mpro are essentially the focus of drug design and development against the ongoing COVID fatal epidemic disease, including SARS-CoV. and MERS – CoV [2].

Currently, there is no known effective treatment or vaccine that can mitigate/inhibit SARS-CoV-2. Available clinical interventions for COVID-19 are only palliative and limited to support [3].

In the absence of an effective vaccine and specific drug, the only option is immunity-boosting nutraceuticals and symptomatic treatment. It is no wonder that medicinal plants and their phytochemical compounds could be employed as a potent weapon against COVID-19. In the present study, the phytochemicals extract of leaves, stem, seeds of *Coriandrum sativum* (also known as curry leaves) have been screened in silico against the main protease of SARS-CoV-2 to investigate the potent inhibitors [4]. The below Fig. 1 shows the structure of SARS-COV-2.

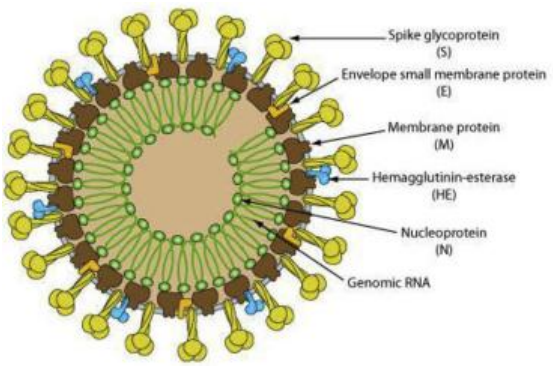


Fig. 1. structure of SARS-COV-2 [5]

2. MATERIALS AND METHODS

2.1 Software and Program

Discovery Studio Biovia 2020 (developed and distributed by Dassault Systemes BIOVIA) was employed to visualize and modify receptor and ligand structures.

2.2 Protein Preparation

RCSB (Research Collaboratory for Structural Bioinformatics) Protein Data Bank (https://www.rcsb.org/) was used to retrieve the three-dimensional crystal structure of novel SARS CoV- 2 (COVID-19) main protease with inhibitor GC- 376 (Protein ID: 6WTT) was derived in pdb. format. It was used as it is a well-annotated model in the database that constitutes three chains A, B, and C with a good resolution of 2.15 Å. This model was employed because it has the largest number of non-hydrogen atoms in the deposited model (7,430) and the most recent release date (2020-05-20). Moreover, the 3D structure of the target protein was sterilized using the Discovery Studio Biovia 2020 (DS 4.0) software to remove the original ligand [6,7].

Protein preparation was done with the help of the 'Prepare protein' protocol of Discovery studio 4.0 (DS 4.0). Water molecules and heteroatoms present in the crystal structure were removed at physiological pH 7.4 using DS 4.0. Further, the prediction of the active site in the prepared protein was done by using the receptor cavities option in the DS 4.0.

2.3 Ligands Selection

For the documentation of potential inhibitors of the main protease of SARS-CoV-2, a total of seventy-three active phytochemicals of *Coriandrum sativum* were retrieved from the literature. PubChem compound database (https://pubchem.ncbi.nlm.nih.gov/) was used for the retrieval of phytochemical structures in 2-dimensional SDF (Structure Data File) format. Afterward ligand optimization, energy minimization, and conversion of retrieved ligands to 3-D PDB format and clean geometry were done with the help of Discovery Studio client 4.0 [8].

A. Phytochemicals of Coriander (*Coriandrum sativum*)

The result of the phytochemical screening of coriander leaf, stem, and fruit powder extracted with methanol, chloroform, and distilled water for different phytochemical tests and the identification of different groups are obtained from already published study [9] has used for our study. The phytochemical screening of leaf, stem, and fruit extract of coriander using three different solvents namely chloroform, methanol, dilution with water has shown following results as listed in the Tables 1,2, and 3. Further individual ligands along with their simile IDs retrieved from respective PubChem webpage [10] are listed in Table 4.

Table 1. Phytochemical screening of *Coriander sativum* leaf extract

S.NO	Phytocompounds	Chloroform	Methanol	D/w
1	Cardiac glycosides	-	+	+
2	Terpenoids	+	+	+
3	Steroid	+	+	+
4	Saponin	-	-	+
5	Tannin	-	-	-
6	Flavonoid	-	-	-
7	Alkaloid	-	-	-

Table 2. Phytochemical screening of *Coriander sativum* stem extract

S.NO	Phytocompounds	Chloroform	Methanol	D/w
1	Cardiac glycosides	+	+	+
2	Terpenoids	+	+	+
3	Steroid	+	+	+
4	Saponin	-	-	-
5	Tannin	-	-	-
6	Flavonoid	-	-	-
7	Alkaloid	-	-	-

Table 3. Phytochemical screening of *Coriander sativum* fruit extract

S.NO	Phytocompounds	Chloroform	Methanol	D/w
1	Cardiac glycosides	+	+	+
2	Terpenoids	+	+	+
3	Steroid	+	+	+
4	Saponin	-	+	-
5	Tannin	-	+	-
6	Flavonoid	-	-	+
7	Alkaloid	-	+	-

Table 4. List of Active Phytochemical Composition in *Coriandrum sativum*

S.No	Active ingredients	SIMILES (Simplified Molecular Input Line Entry System)
1	Aniseed	C[C@@H]1O[C@@H](OCC2O[C@@H](O)[C@H]([C@H]([C@@H]2O)O)O)[C@@H]([C@@H]([C@H]1O)O)O.Oc1cc(O)c2c(c1)oc(c(c2=O)O)c1ccc(c(c1)O)O.O=c1ccc2c(o1)cccc2.C/C=C/c1ccc(cc1)OC
2	Coriandrone D	COc1cc2C[C@H](C)OC(=O)c2c(c1CC(C(O)(C)C)OC(=O)C)O
3	Phytosterols	CC[C@H](C(C)C)CC[C@H]([C@H]1CCC2[C@]1(C)CC[C@H]1[C@H]2CC=C2[C@]1(C)CC[C@@H](C2)O)C
4	Sinapaldehyde Glucoside	O=CC=Cc1cc(OC)c(c(c1)OC)OC1O[C@H](CO)[C@H]([C@@H]([C@H]1O)O)O
5	Linalool	C=C[C@@](CCC=C(C)C)(O)C
6	1-Decanol	CCCCCCCCCCO
7	1-Dodecanol	CCCCCCCCCCCCO

S.No	Active ingredients	SIMILES (Simplified Molecular Input Line Entry System)
8	Z-Ligustilide	CCCC=C1OC(=O)C2=C1CCC=C2
9	1-Tricosanol	CCCCCCCCCCCCCCCCCCCCCCCC
10	2-(4-Hydroxyphenyl) Ethanol	OCCc1ccc(cc1)O
11	2-Tridecenal	CCCCCCCCCC/C=C/C=O
12	2,4-Dihydroxycinnamic Acid	OC(=O)/C=C/c1ccc(cc1O)O
13	3-Carene	CC1=CCC2C(C1)C2(C)C
14	3-Hydroxycoumarin	O=c1oc2ccccc2cc1O
15	3-O-Caffeoyl-D-Quinic Acid	O=C(O[C@@H]1C[C@@](O)(C[C@H]([C@H]1O)O)C(=O)[O-])/C=C/c1ccc(c(c1)O)O
16	3-O-Methylquercetin	COc1c(oc2c(c1=O)c(O)cc(c2)O)c1ccc(c(c1)O)O
17	3-Octenal	CCCC/C=C/CC=O
18	4-Hydroxybenzoic Acid	Oc1ccc(cc1)C(=O)O
19	5-Decenal	CCCC/C=C/CCCC=O
20	6-Methylsulfinylhexyl Isothiocyanate	S=C=NCCCCCCS(=O)C
21	AC1N75QA	CC1S/C(=Nc2ccccc2Cl)/N(C1)C(=O)c1ccc(cc1)F
22	Acetylcholine	CC(=O)OCC[N+](C)(C)C
23	Aflatoxin B1	COc1cc2O[C@@H]3[C@H](c2c2c1c1CCC(=O)c1c(=O)o2)C=CO3
24	Aflatoxin B2	COc1cc2O[C@@H]3[C@H](c2c2c1c1CCC(=O)c1c(=O)o2)CCO3
25	Alpha-Eleostearic Acid	CCCC/C=C/C=C/C=CCCCCCCCC(=O)O
26	Astragalin	OC[C@H]1O[C@@H](Oc2c(oc3c(c2=O)c(O)cc(c3)O)c2ccc(cc2)O)[C@@H]([C@H]([C@@H]1O)O)O
27	Beta-Phellandrene	CC(C1CCC(=C)C=C1)C
28	Choline	OCC[N+](C)(C)C
29	Cis-Anethole	C/C=Cc1ccc(cc1)OC
30	Coriandrone C	COc1c2c(=O)oc(cc2cc2c1cco2)CO
31	Cosmosiin	OC[C@H]1OC(Oc2cc(O)c3c(c2)oc(cc3=O)c2ccc(cc2)O)[C@@H]([C@H]([C@@H]1O)O)O
32	Coumarin	O=c1ccc2c(o1)cccc2
33	Cyclodecane	C1CCCCCCCCC1
34	Cyclododecanol	OC1CCCCCCCCCCC1
35	Cynaroside	OC[C@H]1O[C@@H](Oc2cc(O)c3c(c2)oc(cc3=O)c2ccc(c(c2)O)O)[C@@H]([C@H]([C@@H]1O)O)O
36	D-Citronellol	OCC[C@@H](CCC=C(C)C)C
37	Daucosterol	CC[C@@H](C(C)C)CC[C@H]([C@H]1CC[C@@H]2[C@]1(C)CC[C@H]1[C@H]2CC=C2[C@]1(C)CC[C@@H](C2)O[C@@H]1O[C@H](CO)[C@H]([C@@H]([C@H]1O)O)O)C
38	Dipentene	CC1=CCC(CC1)C(=C)C
39	Dodecanal	CCCCCCCCCCCC=O
40	Epoxyoleic Acid	CCCCCCCC[C@H]1O[C@H]1CCCCCCCC(=O)O
41	Erucic Acid	CCCCCCCC/C=CCCCCCCCCCCCC(=O)O
42	Eugenol	C=CCc1ccc(c(c1)OC)O

S.No	Active ingredients	SIMILES (Simplified Molecular Input Line Entry System)
43	Eupatin	COc1cc2oc(c3ccc(c(c3)O)OC)c(c(=O)c2c(c1OC)O)O
44	Falcarindiol	CCCCCCC/C=C[C@@H](C#CC#C[C@@H](C=C)O)O
45	Galactitol	OC[C@H]([C@@H]([C@@H]([C@H](CO)O)O)O)O
46	Geraniol	OC/C=C(/CCC=C(C)C)C
47	Geranyl Acetate	C/C(=CCOC(=O)C)/CCC=C(C)C
48	Hex-3-En-1-Ol	OCCC=CCC
49	Isokaempferide	COc1c(oc2c(c1=O)c(O)cc(c2)O)c1ccc(cc1)O
50	Isoquercitin	OC[C@@H]1O[C@H](Oc2c(oc3c(c2=O)c(O)cc(c3)O)c2ccc(c(c2)O)O)[C@H]([C@@H]([C@H]1O)O)O
51	L-Ascorbic Acid	OC[C@@H]([C@H]1OC(=O)C(=C1O)O)O
52	L(-)-Borneol	O[C@@H]1C[C@@H]2C([C@]1(C)CC2)(C)C
53	Linalyl Acetate	C=CC(OC(=O)C)(CCC=C(C)C)C
54	Neryl Acetate	C/C(=C/COC(=O)C)/CCC=C(C)C
55	Octanal	CCCCCCCC=O
56	Oleic Acid	CCCCCCCC/C=CCCCCCCCC(=O)O
57	Petroselinic Acid	CCCCCCCCCCCC/C=CCCCCC(=O)O
58	Phthalide	O=C1OCc2c1cccc2
59	Phytol	OCC=C(CCCC(CCCC(CCCC(C)C)C)C)C
60	Pimentol	C=CCc1cc(O[C@@H]2O[C@H](COC(=O)c3cc(O)c(c(c3)O)O)[C@H]([C@@H]([C@H]2O)O)O)c(c(c1)OC)O
61	Rosmarinic Acid	O=C(O[C@@H](C(=O)O)Cc1ccc(c(c1)O)O)/C=C/c1ccc(c(c1)O)O
62	Scopoletin	COc1cc2ccc(=O)oc2cc1O
63	Tetradec-13-Enal	C=CCCCCCCCCCCCC=O
64	Tetradecanal	CCCCCCCCCCCCCC=O
65	Trans-2-Decenal	CCCCCCC/C=C/C=O
66	Trans-2-Dodecenal	CCCCCCCCC/C=C/C=O
67	Trans-2-Hexen-1-Ol	CCC/C=C/CO
68	Triacontane	CCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
69	Undecanal	CCCCCCCCCC=O

2.4 *In Silico* ADME Properties

The pharmacokinetics (ADME) properties of the selected compounds were predicted using the Swiss ADME web tool (http://www.swissadme.ch/). The phytochemical compounds' structure was retrieved from databases using the import tool on the input zone of the Swiss ADME submission page and converted into respectively SMILES format, and then calculations were run [11].

2.5 *In Silico* Toxicity Risks' Assessment and Drug Likeliness

OSIRIS Property Explorer's open-source program was used to evaluate the toxicity risks of the compounds retrieved from PubChem. (http://www.organicchemistry.org/prog/peo/)

2.6 SARS-CoV-2 (COVID-19) Main Protease

The 3-dimensional crystallographic structural coordinate files of the SARS-CoV-2 (COVID-19) main protease with inhibitor GC-376 (PDB ID 6WTT), was downloaded from the protein data bank (https://www.rcsb.org/pdb) and it is opened in Discovery studio module of Biovia client 2020 software for further visualization and docking studies.

3. RESULTS AND DISCUSSION

3.1 Molecular Docking

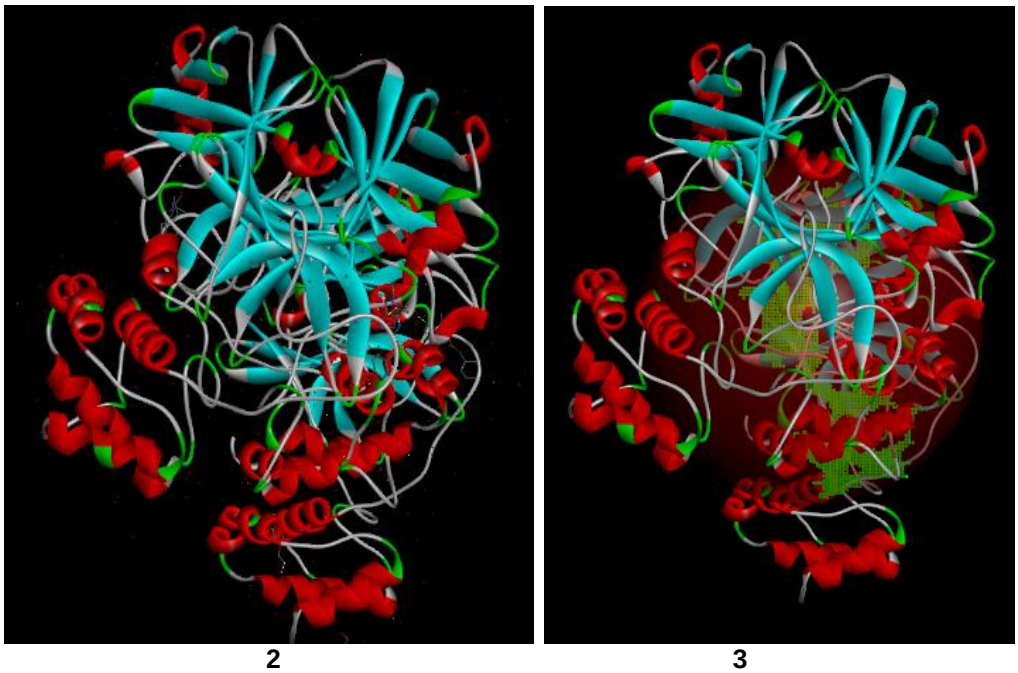
Molecular docking is a popular tool used in computer-assisted drug design and structural molecular biology. It is been widely used to screen the phytochemicals from the plant extract, which acts as a ligand especially when the 3D

structure of the target protein is available. This method could help predict both the binding affinity between protein and ligand and the structure of the protein-ligand complex, which is useful information for lead optimization. Indeed, molecular docking is routinely been applied for more than two decades and a great number of novel drug leads have been discovered and developed accordingly. The Discovery studio module of Biovia client 2020 software was used to perform molecular docking and to identify molecular interaction of the protein-ligand complex [12]. And the ligand-binding site in the main protease and interaction of ligands with residues in the cavity is depicted in Fig. 2 and Fig. 3 below.

In this process first, the Sdf. files of the phytochemicals found in the *Coriandrum sativum* plant were downloaded from the website (https://cb.imsc.res.in/imppat/basicsearchauth). The protein database code of screened phytochemical compounds was identified from the same website. In the same way, target protein (PDB id: 6WTT) was retrieved in PDB. the format from protein data bank (https://www.rcsb.org/). After loading the protein and the ligands, the active site of the target protein was identified via the “receptor cavities” protocol found under the "receptor-ligand interaction" menu. Molecular docking was done using the Dock ligands (LibDock) protocol of Biovia software under “receptor-ligand interaction”. The target protein (enzyme) molecule was treated as the receptor molecule and the identified phytochemicals were treated as the ligands. The “LibDock score", Binding energy, Relative energy, and the number of hydrogen atoms involved in the docking interaction were used as indicators to access the quality of performed molecular docking. The high positive LibDock score of those indicators presented a good interaction between the ligand and the receptor.

Further, the results dock score of phytochemicals with the target protein along with its relative energy are listed in Table 5.

Further the amino acid residues involved in the interaction between the highest LibDock score against the main covid target protein shown in Fig. 4. and the resultant amino acids involved in the interaction re noted for further investigation and studies, especially for molecular dynamics to validate its interactions [13].



2 **3**

Fig. 2. Represents the 3D structure of the main protease of SARS-CoV-2 virus with inhibitor GC-376

Fig. 3. close up of the active site with residues involved in the interaction with the protein (PDB ID 6WTT)

Table 5. Results of Docking of phytochemicals with target protein (PDB id: 6WTT)

S.No	Ligand	LibDock score	No. of H-bonds	Interacting residues	Absolute Energy	Relative Energy
1	Aniseed	118.151	44	Lys5, Phe3, Leu282, Glu288, Gly288, Ser284,Leu286, Ala285	27.9456	4.15725
2	Coriandrone D	123.134	49	Arg4, Lys5, Gln125,Ala7,Try126	57.7703	11.4375
3	Phytosterols	116.066	80	Lle249,His Pro108,Pro293, Lle249, Val202	51.7923	16.0754
4	Sinapaldehyde Glucoside	114.956	48	Tyr126,Arg4,Glu127,Lys5,Val125,Tyr126,Val125,Lys5,Leu285	57.401	6.99006
5	Linalool	74.2154	29	Arg105,Pro241,Ala234,Met235,Asn238,Tyr239	31.7648	7.89998
6	1-Decanol	78.5364	29	Gly183,Asn231,Phe134,Met235,Pro241	10.5379	0.074453
7	1-Dodecanol	91.4449	37	Ala234,Phe134,Met235,Pro241, Arg105	6.82342	8.66001
8	Z-Ligustilide	86.7166	28	Lys5,Arg4,Tyr126,Glu127,Ala7	24.5875	0.338344
9	1-Tricosanol	133.595	72	Arg4,Lys5,Phe291,Ala7	13.3024	10.9539
10	2-(4-Hydroxyphenyl)Ethanol	78.6807	20	Arg4,Lys5,Ala7,Val125	18.2502	6.00369
11	2-Tridecenal	105.588	43	Lys5,Ala7,Trp207,Phe3,Arg4	17605	5.12637
12	2,4-Dihydroxycinnamic Acid	63.5768	21	Lys5, Gly127	25.7424	0.219025
13	3-Carene	47.283	26	Lys90, Lys88, Val35, Phe134	6.53094	0
14	3-Hydroxycoumarin	81.1711	18	Glu83,Glu107,Pro108,Glu240,Asn8,Asn180,His 246,Val202,Ile200	15.9292	0
15	3-O-Caffeoyl-D-Quinic Acid	133.729	42	Trp207,Arg4,Lys5,Try126,Ala7,Gly283	48.5074	6.37039
16	3-O-Methylquercetin	81.9545	35	Asp187,Arg188,Pro52,Glu55,Tyr54	47.9591	1.56
17	3-Octenal	68.4019	23	Phe134,Gly138,Pro241,Met235	8.60701	3.64684
18	4-Hydroxybenzoic Acid	66.2651	16	Arg298,Met6,Ser123,Phe8	13.5963	0
19	5-Decenal	78.5364	29	Glu183,Asn231,Phe134,Met235,Pro241	6.82342	0.0744534
21	6-Methylsulfinyl Hexyl Isothiocyanate	80.0797	28	Asn231,Arg105	0.680324	1.76116
22	AC1N75QA	103.051	37	Trp207,Leu282,Glu288,Arg4,Lys5,Phe291	56.6422	0

S.No	Ligand	LibDock score	No. of H-bonds	Interacting residues	Absolute Energy	Relative Energy
23	Acetylcholine	70.1588	26	Val125,Lys5,Gln127,Tyr126,Arg4	25.3034	6.9487
24	Aflatoxin B1	61.817	35	Ile152,Phe8,Pro9,Ser121,Ser123	78.8822	6.63177
25	Aflatoxin B2	102.887	37	Glu288,Trp207,Phe291,Arg4,Lys5	38.8822	1.12275
26	Alpha-Eleostearic Acid	132.627	50	Ala7,Lys5,Leu286,Ala285	32.7699	17.2519
27	Astragalin	110.33	52	Asp289,Glu288Glu290,Ser284,Ala285,Leu286, Lys5,Arg4,Phe3	67.273	15.4238
28	Beta-Phellandrene	66.7045	26	Lys5, Ala7	13.5804	0
29	Choline	48.4115	21	Val125,Lys5,Glu127,Arg4	23.932	1.72103
30	Cis-Anethole	49.2831	23	Ser284,Ala285,Leu286,Glu288	33.839	0
31	Coriandrone C	107.932	28	Lys5,Val125,Gly127,Try126,Arg4	110.9	0.0431361
32	**Cosmosiin**	**141.405**	**51**	**Lys5,Val125,Gly127,Try126,Arg4**	**68.9448**	**19.5372**
33	Cyclodecane	47.4703	30	Lys5	9.68652	0.92814
34	Cynaroside	138.906	52	Phe3,Leu282,Lys137,Arg4,Lys5,Ala7,Val125	52.4034	2.13696
35	D-Citronellol	78.2316	31	Arg4, Lys5, Ala7	16.6225	4.39559
36	Daucosterol	88.33	101	Leu238,Met276,Leu237,Lys137,Asp197	63.7068	16.1358
37	Dillenetin	91.4346	38	Ser284,Glu288,Lys5,Arg4,Ala7	65.0223	3.61216
38	Dipentene	67.0584	26	Arg4,Tyr126,Lys5,Ala7	22.8945	13.1956
39	Dodecanal	92.4528	37	Ala7, Arg4, Lys5	3.66006	1.78216
40	Epoxy Oleic Acid	133.906	55	Arg4,Ala7,Lys5,Glu288	19.5827	5.03521
41	**Erucic Acid**	**138.34**	**66**	**Phe291,Trp207,LYS5,Arg4,Val125**	**28.5827**	**12.6351**
42	Eugenol	78.441	24	Ala7, Val125, Gly127, Tyr126, Lys5	30.5116	7.04983
43	Eupatin	124.066	42	Ala285,Ser284,Glu288,Arg4,Lys5,Glu127,Tyr126	94.7884	19.2729
44	Falcarindiol	118.907	43	Lys5,Val125,Ala7,Leu286	24.2959	8.5714
45	Galactitol	61.0296	26	Trp207,Leu282,Phe3	30.4851	15.9603
46	Geraniol	77.1257	29	Arg4,Lys5,Ala7,Val125	29.2909	13.0908
47	Geranyl Acetate	93.2983	34	Leu286,Ala285,Leu282,Phe291,Trp207,Phe3	36.2569	14.3989
48	Hex-3-En-1-Ol	59.8697	19	Lys5	6.62332	0.88783
49	Isokaempferide	68.7736	34	Ser284,Ala285,Glu288	45.5596	0
50	Isoquercitrin	77.0977	53	Glu290,Arg4,Lys137,Leu282,Gly283	8.79095	8.79095
51	L-Ascorbic Acid	73.0891	20	Phe3,Leu282,Ile281,Ser284	16.8568	0.175813
52	L(-)-Borneol	59.7107	28	Lys5	5.75242	0

S.No	Ligand	LibDock score	No. of H-bonds	Interacting residues	Absolute Energy	Relative Energy
53	Linalyl Acetate	66.6891	34	Lys5, Arg4	32.8924	2.0246
54	Neryl Acetate	86.0377	34	Phe291,Trp207,Leu282,Ala285,Leu286	34.4921	12.3707
55	Octanal	67.5401	25	Ala7, Lys5	5.86413	4.34243
56	Oleic Acid	127.665	54	Arg4,Ala7,Lys5,Glu288	23.6839	8.05438
57	Petroselinic Acid	127.143		Ala7,Arg4,Lys5,Phe291,Try207,Glu288	29.5445	13.8553
58	Phthalide	50.4438	16	Leu282,Phe291,Ser284,Trp207	44.8596	0
59	Phytol	116.177	61	Ala7,Lys5,Phe291,Trp207	34.5686	14.6342
60	**Pimentel**	**148.609**	**61**	**Glu288,Phe3,Lys5,,Lys286,Ala285**	**64.6044**	**13.6068**
61	**Rosmarinic Acid**	**133.894**	**42**	**Val125,Ala7,Lys5,Glu288,Phe3**	**49.1213**	**6.85707**
62	Scopoletin	70.8988	22	Glu288,Ser284	24.0601	0
63	Tetradec-13-Enal	104.476	41	Ala7,Lys5,Trp207,Phe291	7.41774	1.38985
64	Tetradecanal	105.588	43	Ala7,Lys5,Trp207,Phe3,Arg4	7.17605	5.12637
65	Trans-2-Decenal	78.8444	29	Phe3,Met6,Gln127	9.30399	4.2512
66	Trans-2-Dodecenal	90.0352	35	Pro241,Met235,Arg105	9.20399	0
67	Trans-2-Hexen-1-Ol	60.2978	19	Met165,Met45,Clu189,Asp197	4.57	1.89929
68	Triacontane	133.946	92	Arg105,Met235,Pro241,Ala234,Phe134,Try237, Try239,Leu287	24.6	9.7126
69	Undecanal	80.4531	34	Pro234,Ala234,Met235,Pro108,Leu232,Phe134	67.1	14.8472

2- Dimensional Image of the Amino Acids Involved in the Protein-ligand Interaction

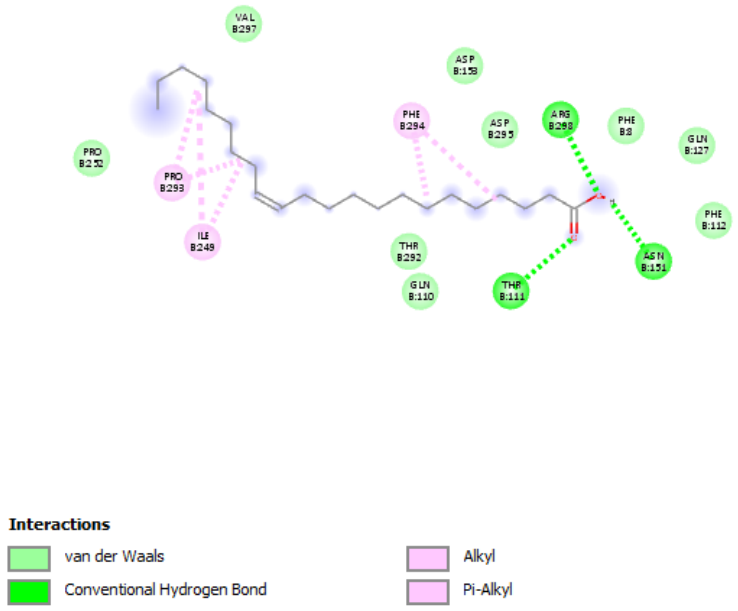


Fig. 4. Represents the 2D structure of the amino acid involved in the interaction between main protease of SARS-CoV-2 virus with Pimentel phytochemical compound of *Coriandrum sativum*

SARS-CoV-2 protein (PDB ID 6WTT) interplays with the top three ligands identified by molecular docking analysis, namely, Cosmosiin, erucic acid, Pimental. No hydrogen bond was detected between Undecanal and the target protein. Cosmosiin bonded with five different amino acid residues, i.e., Lys5, Val125, Gly127, Try126, Arg4. Similarly, Erucic acid and Rosmarinic Acid bonded with five amino acids, i.e., Phe291, Trp207, LYS5, Arg4, Val125, and Val125, Ala7, Lys5, Glu288, Phe3 respectively. In both Cosmossin and Pimental, hydrogen bonds occurred between the ligand and the target protein. Hydrogen bonds are common and are usually essential for various interactions such as protein–ligand interactions, protein folding, and catalysis. By promoting molecular interactions, hydrogen bonds diversify a variety of biological activities; they are usually considered to facilitate protein–ligand binding [14-20].

4. CONCLUSION

In this study, the bioactive compounds in *Coriandrum sativum* were subjected to several experiments, such as Lipinski's rule of five, pharmacokinetics, and molecular dynamics simulations, evaluation with the protein target 6WTT of SARS-CoV-2. Among all the photoactive ligands, Cosomosiin, Erucic acid, Rosmarinic Acid and Pimentel exhibited excellent stability during molecular docking analysis using discovery studio software. Further investigation, particularly molecular dynamic and pathway prediction, are recommended to confirm its interaction properties.

HIGHLIGHTS

- Active phytoconstituents of Ayurvedic medicinal plant *Coriandrum sativum* are predicted to significantly hinder the main protease of SARS-CoV-2.
- Through molecular docking and molecular dynamics simulation study, Cosomosiin, Erucic acid, Rosemarinic acid, and Pimentel were anticipated to impede the activity of the main protease of SARS-CoV-2.
- Further, drug-likeness and ADMET profile prediction of best-docked compounds from the present study were predicted to be safe, drug-like compounds with no toxicity.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Available:https://proteopedia.org/wiki/index.php/6wtt
2. Available:https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01241-1/fulltext
3. Abella BS, Jolkovsky EL, Biney BT. Efficacy and safety of hydroxychloroquine vs placebo for pre-exposure SARS-CoV-2 prophylaxis among health care workers: A randomized clinical trial. JAMA Intern Med. 2021;181(2):195–202.
   DOI: 10.1001/jamainternmed.2020.6319. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
4. Saag MS. Misguided use of hydroxychloroquine for COVID-19: The infusion of politics into science. JAMA. 2020;324(21):2161–2162.
   DOI: 10.1001/jama.2020.22389. [PubMed] [CrossRef] [Google Scholar].
5. Available:https://www.sciencedirect.com/science/article/pii/S1684118220300827
6. ICMR Advisory on the use of Hydroxychloroquine as prophylaxis for SARS-CoV-2 infection dated; 2020.
   Available:https://www.icmr.gov.in/pdf/covid/techdoc/V5_Revised_advisory_on_the_use_of_HCQ_SARS_CoV2_infection.pdf.
   As accessed on July 6, 2021.
7. Available:https://cb.imsc.res.in/imppat/basicsearchauth
8. Ministry of AYUSH advisory page 8,
   Available:https://www.ayush.gov.in/docs/ayurved-guidlines.pdf.
   As accessed on June 15, 2021.
9. Verma N, Gupta SK, Tiwari S. Safety of Ashwagandha root extract: A randomized, placebo-controlled, study in healthy volunteers. Complement Ther Med. 2021;57.
   DOI: 10.1016/j.ctim.2020.102642. [PubMed] [CrossRef] [Google Scholar]
10. Available:https://pubchem.ncbi.nlm.nih.gov/compound/101995280
11. Deepak Kumar Shrivastava. Phytochemical analysis of a miracle herb *Coriander sativum*. Indian J.Sci.Res. 2017;13 (2): 09-14,
12. Stierand K, Maaß P, Rarey M. Molecular complexes at a glance: Automated generation of two-dimensional complex diagrams. Bioinformat. 2006;22:1710–1716.
    Available:https://doi.org/10.1093/bioinformatics/btl150
13. Badyal DK, Mahajan R. Chloroquine: Can it be a novel drug for COVID-19. Int J Appl Basic Med Res. 2020;10(2):128–130
14. Sahu A Leptin, Neuroendocrinology. Ch.4, In Leptin (Eds.Castracane VD and Henson MC) Springer Science & Business Media NY,USA. 2006;53-77.
15. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Molecular biology york, garland science; 2002.
    Available:https://www.ncbi.nlm.nih.gov/books/NBK21054
16. Dunn MF. Protein-ligand interactions: General description. Ency. Life Sci; 2010.
    Available:https://doi.org/10.1002/9780470015902.a0001340.pub2.
17. Chopra GL. Angiosperms: Systematics and life cycle. S. Nagin & Co., Jalandhar, Punjab, India. 1969;361–365
18. Beegum J, Suhara GR, Beevy S, Sugunan VS. Nutritive and anti-nutritive properties of *Boerhaavia diffusa* L. Journal of Pharmacognosy and Phytochemistry. 2014;2(6):147-151.
19. Ahmad K, Ashfaq A, Khan ZI, Ashraf M, Akram NA, Yasmin S, Batool AI, Sher M, Shad HA, Khan A, Rehman SU, Ullah MF, Noorka IR. 2016;22:597–610.
20. Pandey B, Deshpande B, Singh S, Chandrakar V. Estimation of elemental contents of cordia myxa and its antimicrobial activity against various pathogenic microorganisms" Indian J.Sci.Res. 2014;4(1):39-44. ISSN: 0976-2876.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/85408