BT5230: Molecular Modelling and Drug Design
Final Assignment: Covid-19
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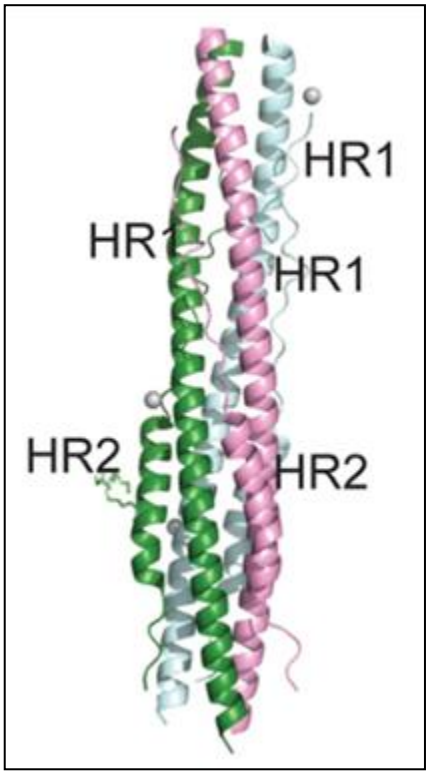
Select one target of SARS cov2. Identify about 4 to 5 ligands /drugs reported for inhibiting the target- from literature search. Develop a pharmacophore model and search the Zinc data base for molecules with similar pharmacophore features. Dock them to the target and identify about 10 molecules which show best binding affinity. If 3D structures of the proteins are not available you may have to do a homology model. If commercial drugs are reported for the target dock them also and compare their docking score. Estimate their PK and the drug likeness properties/ADME etc. Compare these molecules with reported drugs.

Submit a report and comment on the results in detail. Compare the reported and new compounds identified by you. A comprehensive report with discussions is expected, not just results.

Target:

We have chosen the spike protein S2 domain as our main target which plays as important role in cell fusion.

PDB id: 6LXT (HR – 6 alpha helix bundle)



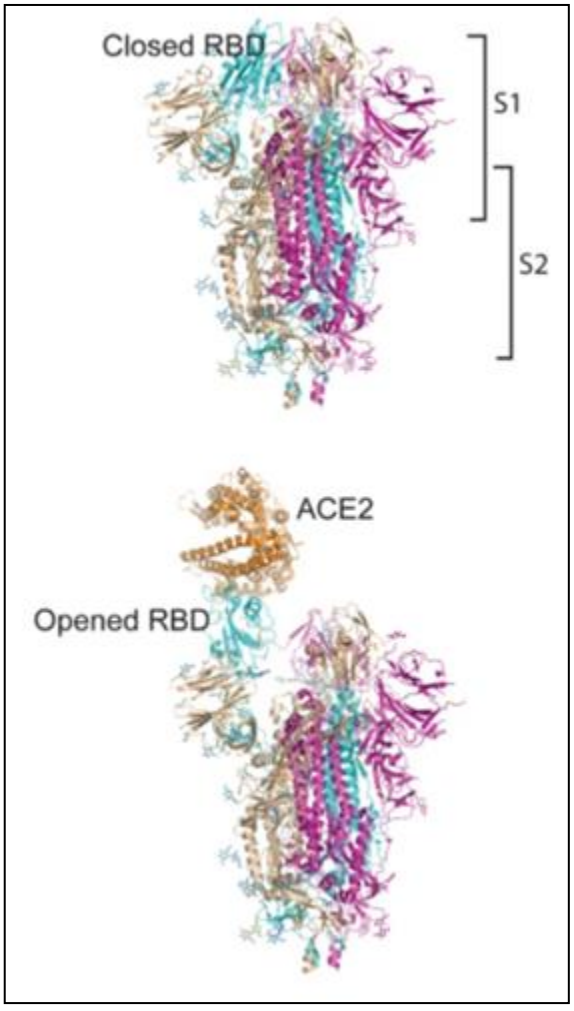
Structure of S- protein:

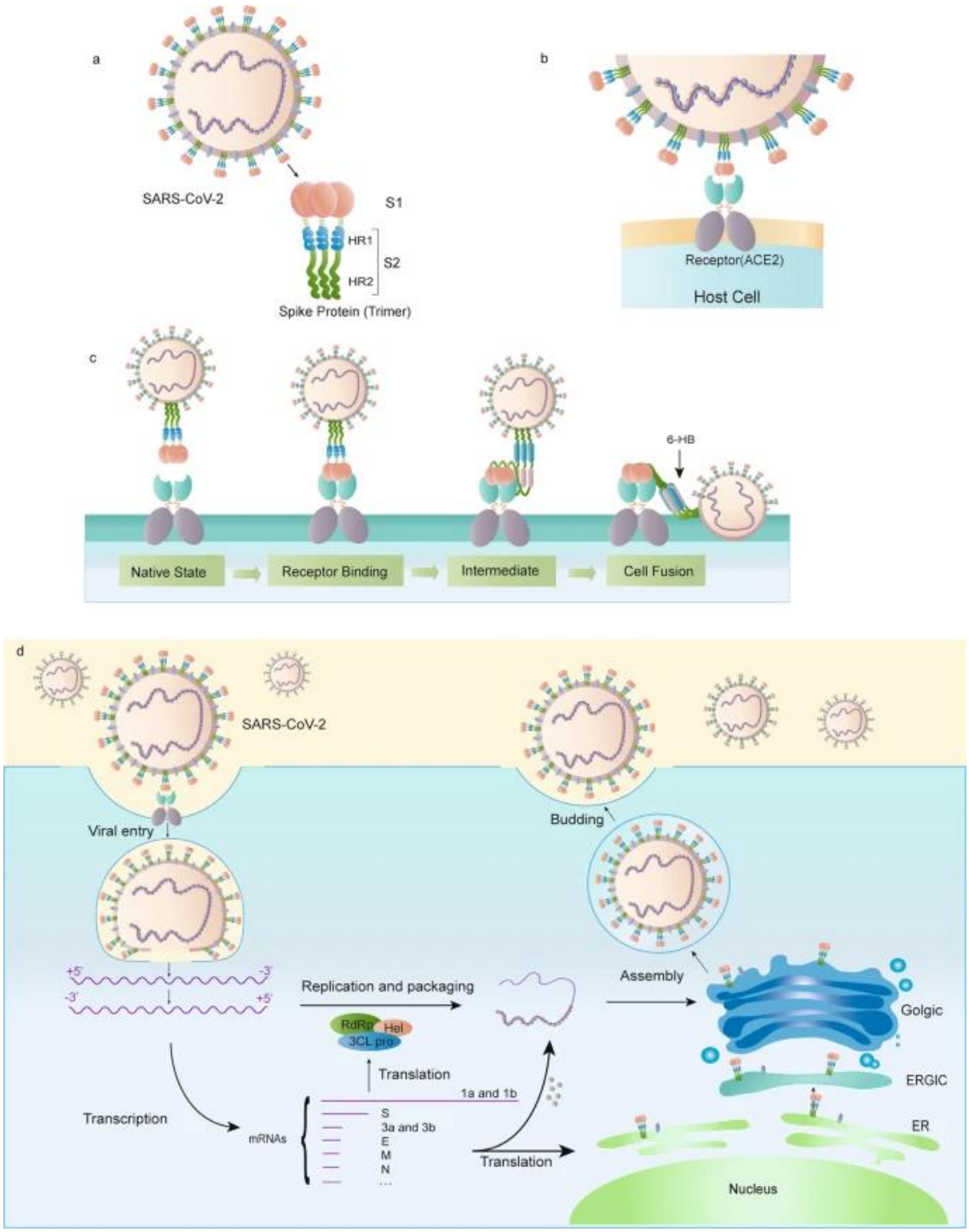
The spike protein has two main subunits S1 and S2.

- The S1 subunit contains a receptor-binding domain that recognizes and binds to the host receptor angiotensin-converting enzyme 2(ACE2) which is distributed in lungs, intestine, heart and kidney.
- The S2 subunit mediates viral cell membrane fusion by forming a six-helical bundle via the two-heptad repeat domain.

The spike protein is activated by a type 2TM serine protease (TMPRSS2) which is located on the host cell membrane promoting viral entry.

S1 subunit: N-terminal domain (14–305 residues) and a receptor-binding domain (RBD, 319–541 residues)
S2 subunit: The fusion peptide (FP) (788–806 residues), heptapeptide repeat sequence 1 (HR1) (912–984 residues), HR2 (1163–1213 residues), TM domain (1213–1237 residues), and cytoplasm domain (1237–1273 residues).





Reference: Huang, Y., Yang, C., Xu, Xf. et al. Structural and functional properties of SARS-CoV-2 spike protein: potential antivirus drug development for COVID-19. Acta Pharmacol Sin 41, 1141–1149 (2020). https://doi.org/10.1038/s41401-020-0485-4

The RBD region is a critical target for neutralizing antibodies (nAbs), and SARS-CoV-2 and SARS-CoV RBD are ~73%–76% similar in sequence. But it has been found that some murine monoclonal antibodies (mAbs) and polyclonal antibodies against SARS-RBD are unable to interact with the SARS-CoV-2 S protein, revealing differences in antigenicity between SARS-CoV and SARS-CoV-2.

Structure of the S2 subunit:

The S2 subunit, composed successively of a FP, HR1, HR2, TM domain, and cytoplasmic domain fusion (CT), is responsible for viral fusion and entry.

FP is a short segment of 15–20 conserved amino acids of the viral family, composed mainly of hydrophobic residues, such as glycine (G) or alanine (A), which anchor to the target membrane when the S protein adopts the pre-hairpin conformation. FP plays an essential role in mediating membrane fusion by disrupting and connecting lipid bilayers of the host cell membrane.

HR1 and HR2 are composed of a repetitive heptapeptide: HPPHCPC, where H is a hydrophobic or traditionally bulky residue, P is a polar or hydrophilic residue, and C is another charged residue. HR1 and HR2 form the six-helical bundle (6-HB), which is essential for the viral fusion and entry function of the S2 subunit. HR1 is located at the C-terminus of a hydrophobic FP, and HR2 is located at the N-terminus of the TM domain. The downstream TM domain anchors the S protein to the viral membrane, and the S2 subunit ends in a CT tail.

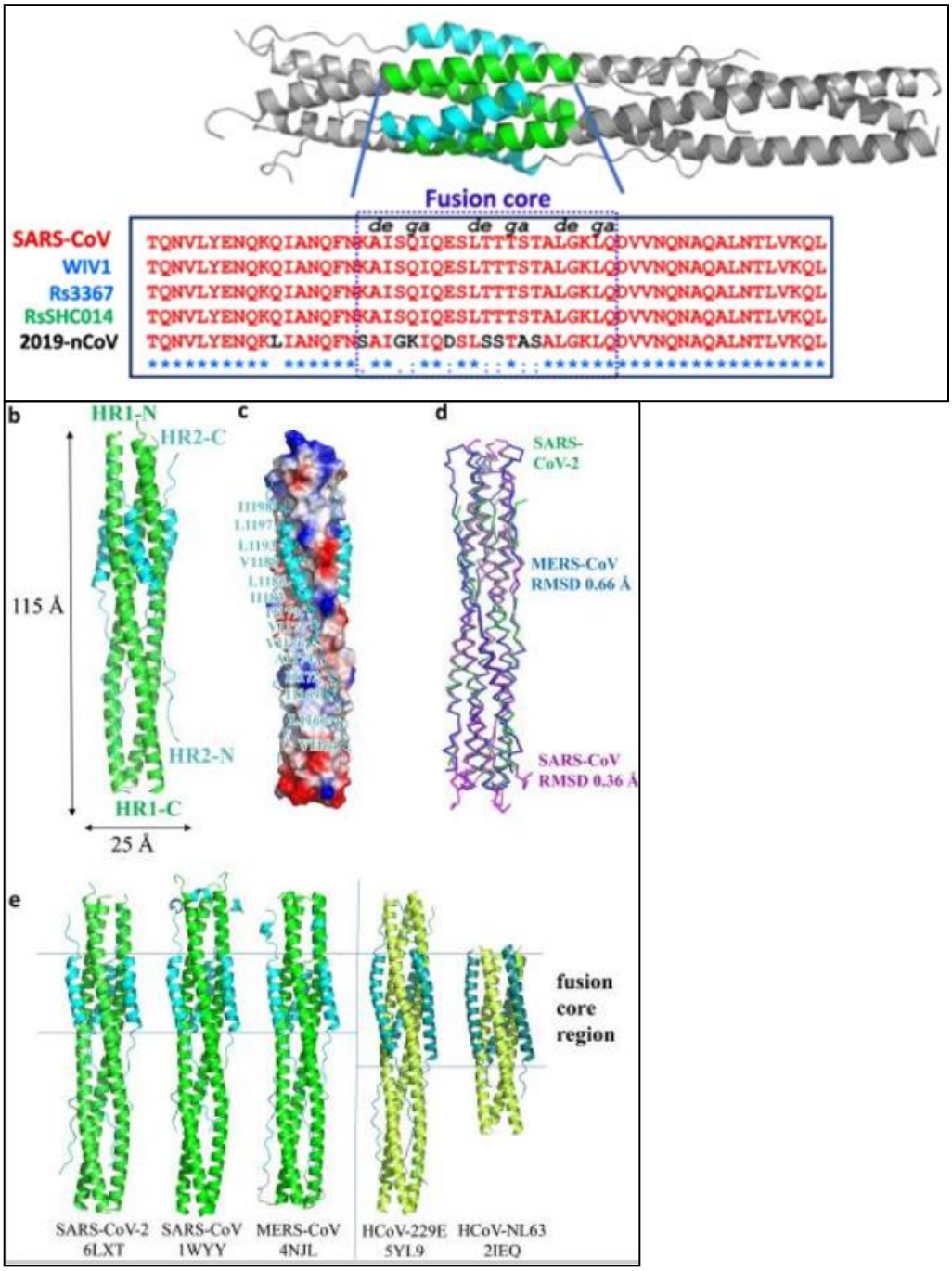
RBD binds to ACE2, and S2 changes conformation by inserting FP into the target cell membrane, exposing the pre-hairpin coiled-coil of the HR1 domain and triggering interaction between the HR2 domain and HR1 trimer to form 6-HB, thus bringing the viral envelope and cell membrane into proximity for viral fusion and entry. HR1 forms a homo-trimeric assembly in which three highly conserved hydrophobic grooves on the surface that bind to HR2 are exposed. The HR2 domain forms both a rigid helix and a flexible loop to interact with the HR1 domain. In the post-fusion hairpin conformation of CoVs, there are many strong interactions between the HR1 and HR2 domains inside the helical region, which is designated the “fusion core region” - (HR1core and HR2core regions).

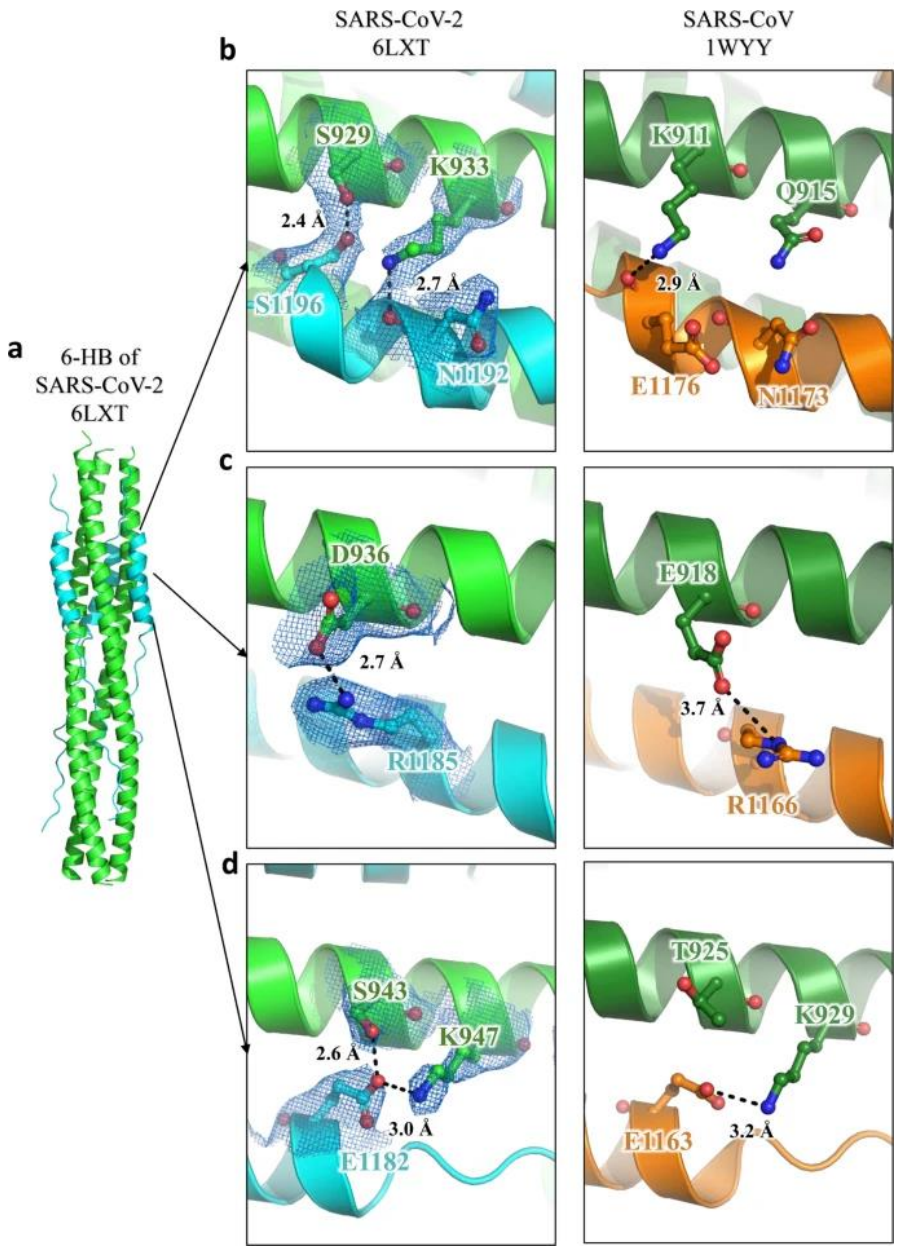
Since the formation of 6-HB is essential for viral fusion, targeting the heptad repeat (HR) has attracted the greatest interest in therapeutic drug discovery.

While the S1 RBD domain is part of a highly mutable region and hence is not an ideal target site for broad-spectrum antiviral inhibitor development. In contrast, the HR region of the S2 subunit plays an essential role in HCoV infections and is conserved among HCoVs, as is the mode of interaction between HR1 and HR2.

The S2 subunits of SARS-CoV-2 and SARS-CoV are highly conserved, with 92.6% and 100% overall homology in HR1 and HR2 domains, respectively. Inside the fusion core region of HR1 domain, there are 8 different residues, which may contribute the enhanced interactions between HR1 and HR2 and stabilize 6-HB conformation of SARS-CoV-2 as revealed by crystallographic analysis, compared with those of SARS-CoV.

Therefore, HR is a promising target for the development of fusion inhibitors against SARS-CoV-2 infection and hence we have chosen this as our target.





Reference: Xia, S., Liu, M., Wang, C. et al. Inhibition of SARS-CoV-2 (previously 2019-nCoV) infection by a highly potent pan-coronavirus fusion inhibitor targeting its spike protein that harbors a high capacity to mediate membrane fusion. Cell Res 30, 343–355 (2020). https://doi.org/10.1038/s41422-020-0305-x

Molecules chosen to bind to fusion core:

No commercial small molecule drugs have been found to bind to HR domain. Several small molecule inhibitor studies and peptides are known to interact with the 6-helix bundle and disrupt viral fusion.

Arbidol, a commercial drug for influenza may be re-purposed for CoV2 to target S2. Exact mechanism of action of SARS CoV2 and arbidol in-vivo need to be studied.

Further due to high conservation in S2 subunits, inhibitors tested on SARS Cov are very likely to work for SARS Cov2.

The following small molecule inhibitors were selected as input to pharmacophore model:

1. Salvionalic acid C (ZINC14690026)
2. Arbidol (ZINC19907652)
3. Luteolin (ZINC18185774)
4. Quercetin (ZINC3869685)

References for molecules:

Xiu S, Dick A, Ju H, et al. Inhibitors of SARS-CoV-2 Entry: Current and Future Opportunities. *J Med Chem*. 2020;63(21):12256-12274. doi:10.1021/acs.jmedchem.0c00502

Yi L, Li Z, Yuan K, et al. Small molecules blocking the entry of severe acute respiratory syndrome coronavirus into host cells. *J Virol*. 2004;78(20):11334-11339. doi:10.1128/JVI.78.20.11334-11339.2004

Yang, C., Pan, X., Xu, X. et al. Salvianolic acid C potently inhibits SARS-CoV-2 infection by blocking the formation of six-helix bundle core of spike protein. Sig Transduct Target Ther 5, 220 (2020). https://doi.org/10.1038/s41392-020-00325-1

TGG and luteolin, can bind avidly to the SARS-CoV S2 protein and inhibit viral entry of SARS-CoV into Vero E6 cells with IC_{50} values of 4.5 and 10.6 μM. Quercetin an analogue of luteolin also showed antiviral activity against SARS-CoV.

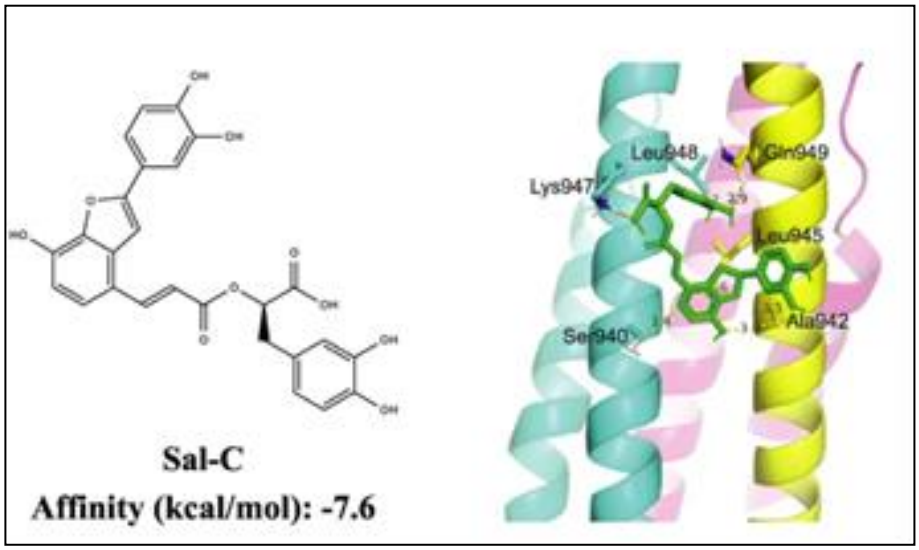
Arbidol, a broad-spectrum drug, has been licensed against influenza by binding to the HA protein to block the viruses–cell fusion. It can inhibit SARS-CoV-2 virus infection in vitro with an IC50 value of 4.11 μM.

Docked input molecules to fusion core:

1. Salvionalic acid C (ZINC14690026)

∆G = -7.6kcal/mol (Paper)

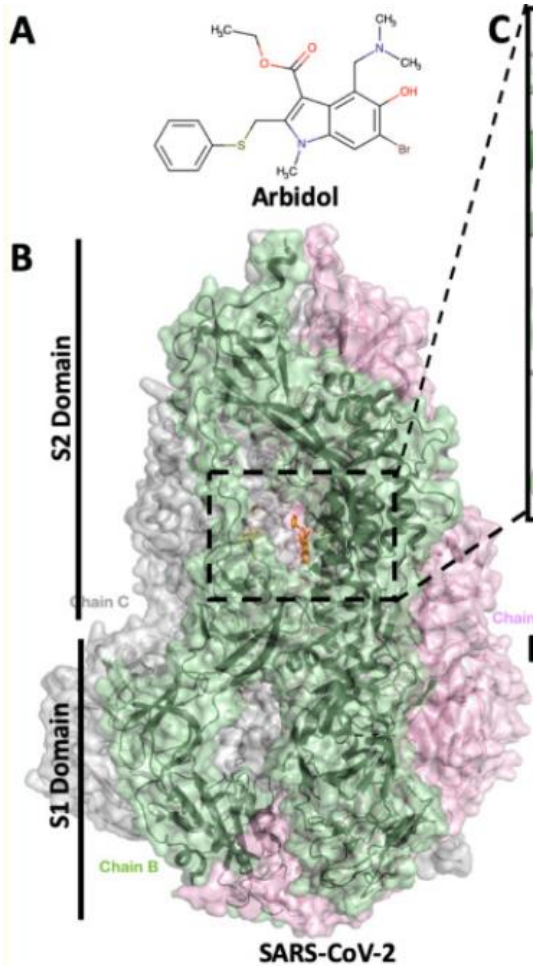
Chemical structure and schematic diagram of molecular docking between Sal-C and the post-fusion core of 6-HB. The affinity of Sal-C with the post-fusion core of 6-HB was −7.6kcal/mol. (*Yang, C., Pan, X., Xu, X. et al. Salvianolic acid C potently inhibits SARS-CoV-2 infection by blocking the formation of six-helix bundle core of spike protein. Sig Transduct Target Ther 5, 220 (2020).* https://doi.org/10.1038/s41392-020-00325-1)

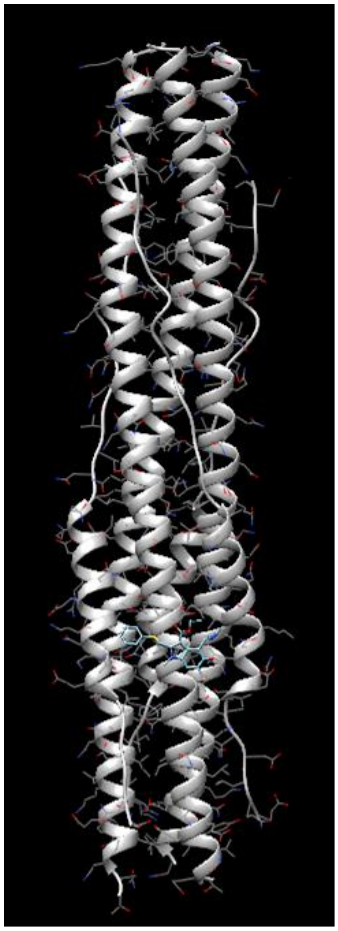


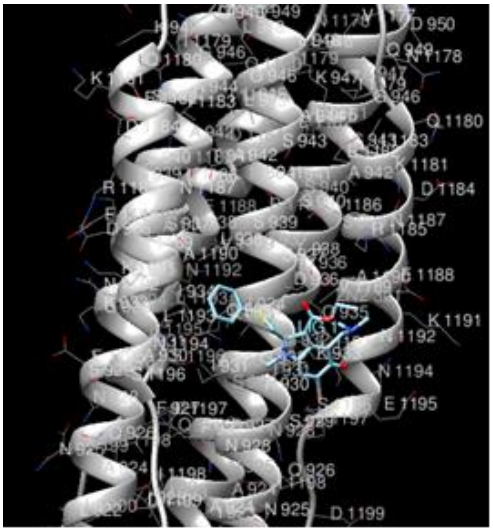
Sal-C can interact with residues Ser940, Thr941, Ala942, Leu945, Lys947, Leu948, and Gln949 in the HR1 pocket of the 6-HB core, providing insight into its molecular structure relationship with the 6-HB core region.

2. Arbidol (ZINC19907652)

∆G = -7.24kcal/mol (SwissDock)

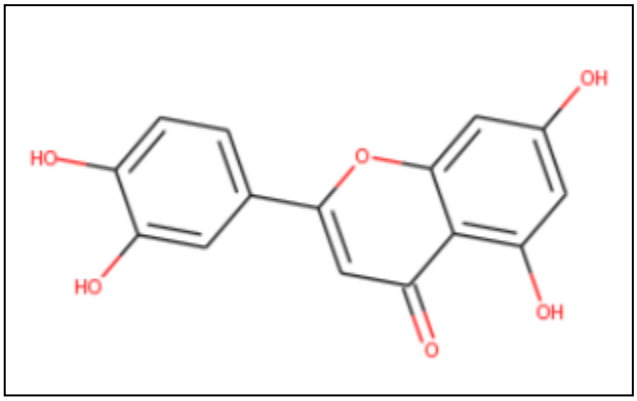


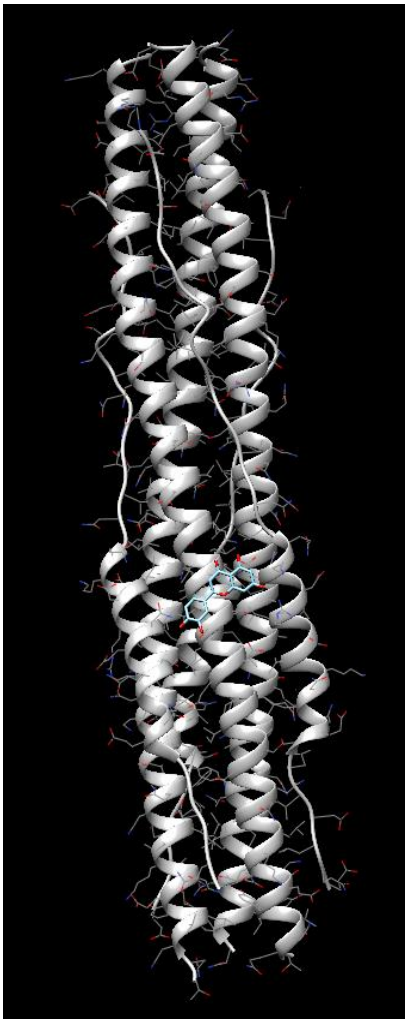


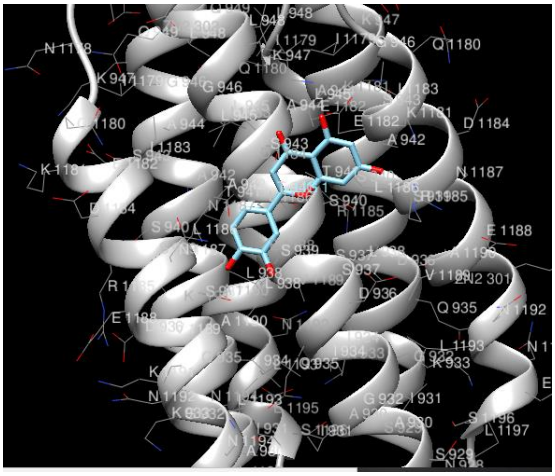


3. Luteolin (ZINC18185774)

∆G = -8.04kcal/mol (SwissDock)

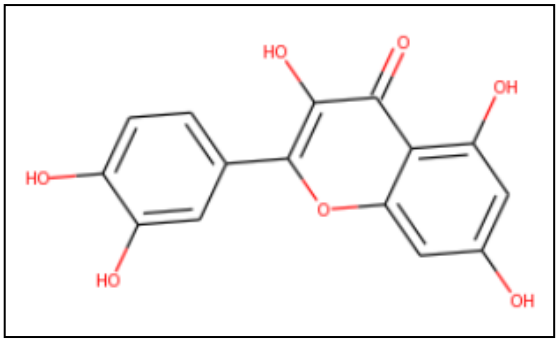


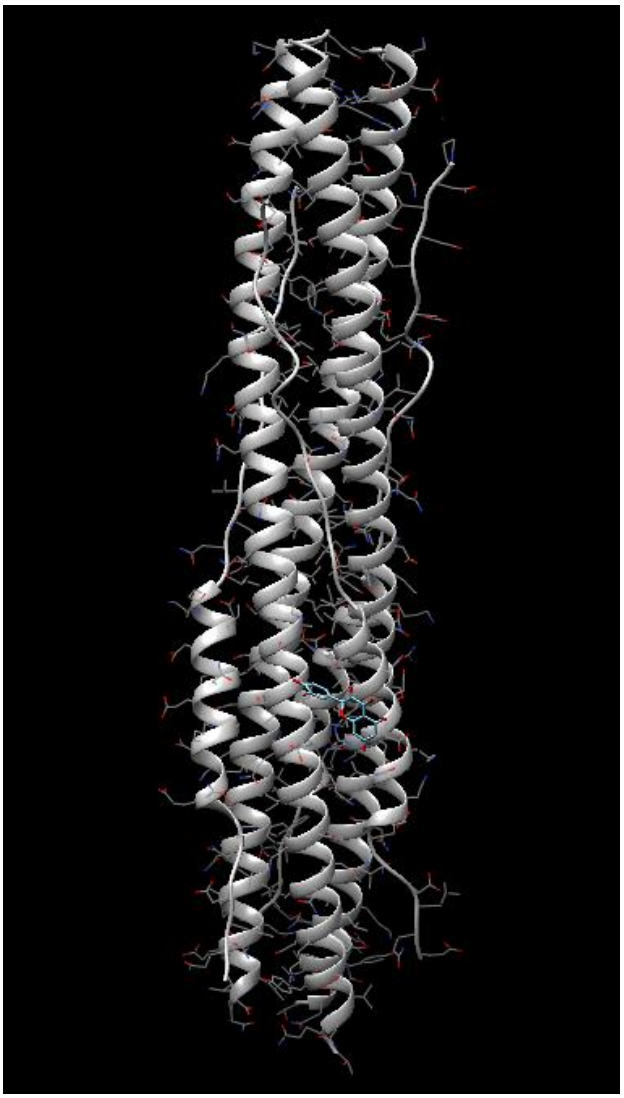


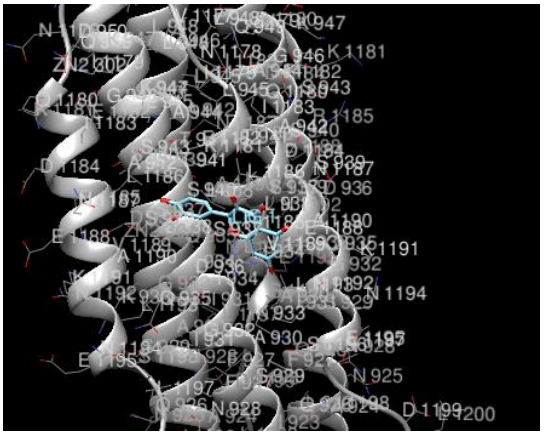


4. Quercetin (ZINC3869685)

∆G = -6.12kcal/mol (SwissDock)







Pharmacophore model:

Output from pharmagist:

Input Molecules view details: visualization of the detected features

#	Molecule	Atoms	Features	Spatial Features	Aromatic	Hydrophobic	Donors	Acceptors	Negatives	Positives
1	salvionalic_acid.mol2	58	27	20	1	9	7	10	0	0
2	luteolin.mol2	31	14	10	1	3	4	6	0	0
3	quercetin.mol2	32	15	10	0	3	5	7	0	0
4	arbidol.mol2	58	16	15	2	8	1	5	0	0

Sort by score

Number of Aligned Molecules: 4

Score	Jmol	Features	Spatial Features	Aromatic	Hydrophobic	Donors	Acceptors	Negatives	Positives	Molecules
11.482	Jmol	4	3	0	0	1	3	0	0	arbidol.mol2 salvionalic_acid.mol2 luteolin.mol2 quercetin.mol2
8.731	Jmol	3	3	0	1	0	2	0	0	arbidol.mol2 salvionalic_acid.mol2 luteolin.mol2 quercetin.mol2
8.543	Jmol	4	3	0	1	1	2	0	0	arbidol.mol2 luteolin.mol2 quercetin.mol2 salvionalic_acid.mol2
5.879	Jmol	4	4	0	3	0	1	0	0	arbidol.mol2 luteolin.mol2 quercetin.mol2 salvionalic_acid.mol2
5.556	Jmol	3	3	0	2	0	1	0	0	arbidol.mol2 salvionalic_acid.mol2 luteolin.mol2 quercetin.mol2
5.556	Jmol	3	3	0	2	0	1	0	0	arbidol.mol2 salvionalic_acid.mol2 luteolin.mol2 quercetin.mol2

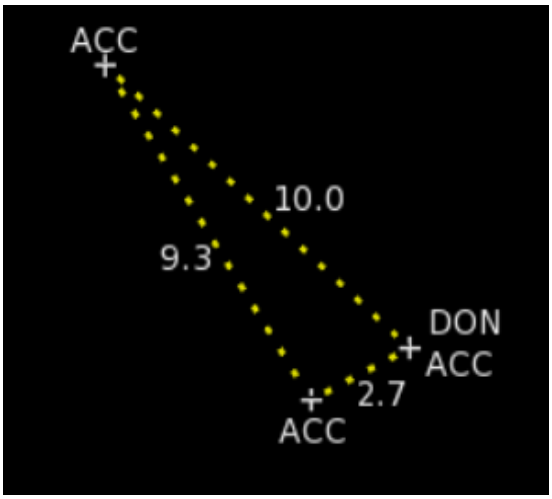
Pharmacophore features:

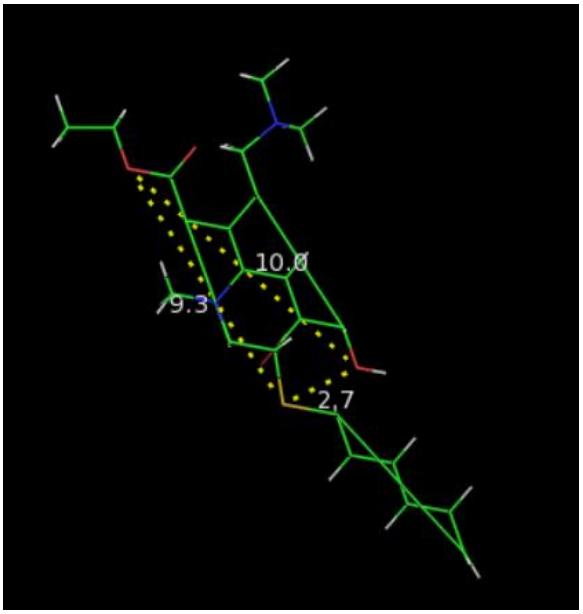
Score	Features	Spatial Features	Aromatic	Hydrophobic	Donors	Acceptors	Negatives	Positives
11.482	4	3	0	0	1	3	0	0

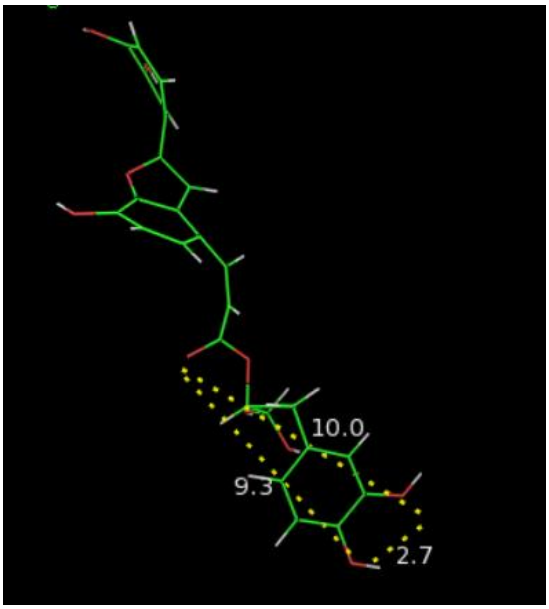
Molecule Name	Show Molecule:	Show Features:
arbidol*		
salvionalic_acid		
luteolin		
quercetin		

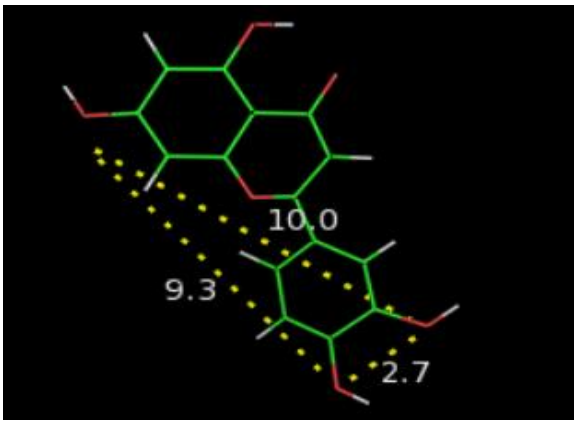
* pivot molecule

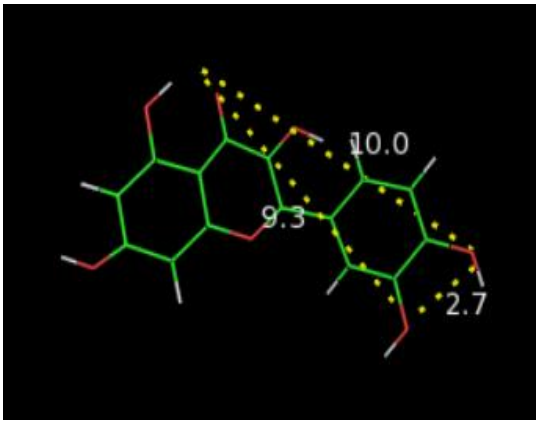
Pharmacophore & Alignment file

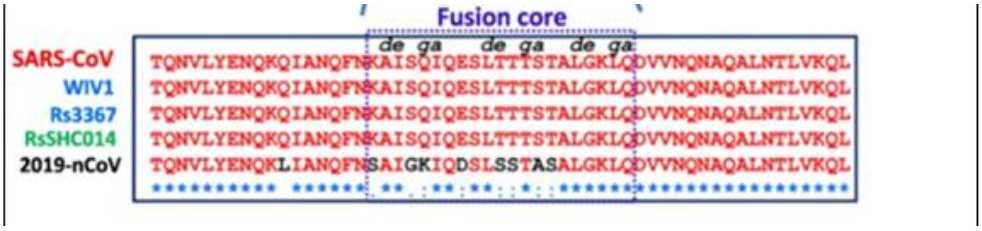












Observations:

The pharmacophore model results in three acceptors and one donor. We observed that there are more Ser residues in the fusion core of HR region which can act as both donor and acceptor of hydrogen atom. Gln an amide can also act as both donor and acceptor. The basic residue Lys could act as acceptor.

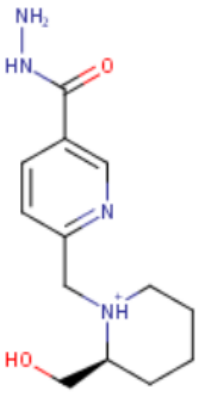
So, based on these observations, these molecules may fit the fusion core.

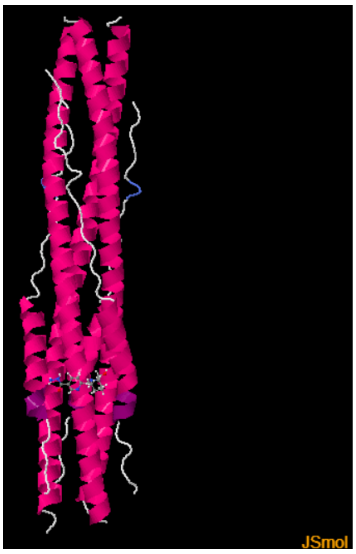
Zinc Pharmer output:

Molecules with low RMSD and ΔG obtained by docking using SwissDock.

S. No.	Zinc id	RMSD	ΔG(kcal/mol)
1	ZINC94763924	0.005	-5.99
2	ZINC81318565	0.006	-6.58
3	ZINC36369755	0.008	-6.89
4	ZINC81318568	0.009	-6.17
5	ZINC68601187	0.009	-8.71
6	ZINC09559961	0.009	-5.95
7	ZINC12745518	0.01	-6.38
8	ZINC14962356	0.01	-6.01
9	ZINC38143804	0.01	-7.9
10	ZINC09970504	0.01	-6.67
11	ZINC94797964	0.011	-6.53

1. ZINC94763924





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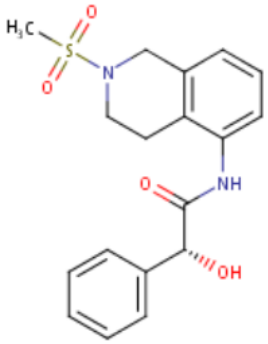

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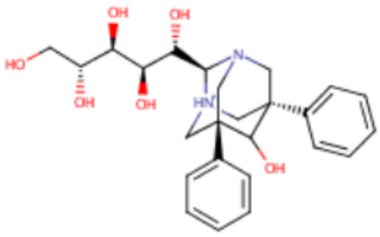

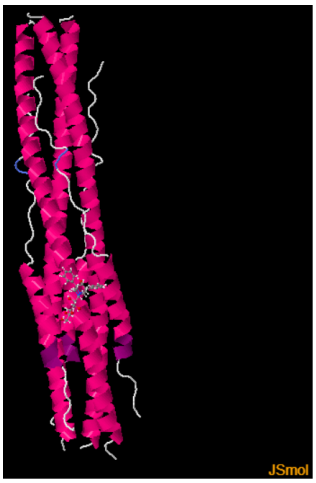

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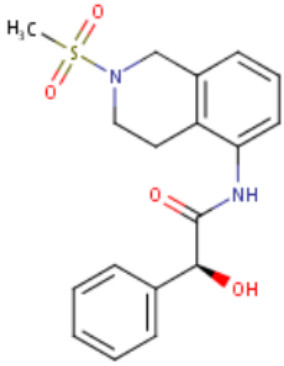
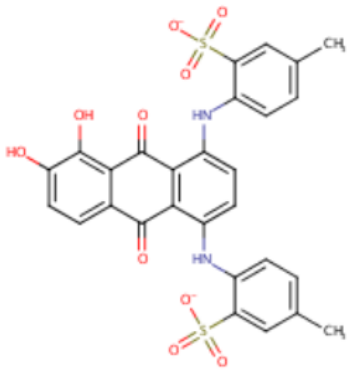
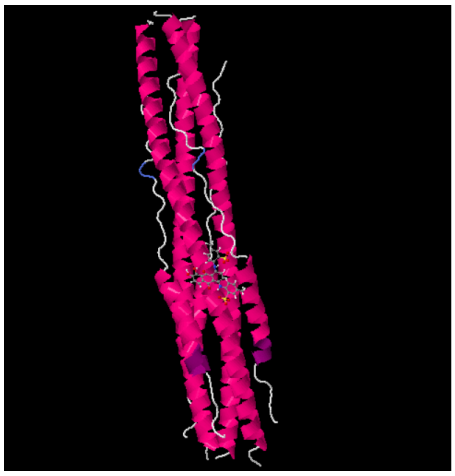
4. ZINC81318568



○	25	1	-2921.75	-5.84
○	25	2	-2912.15	-5.92
○	25	3	-2912.09	-5.90
○	25	4	-2912.02	-5.91
○	25	5	-2906.11	-6.02
○	25	6	-2906.09	-6.07
○	25	7	-2905.20	-6.01
○	26	0	-2921.37	-6.18
○	26	1	-2921.37	-6.18
○	26	2	-2921.37	-6.17
◉	26	3	-2921.36	-6.17
○	26	4	-2921.36	-6.17
○	26	5	-2921.36	-6.17
○	26	6	-2921.36	-6.17
○	26	7	-2921.36	-6.17
○	27	0	-2920.92	-5.68
○	27	1	-2920.92	-5.68
○	27	2	-2920.62	-5.65
○	27	3	-2920.62	-5.65
○	27	4	-2920.62	-5.65
○	27	5	-2920.62	-5.65
○	27	6	-2919.31	-5.57
○	27	7	-2919.31	-5.57
○	28	0	-2920.61	-5.90
○	28	1	-2920.49	-5.89

5. ZINC68601187





○	5	0	-2900.21	-6.53
○	5	1	-2900.21	-6.53
○	5	2	-2900.21	-6.53
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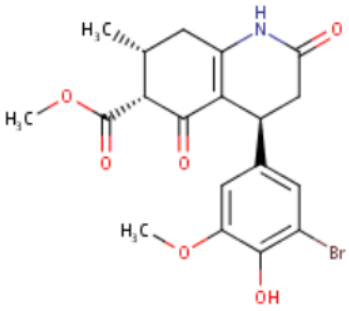
○	5	4	-2899.71	-6.49
○	5	5	-2899.71	-6.49
○	5	6	-2899.67	-6.50
○	5	7	-2899.67	-6.50
◉	6	0	-2900.12	-8.71
○	6	1	-2900.12	-8.71
○	6	2	-2900.12	-8.71
○	6	3	-2900.12	-8.71
○	6	4	-2900.12	-8.41
○	6	5	-2900.12	-8.41
○	6	6	-2896.41	-8.53
○	6	7	-2896.41	-8.53
○	7	0	-2899.53	-7.27
○	7	1	-2899.53	-7.27
○	7	2	-2899.53	-7.27
○	7	3	-2897.50	-7.13
○	7	4	-2897.50	-7.13
○	7	5	-2897.50	-7.13
○	7	6	-2897.50	-7.13
○	7	7	-2895.63	-7.01

6. ZINC09559961



○	25	3	-2948.02	-5.85
○	25	4	-2948.02	-5.85
○	25	5	-2947.37	-5.86
○	25	6	-2947.37	-5.86
○	25	7	-2947.37	-5.86
◉	26	0	-2948.62	-5.95
○	26	1	-2948.58	-5.95
○	26	2	-2948.58	-5.95
○	26	3	-2948.58	-5.95
○	26	4	-2948.58	-5.95
○	26	5	-2948.58	-5.95
○	26	6	-2948.58	-5.95
○	26	7	-2948.43	-5.96
○	27	0	-2948.50	-5.86
○	27	1	-2948.50	-5.86
○	27	2	-2948.50	-5.86
○	27	3	-2948.35	-5.87
○	27	4	-2948.31	-5.87
○	27	5	-2948.31	-5.87
○	27	6	-2948.31	-5.87
○	27	7	-2948.31	-5.87
○	28	0	-2947.94	-6.13
○	28	1	-2947.94	-6.13
○	28	2	-2947.94	-6.13
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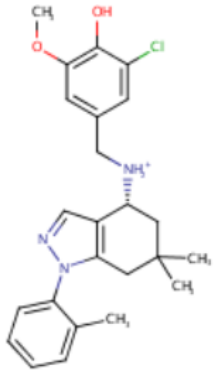
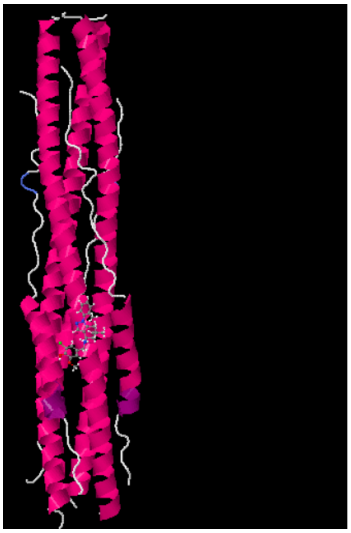
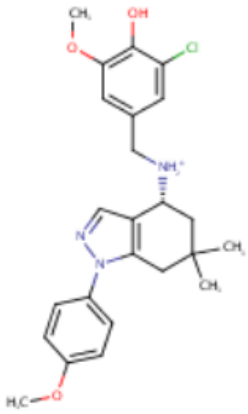
7. ZINC12745518





○	15	6	-2893.81	-6.27
○	15	7	-2893.81	-6.27
○	16	0	-2896.83	-7.18
○	16	1	-2896.83	-7.18
○	16	2	-2896.44	-7.07
○	16	3	-2896.44	-7.07
○	16	4	-2896.35	-7.05
○	16	5	-2896.35	-7.05
○	16	6	-2896.35	-7.05
○	16	7	-2896.35	-7.05
◉	17	0	-2896.54	-6.38
○	17	1	-2896.54	-6.38
○	17	2	-2896.54	-6.38
○	17	3	-2896.44	-6.38
○	17	4	-2896.23	-6.39
○	17	5	-2896.23	-6.39
○	17	6	-2896.23	-6.39
○	17	7	-2896.23	-6.39
○	18	0	-2896.35	-6.26
○	18	1	-2896.35	-6.26
○	18	2	-2896.35	-6.26
○	18	3	-2896.22	-6.24
○	18	4	-2896.22	-6.24
○	18	5	-2895.89	-6.22

8. ZINC14962356



○	28	0	-2964.69	-6.84
○	28	1	-2964.69	-6.84
○	28	2	-2964.69	-6.84
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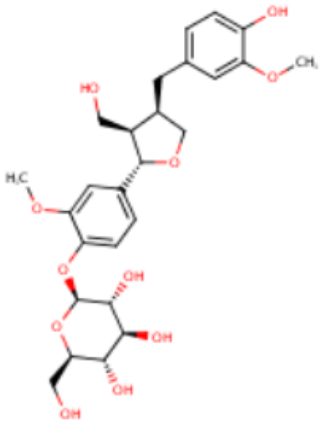
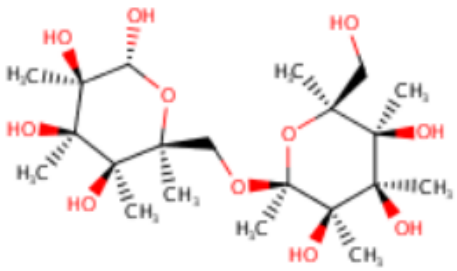
○	28	4	-2960.95	-6.64
○	28	5	-2960.95	-6.64
○	28	6	-2959.85	-6.73
○	28	7	-2959.85	-6.73
○	29	0	-2964.44	-5.36
○	29	1	-2964.44	-5.36
○	29	2	-2964.31	-5.33
○	29	3	-2964.31	-5.33
○	29	4	-2964.31	-5.33
○	29	5	-2964.31	-5.33
○	29	6	-2964.31	-5.33
○	29	7	-2964.31	-5.32
◉	30	0	-2964.43	-6.01
○	30	1	-2964.43	-6.01
○	30	2	-2963.11	-5.94
○	30	3	-2963.11	-5.94
○	30	4	-2963.11	-5.94
○	30	5	-2962.82	-5.92
○	30	6	-2962.82	-5.92
○	30	7	-2962.82	-5.92

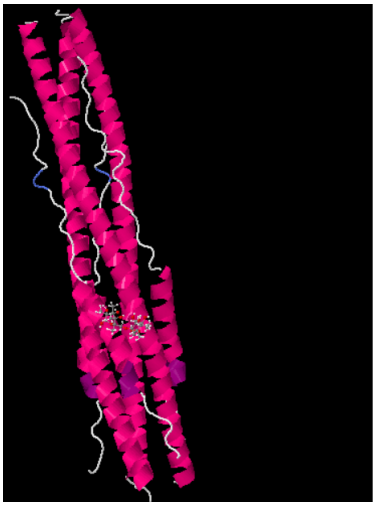
9. ZINC38143804



○	6	3	-2813.73	-7.29
○	6	4	-2813.73	-7.29
○	6	5	-2813.73	-7.29
○	6	6	-2813.69	-7.29
○	6	7	-2813.69	-7.29
◉	7	0	-2814.26	-7.90
○	7	1	-2814.26	-7.90
○	7	2	-2814.26	-7.90
○	7	3	-2814.19	-7.66
○	7	4	-2814.19	-7.66
○	7	5	-2814.18	-7.66
○	7	6	-2814.18	-7.66
○	7	7	-2814.18	-7.66
○	8	0	-2813.88	-7.03
○	8	1	-2812.54	-6.81
○	8	2	-2812.54	-6.81
○	8	3	-2812.54	-6.81
○	8	4	-2812.54	-6.81
○	8	5	-2812.38	-6.84
○	8	6	-2812.38	-6.84
○	8	7	-2812.38	-6.84
○	9	0	-2813.59	-7.99
○	9	1	-2813.59	-7.99
○	9	2	-2813.59	-7.99
○	9	3	-2813.34	-8.08

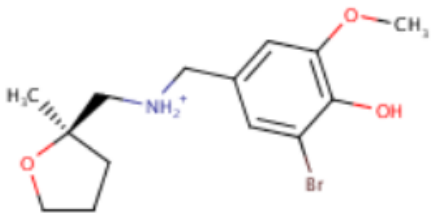
10. ZINC09970504





○	13	3	-2697.07	-6.54
○	13	4	-2697.07	-6.54
○	13	5	-2696.61	-6.49
○	13	6	-2696.61	-6.49
○	13	7	-2696.61	-6.49
○	14	0	-2698.64	-4.46
○	14	1	-2698.64	-4.46
○	14	2	-2697.35	-4.54
○	14	3	-2697.35	-4.54
○	14	4	-2697.35	-4.54
○	14	5	-2697.35	-4.54
○	14	6	-2697.11	-4.32
○	14	7	-2697.11	-4.32
◉	15	0	-2698.30	-6.67
○	15	1	-2698.30	-6.67
○	15	2	-2698.30	-6.67
○	15	3	-2696.72	-6.64
○	15	4	-2696.72	-6.64
○	15	5	-2694.18	-6.51
○	15	6	-2694.18	-6.51
○	15	7	-2694.18	-6.51
○	16	0	-2697.78	-5.88
○	16	1	-2697.57	-5.82
○	16	2	-2697.57	-5.82

11. ZINC94797964



7	0	-2909.76	-7.01
7	1	-2909.76	-7.01
7	2	-2909.76	-6.98
7	3	-2909.76	-6.98
7	4	-2909.76	-6.98
7	5	-2909.76	-6.98
7	6	-2909.76	-6.98
7	7	-2909.70	-7.01
8	0	-2908.97	-6.05
8	1	-2908.90	-6.04
8	2	-2908.90	-6.04
8	3	-2908.90	-6.04
8	4	-2908.90	-6.04
8	5	-2905.88	-5.85
8	6	-2905.88	-5.85
8	7	-2905.88	-5.85
9	0	-2908.69	-6.53
9	1	-2908.69	-6.53
9	2	-2908.69	-6.53
9	3	-2908.69	-6.53
9	4	-2908.69	-6.53
9	5	-2908.69	-6.53
9	6	-2908.69	-6.53
9	7	-2908.60	-6.51
10	0	-2908.61	-7.74

ADME, Drug Likeness, PK, Toxicity properties:

ADME, Drug Likeness

Molecule	ΔG(kcal/mol)	MW	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	log Kp (cm/s)	Lipinski #violations	Ghose #violations	Veber #violations	Egan #violations	Muegge #violations	Bioavailability Score	PAINS #alerts	Brenk #alerts	Leadlikeness #violations
ZINC94763924	-5.99	265.33	High	No	Yes	No	No	No	No	No	-8.29	0	1	0	0	0	0.55	0	2	0
ZINC81318565	-6.58	360.43	High	No	Yes	No	No	No	No	No	-7.6	0	0	0	0	0	0.55	0	0	1
ZINC36369755	-6.89	457.54	Low	No	Yes	No	No	No	No	No	-9.42	1	1	0	0	1	0.55	0	0	1
ZINC81318568	-6.17	360.43	High	No	Yes	No	No	No	No	No	-7.6	0	0	0	0	0	0.55	0	0	1
ZINC68601187	-8.71	608.6	Low	No	No	No	No	No	No	No	-6.38	2	3	1	2	3	0.11	3	2	2
ZINC09559961	-5.95	438.27	High	No	Yes	No	No	No	No	Yes	-7.49	0	0	0	0	0	0.55	0	1	1
ZINC12745518	-6.38	426.96	High	Yes	Yes	Yes	No	Yes	No	No	-5.35	0	0	0	0	1	0.55	0	0	2
ZINC14962356	-6.01	442.96	High	Yes	No	Yes	No	Yes	No	No	-5.72	0	0	0	0	0	0.55	0	0	2
ZINC38143804	-7.9	522.54	Low	No	Yes	No	No	No	No	No	-9.06	3	2	1	1	3	0.17	0	0	2
ZINC09970504	-6.67	468.54	Low	No	Yes	No	No	No	No	Yes	-11.34	2	2	1	1	4	0.17	0	0	1
ZINC94797964	-6.53	331.23	High	Yes	No	Yes	No	No	No	No	-6.77	0	0	0	0	0	0.55	0	0	0
1. Salvionalic acidC	-7.6	492.43	Low	No	No	No	No	Yes	No	No	-6.41	1	1	1	1	2	0.11	1	2	3
2. Arbidol	-7.24	477.41	High	No	No	No	Yes	Yes	Yes	Yes	-6.07	0	0	0	0	0	0.55	1	0	3
3. Luteolin	-8.04	286.24	High	No	No	Yes	No	No	Yes	Yes	-6.25	0	0	0	0	0	0.55	1	1	0
4. Quercetin	-6.12	302.24	High	No	No	Yes	No	No	Yes	Yes	-7.05	0	0	0	0	0	0.55	1	1	0

PK

Molecule	TPSA	iLOGP	XLOGP3	WLOGP	MLOGP	Silicos-IT Log P	Consensus Log P	ESOL Log S	ESOL Solubility (mg/ml)	ESOL Solubility (mol/l)	ESOL Class	Ali Log S	Ali Solubility (mg/ml)	Ali Solubility (mol/l)	Ali Class	Silicos-IT LogSw	Silicos-IT Solubility (mg/ml)	Silicos-IT Solubility (mol/l)	Silicos-IT class
ZINC94763924	92.68	1.55	-0.52	-1.92	-3.65	0.15	-0.88	-1.06	2.30E+01	8.69E-02	Very soluble	-0.96	2.92E+01	1.10E-01	Very soluble	-2.4	1.06E+00	4.01E-03	Soluble
ZINC81318565	95.09	2.26	1.26	1.71	0.89	1.38	1.5	-2.89	4.60E-01	1.28E-03	Soluble	-2.86	5.03E-01	1.39E-03	Soluble	-4.82	5.46E-03	1.51E-05	Moderately soluble
ZINC36369755	129.06	2.2	-0.47	-3.55	-3.7	0.44	-1.01	-2.19	2.97E+00	6.49E-03	Soluble	-1.77	7.70E+00	1.68E-02	Very soluble	-2.33	2.13E+00	4.66E-03	Soluble
ZINC81318568	95.09	2.02	1.26	1.71	0.89	1.38	1.45	-2.89	4.60E-01	1.28E-03	Soluble	-2.86	5.03E-01	1.39E-03	Soluble	-4.82	5.46E-03	1.51E-05	Moderately soluble
ZINC68601187	229.82	-0.04	5.12	5.95	1.66	1.92	2.92	-6.87	8.29E-05	1.36E-07	Poorly soluble	-9.69	1.24E-07	2.04E-10	Poorly soluble	-8.39	2.48E-06	4.07E-09	Poorly soluble
ZINC09559961	101.93	2.61	2.09	2.04	1.35	2.83	2.18	-3.77	7.37E-02	1.68E-04	Soluble	-3.86	6.04E-02	1.38E-04	Soluble	-4.76	7.65E-03	1.75E-05	Moderately soluble
ZINC12745518	63.89	3.89	5.01	3.85	-0.01	4.84	3.52	-5.73	7.90E-04	1.85E-06	Moderately soluble	-6.09	3.46E-04	8.10E-07	Poorly soluble	-8	4.30E-06	1.01E-08	Poorly soluble
ZINC14962356	73.12	4.17	4.62	3.55	-0.56	4.38	3.23	-5.51	1.38E-03	3.11E-06	Moderately soluble	-5.88	5.83E-04	1.32E-06	Moderately soluble	-7.72	8.40E-06	1.90E-08	Poorly soluble
ZINC38143804	167.53	3.01	0.6	-0.2	-1.05	0.79	0.63	-3.1	4.11E-01	7.87E-04	Soluble	-3.69	1.06E-01	2.03E-04	Soluble	-2.6	1.30E+00	2.48E-03	Soluble
ZINC09970504	189.53	0.81	-3.07	-1.89	-2.16	0.11	-1.24	-0.55	1.33E+02	2.84E-01	Very soluble	-0.35	2.11E+02	4.51E-01	Very soluble	-1.1	3.75E+01	8.00E-02	Soluble
ZINC94797964	55.3	3.38	2.19	1.64	-1.95	3.35	1.72	-3.18	2.20E-01	6.65E-04	Soluble	-2.99	3.43E-01	1.03E-03	Soluble	-4.86	4.55E-03	1.37E-05	Moderately soluble
1. Salvionalic acidC	177.89	1.67	4.07	3.77	0.88	3.09	2.7	-5.36	2.15E-03	4.36E-06	Moderately soluble	-7.51	1.52E-05	3.09E-08	Poorly soluble	-4.88	6.45E-03	1.31E-05	Moderately soluble
2. Arbidol	80	3.79	4.43	4.87	3.59	4.61	4.26	-5.45	1.71E-03	3.58E-06	Moderately soluble	-5.83	7.09E-04	1.49E-06	Moderately soluble	-7	4.80E-05	1.00E-07	Poorly soluble
3. Luteolin	111.13	1.86	2.53	2.28	-0.03	2.03	1.73	-3.71	5.63E-02	1.97E-04	Soluble	-4.51	8.84E-03	3.09E-05	Moderately soluble	-3.82	4.29E-02	1.50E-04	Soluble
4. Quercetin	131.36	1.63	1.54	1.99	-0.56	1.54	1.23	-3.16	2.11E-01	6.98E-04	Soluble	-3.91	3.74E-02	1.24E-04	Soluble	-3.24	1.73E-01	5.73E-04	Soluble

Toxicity

ID	algae_at	Ames_test	Carcino_ Mouse	Carcino_ Rat	daphnia_ at	hERG_inhibition	medaka_at	minnow_at	TA100_10 RLI	TA100_NA	TA1535_10RLI	TA1535_ NA
ZINC94763924	0.148936	mutagen	negative	negative	2.20555	low_risk	5.89066	3.54502	negative	positive	positive	negative
ZINC81318565	0.072873	mutagen	negative	negative	0.287705	ambiguous	0.156377	0.272897	negative	negative	negative	negative
ZINC36369755	0.039221	mutagen	negative	negative	1.57244	ambiguous	4.02375	7.62481	positive	negative	negative	negative
ZINC81318568	0.072873	mutagen	negative	negative	0.287705	ambiguous	0.156377	0.272897	negative	negative	negative	negative
ZINC68601187	0.00019	non-mutagen	negative	negative	0.001699	ambiguous	1.37E-05	1.82E-05	negative	negative	negative	negative
ZINC09559961	0.038886	mutagen	negative	negative	0.093687	low_risk	0.0181787	0.0389529	negative	negative	negative	negative
ZINC12745518	0.002522	non-mutagen	negative	negative	0.004731	medium_risk	5.80E-05	0.000288297	negative	negative	negative	negative
ZINC14962356	0.003673	non-mutagen	negative	negative	0.009507	medium_risk	0.000223338	0.000575361	negative	negative	negative	negative
ZINC38143804	0.012985	non-mutagen	negative	negative	0.362495	high_risk	0.252184	0.788902	negative	negative	negative	negative
ZINC09970504	0.007928	non-mutagen	negative	positive	0.276523	low_risk	0.113218	0.104346	negative	negative	negative	negative
ZINC94797964	0.028291	mutagen	negative	positive	0.198536	medium_risk	0.0606247	0.0628624	negative	positive	positive	positive
Salvionalic acid C	0.001543	mutagen	positive	positive	0.006048	high_risk	0.000112165	0.000200147	negative	positive	negative	positive
Arbidol	0.003904	non-mutagen	negative	positive	0.004259	medium_risk	5.84E-05	0.000166726	negative	negative	negative	negative
Luteolin	0.041631	mutagen	positive	positive	0.139325	medium_risk	0.0329883	0.0169052	negative	positive	negative	negative
Quercetin	0.037814	mutagen	negative	positive	0.214345	medium_risk	0.0778806	0.0335026	negative	positive	negative	negative

Observations:

We find that the molecules ZINC68601187(ΔG = - 8.71kcal/mol) and ZINC38143804 (ΔG = - 7.9 kcal/mol) have the best binding energy, better than the input molecules used. But they have poor drug-likeness properties, as they violate all the rules and have poor bioavailability of 0.11 and 0.17 respectively.

Luteolin (ΔG = - 8.04kcal/mol) and seems to be the best among molecules with good binding affinity followed by Arbidol (ΔG = - 7.24kcal/mol) and satisfying drug-likeness rules. Salvionalic acid C part of ancient Chinese herbals has poor drug-likeness properties.

Among the output molecules form ZincPharmer, the best molecules satisfying ADME rules with good GI absorption are ZINC81318565 (ΔG = -6.58kcal/mol) and ZINC94797964 (ΔG = -6.53 kcal/mol).
