Supplementary data

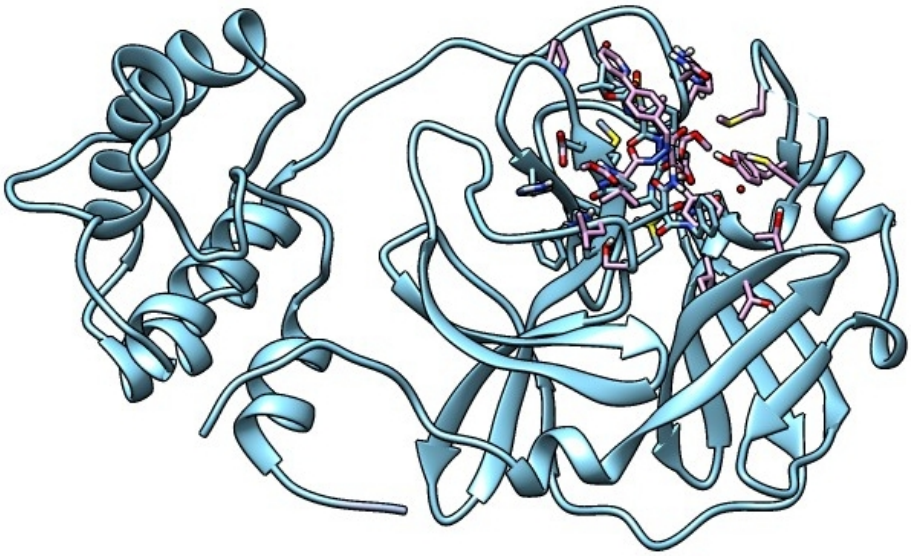


Figure S1: Superimposed protein three dimensional X-ray crystal structures of SARS-CoV-2 M^{pro}, (PDB ID: 6Y2F in blue) and (PDB ID: 5R7Z in light yellow).

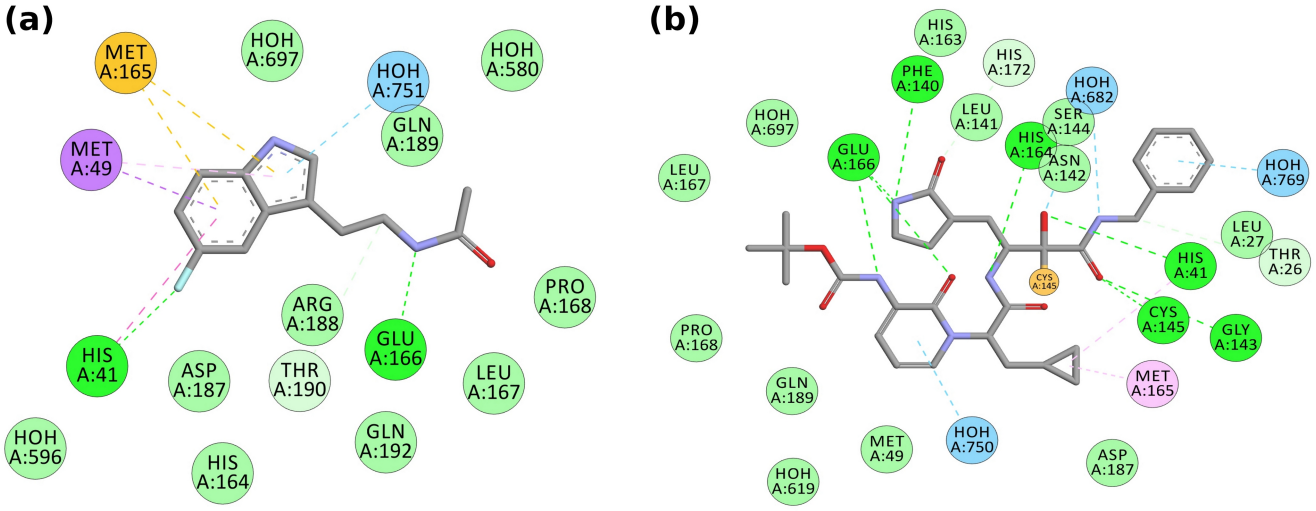
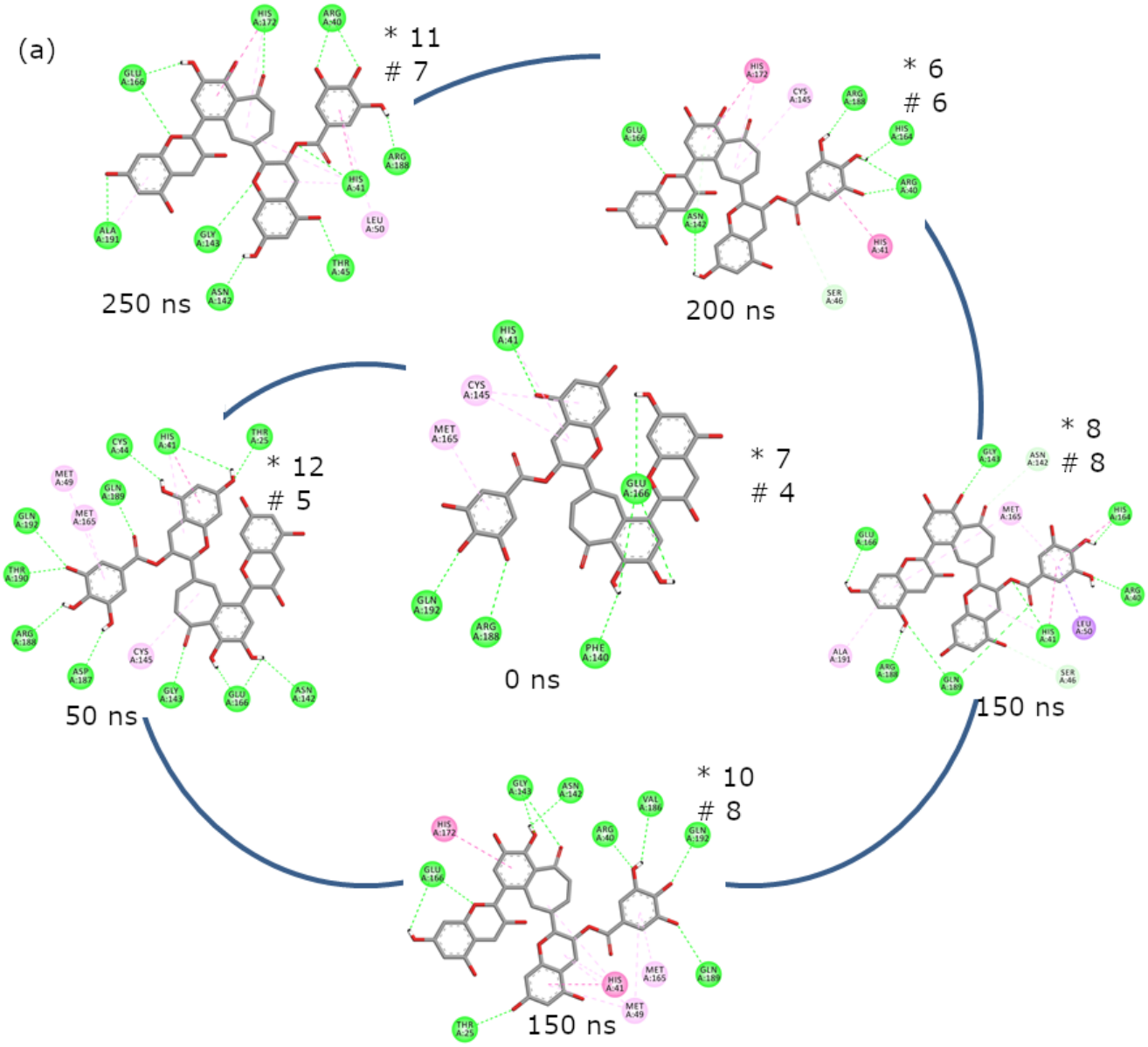
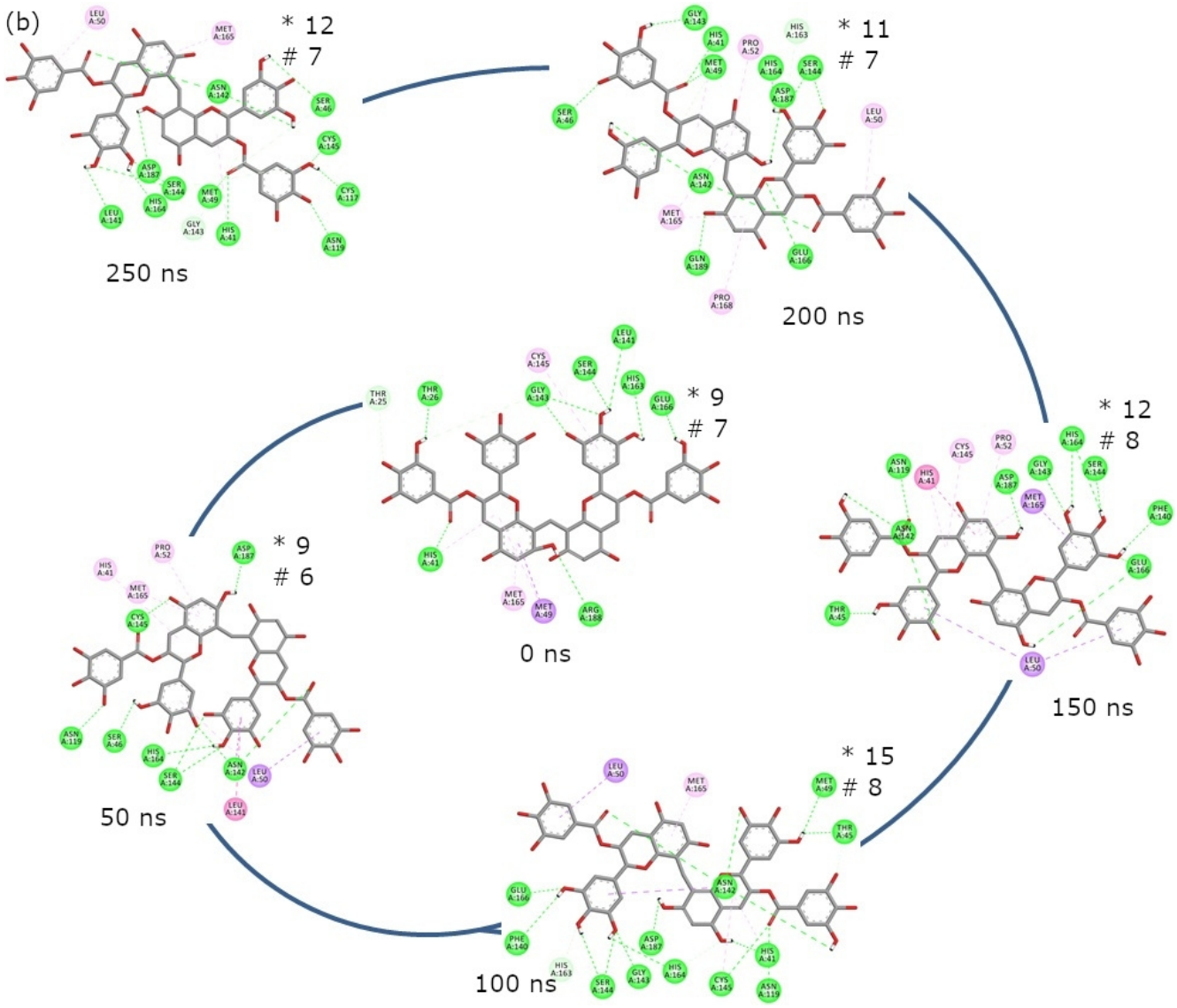
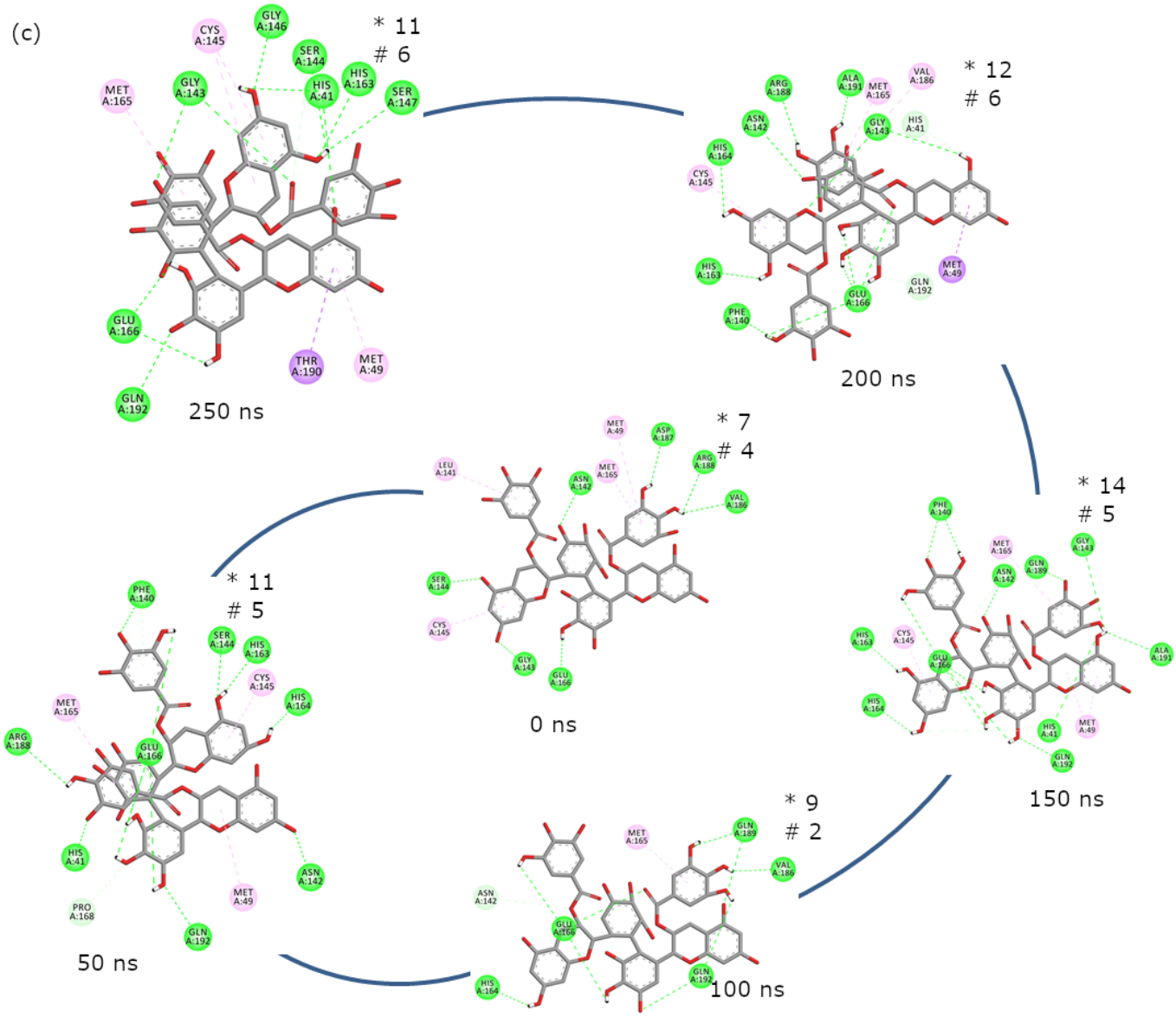


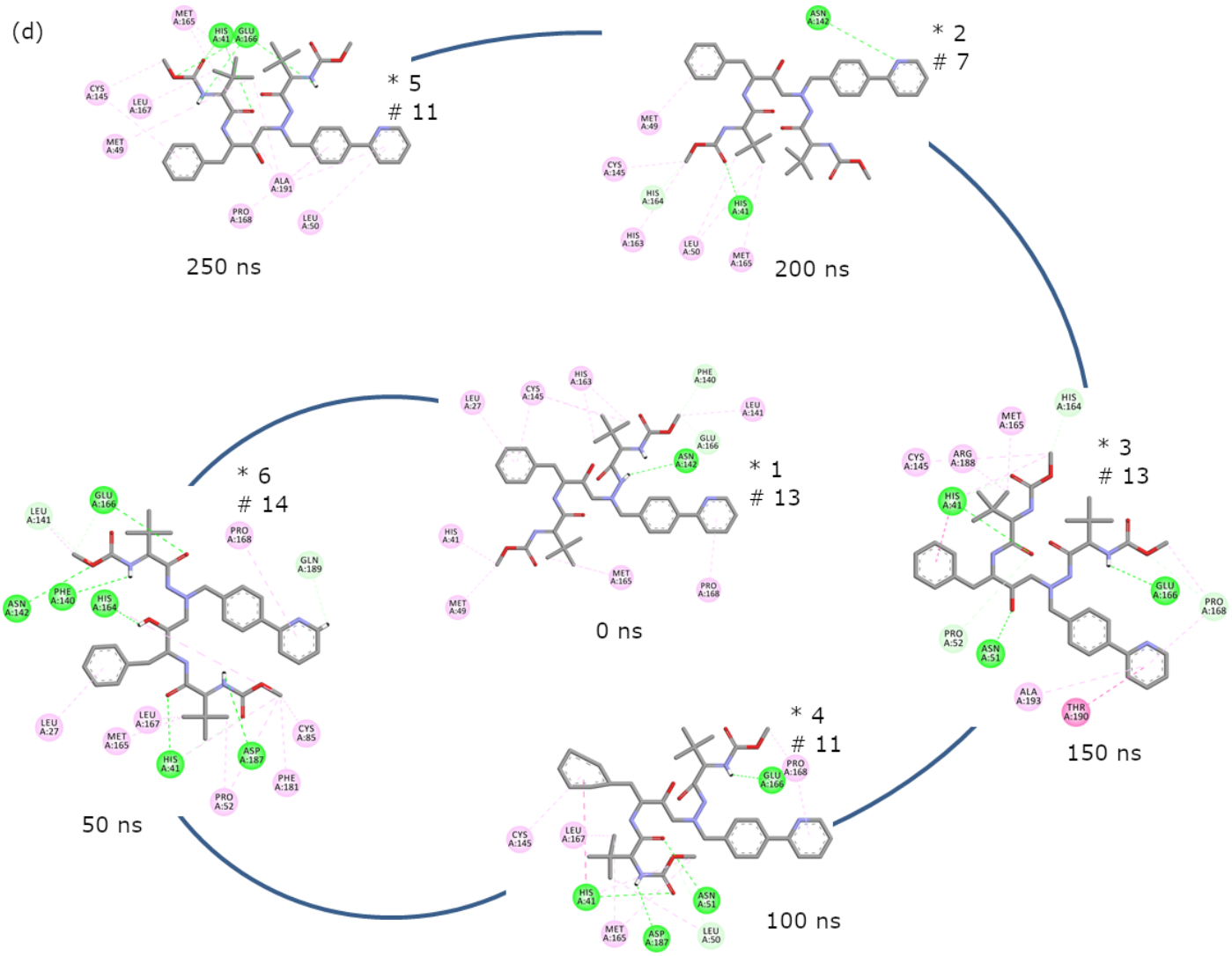
Figure S2: Binding pattern of co-crystallized ligand of SARS-CoV-2 M^{pro}, (a) PDB ID: 5R7Z (b) PDB ID: 6Y2F.

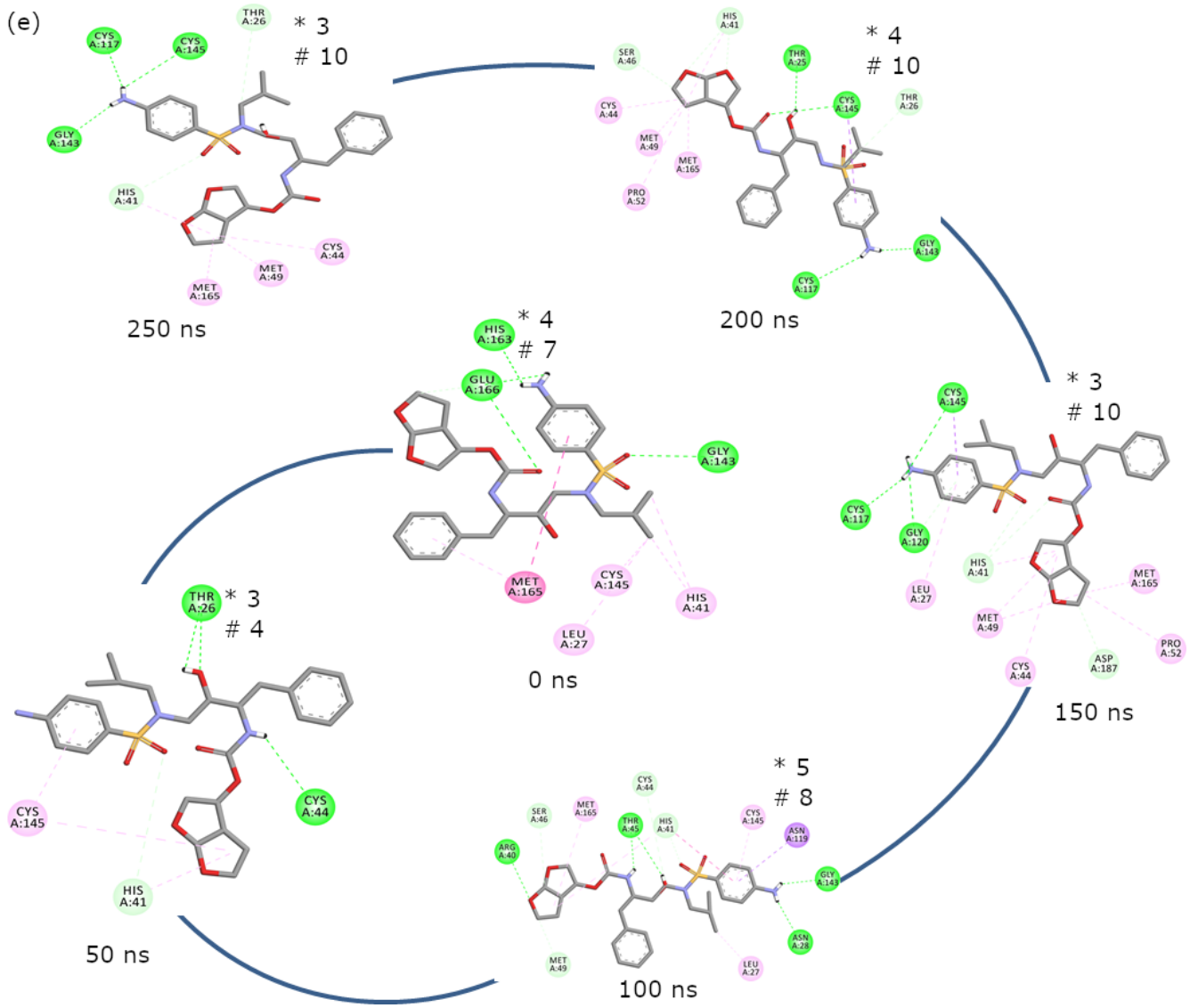

(a)
* 11
# 7
250 ns
* 6
# 6
200 ns
* 8
# 8
150 ns
* 10
# 8
150 ns
* 12
# 5
50 ns
* 7
# 4
0 ns


(b)
* 12
# 7
250 ns
* 11
# 7
200 ns
* 12
# 8
150 ns
* 15
# 8
100 ns
* 9
# 6
50 ns
* 9
# 7
0 ns

(c)




(d)
* 5
# 11
250 ns
* 2
# 7
200 ns
* 3
# 13
150 ns
* 4
# 11
100 ns
* 1
# 13
0 ns
* 6
# 14
50 ns


(e)
* 3
# 10
250 ns
* 4
# 10
200 ns
* 3
# 10
150 ns
* 5
# 8
100 ns
* 3
# 4
50 ns
* 4
# 7
0 ns

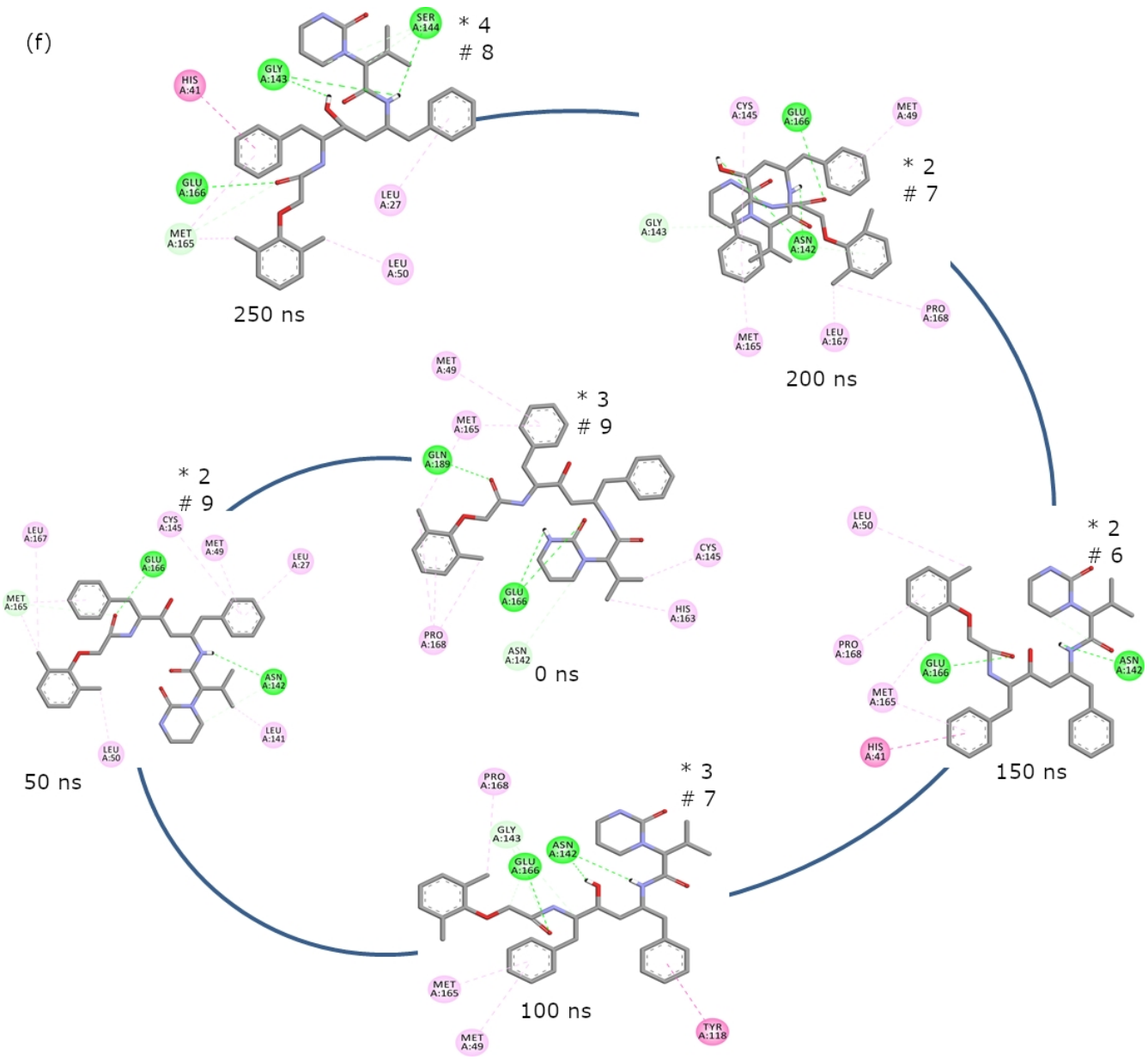


Figure S3: 2D interactions showing hydrogen bonds (green) and hydrophobic interactions (Pink, light pink, blue, and cyan) at different time period of MD-simulations in the binding pocket of the SARS-CoV-2 M^{pro} visualized by Discovery studio. (a) Theaflavin-3-O-gallate (b) Oolonghomobisflavan-A (c) Theasinensin-D (d) Atazanavir (e) Darunavir, and (f) Lopinavir.

* No. of hydrogen bonds

No. of hydrophobic interactions

Table S1: CDOCKER interaction energies of selected 65 bio-active molecules and 3 FDA approved drugs.

S. No.	Molecules	-CDOCKER Interaction Energy
1.	Oolonghomobisflavan A	75.54
2.	Theasinensin D	71.58
3.	Theaflavin-3'-O-Gallate	71.56
4.	Isotheaflavin	71.22
5.	Epigallocatechin-3,5-Di-O-Gallate	66.99
6.	Oolonghomobisflavan B	66.87
7.	Atazanavir	64.85
8.	Epigallocatechin-3,4-Di-O-Gallate	63.33
9.	Vicenin 2	60.82
10.	Epicatechin-3,5-Di-O-Gallate	60.22
11.	Rutin	58.07
12.	Proanthocyanidin	57.83
13.	Pheophytin	56.29
14.	Lopinavir	56.17
15.	Epitheaflavic Acid 3'-Gallate	54.32
16.	Epigallocatechin Gallate	53.14
17.	Theasinensin E	52.96
18.	Myricitrin	52.69
19.	Theaflavin	52.63
20.	Epicatechin Gallate	51.99
21.	Kaempferitrin	51.04
22.	Isoquercetin	48.84
23.	Epiafzelechin 3-O-Gallate	48.34
24.	Pheophorbide	47.31
25.	Epigallocatechin 3-O-P-Coumarate	46.53
26.	Pheophorbide	46.34
27.	Darunavir	46.02
28.	Cryptoxanthin	45.08
29.	Isovitexin	44.92
30.	Vitexin	44.63
31.	Chlorogenic Acid	42.95
32.	Coumaroyl Quinic Acid	42.94
33.	Epigallocatechin	42.09
34.	Theaflavic Acid	40.64
35.	Barrigenol R1	40.63
36.	Barringtogenol	40.14
37.	Camelliagenin	39.18
38.	Gallocatechin	39
39.	Catechin	36.99
40.	Epicatechin	36.39
41.	Epiafzelechin	33.85
42.	Quercetin	33.59
43.	Cryptoxanthin	33.42
44.	Myricetin	33.3

45.	Apigenin	33.25
46.	Nerolidol	33.11
47.	Kaempferol	32.04
48.	Theanine	31.93
49.	Ascorbic Acid	30.14
50.	Quinic Acid	29.07
51.	Succinic Acid	25.3
52.	Methyl Salicylate	25.19
53.	Theobromine	24.36
54.	Caffeine	24.21
55.	Xanthine	23.73
56.	Linalool Oxide	23.71
57.	Phenylacetaldehyde	23.02
58.	Methylxanthine	22.66
59.	Theophylline	22.38
60.	Geraniol	21.81
61.	Hexanal	21.32
62.	Diphenylamine	20.57
63.	Trans-2-Hexenal	20.22
64.	Linalool	20.19
65.	Phenylethanol	18.82
66.	Cis-3-Hexenol	18.21
67.	Benzaldehyde	18.2
68.	Oxalic Acid	17.91

Table S2: Energy contribution of the key residues computed by MM-PBSA method.

S. No.	Molecules	Residues with contribution energy (kJ/mol)
1.	Atazanavir	HIS41 (-3.82), MET49 (-10.69), MET165 (-14.52), GLU166 (-4.29)
2.	Darunavir	HIS41 (-6.83), MET165 (-10.14), GLU166 (-3.11)
3.	Lopinavir	LEU50 (-9.52), MET165 (-10.30), GLU166 (-4.33)
4.	Oolonghomobisflavan-A	MET49 (-15.47), PHE140 (-12.08), MET165 (-4.90), GLU166 (-18.58)
5.	Theasinensin-D	LEU50 (-10.89), PHE140 (-8.43), MET165 (-10.97), GLU166 (-6.02)
6.	Theaflavin-3'-O-Gallate	HIS41 (-6.79), LEU50 (-10.50), MET165 (-17.60), GLU166 (-17.00)