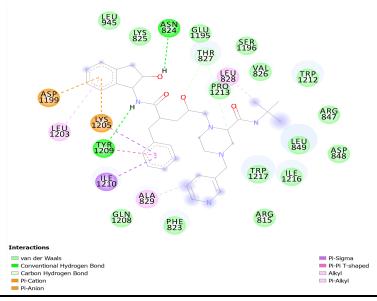
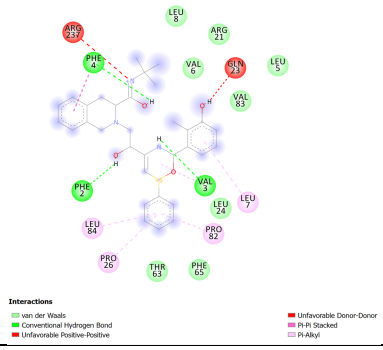
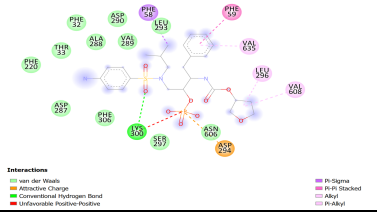
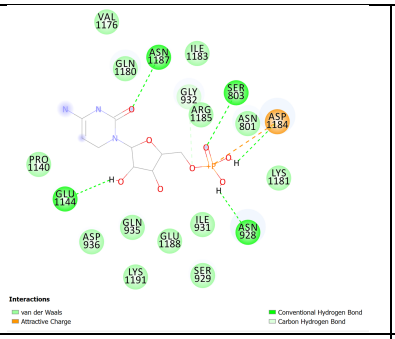
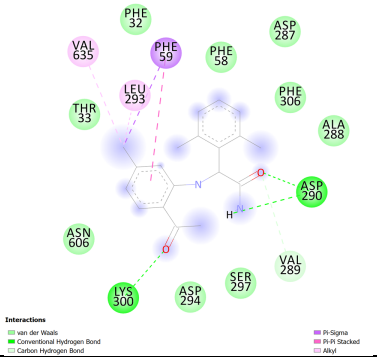
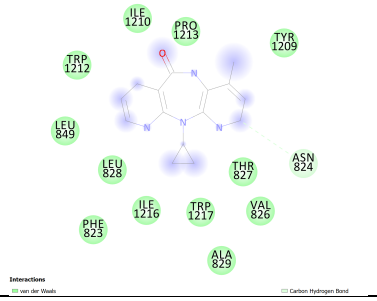
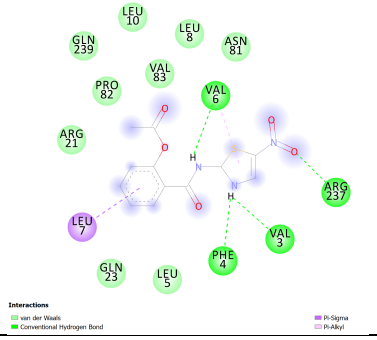
Supplementary Tables

Table S1: List of the ten top hits of antiviral drugs against SARS-CoV-2 Spike protein by order of lowest to highest binding energy value. Indinavir seems to exhibit the lowest binding energy (-9.8 kcal/Mol) when docked with Spike protein, whereas Cobicistat exhibits the highest binding energy (-6.37 kcal/Mol).

	Antivirals	**Binding energy (kcal/Mol)**	**2D interaction**	**Interface amino acids**	**Type of interactions**
1	Indinavir (C36H47N5O4), 5362440	-9.8		Ala, 2Arg, Asn, 2Asp, Gln, Glu, 2Ile, 4Leu, 2Lys, Phe, Pro, Ser, Thr, 2Trp, Tyr	1Alk, 1CHB, 2HB, 1Pi-An, 3Pi-Alk, 1Pi-Cat, 2Pi-Sig,1Pi-Pi-T, 14VW
2	Nelfinavir (C32H45N3O4S), 64143	-9		2Arg, Gln, 5Leu, 3Phe, 2Pro, Thr, 3Val	3HB, 5Pi-Alk, Pi-Pi-Stk, 7VW, 1UDD, 1UPP
3	Fosamprenavir (C25H36N3O9PS), 131536	-8.2		Ala, Asn, 3Asp, 5Phe, 2Leu, Lys, Ser, 3Val	1AC, 2Alk, 1HB, 1Pi-Alk, 1Pi-Pi-Stk, 1Pi-Sig, 1UPP, 11VW
4	Rintatolimod (C28H40N9O25P3), 135537060	-7.6		Arg, 3Asn, 2Asp, 2Gln, 2Glu, Gly, 2Ile, 2Lys, Pro, 2Ser, 1Val	1AC, 1CHB, 5HB, 14VW

					
5	Loviride (C17H16Cl2N2O2), 3963	-7.3		Ala, Asn, 3Asp, Leu, Lys, 4Phe, Ser, Thr, 2Val	2Alk, 1CHB, 3HB, 1Pi-Pi-Stk, 1Pi-Sig, 9VW
6	Nevirapine (C15H14N4O), 4463	-7.3		Ala, Asn, 2Ile, 2Leu, Phe, Pro, Thr, 2Trp, Tyr, Val	1CHB,12VW
7	Nitazoxanide (C12H9N3O5S), 41684	-7.1		2Arg, Asn, 2Gln, Phe, Pro, 4Leu, 3Val	4HB,12Pi-Alk, 1Pi-Sig, 9VW
8	Imiquimod (C14H16N4), 57469	-6.8		Asn, Ile, 2Leu, Lys, Phe, Pro, Thr, Trp, Tyr, Val	2Alk, 2HB, 1Pi-Alk, 5VW

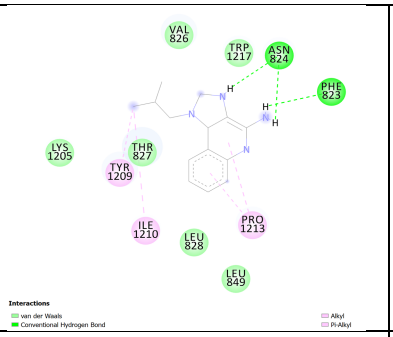
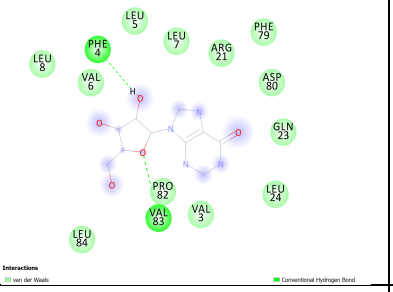
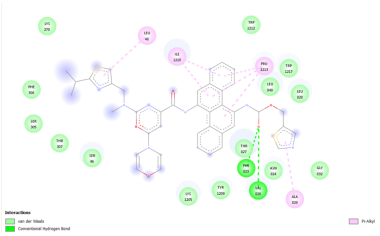
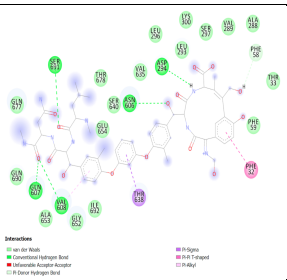
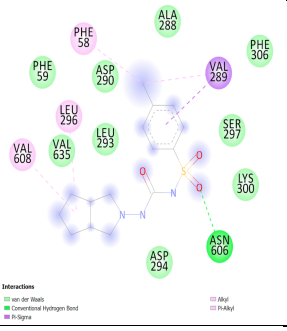
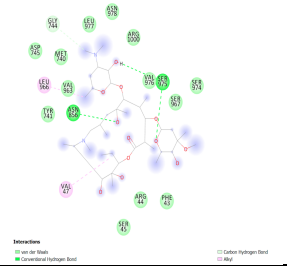
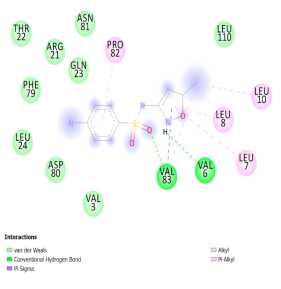
					
9	Inosine (C10H12N4O5), 135398641	-6.5		Arg, Asp, 5Leu, 2Phe, Pro, 3Val	2HB, 12VW
10	Cobicistat (C40H53N7O5S2), 25151504	-6.37		1Ala, 1Asn, 1Gly, 1Ile, 3Leu, 2Lys, 2Phe, 1Pro, 2Ser, 2Thr, 2Trp, 1Tyr, 1Val	2HB, 7Pi-Alk, 14VW

Table S2: List of the ten top hits of antibiotics drugs against SARS-CoV-2 Spike protein by order of lowest to highest binding energy value. Vancomycin seems to exhibit the lowest binding energy (-10.2 kcal/Mol) when docked with Spike protein, whereas Levofloxacin exhibits the highest binding energy (-5.11 kcal/Mol).

	Antibiotics	**Binding energy (kcal/ Mol)**	**2D interaction**	**Interface amino acids**	**Type of interactions**
1	Vancomycin (C66H75Cl2N9O24), 14969	-10.2		2Ala, Asn, Asp, 3Gln, Glu, Gly, Ile, 2Leu, Lys, 3Phe, 3Ser, 3Thr, 2Val	5HB, 1Pi-Alk, 1Pi-DHB, 1Pi-Pi-T, 1Pi-Sig, 17VW
2	Gliclazide (C15H21N3O3S), 3475	-8.6		Ala, Asn, 2Asp, 2Leu, Lys, 3Phe, Ser, 2Val	3Alk, 1HB, 1Pi-Alk, 1Pi-Sig, 9VW
3	Azithromycin (C38H72N2O12), 447043	-7.9		2Arg, 2Asn, Asp, Gly, 2Leu, Met, Phe, 4Ser, Tyr, 3Val	2Alk, 1CHB, 3HB, 13VW
4	Sulfamethoxazole (C10H11N3O3S), 5329	-6.6		Arg, Asn, Asp, Gln, 5Leu, Phe, Pro, Thr, 3Val	3Alk, 2HB, 3Pi-Alk, 1Pi-Sig, 9VW

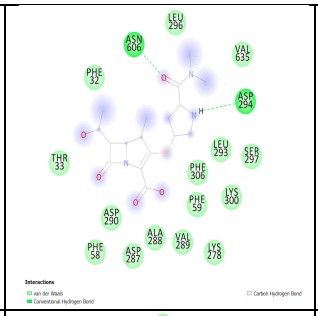
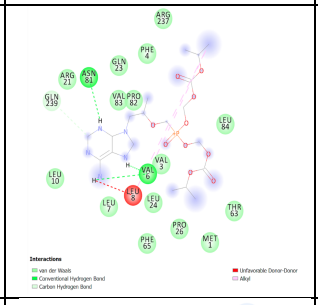
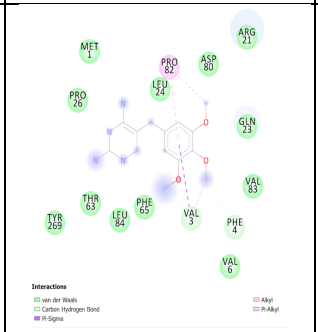
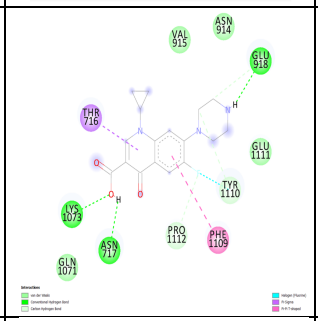
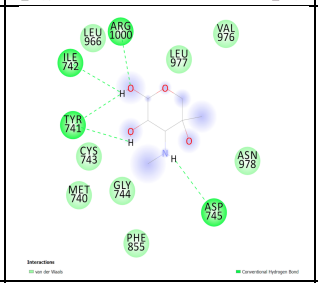
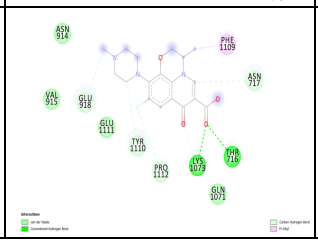
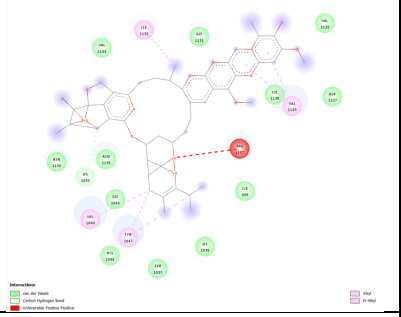
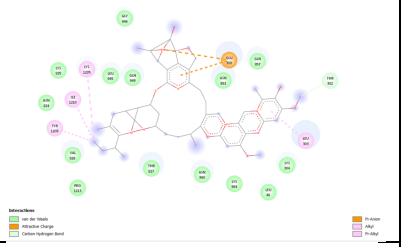
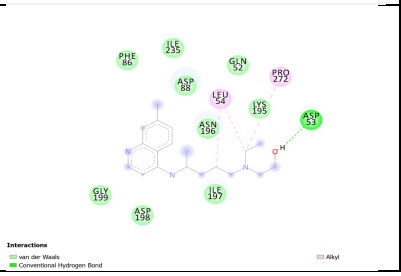
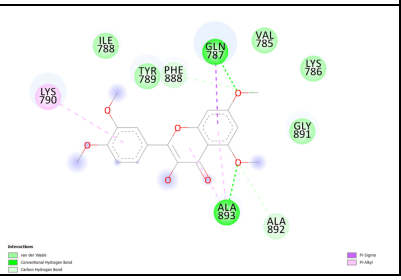
5	Meropenem (C17H25N3O5S), 441130	-6.4		Ala, Asn, 3Asp, 2Leu, 2Lys, 4Phe, Ser, Thr, 2Val	1CHB, 2HB, 15VW
6	Tenofovir Disoproxil (C19H30N5O10P), 5481350	-6.3		2Arg, Asn, 2Gln, 5Leu, Met, 2Phe, 2Pro, Thr, 3Val	2Alk, 1CHB, 2HB, 1UDD, 16VW
7	Trimethoprim (C14H18N4O3), 5578	-6.1		Arg, Asp, Gln, 2Leu, Met, 2Phe, 2Pro, Thr, Tyr, 3Val	2Alk, 2CHB, 1Pi-Alk, 1Pi-Sig, 12VW
8	Ciprofloxacin (C17H18FN3O3), 2764	-5.58		2Asn, 1Gln, 2Glu, 1Lys, 1Phe, 1Pro, 1Thr, 1Tyr, 1Val	3CHB, 1Hal, 3HB, 1Pi-Pi-T, 1Pi-Sig, 4VW
9	Gentamicin (C21H43N5O7), 3467	-5.4		Arg, Asn, Asp, Cys, Gly, Ile, 2Leu, Met, Phe,Tyr, Val	5HB, 8VW
10	Levofloxacin (C18H20FN3O4), 149096	-5.11		2Asn, 1Gn, 2Glu, 1Lys, 1Phe, 1Pro, 1Thr, 1Tyr, 1Val	5CHB, 2HB, 1Pi-Alk, 4VW

Table S3: List of the top hits antiparasitic drugs, flavonoids, and Vitamins against SARS-CoV-2 Spike protein by order of lowest to highest binding energy value. Ivermectin B1a seems to exhibit the lowest binding energy (-9.16 kcal/Mol) when docked with Spike protein, whereas Hydroxychloroquine exhibits the highest binding energy (-2.85 kcal/Mol). In terms of flavonoids Tetramethoxyflavone exhibit, the lowest binding energy (-4.91 kcal/Mol) and Gallocatechin exhibits the highest binding energy (-2.88). Moreover, Vitamin D showed the lowest binding energy (-5.52 kcal/Mol) and Vitamin C the lowest binding energy (-2.95 kcal/Mol).

	Antiparasitic	**Binding energy (kcal/Mol)**	**2D interaction**	**Interface amino acids**	**Type of interactions**
1	Ivermectin B1a (C48H74O14), 6321424	-9.16		1Arg, 2Asn, 1Asp, 2Gly, 1His, 3Ile, 2Lys, 1Ser, 1Tyr, 4Val	4Alk, 1CHB, 2Pi-Alk, 1UPP, 12VW
2	Ivermectin B1b (C47H72O14), 6321425	-8.86		3Asn, 2Gln, 1Glu, 1Gly, 1Ile, 3Leu, 4Lys, 1Pro, 2Thr, 1Tyr, 1Val	2AC, 3Alk, 1CHB, 1Pi-Alk, 14VW
3	Hydroxychloroquine (C18H26ClN3O), 3652	-2.85		Asn, 3Asp, Gln, Gly, 2Ile, Leu, Lys, Phe, Pro	2Alk, 1HB, 9VW
	Flavonoids	**Binding energy (kcal/Mol)**	**2D interaction**	**Interface amino acids**	**Type of interactions**
1	Tetramethoxyflavone (C19H18O6), 471721	-4.91		2Ala, 1Gln, 1Gly, 1Ile, 2Lys, 1Phe, 1Tyr, 1Val	2CHB, 2HB, 3Pi-Alk, 1Pi-Sig, 5VW

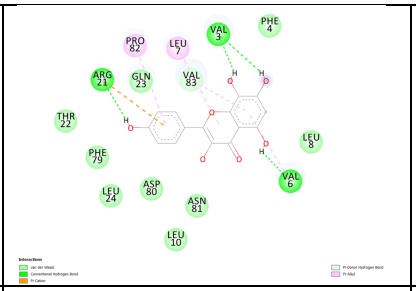
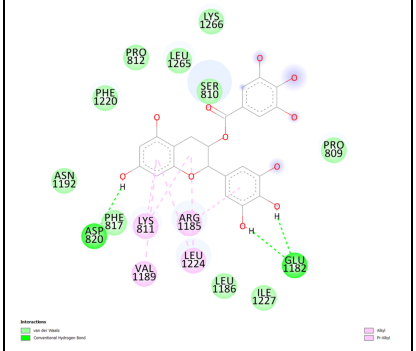
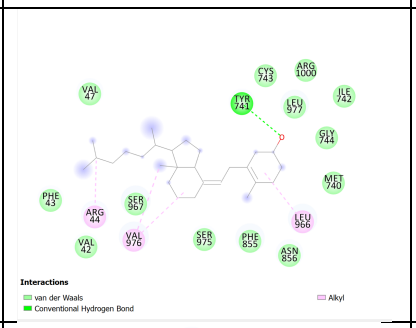
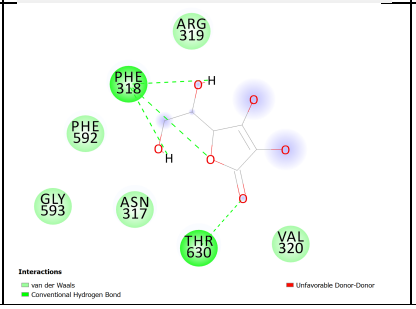
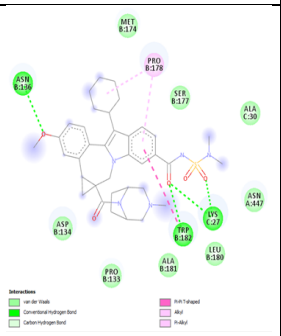
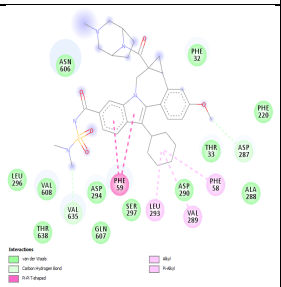
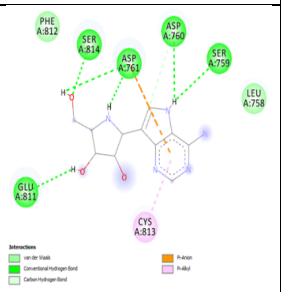
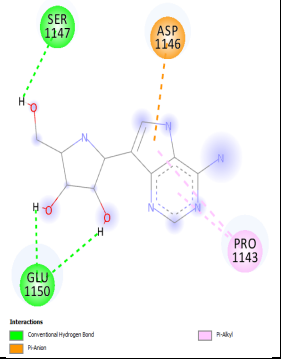
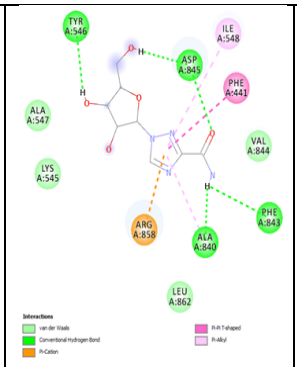
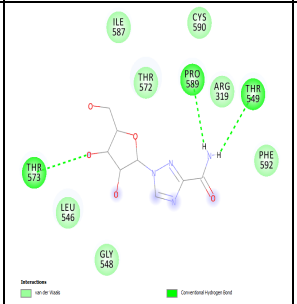
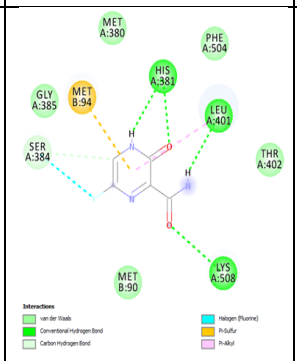
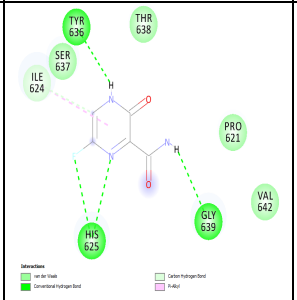
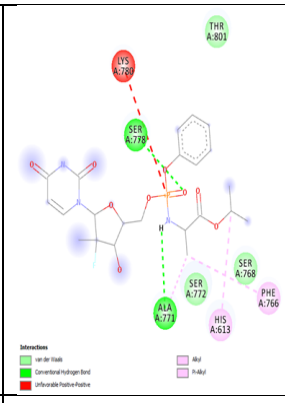
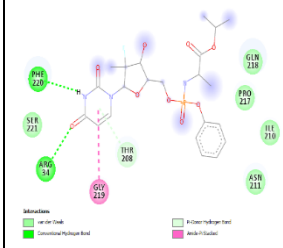
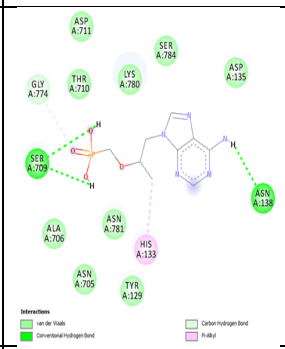
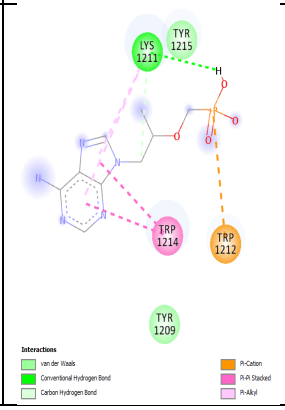
2	Herbacetin (C15H10O7), 5280544	-4.74		1Arg, 1Asn, 1Asp, 1Gln, 4Leu, 2Phe, 1Pro, 1Thr, 3Val	4HB, 4Pi-Alk, 1Pi-Cat, 1Pi-DHB, 9VW
3	Gallocatechin (C15H14O7), 65084	-2.88		1Arg, 1Asn, 1Asp, 1Glu, 1Ile, 3Leu, 2Lys, 1Ser, 2Phe, 2Pro, 1Val	2Alk, 3HB, 4Pi-Alk, 10VW
	Vitamins	**Binding energy (kcal/Mol)**	**2D interaction**	**Interface amino acids**	**Type of interactions**
1	Vitamin D (C27H44O), 5280795	-5.52		2Arg, Asp, Cys, Gly, Ile, 2Leu, Met, 2Phe, 2Ser, Tyr, 3Val	3Alk, 1HB, 12VW
2	Vitamin C (C6H8O6), 54670067	-2.95		Arg, Asn, Gly, 2Phe, Thr, Val	4HB, 5VW

Table S4: A comparative analysis between SARS-CoV-2 RdRP binding affinities and spike protein binding affinities in antivirals which primarily target viral RdRP. These comparisons include binding energy, the specific amino acids that are interacting with the drug, and the types of bonds formed during this interaction.

	Name and PubChem ID	Bound molecule	Binding Energy (kcal)	2D Interaction Plot	Interface Amino Acid	Type of Interactions
1	Beclabuvir (C36H45N5O5S), 49773361	RdRp	-5.63		2Ala, 2Asn, Asp, Leu, Lys, Met, 2Pro, Ser, Trp	4HB, 2Pi-Alk, 1Pi-Pi-T, 8VW
		Spike	-6.64		Ala, Asn, 3Asp, Gln, 2Leu, 4Phe, Ser, 2Thr, 3Val	2Alk, 2CHB, 1Pi-Alk, 2Pi-Pi-T; 12VW
2	Galidesivir (C11H15N5O3), 10445549	RdRp	-4.38		2Asp, Cys, Glu, Leu, Phe, 2Ser	1CHB, 6HB, 1Pi-Alk, 1Pi-Ani, 2VW
		Spike	-3.11		Asp, Glu, Pro, Ser	3HB, 2Pi-Alk, 1Pi-An

3	Ribavirin (C8H12N4O5), 37542	RdRp	-4.2		2Ala, Arg, Asp, Ile, Leu, Lys, 2Phe, Val	5HB, 2Pi-Alk, 1Pi-Cat, 1Pi-Pi, 4VW
		Spike	-3.29		Arg, Cys, Gly, Ile, Leu, Phe, Pro, 3Thr	3HB, 7VW
4	Favipiravir (C5H4FN3O2), 492405	RdRp	-3.09		Gly, His, Leu, Lys, 3Met, Phe, Ser, Thr	1CHB, 1Hal, 4HB, 1Pi-Alk, 1Pi-Sul, 5VW
		Spike	-2.94		Gly, His, Ile, Pro, Ser, Thr, Tyr, Val	1CHB, 4HB, 1Pi-Alk, 4VW

5	Sofosbuvir (C22H29FN3O9P), 45375808	RdRp	-2.95		Ala, His, Lys, Phe, 3Ser, Thr	1Alk, 2HB, 2Pi-Alk, 3VW, 1UPP
		Spike	-3.7		Arg, Asn, Gln, Gly, Ile, Phe, Pro, Ser, Thr	1APS, 2HB, 1Pi-DHB, 5VW
6	Tenofovir (C9H14N5O4P), 464205	RdRp	-2.34		Ala, 3Asn, 2Asp, Gly, His, Lys, 2Ser	1CHB, 3HB, 1Pi-Alk, 9VW
		Spike	-2.75		Lys, 2Trp, 2Tyr	1CHB, 1HB, 2Pi-Alk, 1Pi-Cat, 2Pi-Pi-Stk, 2VW

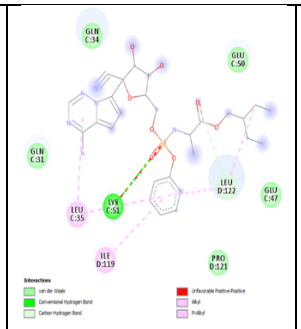
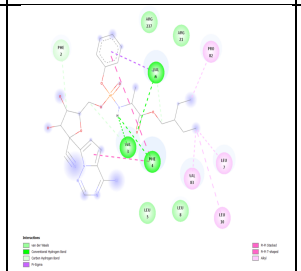
7	Remdesivir (C27H35N6O8P), 121304016	RdRp	-1.28		2Gln, 2Glu, Ile, 2Leu, Lys, Pro	1Alk, 1CHB, 1HB, 4Pi-Alk, 5VW, 1UPP
		Spike	-2.65		2Arg, 4Leu, 2Phe, 1Pro, 3Val	4Alk, 1CHB, 3HB, 1Pi-Pi-T, 1Pi-Pi-Stk, 1Pi-Sig, 4VW

Figure S1

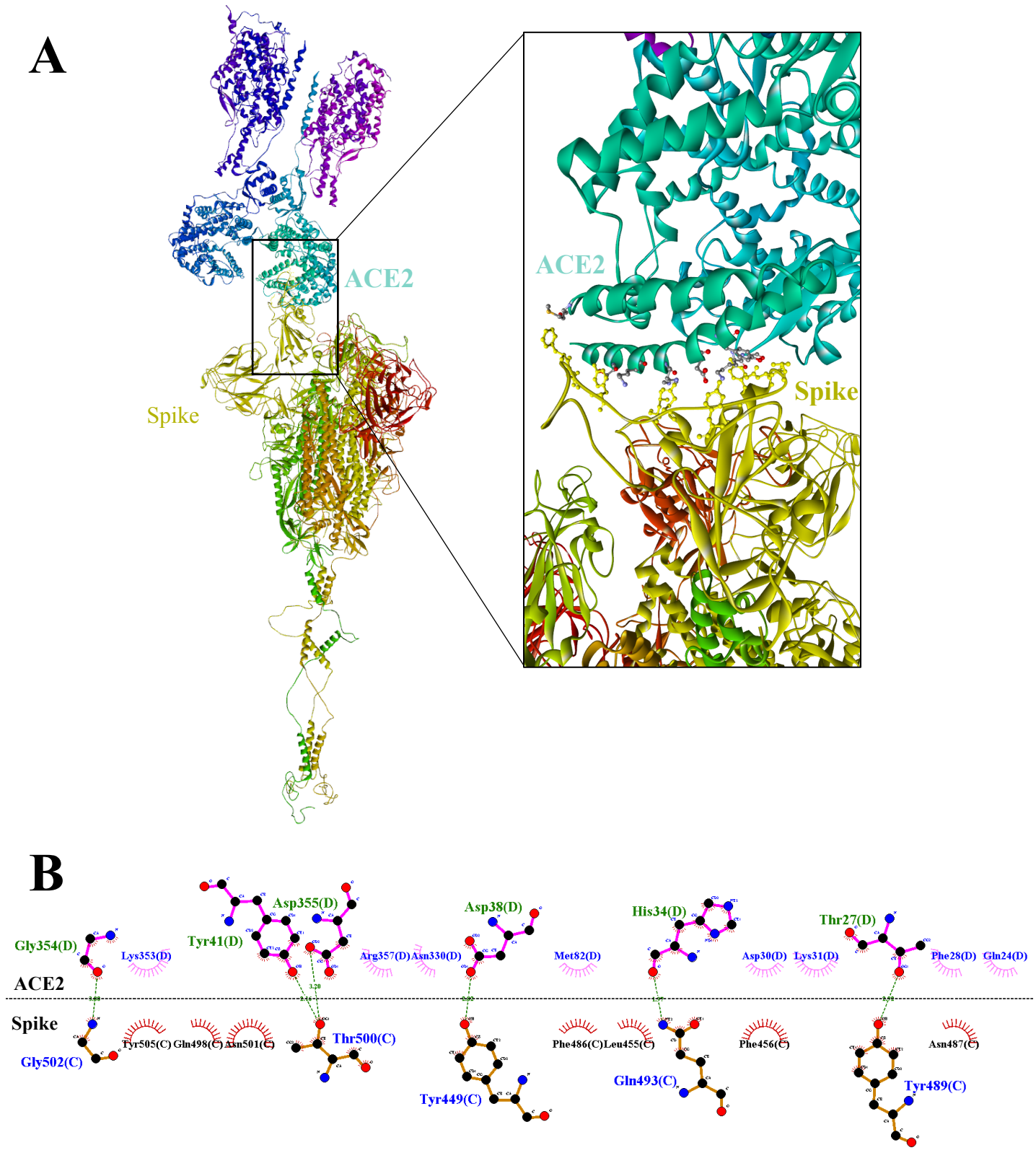
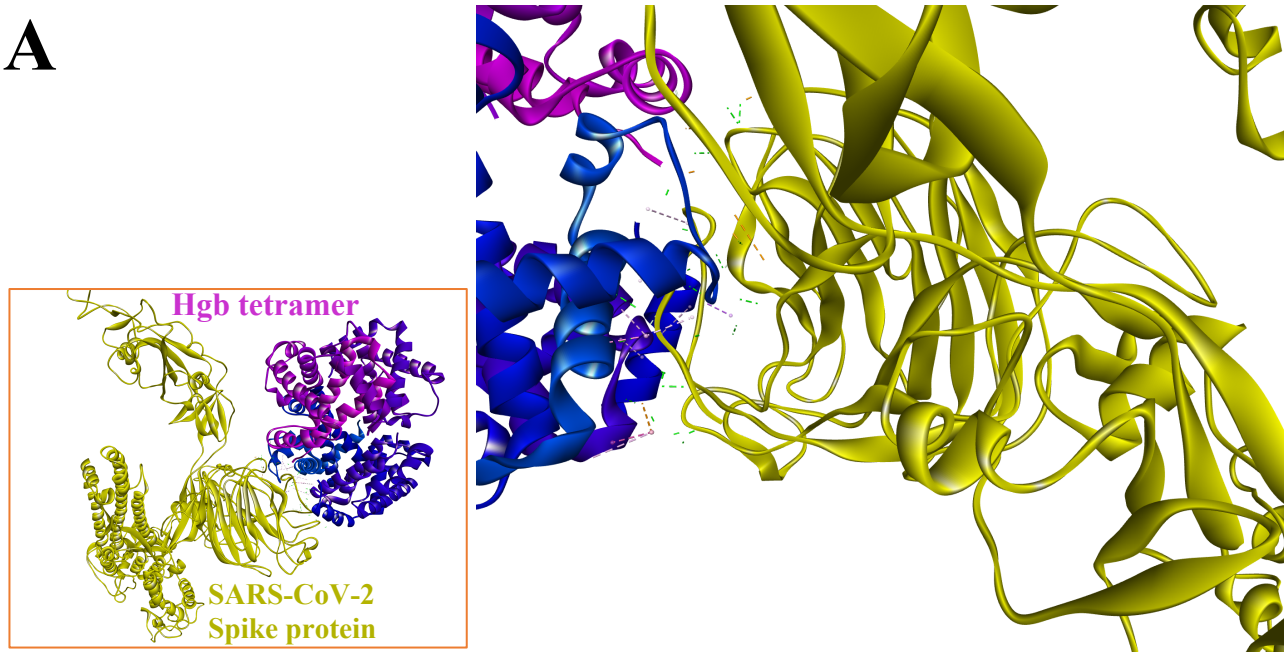

A
ACE2
Spike
ACE2
Spike
B
Gly354(D)
Lys353(D)
Asp355(D)
Tyr41(D)
Arg357(D)
Asn330(D)
Asp38(D)
Met82(D)
His34(D)
Asp30(D)
Lys31(D)
Thr27(D)
Phe28(D)
Gln24(D)
ACE2
Spike
Gly502(C)
Tyr505(C)
Gln498(C)
Asn501(C)
Thr500(C)
Tyr449(C)
Phe486(C)
Leu455(C)
Gln493(C)
Phe456(C)
Asn487(C)
Tyr489(C)

Figure S2

A


Hgb tetramer
SARS-CoV-2
Spike protein

B

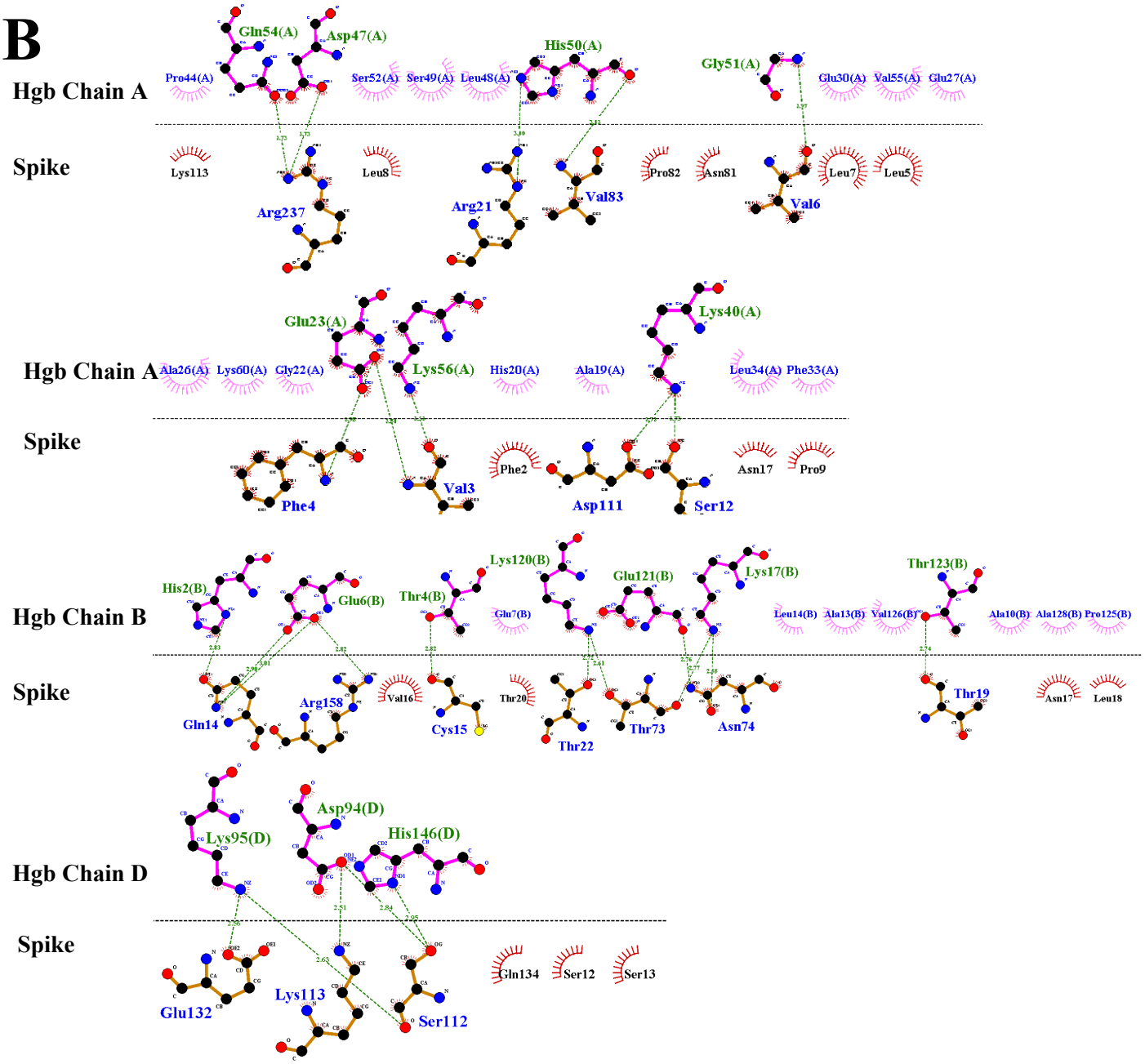
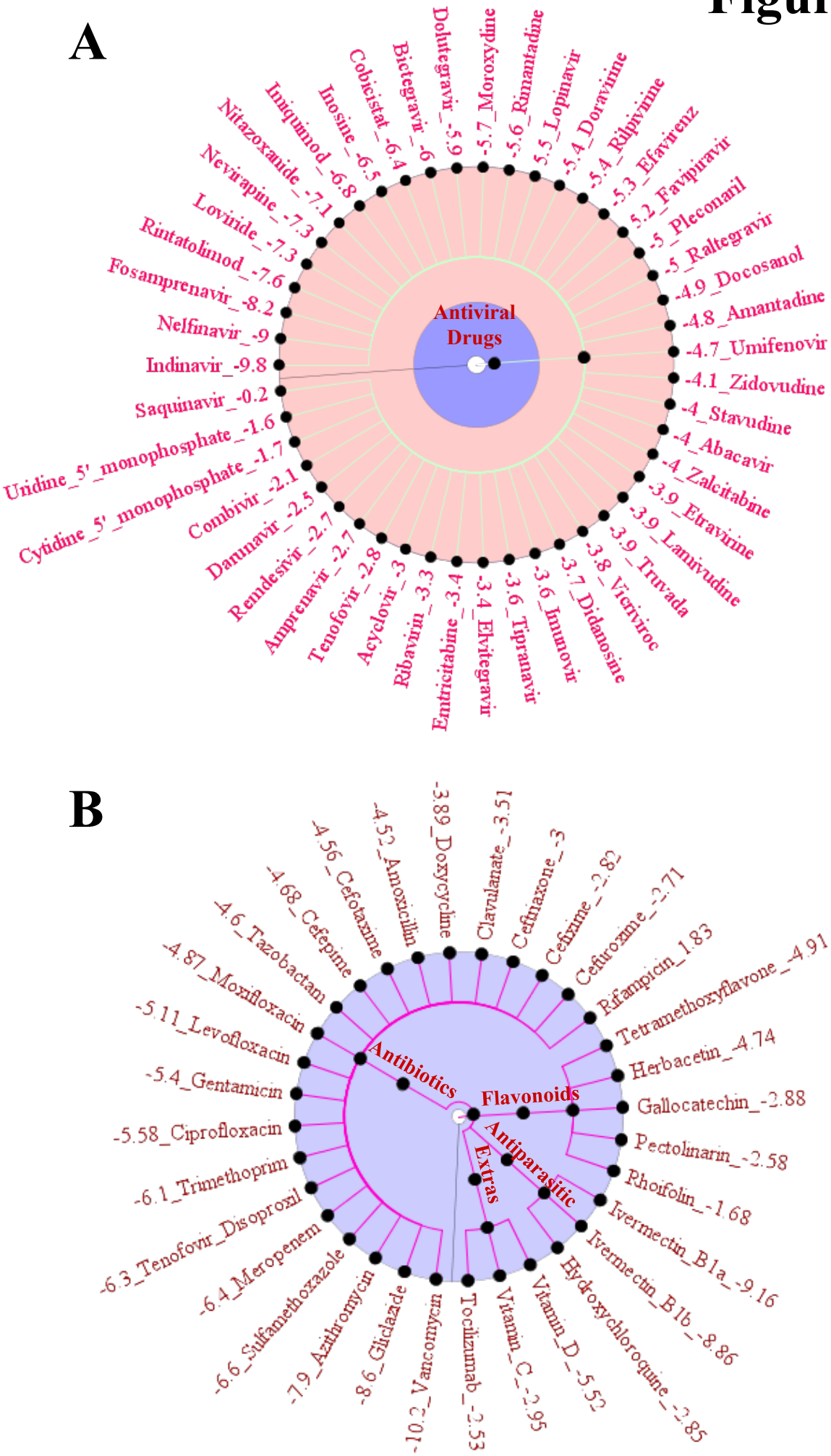

Hgb Chain A
Spike
Gln54(A)
Asp47(A)
Pro44(A)
Ser52(A)
Ser49(A)
Leu48(A)
His50(A)
Gly51(A)
Glu30(A)
Val55(A)
Glu27(A)
Lys113
Leu8
Arg237
Arg21
Val83
Pro82
Asn81
Leu7
Leu5
Val6
Hgb Chain A
Spike
Glu23(A)
Lys40(A)
Ala26(A)
Lys60(A)
Gly22(A)
Lys56(A)
His20(A)
Ala19(A)
Leu34(A)
Phe33(A)
Phe4
Val3
Phe2
Asp111
Ser12
Asn17
Pro9
Hgb Chain B
Spike
His2(B)
Glu6(B)
Thr4(B)
Lys120(B)
Glu121(B)
Lys17(B)
Glu7(B)
Thr123(B)
Leu14(B)
Ala13(B)
Val126(B)
Ala10(B)
Ala128(B)
Pro125(B)
Gln14
Arg158
Val16
Cys15
Thr20
Thr22
Thr73
Asn74
Thr19
Asn17
Leu18
Hgb Chain D
Spike
Asp94(D)
Lys95(D)
His146(D)
Glu132
Lys113
Ser112
Gln134
Ser12
Ser13

Figure S3


A
Antiviral Drugs
Uridine_5'_monophosphate_-1.6
Cytidine_5'_monophosphate_-1.7
Saquinavir_-0.2
Indinavir_-9.8
Nelfinavir_-9
Fosamprenavir_-8.2
Rintatolimod_-7.6
Loviride_-7.3
Nevirapine_-7.3
Nitazoxanide_-7.1
Imiquimod_-6.8
Inosine_-6.5
Cobicistat_-6.4
Bictegravir_-6
Dolutegravir_-5.9
Moroxydine_-5.7
Rimantadine_-5.6
Lopinavir_5.5
Doravirine_-5.4
Rilpivirine_-5.4
Efavirenz_-5.3
Favipiravir_5.2
Pleconaril_-5
Raltegravir_-5
Docosanol_-4.9
Amantadine_-4.8
Umifenovir_-4.7
Zidovudine_-4.1
Stavudine_-4
Abacavir_-4
Zalcitabine_-4
Etravirine_-3.9
Lamivudine_-3.9
Truvada_-3.9
Vicriviroc_-3.8
Didanosine_-3.7
Immunovir_-3.6
Tipranavir_-3.6
Elvitegravir_-3.4
Emtricitabine_-3.4
Ribavirin_-3.3
Acyclovir_-3
Tenofovir_-2.8
Amprenavir_-2.7
Remdesivir_-2.7
Darunavir_-2.5
Combivir_-2.1
B
Antibiotics
Flavonoids
Antiparasitic
Extras
Doxycycline_-3.89
Amoxicillin_-4.52
Cefotaxime_-4.56
Cefepime_-4.68
Tazobactam_-4.6
Moxifloxacin_-4.87
Levofloxacin_-5.11
Gentamicin_-5.4
Ciprofloxacin_-5.58
Trimethoprim_-6.1
Tenofovir_Disoproxil_-6.3
Meropenem_-6.4
Sulfamethoxazole_-6.6
Azithromycin_-7.9
Gliclazide_-8.6
Vancomycin_-10.1
Clavulanate_-3.51
Cefmetazone_-3
Cefixime_-2.82
Cefuroxime_-2.71
Rifampicin_1.83
Tetramethoxyflavone_-4.91
Herbacetin_-4.74
Gallocatechin_-2.88
Pectolinarin_-2.58
Rhoifolin_-1.68
Ivermectin_B1a_-9.16
Ivermectin_B1b_-8.86
Hydroxychloroquine_-2.85
Vitamin_D_-5.52
Vitamin_C_-2.95
Tocilizumab_-2.53