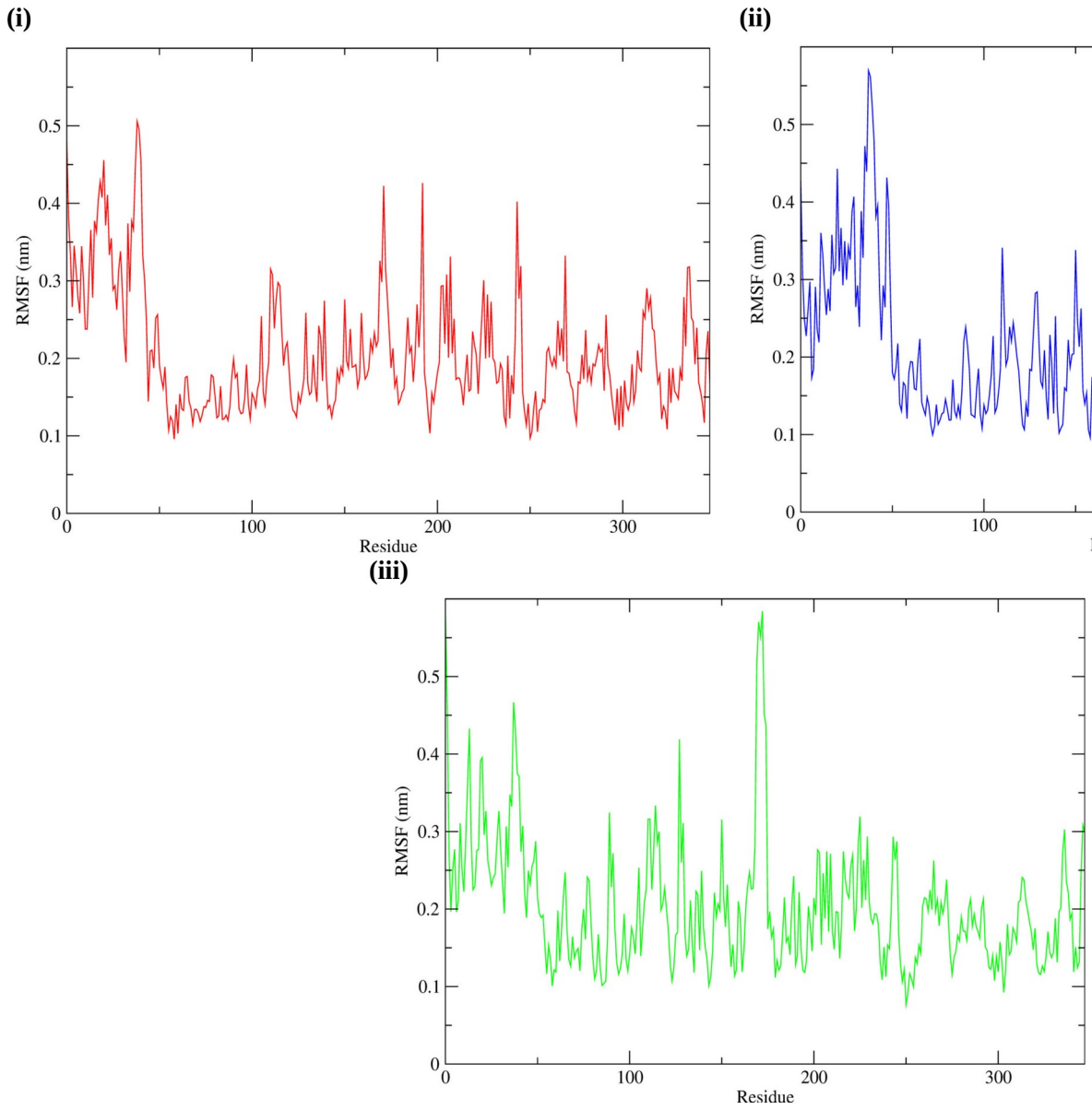
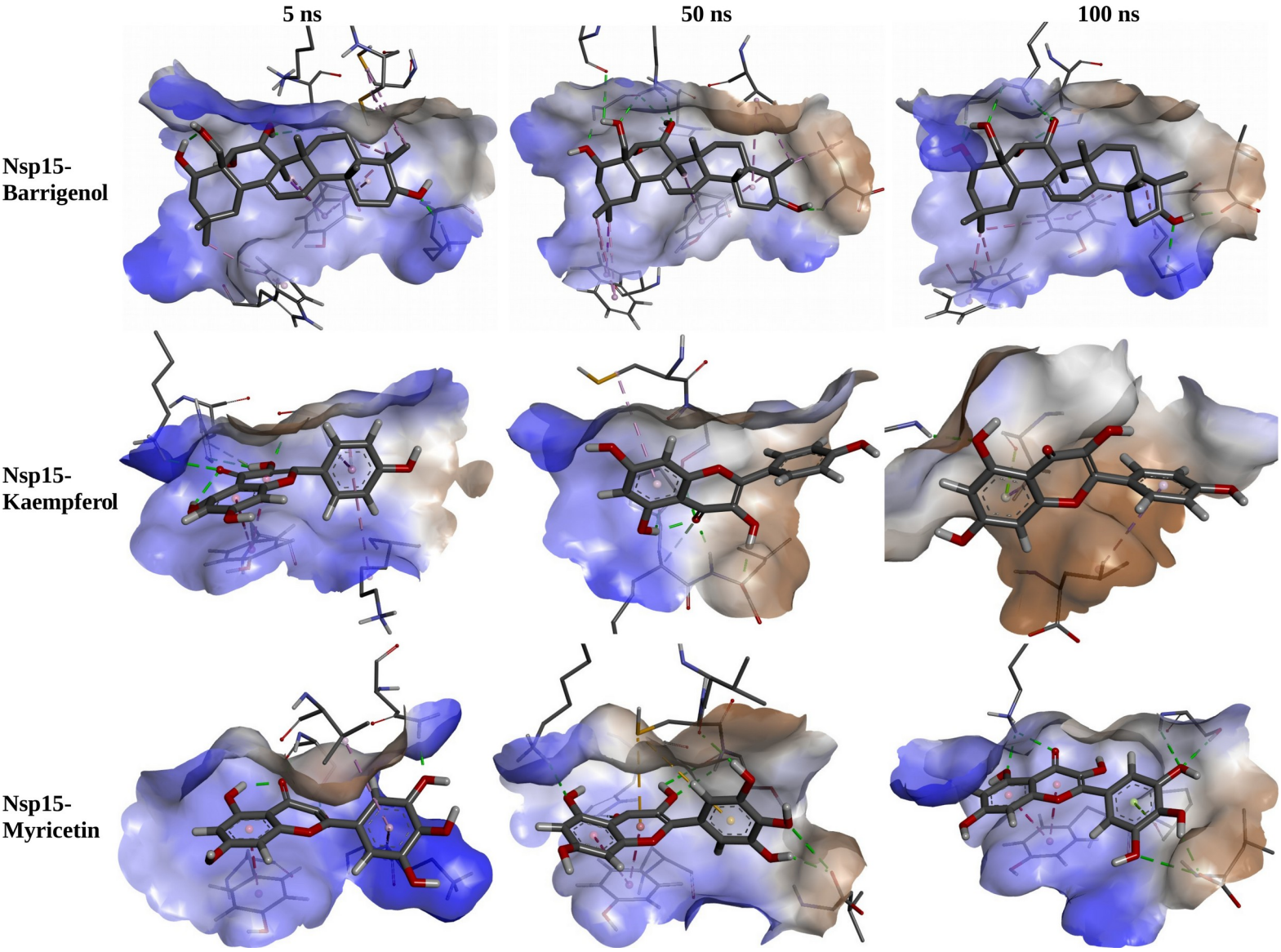
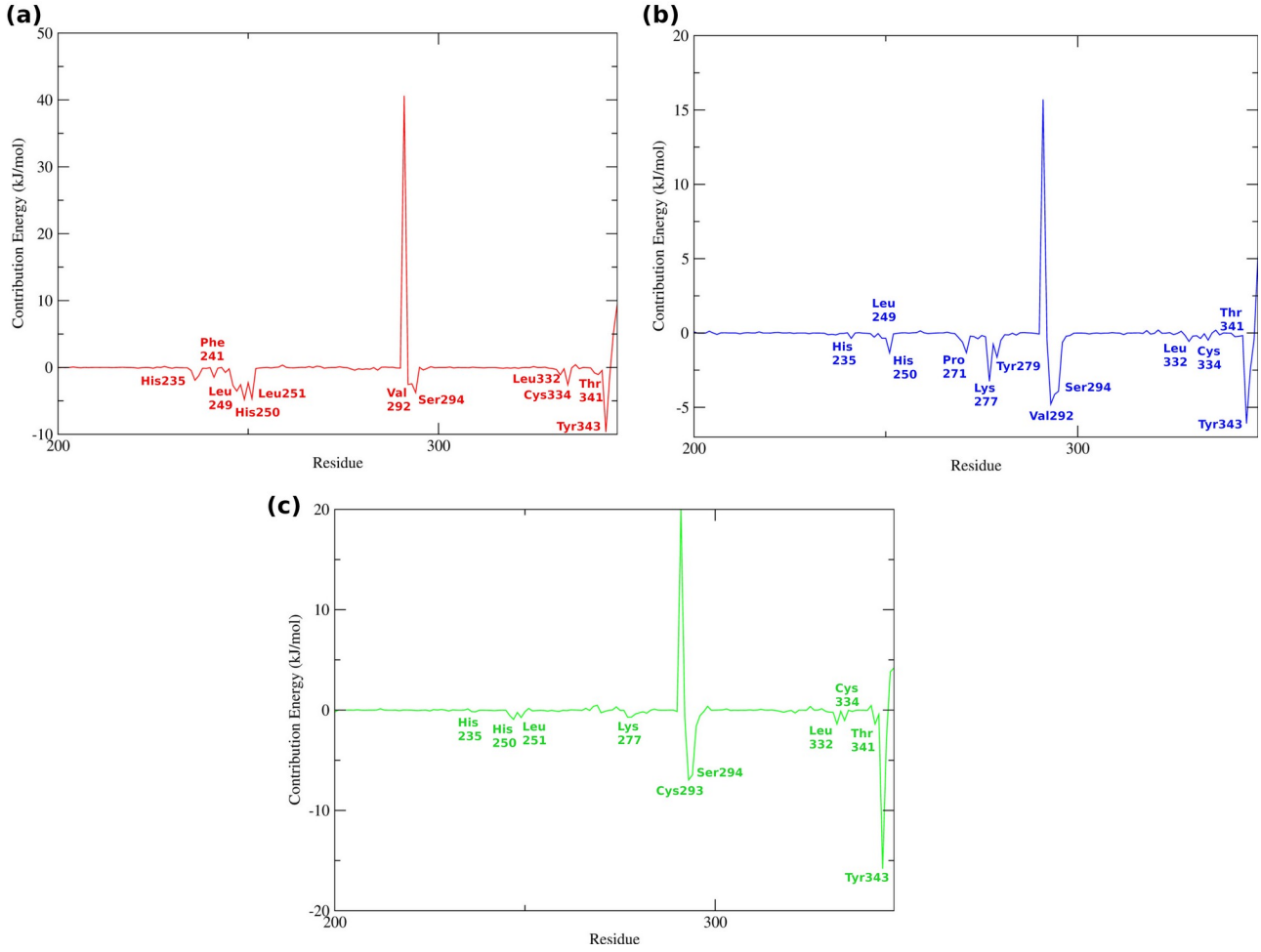


Supplementary Figure S1: RMSF of the Nsp15 residues towards the bioactive moleules : (i)Nsp15-Barrrigenol (Red) (ii)Nsp15-Kaempferol (Blue) (iii)Nsp15-Myricetin (Green)



Supplementary Figure S2: Interactions pattern of the three bioactive molecues inside the active site of Nsp15 in 3D conformational space also showing the hydrophobic interaction surface at the beginning, middle, and end of MD-simulations visualized by Discovery studio.



Supplementary figure S3: Graphical representation of per residue contribution energy of the active site of Nsp15 in complex with bioactives: (i)Nsp15-Barrrigenol (Red) (ii)Nsp15-Kaempferol (Blue) (iii)Nsp15-Myricetin (Green)

Supplementary Table 1: 65 bioactive molecules depicting the total binding energies obtained after docking.

S. No.	Name	Total Binding Energies
1.	Barrigenol	-15.9
2.	Kaempferol	-12.99
3.	Myricetin	-11.9
4.	Theanine	-11.78
5.	Methyl Salicylate	-11.74
6.	Linalool Oxide	-11.27
7.	Epicatechin	-10.53
8.	Quercetin	-10.37
9.	Apigenin	-10
10.	Succinic Acid	-9.88
11.	Coumaroyl Quinic Acid	-9.76
12.	Hexanal	-9.22
13.	Catechin	-9.07
14.	Epigallocatechin	-9.07
15.	Linalool	-8.87
16.	Vitexin	-8.51
17.	Phenylethanol	-7.45
18.	Epicatechin Gallate	-7.41
19.	Geraniol	-6.58
20.	Nerolidol	-6.31
21.	Kaempferitrin	-6.22
22.	Phenylacetaldehyde	-5.9
23.	cis-3-Hexenol	-5.26
24.	Theobromine	-5.08

25.	Caffeine	-4.44
26.	trans-2-Hexenal	-3.57
27.	Theophylline	-3.45
28.	Benzaldehyde	-3.33
29.	Epiafzelechin 3-O-gallate	-2.52
30.	Vicenin	-2.46
31.	Barringtogenol	-2.43
32.	Oxalic Acid	-2.43
33.	Epiafzelechin	-2.29
34.	Quinic Acid	-2.2
35.	Theaflavic Acid	-2.15
36.	Methylxanthine	-2
37.	Ascorbic Acid	-1.49
38.	Gallocatechin	-1.08
39.	Pheophytin	-0.87
40.	Theaflavin	-0.65
41.	Xanthine	-0.61
42.	Epigallocatechin Gallate	-0.55
43.	Isovitexin	-0.24
44.	Theasinensin E	0.28
45.	Rutin	0.69
46.	Chlorogenic Acid	0.79
47.	Isoquercetin	2.57
48.	Diphenylamine	3.89
49.	Epitheaflavic Acid 3-gallate	4.34
50.	Saponarin	4.4
51.	Epicatechin-3,5-di-O-gallate	4.68

52.	Epigallocatechin-3-O-p-coumarate	5.16
53.	Epigallocatechin-3,4-di-O-gallate	6.01
54.	Epigallocatechin-3,5-di-O-gallate	8.49
55.	Camelliagenin	8.49
56.	Cryptoxanthin	9.23
57.	Oolonghomobisflavan A	No Pose Generated
58.	Oolonghomobisflavan B	No Pose Generated
59.	Theasinensin D	No Pose Generated
60.	Theaflavin-3'-O-Gallate	No Pose Generated
61.	Isotheaflavin	No Pose Generated
62.	Theasinensin F	No Pose Generated
63.	Proanthocyanidin	No Pose Generated
64.	Myricitrin	No Pose Generated
65.	Pheophorbide	No Pose Generated

Supplementary Table 2. The interactions between the residues involved in the binding of the selected bioactive molecules with the Nsp15 of SARS-CoV2.

Interactions	Interacting resudues with Barrigenol	Interacting resudues with Kaempferol	Interacting resudues with Myricetin
Conventional Hydrogen bond	Lys290, His235	His250, Lys290, Val292, His235, Thr341	His250, Lys290, Val292, His235, Thr341
Carbon Hydrogen bond	Nil	His250, Lys290	His250, Lys290
Pi-Pi stacked	Nil	Tyr343	Tyr343
Pi-alkyl/alkyl	Val292, Tyr343	Val292	Val292

Supplementary Table 3: Observed contribution energies for the binding site residues of NSP15 towards the ligand molecules

	NSP-15				
Ligands	His235	His250	Ser294	Thr341	Tyr343
Barrigenol	-1.9074	-1.9074	-3.7616	-1.0588	-9.6295
Kaempferol	-0.0871	-1.3389	-3.9235	-0.2284	-6.0896
Myricetin	-0.1470	-0.1591	-6.47	-1.4008	-15.8175