



Supplementary material

Targeting the SARS-CoV-2 HR1 with Small Molecules as Inhibitors of the Fusion Process

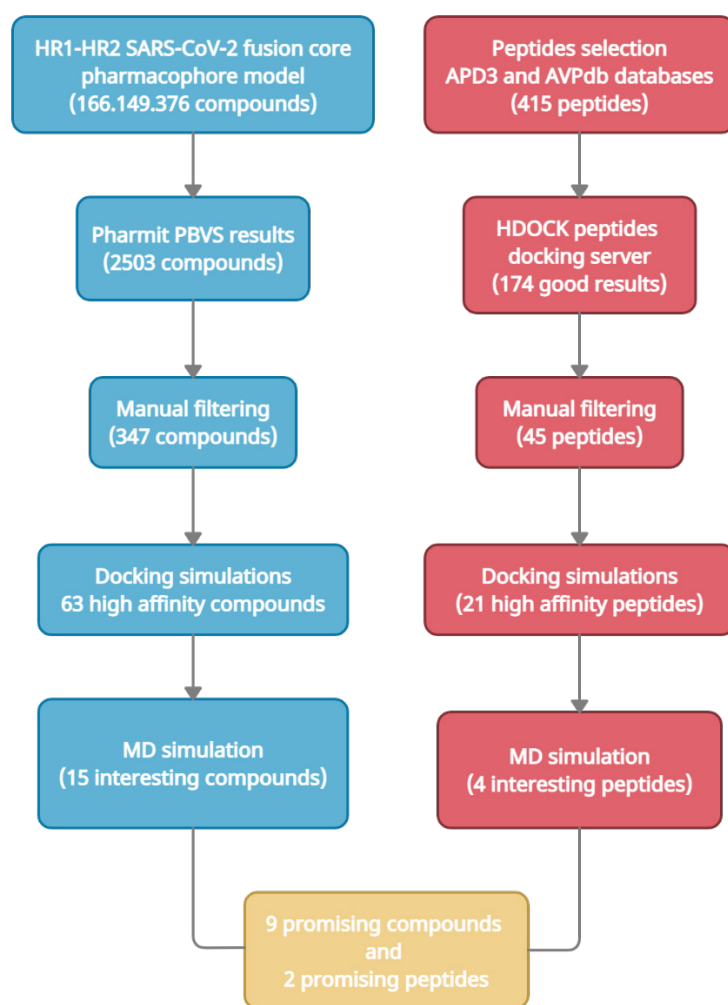
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Scheme S1. Used workflow for the *in-silico* screening.

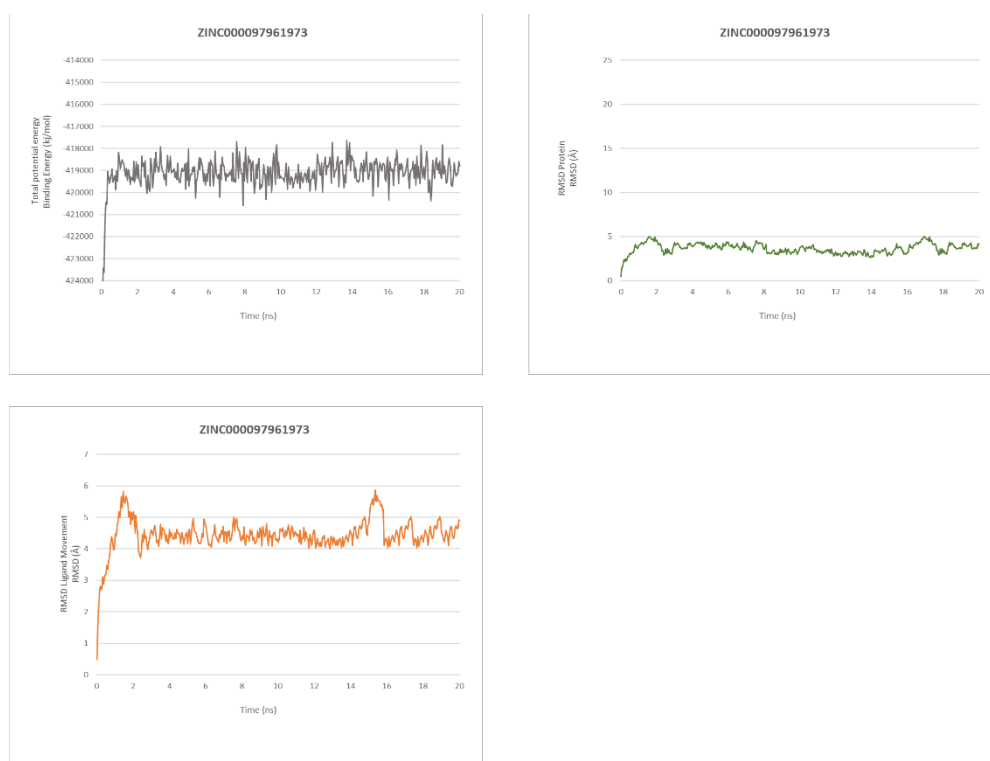


Figure S1. ZINC000097961973@HR1 domain. Total energy (up-left), RMSDs of protein (up-right) and RMSDs of ligand (down-left).

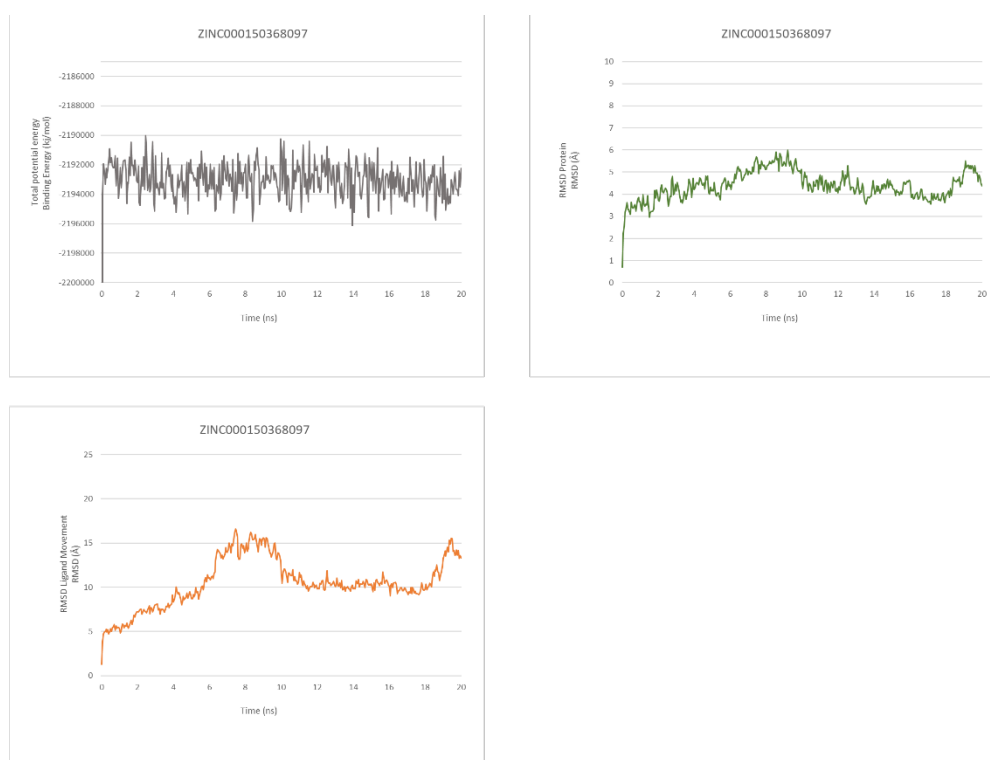


Figure S2. ZINC000150368097@HR1 domain. Total energy (up-left), RMSDs of protein (up-right) and RMSDs of ligand (down-left).

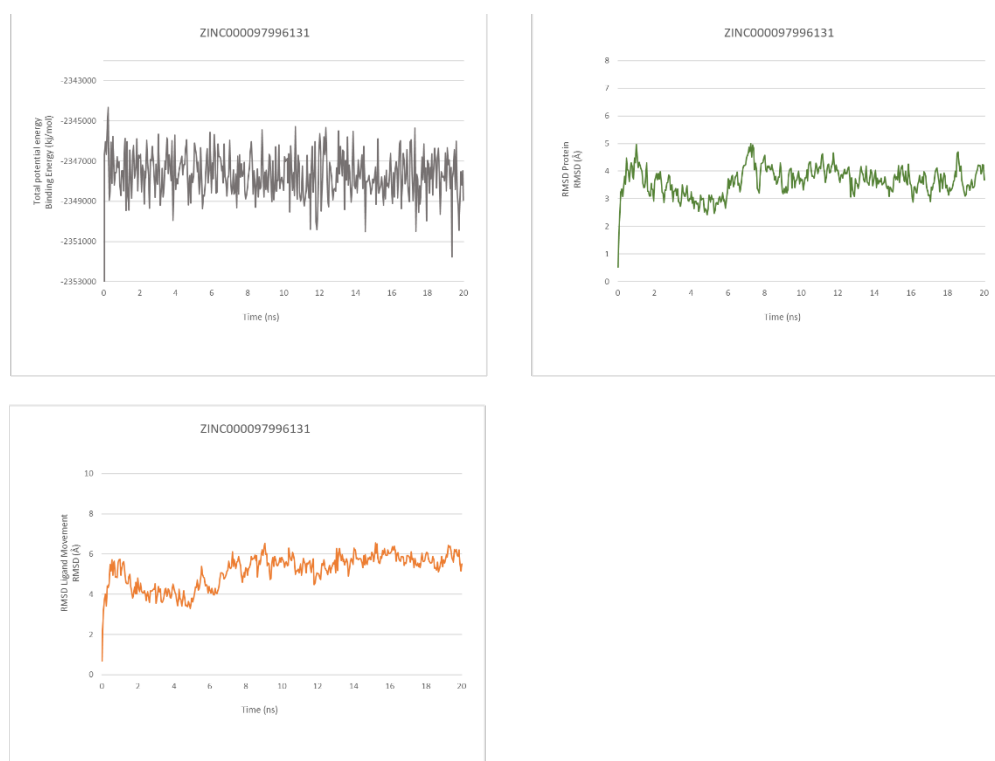


Figure S3. ZINC000097996131@HR1 domain. Total energy (up-left), RMSDs of protein (up-right) and RMSDs of ligand (down-left).

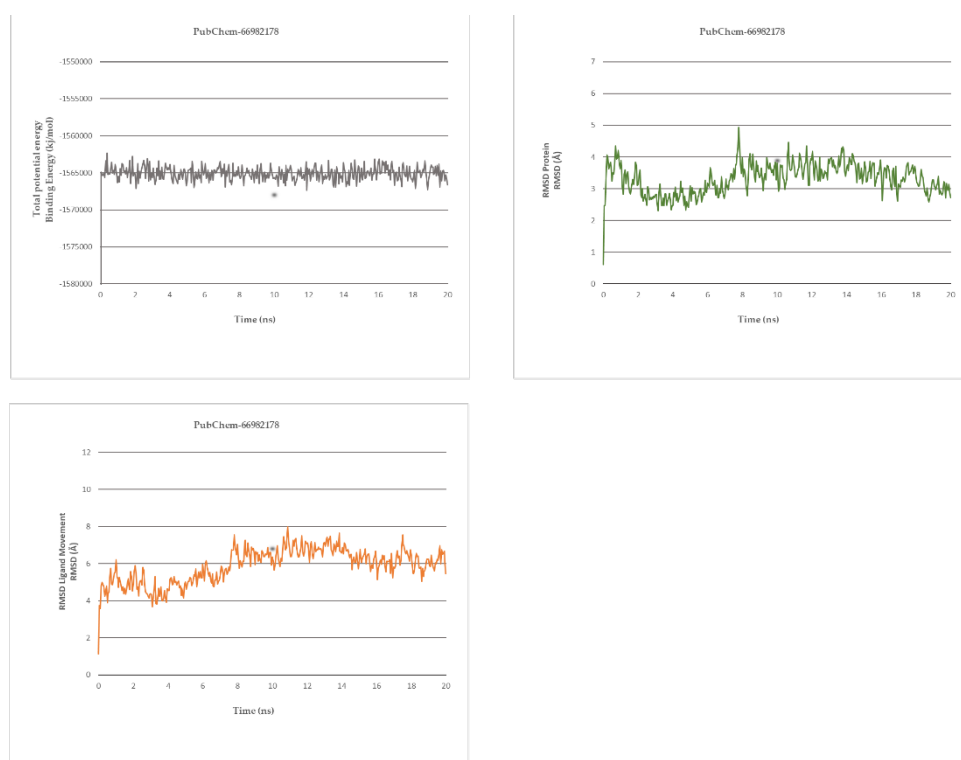


Figure S4. PubChem-66982178@HR1 domain. Total energy (up-left), RMSDs of protein (up-right) and RMSDs of ligand (down-left).

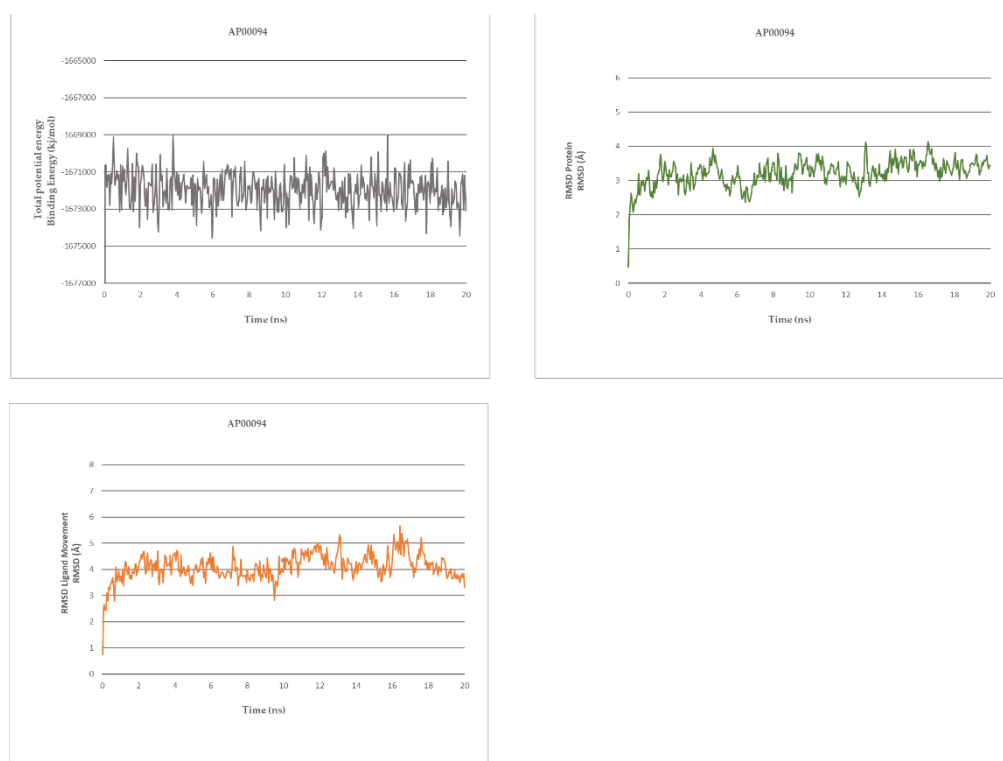


Figure S5. AP00094@HR1 domain. Total energy (up-left), RMSDs of protein (up-right) and RMSDs of ligand (down-left).

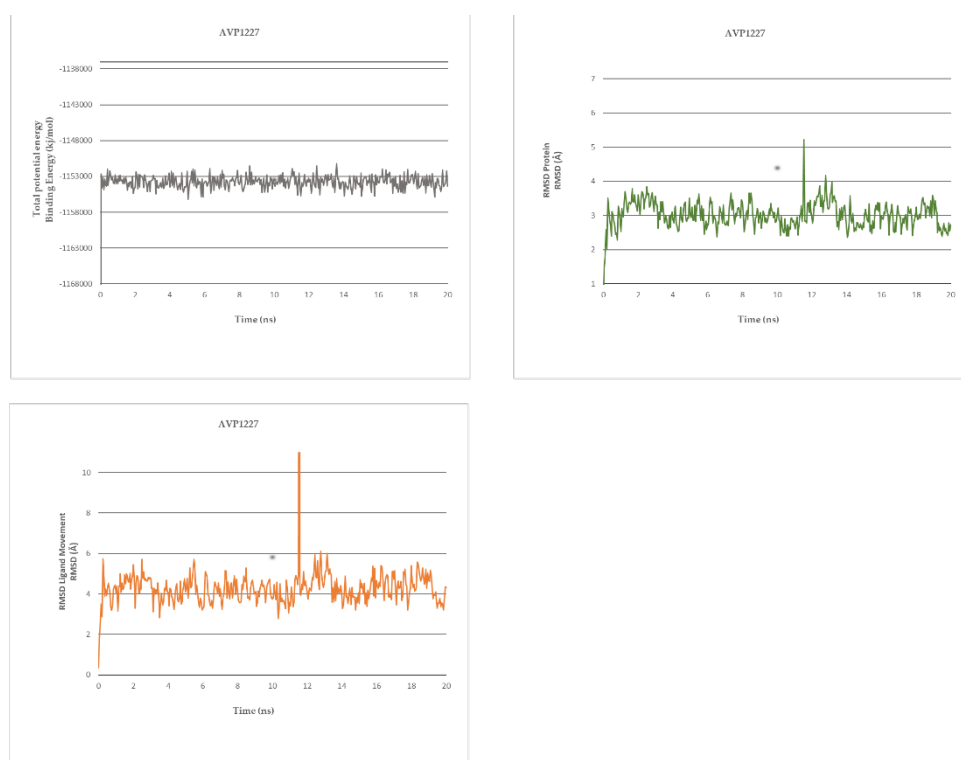


Figure S6. AVP1227@HR1 domain. Total energy (up-left), RMSDs of protein (up-right) and RMSDs of ligand (down-left).

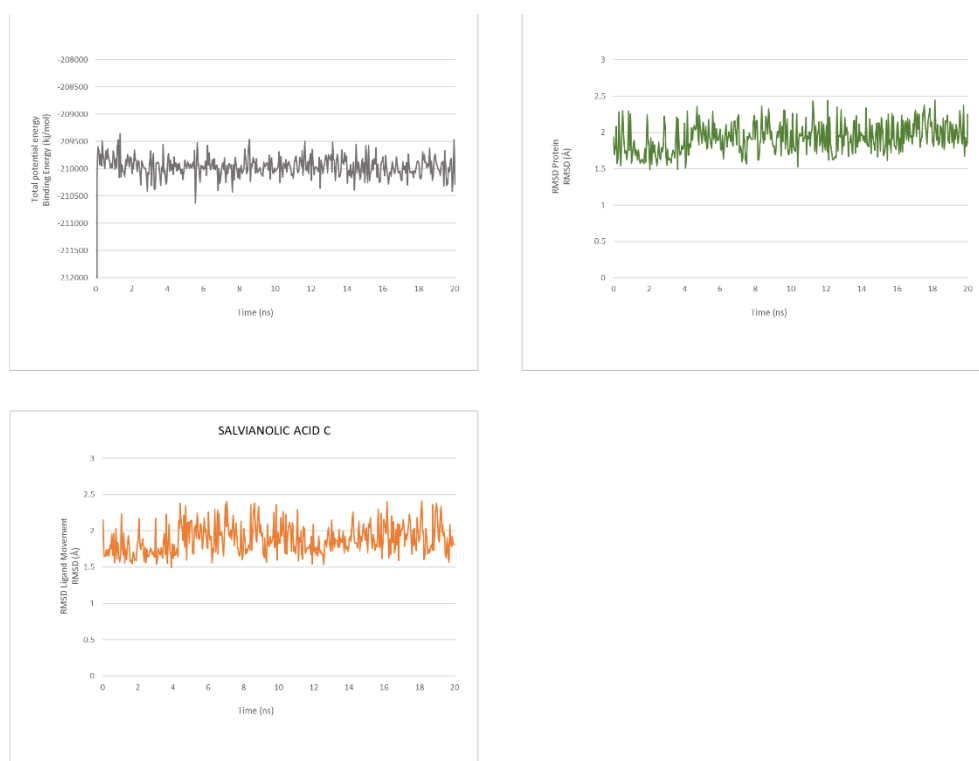


Figure S7. Sal C@HR1 domain. Total energy (up-left), RMSDs of protein (up-right) and RMSDs of ligand (down-left).

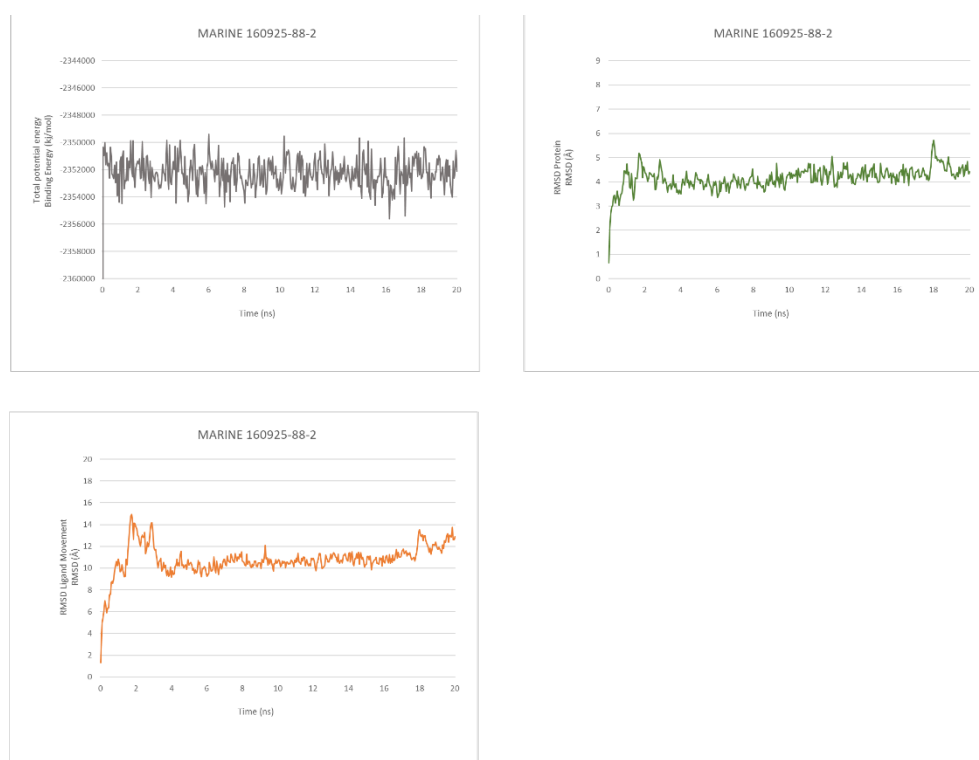


Figure S8. Marine-160925-88-2@HR1 domain. Total energy (up-left), RMSDs of protein (up-right) and RMSDs of ligand (down-left).

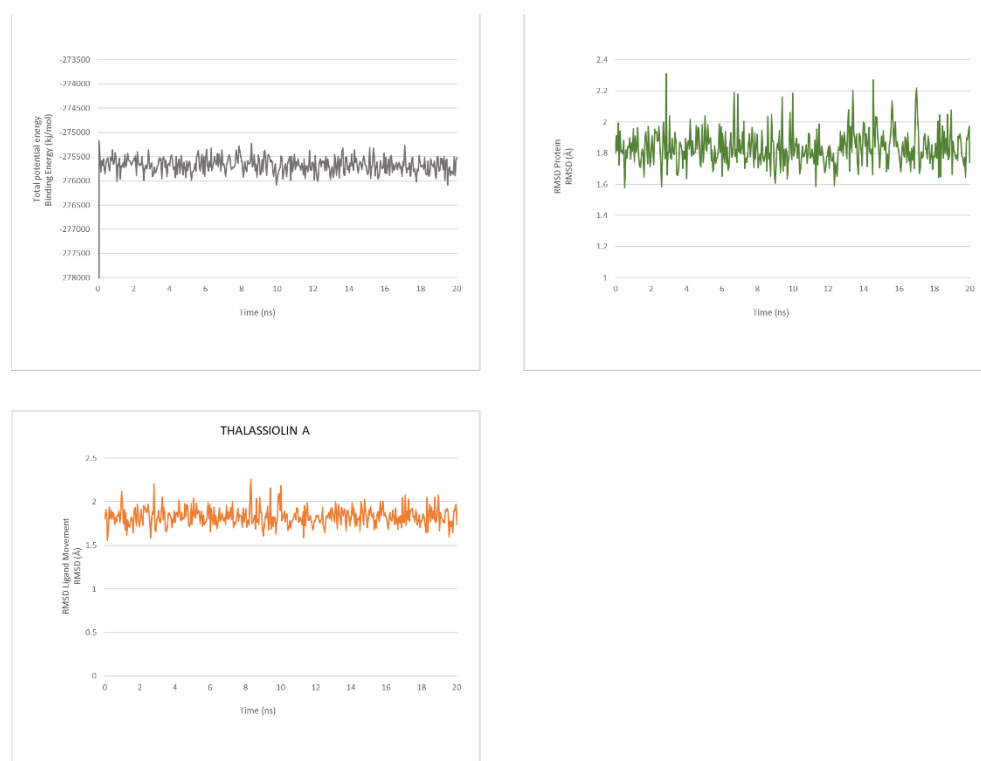


Figure S9. Thalassiolin A@HR1 domain. Total energy (up-left), RMSDs of protein (up-right) and RMSDs of ligand (down-left).

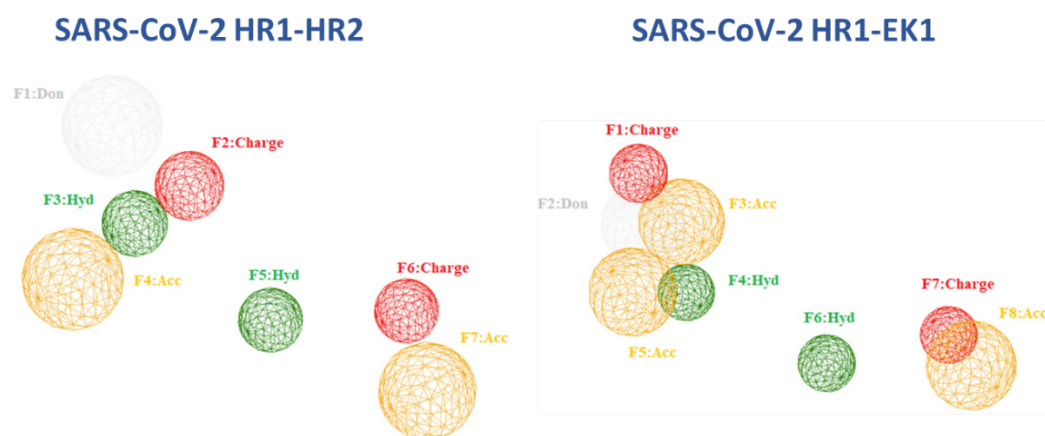
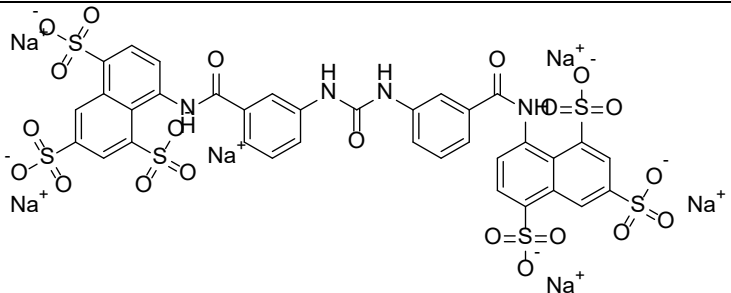
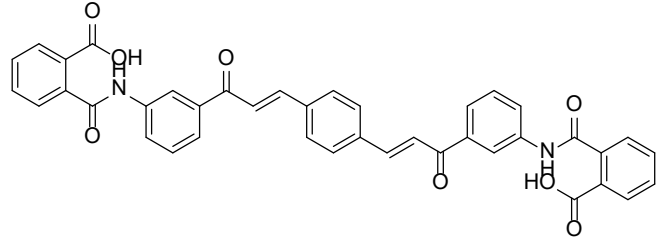
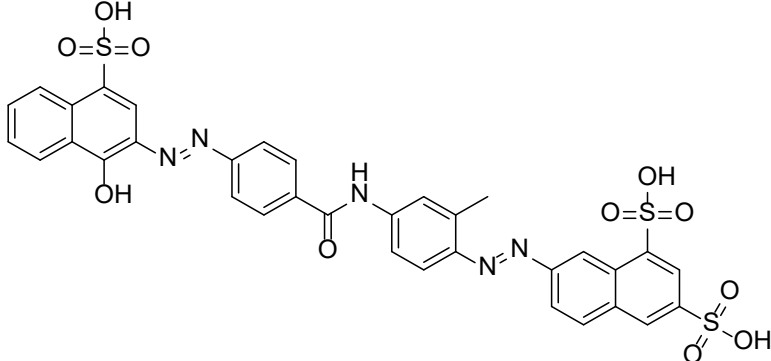
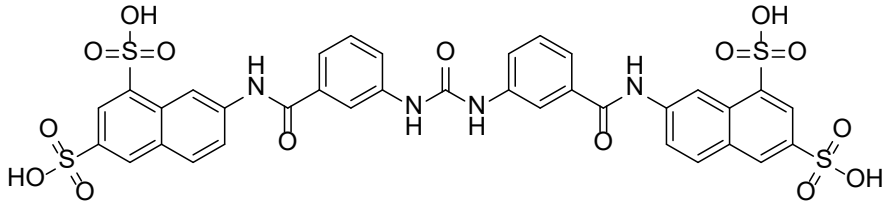
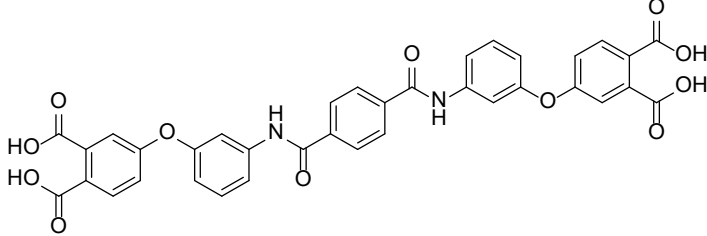
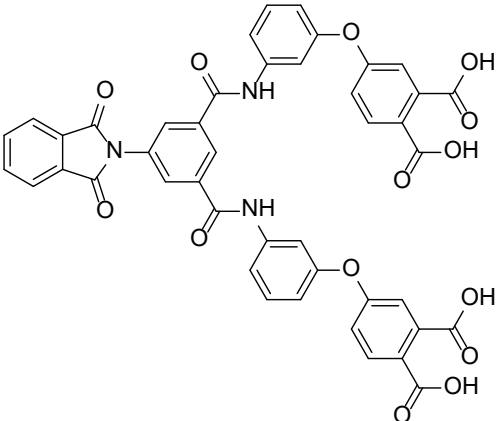
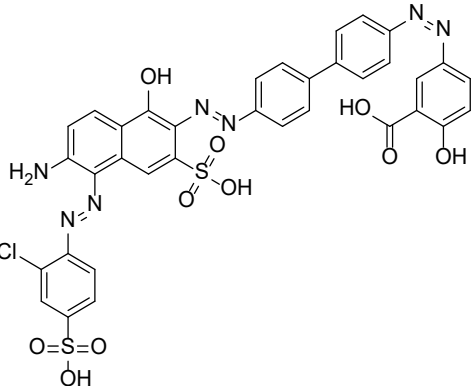
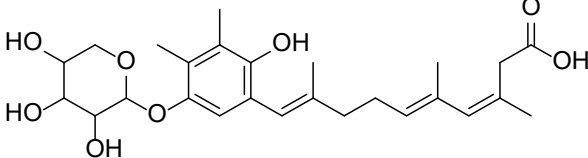
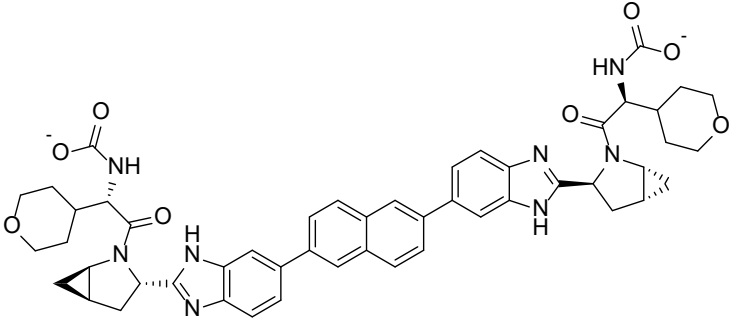
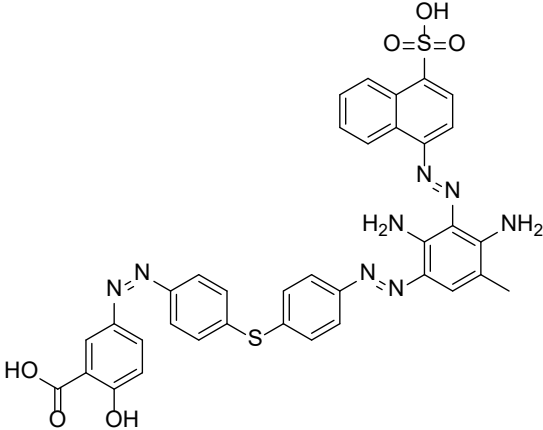
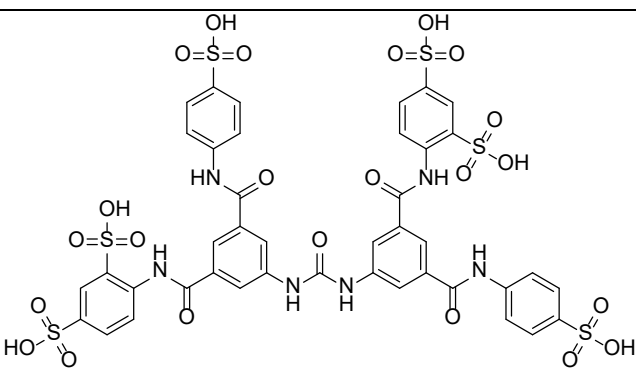
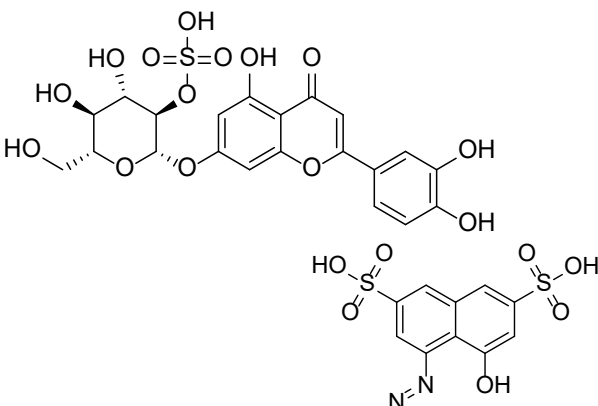
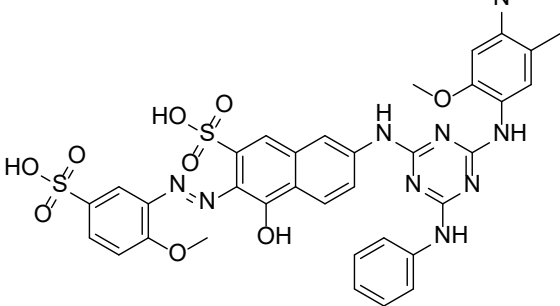
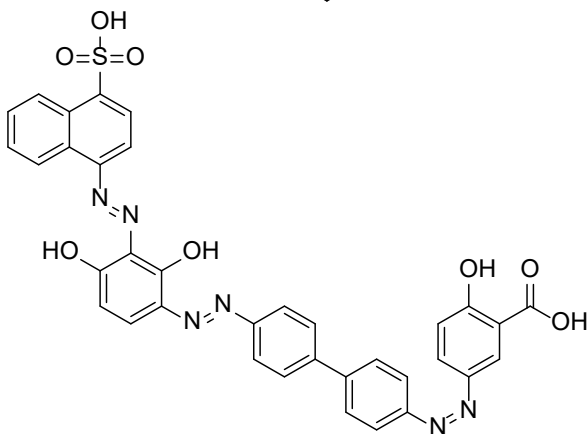


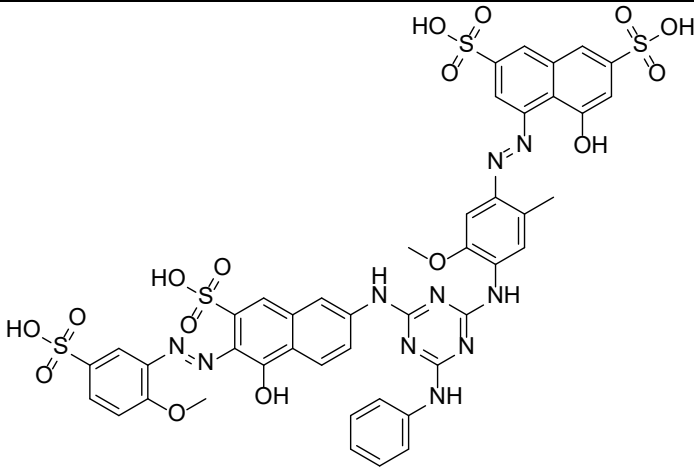
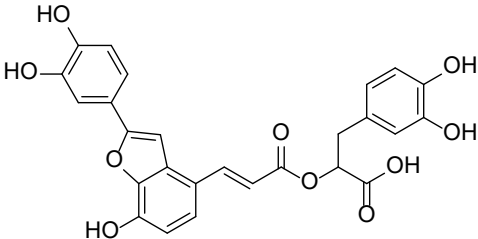
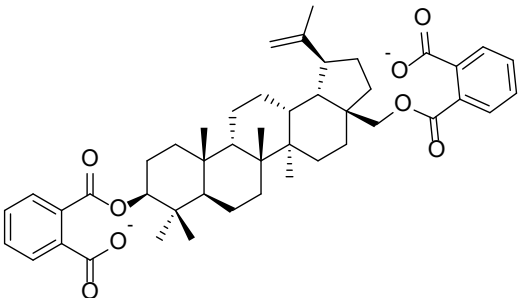
Figure S10. Main interactions described in the pharmacophore model of HR1-HR2 and HR1-EK1.

Table S1. AutodockLGA simulation results for best-scoring compounds.

N.	Name	Structure	ΔG Auto-dock4 kcal/mol
1	NF 023 hydrate PubChem-24278597		-12.03
2	ZINC000097961973		-10.73
3	ZINC000150368097		-10.68
4	ZINC000169332064		-10.59
5	ZINC000097996131		-10.38

6	ZINC000150346512		-10.34
7	ZINC000150631141		-10.31
8	Marine-160925-88-2		-10.21
9	PubChem-66982178		-10.12
10	ZINC000150485530		-10.04

11	PubChem-24742078		-9.94
12	Thalassiolin A		-9.94
13	ADS-J1@SARS-CoV-1 fusion core		-9.76
14	ZINC263603439		-9.73

15	ADS-J1@SARS-CoV-2 fusion core	 <p>The structure shows a complex molecule with multiple sulfonamide and hydroxyl groups. It features a central benzotriazole core substituted with a 4-methoxyphenyl group, a 4-hydroxyphenyl group, and a 4-sulfamoylphenyl group. A 4-sulfamoylphenyl group is also attached to the triazole ring via an azo linkage.</p>	-8.80
16	Salvianolic acid C	 <p>The structure is a polyphenolic compound consisting of a central chromane core. It has a 4-hydroxyphenyl group at position 2, a 4-hydroxyphenyl group at position 7, and a 4-hydroxyphenyl group at position 8. A 4-hydroxyphenyl group is also attached to the chromane core via an ester linkage.</p>	-8.75
17	PubChem-10169258	 <p>The structure is a complex polycyclic molecule with multiple fused rings. It features a central steroid-like core with various functional groups, including a 4-sulfamoylphenyl group, a 4-hydroxyphenyl group, and a 4-sulfamoylphenyl group. A 4-sulfamoylphenyl group is also attached to the steroid core via an ester linkage.</p>	-8.26