Supporting Information

Computational Determination of Potential Inhibitors of SARS-CoV-2 Main Protease

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Table S1. The List of Top-Lead Compounds forming a Large Affinity Obtained via Molecular Docking Simulations.[a]

N⁰	Pubchem	Compound Name	Vietnamese Herb Name	ΔG_{Dock}
1	10621	Hesperidin	Citrus Aurantium	-9.0
2	73330	Strictinin	Castanea Mollissima/ Juglans Regia/ Psidium Guajava	-8.7
3	83489	Eriocitrin	Mentha Piperita	-9.1
4	114777	CHEMBL346119	Camellia Sinensis	-8.7
5	122738	Procyanidin B2	Cinnamomum Cassia	-8.6
6	124356	Physalin F	Physalis Angulata	-8.9
7	156766	Kihadanin B	Phellodendron Amurense	-8.6
8	179651	Limonin	Citrus Aurantium/ Coptis Chinensis/ Phellodendron Amurense/ Citrus Reticulata	-9.0
9	183905	6,8-Di-C-Beta-D-Arabinopyranosyl Apigenin	Camellia Sinensis	-8.7
10	190799	Stephasubine	Stephania Hernandifolia	-9.2
11	196583	Mulberrofuran G	Morus Alba	-9.3
12	442431	Narirutin	Citrus Aurantium/ Cynara Scolymus/ Citrus Sinensis	-8.9
13	480819	Albanol B	Morus Alba	-9.1
14	5281600	Amentoflavone	Garcinia Xanthochymus	-8.6
15	5281613	Diosmin	Pratia Nummularia	-9.1
16	5281627	Hinokiflavone	Rhus Succedanea/ Cycas Revoluta/ Cupressus Funebris	-8.6
17	5317025	Linarin	Mentha Aquatica	-9.1
18	5319276	Marchantin K	Marchantia Polymorpha	-9.0
19	5319278	Marchantin L	Marchantia Polymorpha	-8.7
20	5319933	Mulberrofuran Q	Morus Alba	-8.6
21	5458744	Physalin B 5,6-Epoxide	Physalis Angulata	-8.7
22	6476333	Isoacteoside	Fernandoa Adenophylla/ Stereospermum Cylindricum/ Clerodendrum Inerme/ Markhamia Stipulata/ Rehmannia Glutinosa/ Plantago Asiatica/	-8.8

			Acanthus Ebracteatus	
23	6711179	Hypopistephanine	Stephania Japonica	-9.8
24	9851181	Isorhoifolin	Mentha Aquatica/ Citrus Paradisi/ Pratia Nummularia	-9.0
25	10456516	Cinchonain-Ib	Kandelia Candel	-8.6
26	10461109	Luteolin-7-O-Beta-Rutinoside	Capsella Bursa/ Mentha Aquatica/ Pratia Nummularia	-9.2
27	11827970	Diosgenin Glucoside	Borassus Flabellifer	-9.3
28	15086398	Cannabisin A	Cannabis Sativa	-8.8
29	16760075	Didymin	Citrus Sinensis	-9.0
30	21123844	Gamma-Chaconine	Solanum Tuberosum	-8.9
31	44558930	Anabsinthin	Artemisia Absinthium	-9.0
32	71437113	2,3-Dihydrohinokiflavone	Cycas Revoluta	-8.8
33	71448965	Cannabisin D	Cannabis Sativa	-8.6
34	90473381	(1*R*,2*S*,5*S*,8*S*,9*R*,14*R*,15*R*,17*R*,18*R*,21*S*,24*R*,26*R*,27*S*)-5,14,15-Trihydroxy-2,9,26-Trimethyl-3,19,23,28-Tetraoxaoctacyclo[16.9.1.1^{18,27}.0^{1,5}.0^{2,24}.0^{8,17}.0^{9,14}.0^{21,26}]Nonacos-11-Ene-4,10,22,29-Tetrone	Physalis Angulata/ Physalis Minima	-9.1
35	101764560	Quercetin-7-O-Rutinoside	Platycodon Grandiflorum	-9.2
36	65016	Amprenavir		-6.6
37	148192	Atazanavir		-6.6
38		Aza-Peptide Epoxide		-6.4
39	213039	Darunavir		-6.9
40	5362440	Indinavir		-7.6
41	92727	Lopinavir		-7.0
42	64143	Nelfinavir		-7.0
43	392622	Ritonavir		-6.5
44	441243	Saquinavir		-7.6

[a]The Docking Binding Free Energy Was Obtained by Autodock Vina. The Mean Rupture Force ΔF_{Max} and The Mean Pulling Work ΔW were Obtained from 8 Independent Trajectories of SMD Simulations. The Error is Standard Error of the Mean. The Unit of Energy/Work and Force are pN and kcal/mol, respectively.

Table S2. The Two-Dimensional Protein-Ligand Interaction Diagrams.[a]

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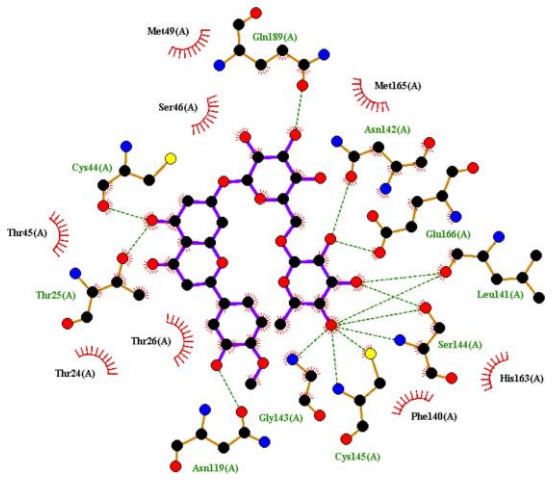

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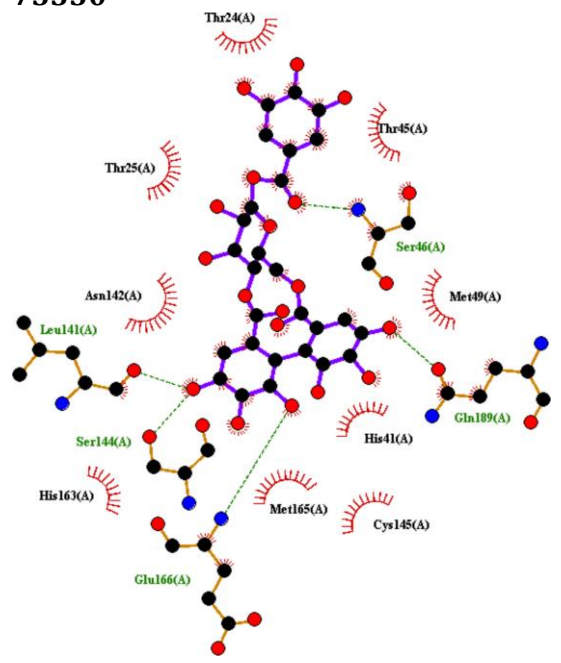

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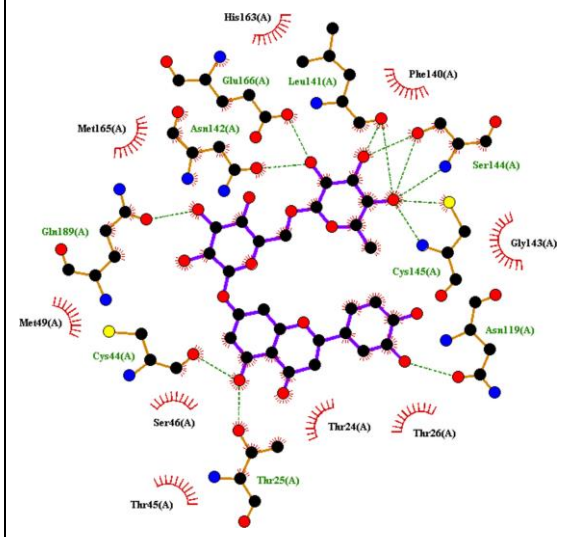

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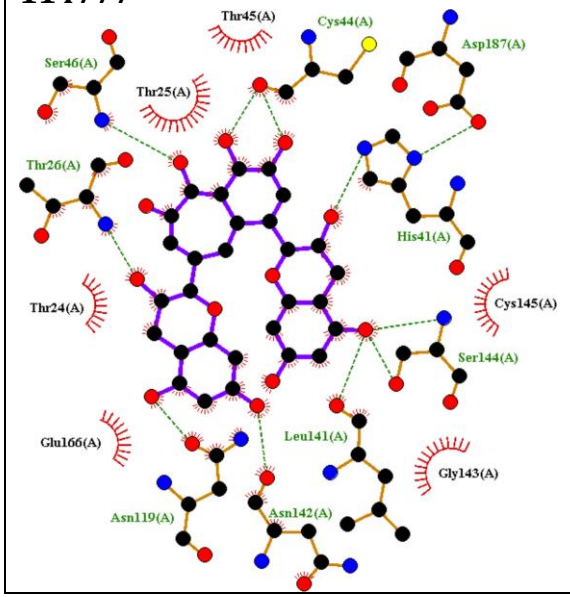

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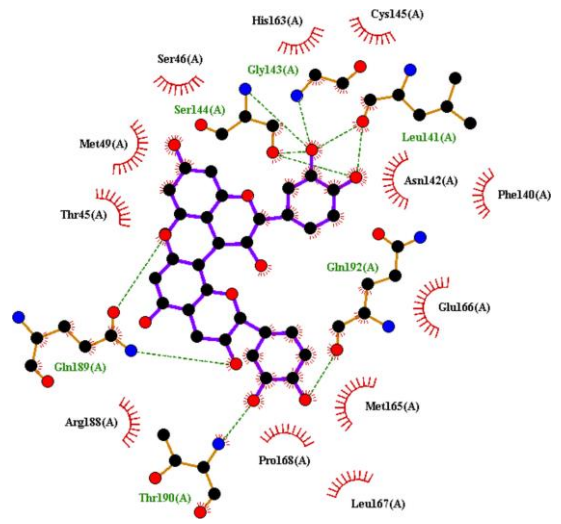

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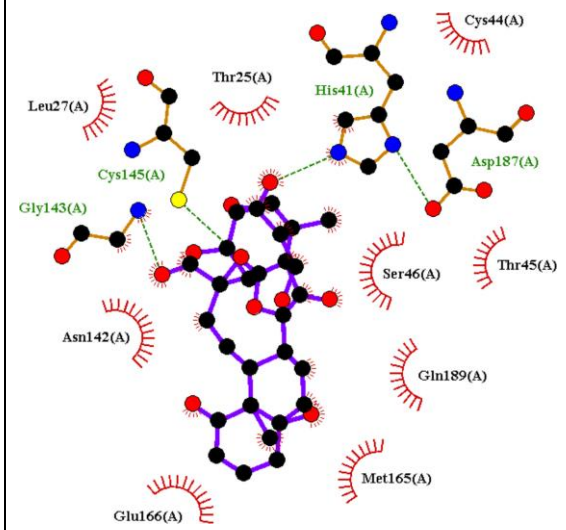

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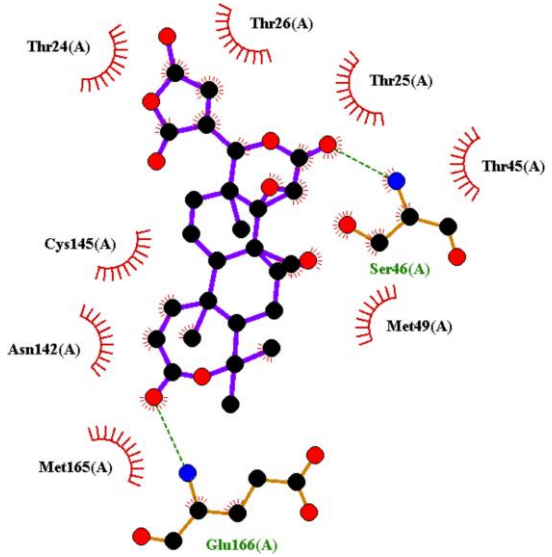

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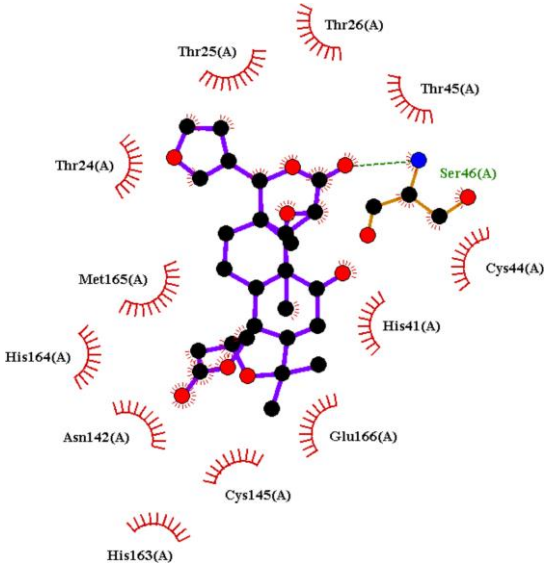

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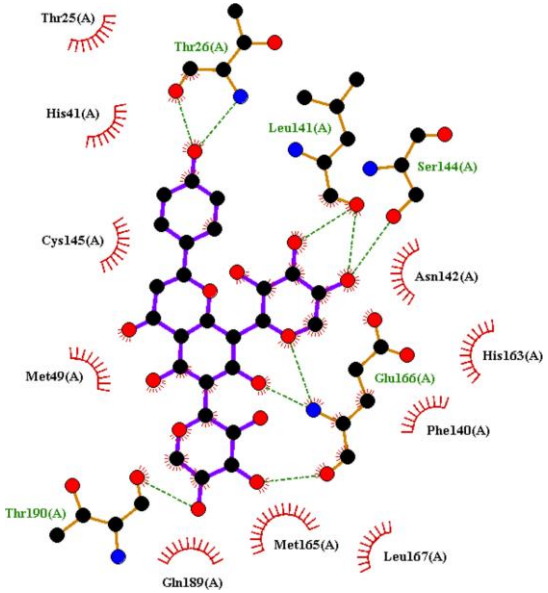

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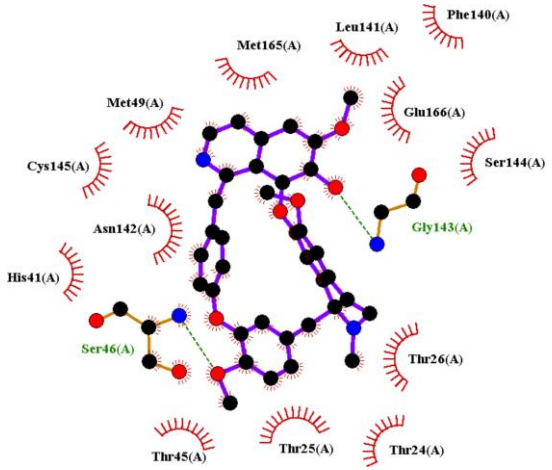

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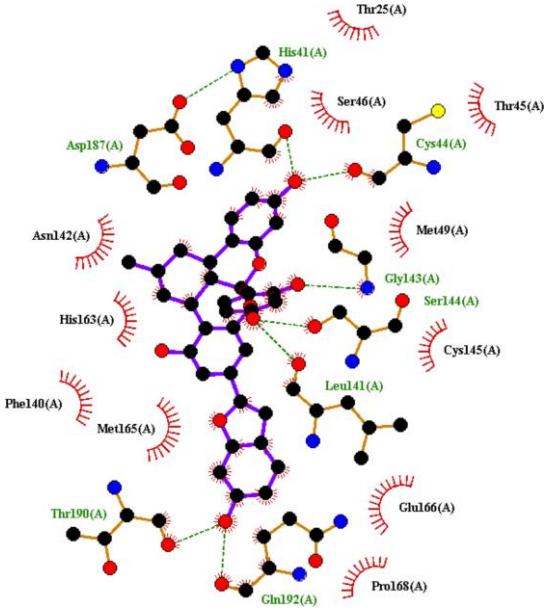

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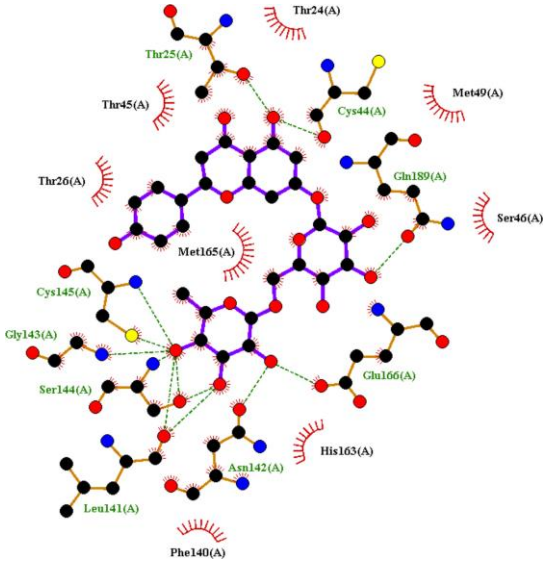

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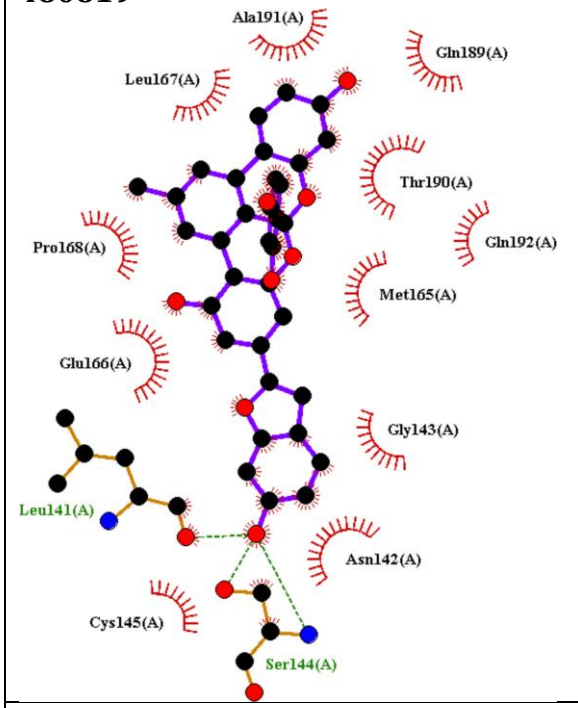

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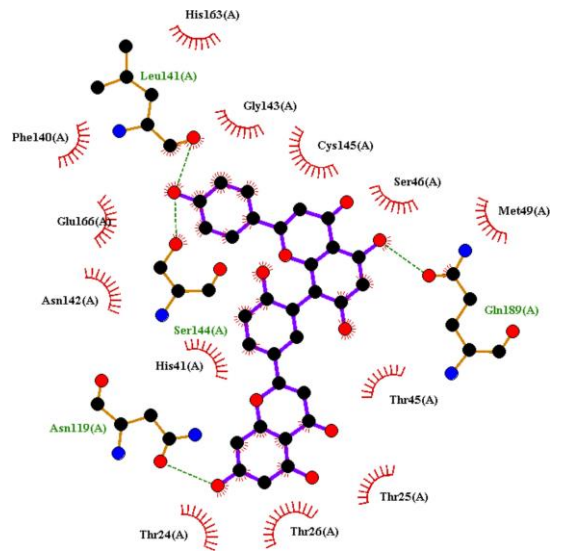

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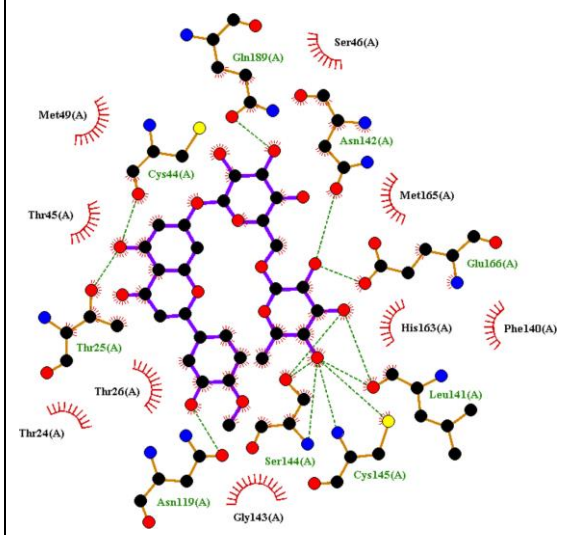

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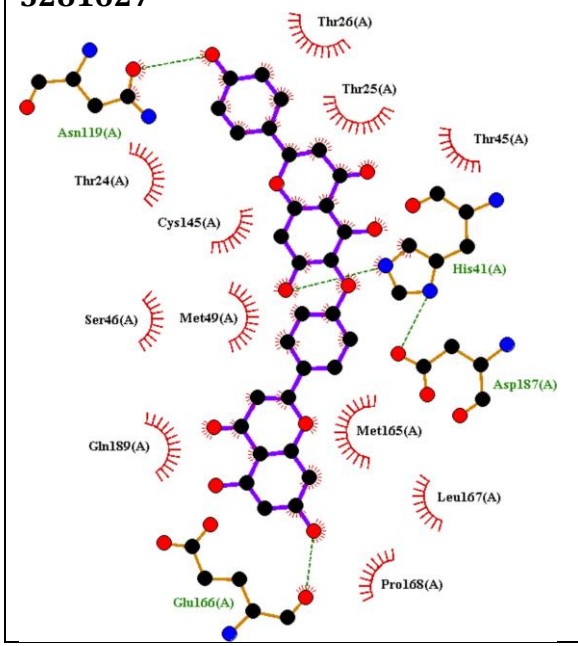

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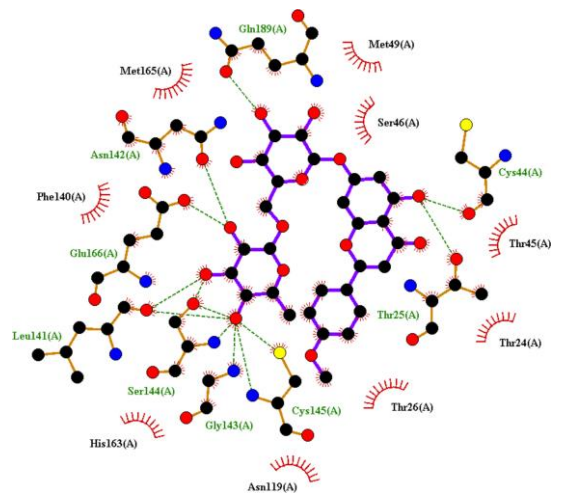

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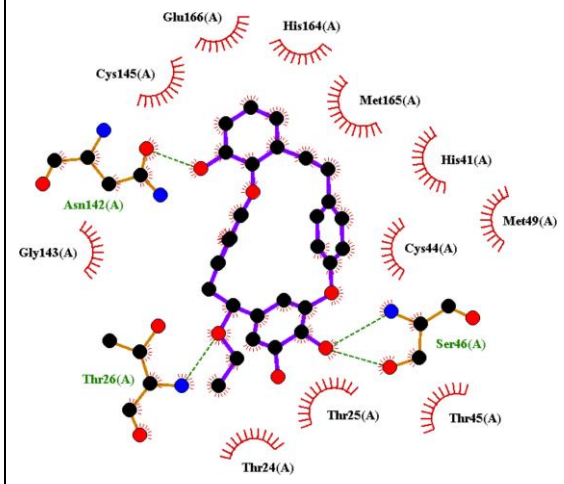

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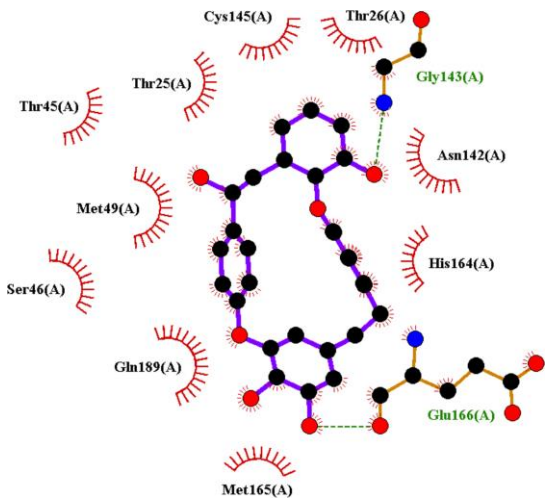

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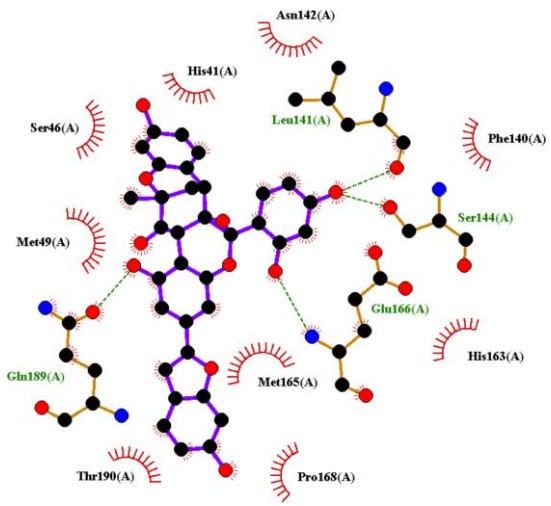

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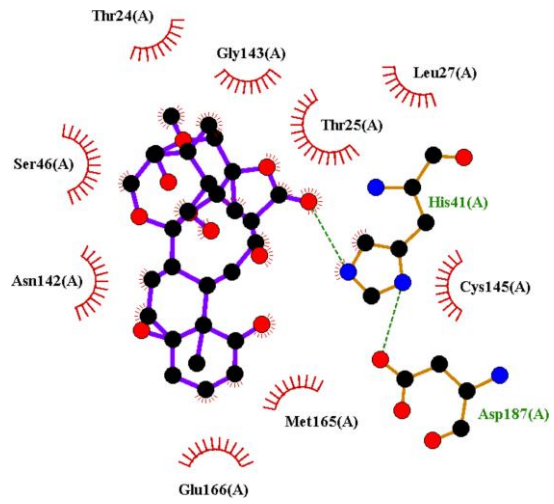

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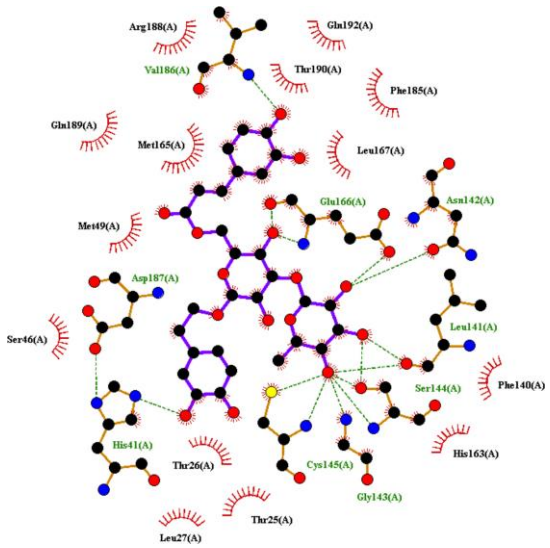

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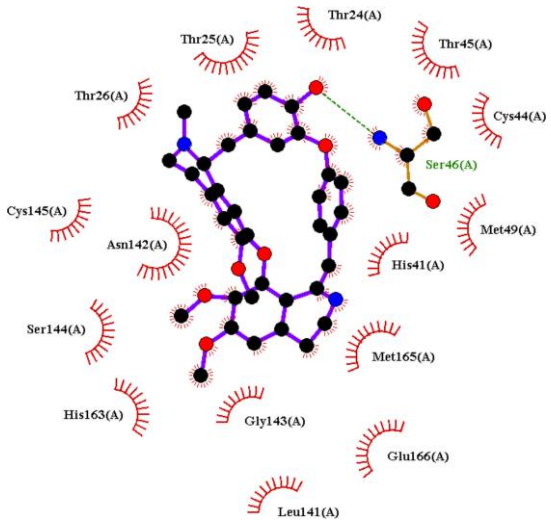

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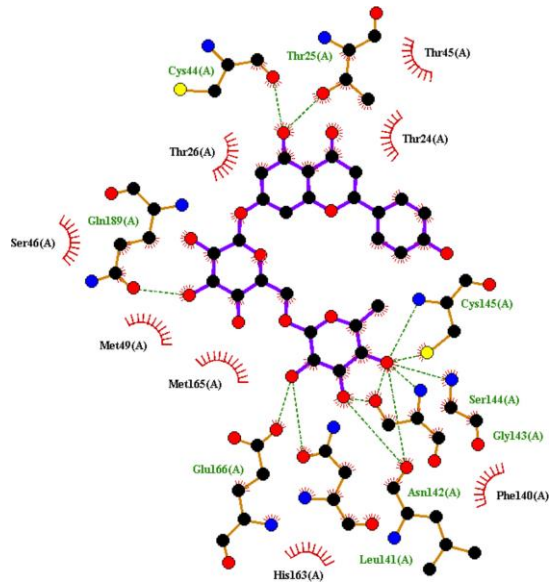

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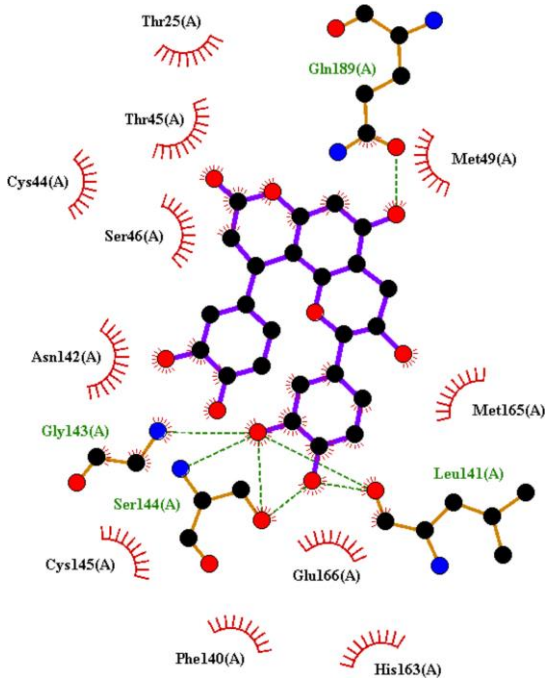

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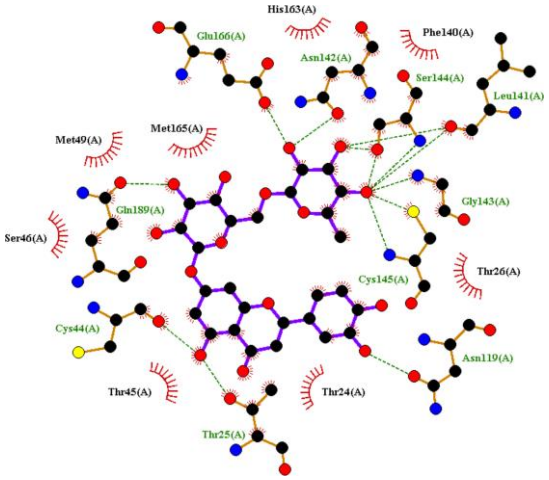

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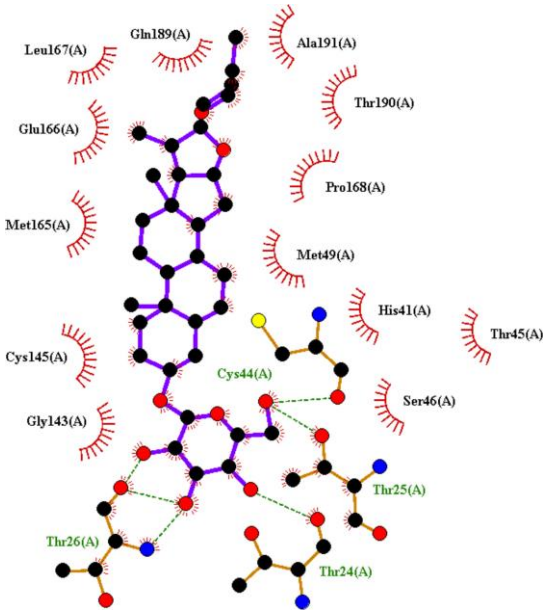

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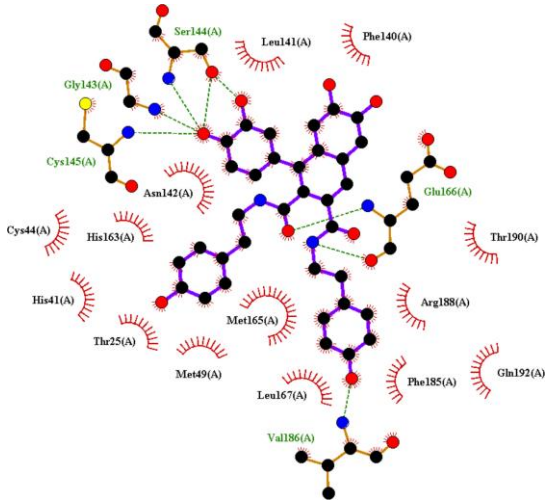

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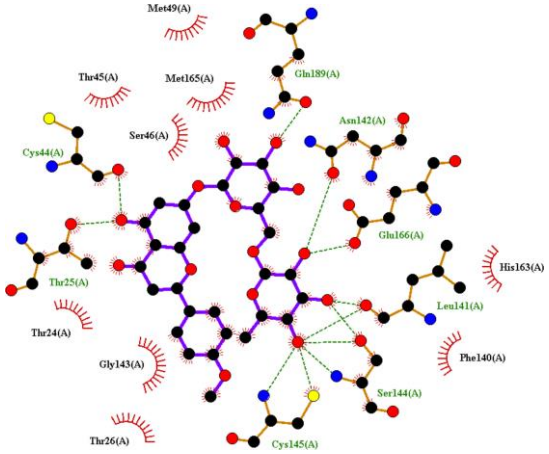

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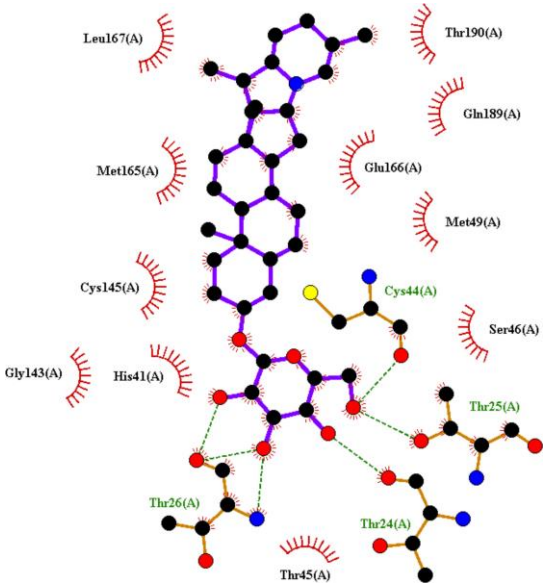

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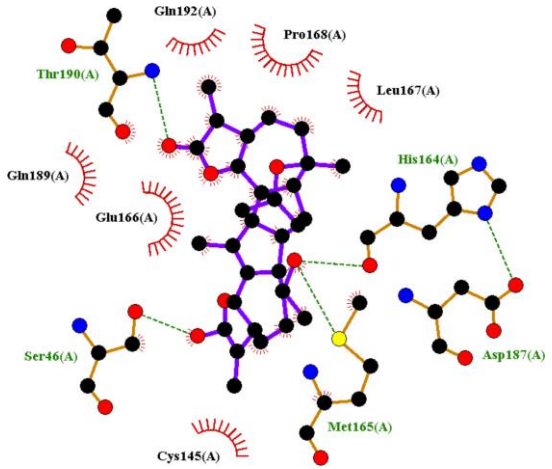

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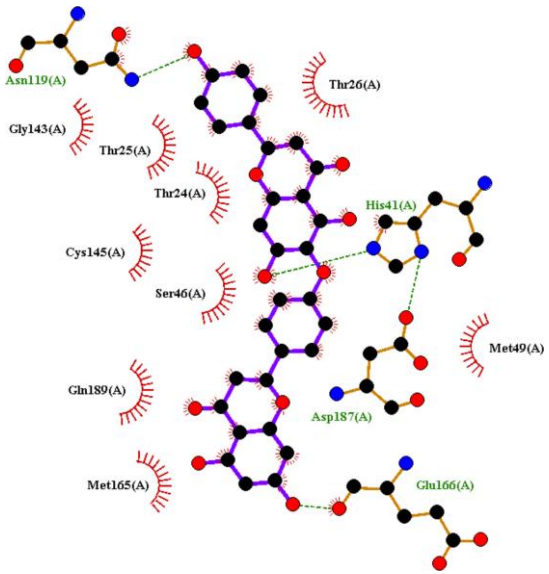

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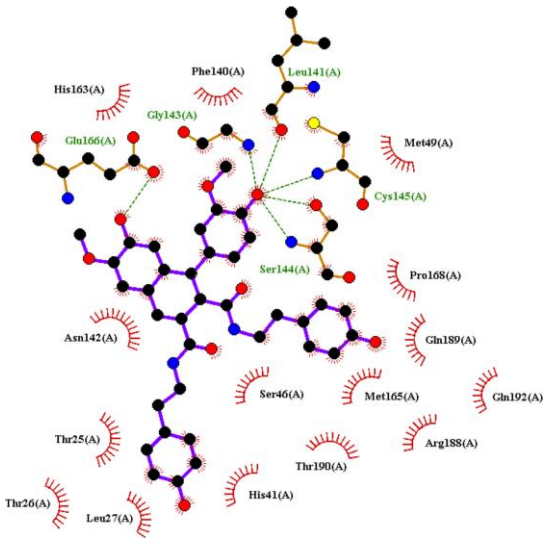

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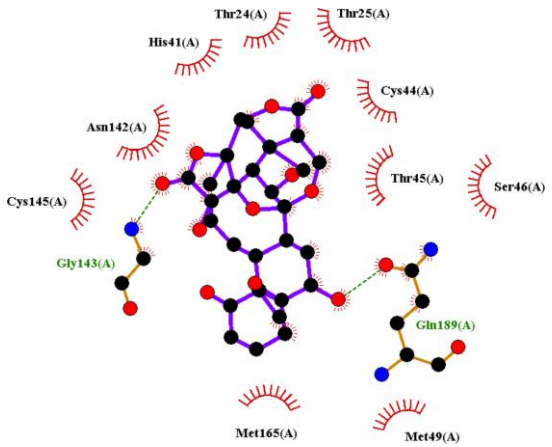

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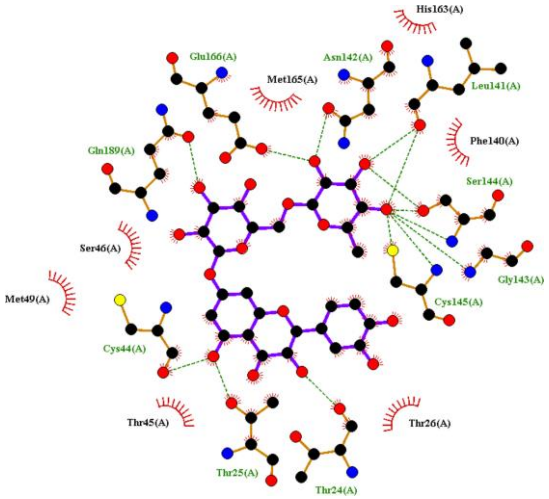

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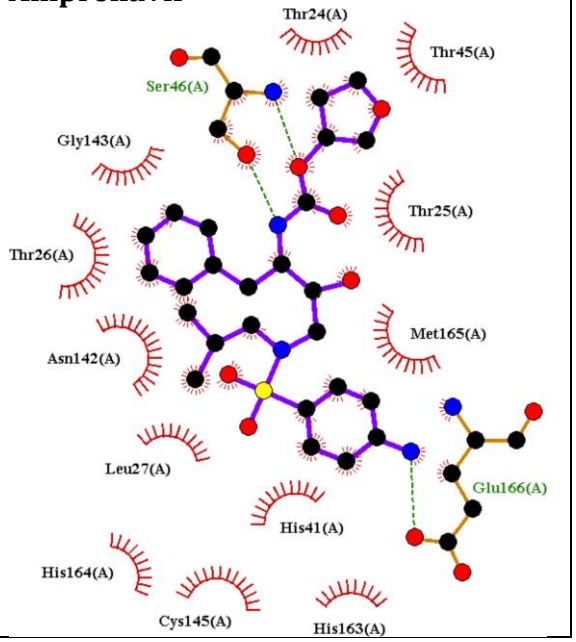

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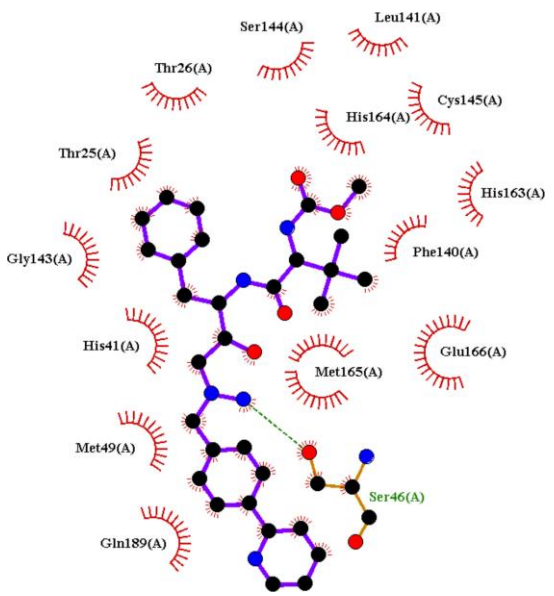

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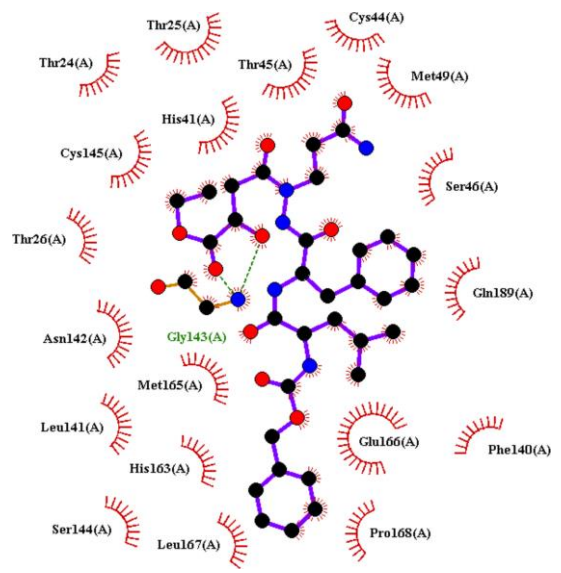

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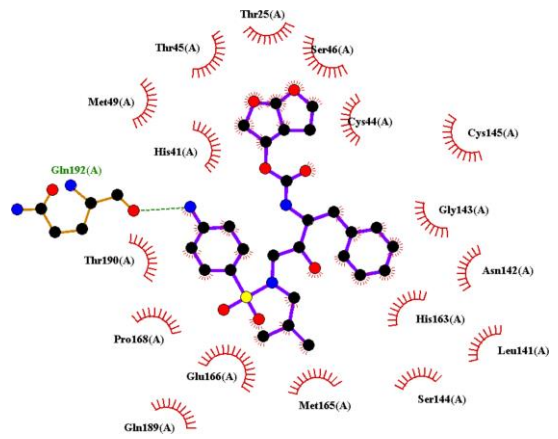

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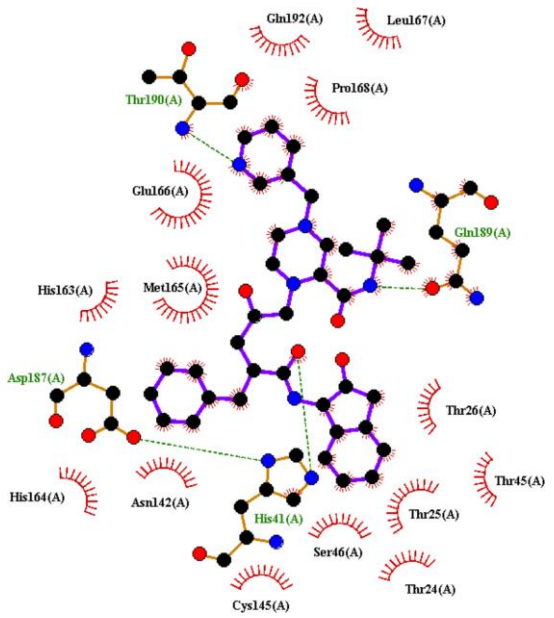

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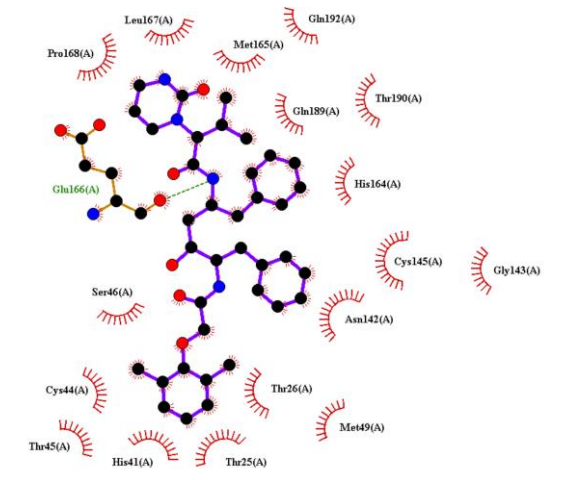

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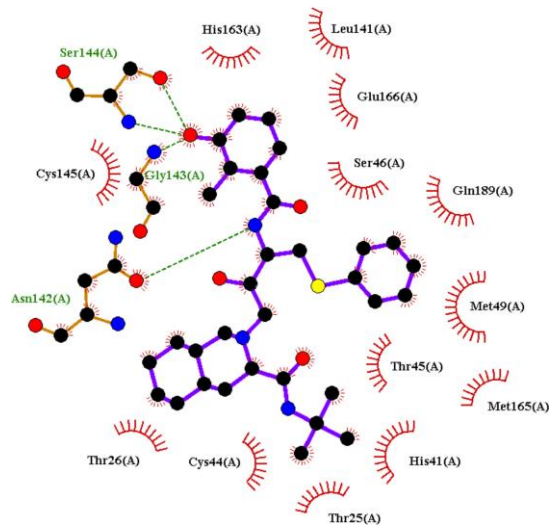

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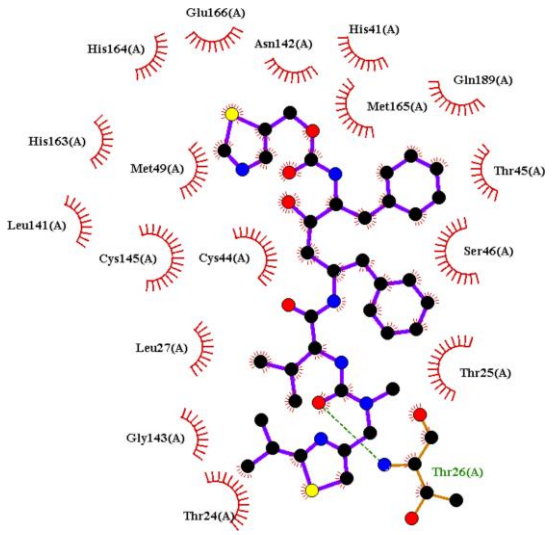
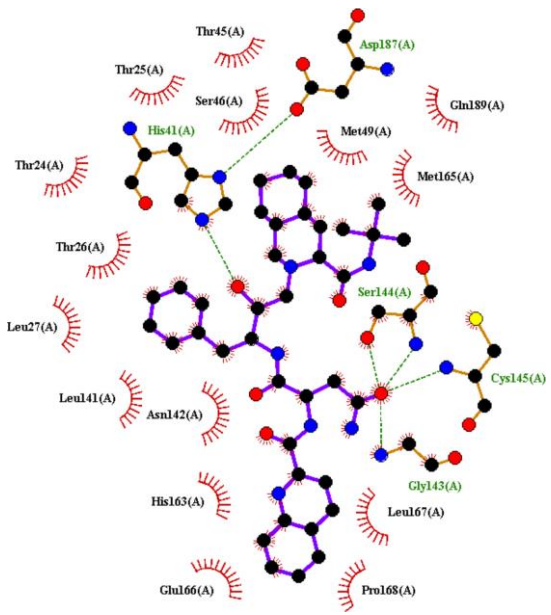
		

[a]The Obtained Results were Prepared via the LigPlot++ package.[1]

Figure S1. Super position between the modelled SARS-COV-2 Mpro[2] and the experimental structure.[3] The C_α RMSD between two structures is of 0.05 nm.

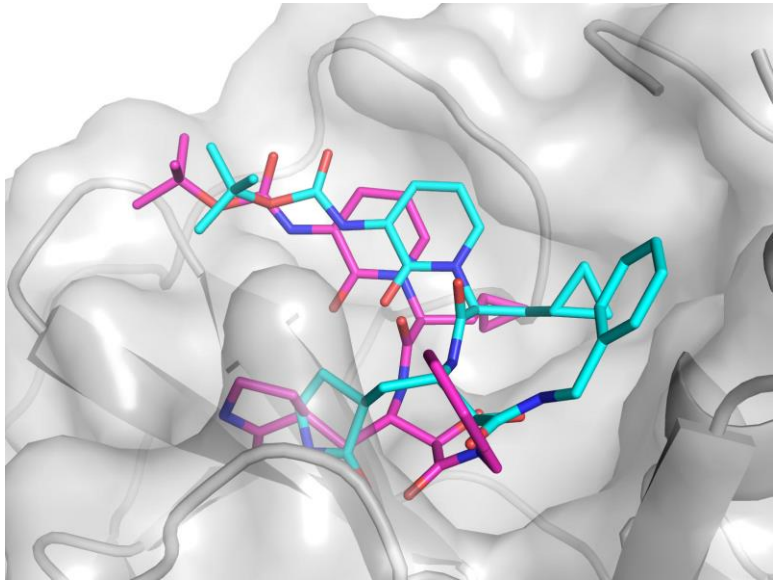
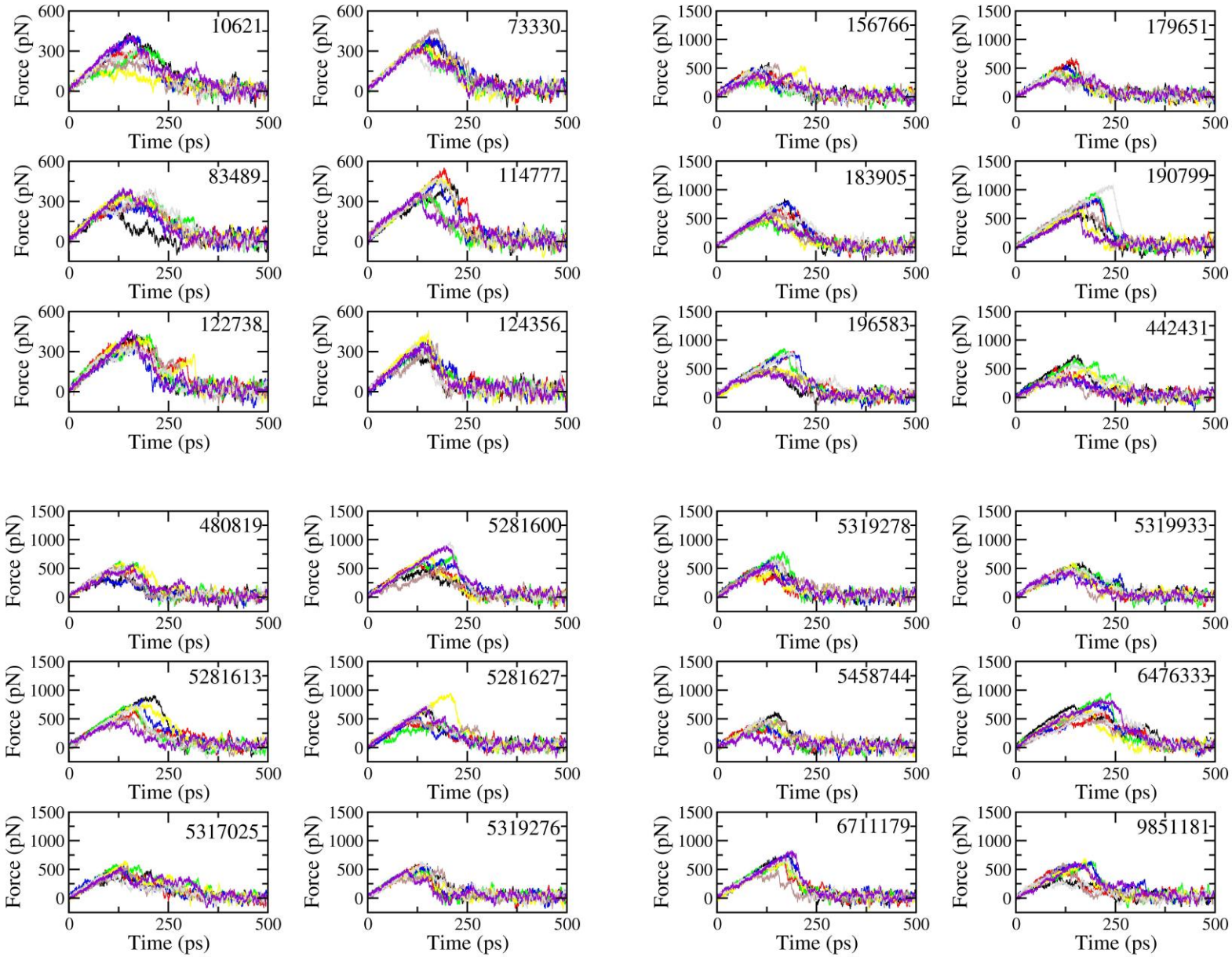


Figure S2. Super position between the experimental (purple)[3] and computational (cyan) poses between compound **13b** and SARS-COV-2 Mpro. The C_α RMSD between two structures is of 0.19 nm.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6711179
9851181
Force (pN)
Time (ps)

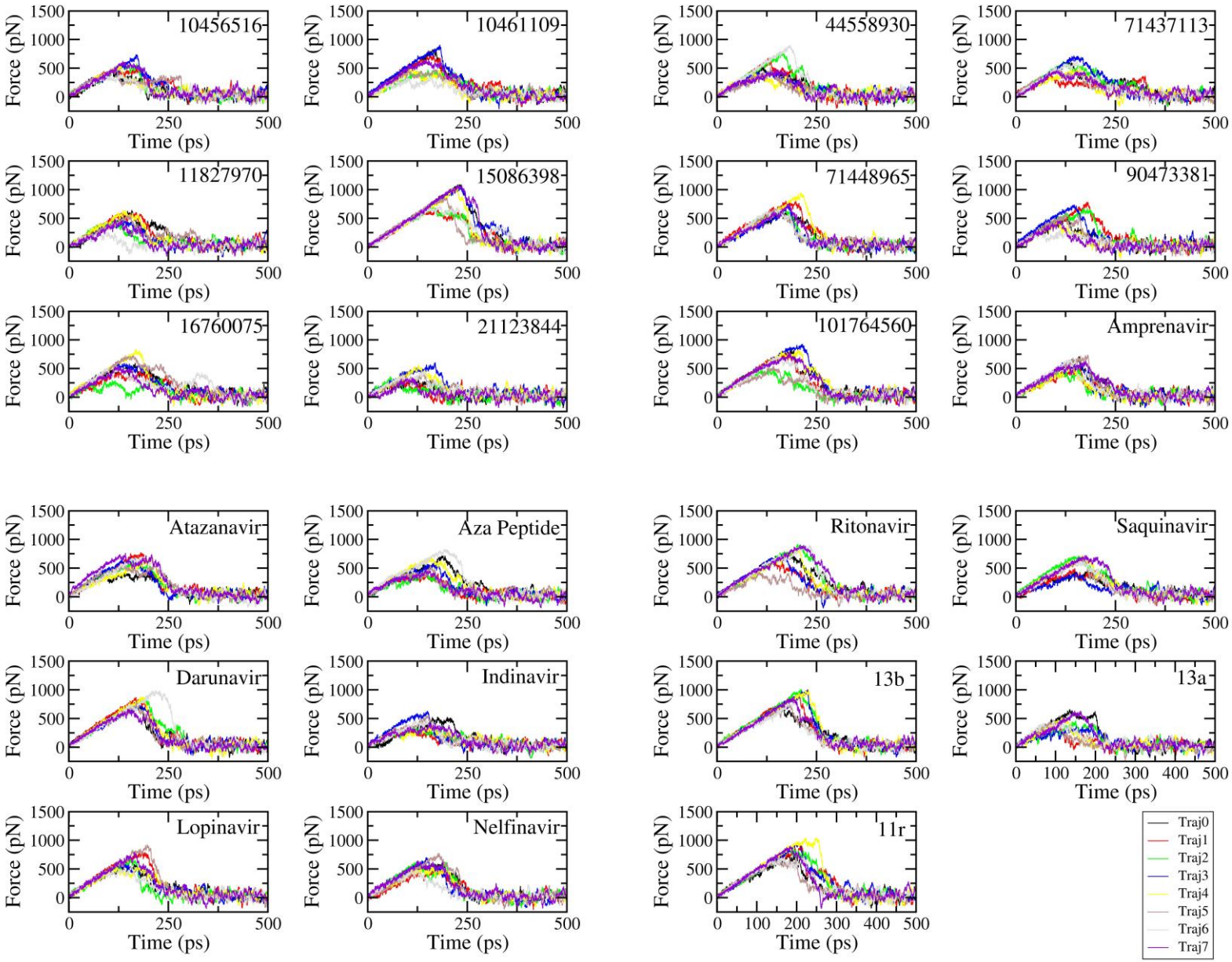

Figure S3. The pulling force in time dependence over 8 independent SMD trajectories.

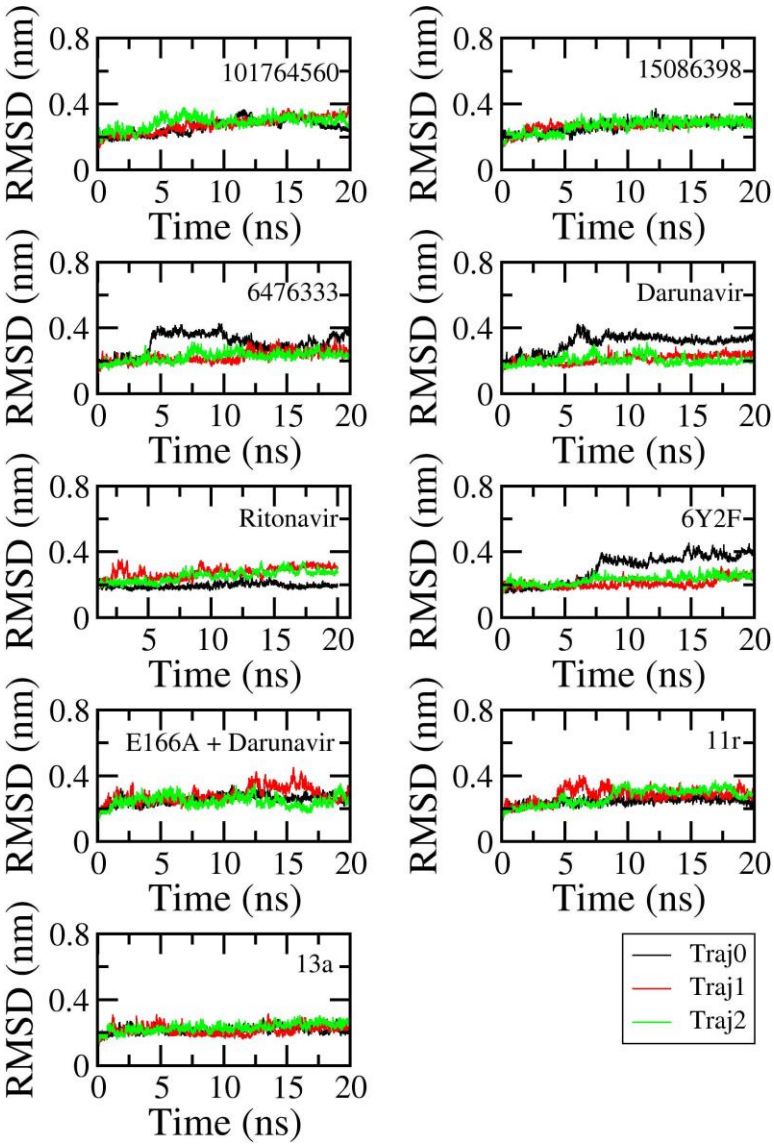

Figure S4. All-atoms RMSD of SARS-COV-2 Mpro + Inhibitors over 3 independent MD simulations with length of 20 ns.

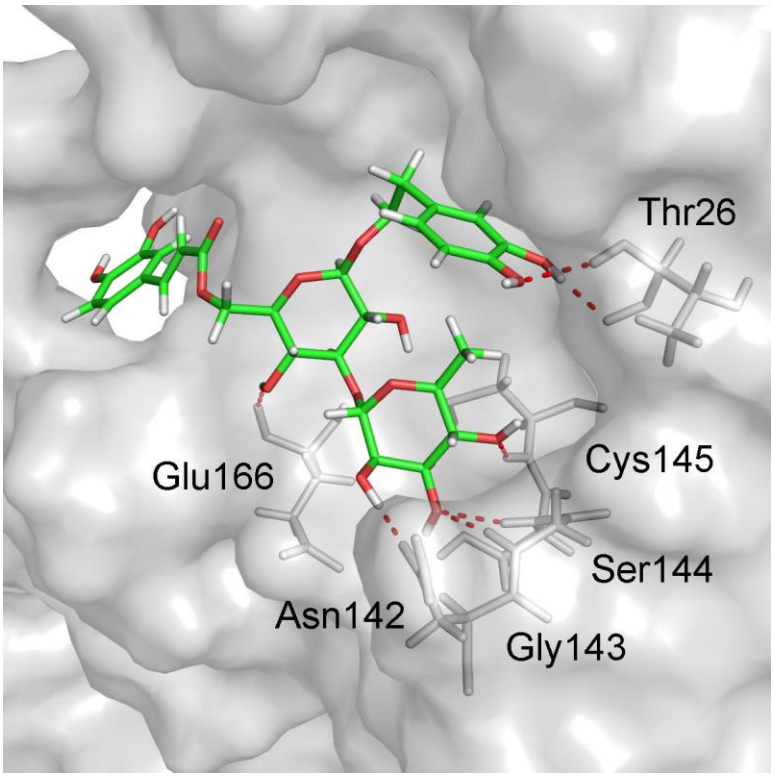

Figure S5. The binding pose of the SARS-COV-2 PR + *isoacteoside* system. This result was obtained by all-atom clustering with a cutoff 0.3 nm using 3000 equilibrium snapshots.

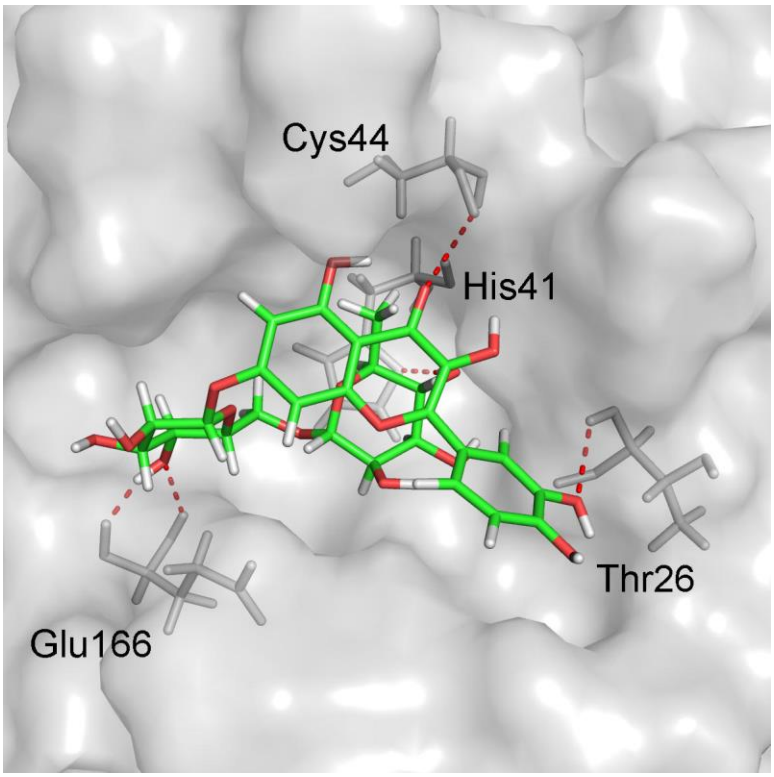

Figure S6. The binding pose of the SARS-COV-2 PR + *quercetin 7-o-rutinoside* system. This result was obtained by all-atom clustering with a cutoff 0.3 nm using 3000 equilibrium snapshots.

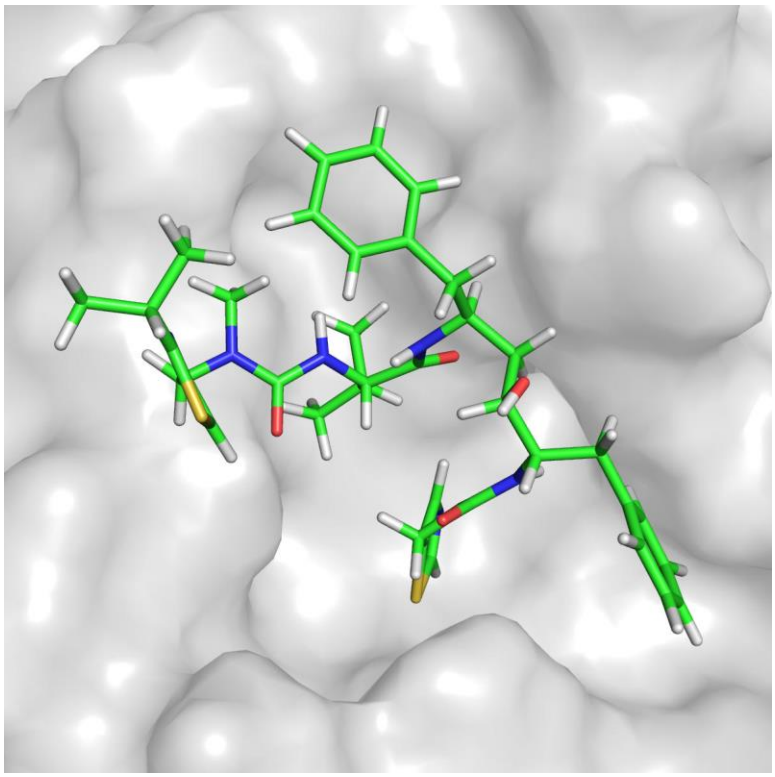

Figure S7. The binding pose of the SARS-COV-2 PR + *ritonavir* system. This result was obtained by all-atom clustering with a cutoff 0.3 nm using 3000 equilibrium snapshots.

Video S1. The dynamics of SARS-CoV-2 Mpro + *cannabisin A* during MD simulations.

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