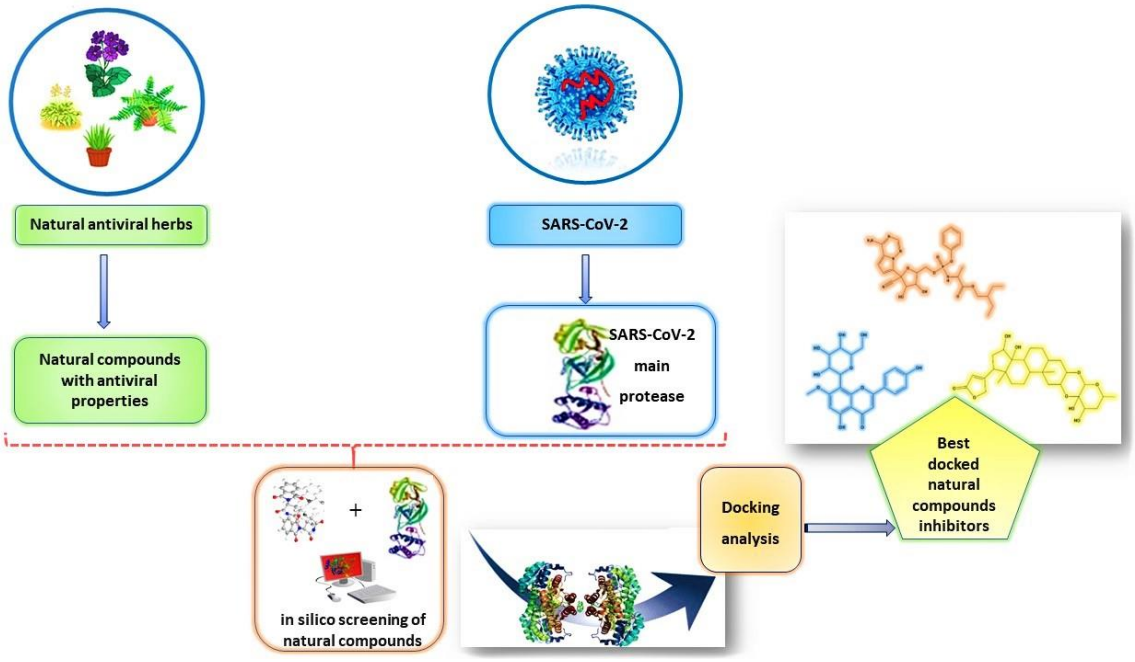
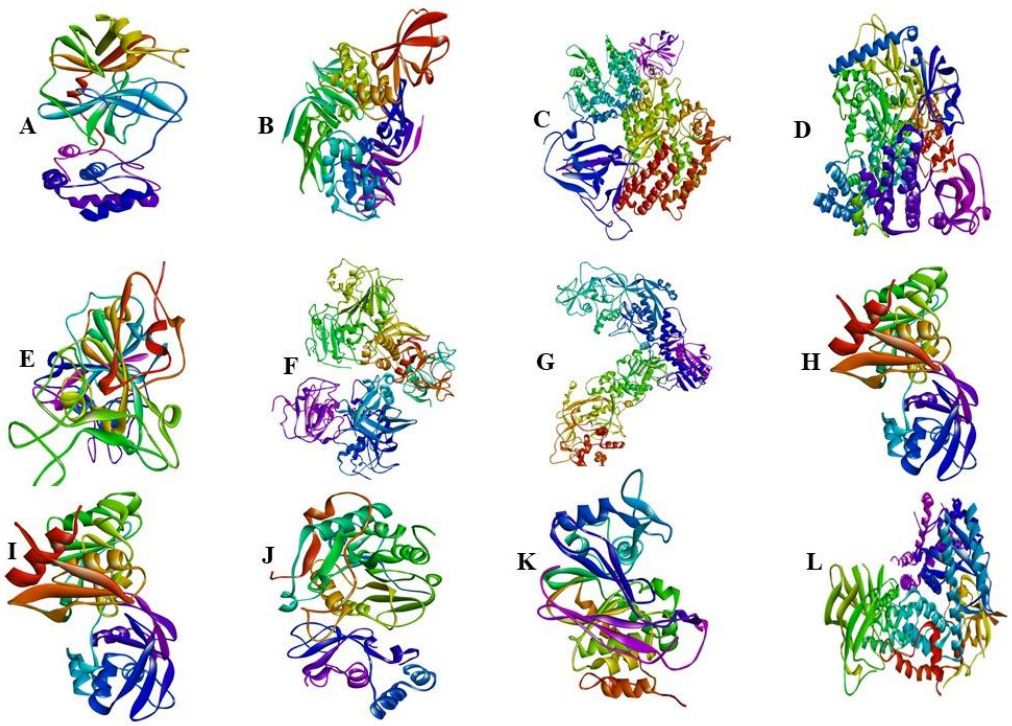
Supplementary material to “In silico Screening of Natural Products as Potential Inhibitors of SARS-CoV-2 using Molecular Docking Simulation”

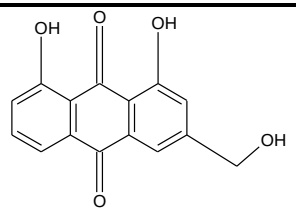
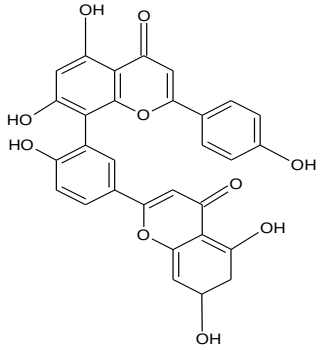


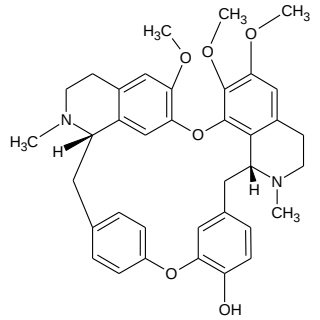
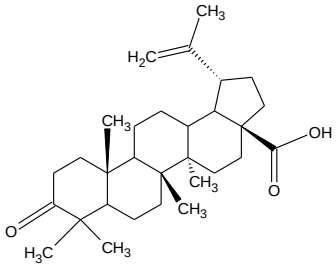
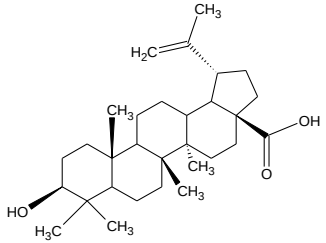
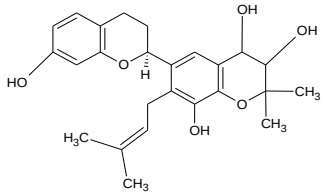
Appendix 1. The flow chart of the study.

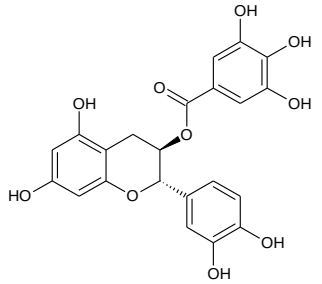
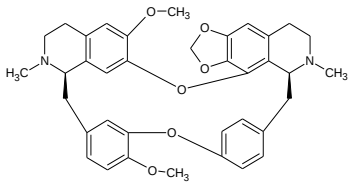
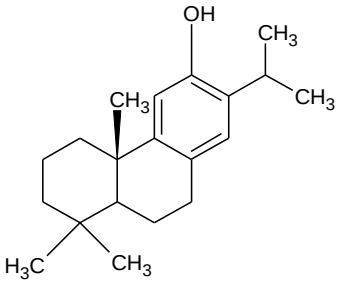
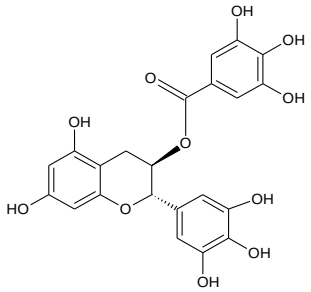


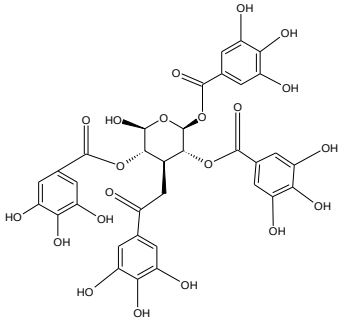
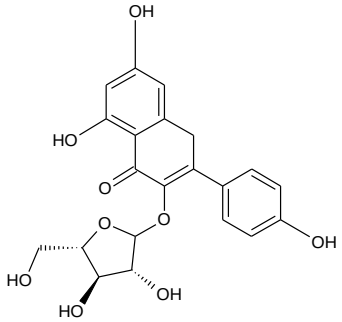
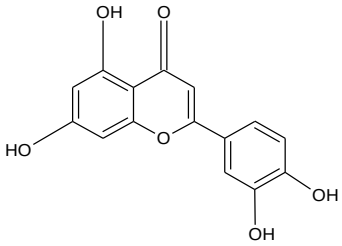
Appendix 2. Three dimensional structures of the SARS-CoVproteins [(**A**) 3-chymotrypsin-*like* protease ($3CL^{PRO}$) (PDB 6LU7), (**B**) Papain-*like* proteases (PL^{PRO}) (PDB 4OW0), (**C**) Human angiotensin converting enzyme 2 receptor (hACE2R) (PDB 2AJF), (**D**) RNA-dependent RNA polymerase (RdRp) (PDB 6NUR), (**E**) SARS spike glycoprotein (S protein) (PDB 2GHV), (**F**) Non-structural protein 13 (nsp13, helicase) (PDB 6JYT), (**G**) Non-structural protein 14 (nsp14) (PDB 5C8S), (**H**) Non-structural protein 15 (nsp15) (PDB 2H85), (**I**) Non-structural protein 16 (nsp16) (PDB 3R24), (**J**) Non-structural protein 10 (nsp10) (PDB 2XYR), (**K**) Calcineurin–NFAT (PDB 2JOG) and (**L**) ABL1 (PDB 6T3B).

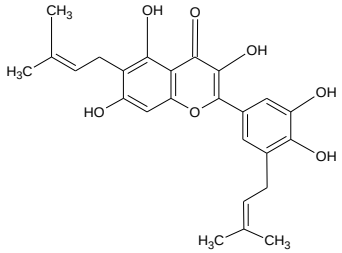
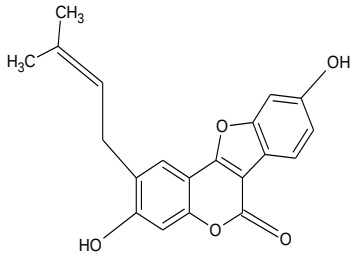
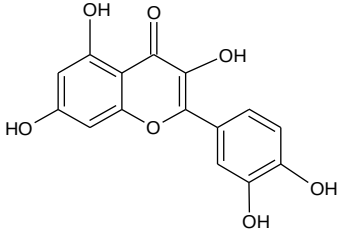
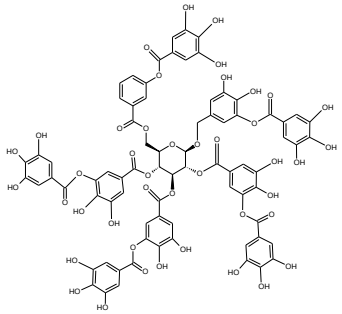
Appendix 3. Examples of natural product-derived against SARS-CoV-2 potential candidates

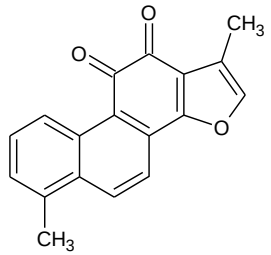
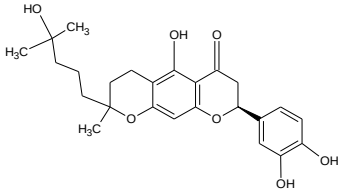
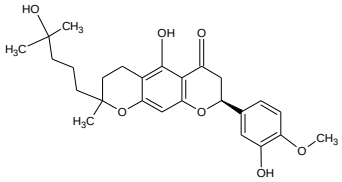
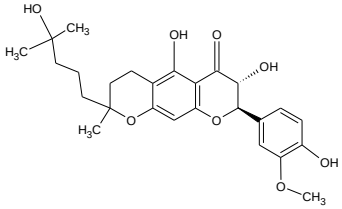
Natural Compounds/ Chemical group	Chemical structures	Coronavirus type targeted/ SARS-CoV viral proteases	Mechanism of action	IC_{50} /EC_{50} value	Ref
Aloe emodin/ Anthraquinone		SARS-CoV	Inhibition of $3CL^{PRO}$	8.3 µM	(20)
Amentoflavone/ Flavonoid		SARS-CoV	Inhibition of $3CL^{PRO}$	8.3 µM	(21)

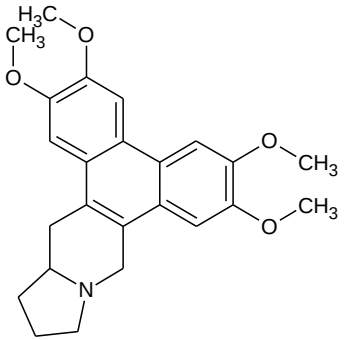
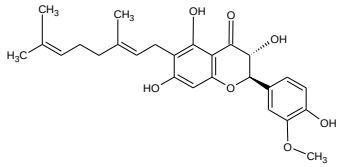
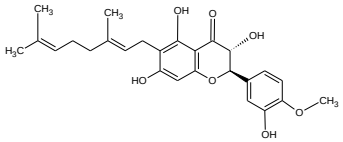
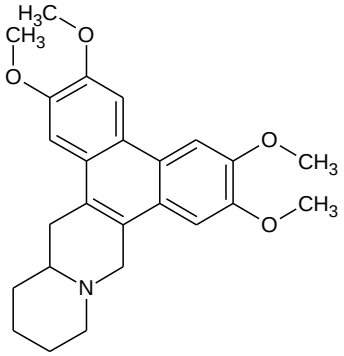
Berbamine/ Alkaloid		HCoV-NL63	Unknown	1.48 µM	(22)
Betulonic acid/ Triterpenoid derivative		SARS-CoV	Inhibition of virus replication.	0.63 µM	(23)
Betulinic acid/ Triterpenoid derivative		SARS-CoV	Inhibition of $3CL^{PRO}$.	10 µM	
Broussoflavan A/ Flavonol		$3CL^{PRO}$ and PL^{PRO}	Inhibition of PL^{PRO}.	9.2 µM	(24)

(−)-Catechin gallate/ Flavonoid		SARS-CoV	Inhibition of nanoparticle-based RNA oligonucleotide.	-	(19)
Cepharanthine/ Alkaloid		SARS-CoV	Protease inhibition.	9.5 µg/mL	(25)
Ferruginol/ Diterpenoid		SARS-CoV	Inhibition of virus replication.	1.39 µM	(23)
(−)-Gallocatechin gallate/ Polyphenol		SARS-CoV	Inhibition of nanoparticle-based RNA oligonucleotide.	-	(19)

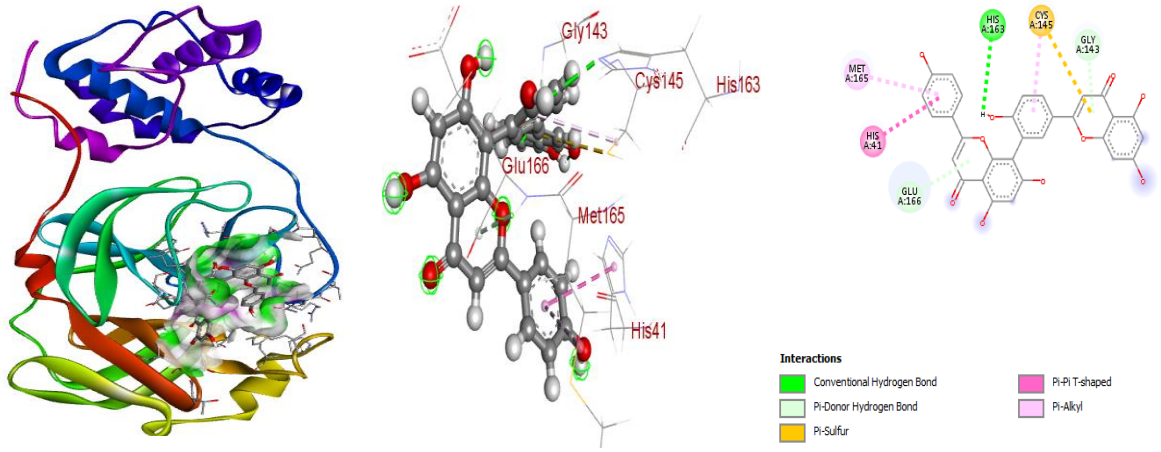
Glucogallin/ Polyphenol		SARS-CoV	Blocking the viral entry.	4.5µM	(26)
Juglanin/ Flavonoid		SARS-CoV	Blocks the 3a channel.	2.3 µM	(27)
Luteolin/ Flavonoid		SARS-CoV	Blocking the viral entry.	9.02 µM	(26)

Papyriflavonol A/ Flavonol		3CL^{PRO} and PL^{PRO}	Protease inhibition.	3.7 µM	(24)
Psoraldin/ Coumarin		SARS-CoV	Inhibition of PL^{PRO}	4.2±1.0 µM	(19)
Quercetin/ Flavonoid		3CL^{PRO} and PL^{PRO}	Inhibition of PL^{PRO}.	8.7 µM	(24)
Tannic acid/ Polyphenol		SARS-CoV	Inhibition of virus replication.	1.57 µM	(23)

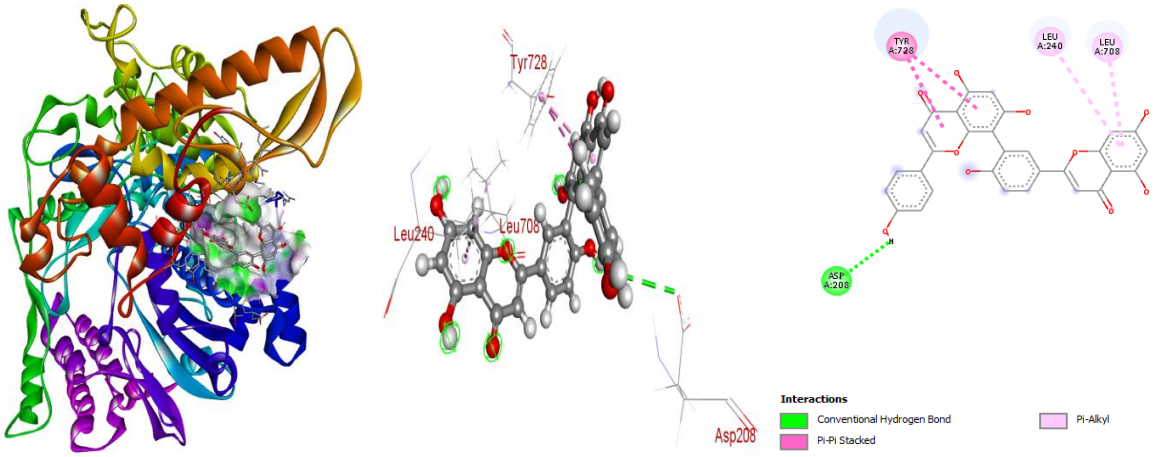
Tanshinone I/ Diterpene		SARS-CoV	Inhibition of SARS-CoV viral infection and replication.	0.7 µM	(34)
Tomentin A/ Flavonoid		SARS-CoV	Inhibition of PL^{PRO}.	6.2 ± 0.04 µM	
Tomentin B/ Flavonoid		SARS-CoV	Inhibition of PL^{PRO}.	6.1 ± 0.02 µM	(29)
Tomentin E/ Flavonoid		SARS-CoV	Inhibition of PL^{PRO}.	5.0 ± 0.06 µM	

Tylophorine/ Alkaloid		SARS-CoV	Protease inhibition.	0.018 µM	(28)
3′-*O*-methyldiplacol/ Flavone		SARS-CoV	Inhibition of PL^{PRO}	9.5 ± 0.10 µM	(29)
4′-*O*-methyldiplacol/ Flavone		SARS-CoV	Inhibition of PL^{PRO}	9.2 ± 0.13 µM	(29)
7-methoxycryptopleurine/ Flavone		SARS-CoV	Protease inhibition.	<0.005 µM	(28)

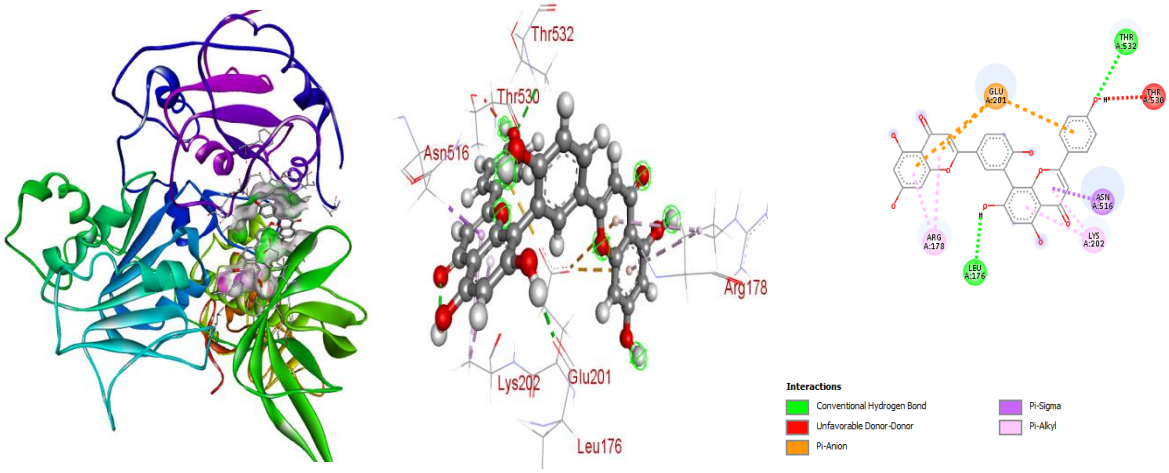
Abbreviations: papain-like protease (PL^{pro}), 3-chymotripsin-like protease ($3CL^{pro}$), severe acute respiratory syndrome coronavirus (SARS-CoV), Human coronavirus NL63 (HCoV-NL63)



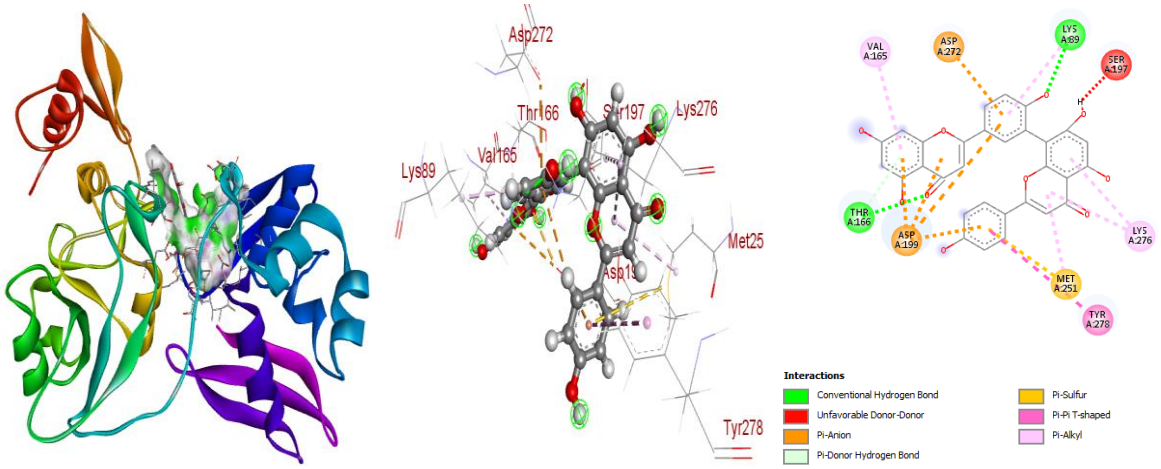
(A) Amentoflavone - 3CL^{PRO}



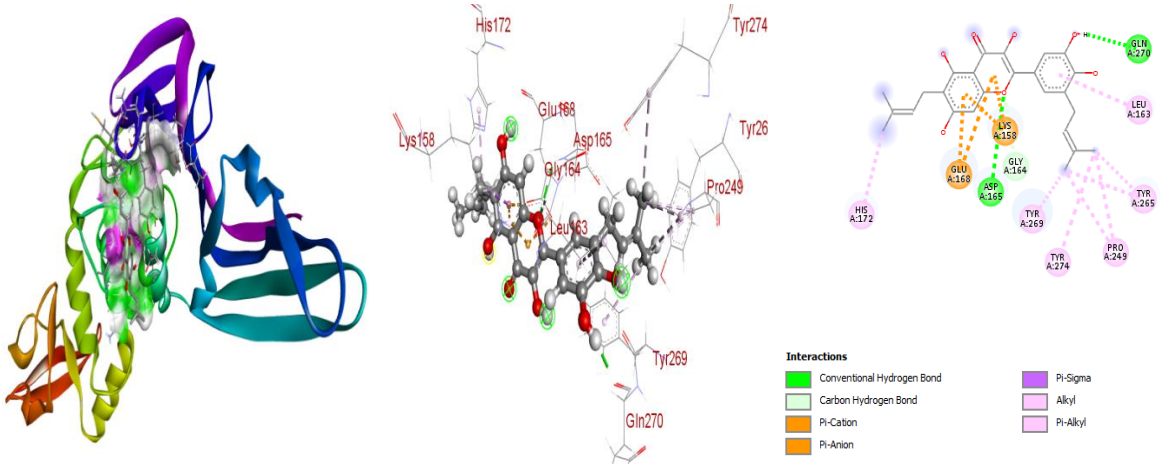
(B) Amentoflavone - RdRp



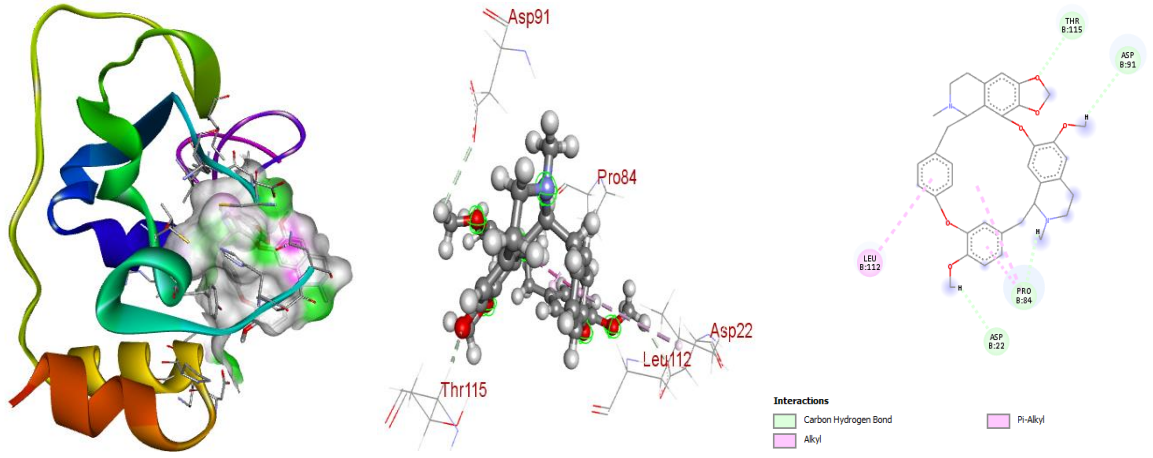
(C) Amentoflavone – nsp13



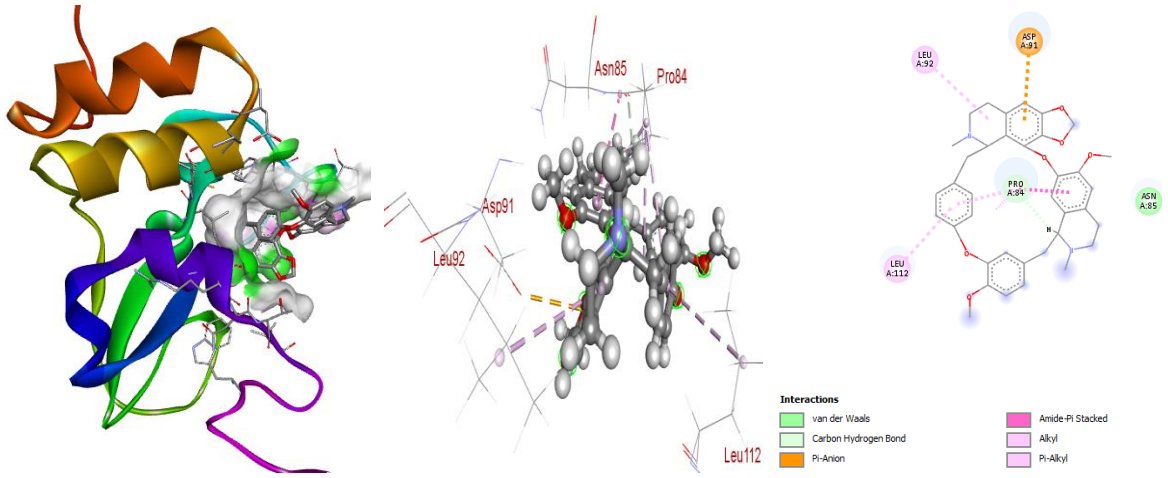
(D) Amentoflavone - nsp15



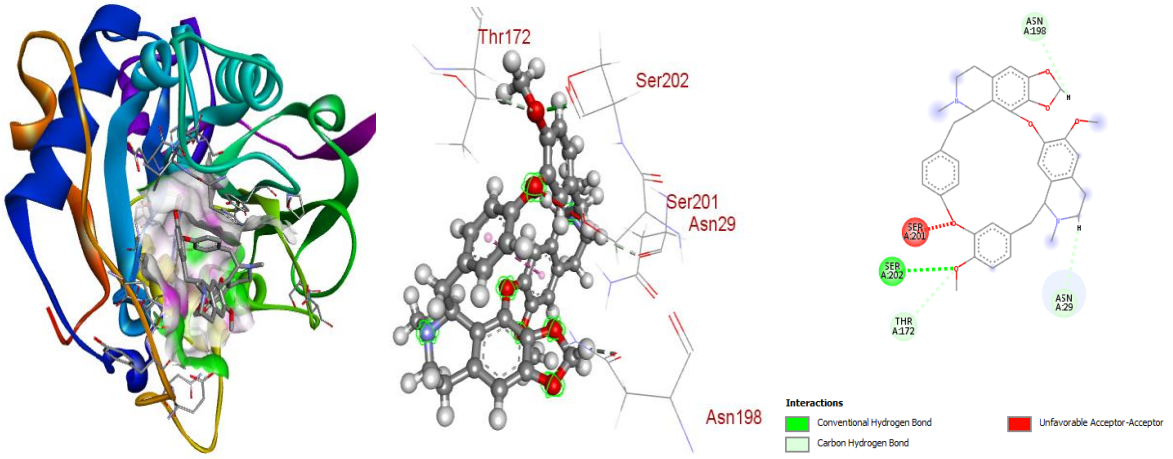
(E) Papyriflavonol A - PL^{PRO}



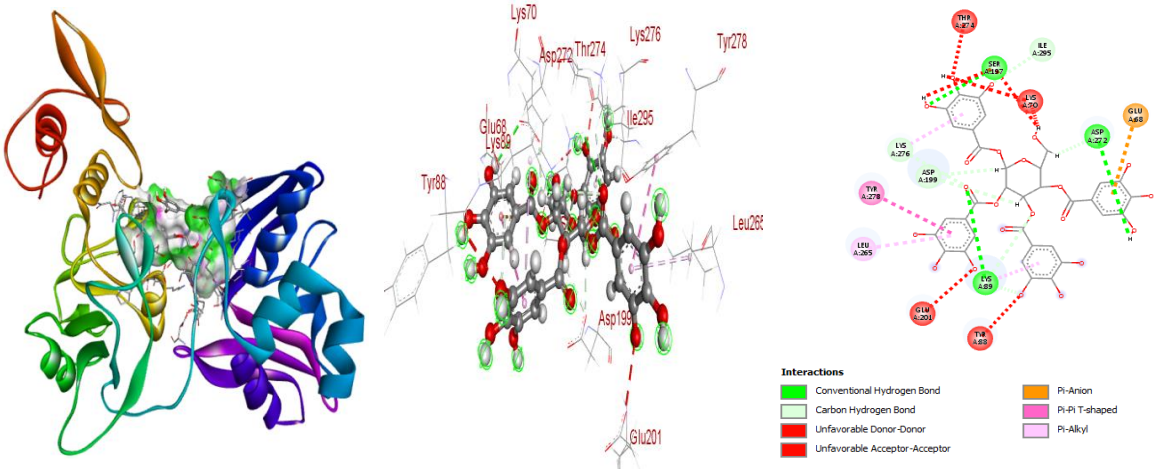
(F) Cepharanthine – nsp10



(G) Cepharanthine – nsp14

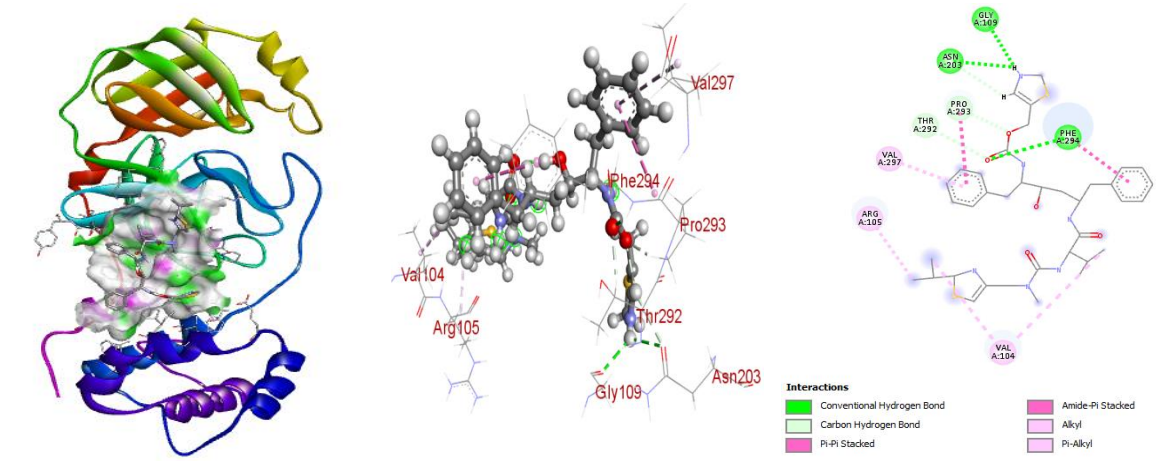


(H) Cepharanthine – nsp16

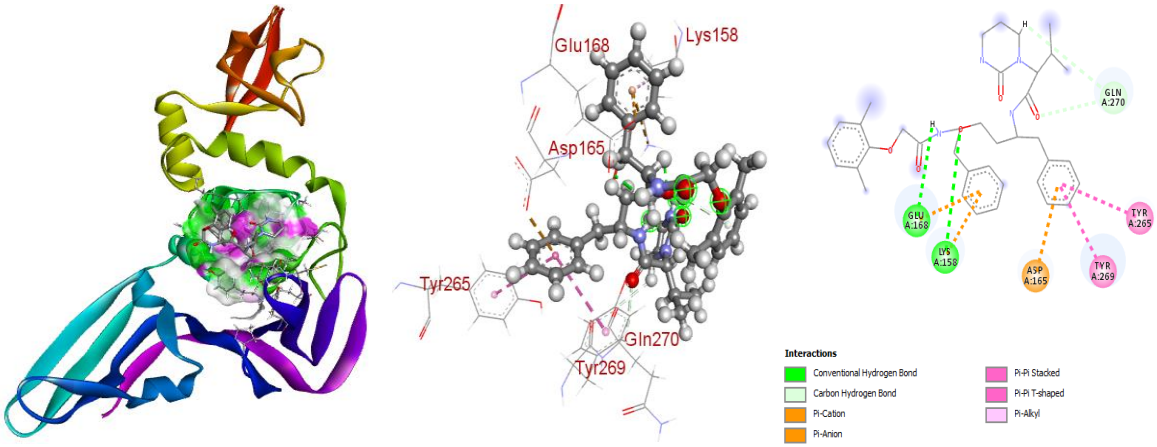


(I) Glucogallin – nsp15

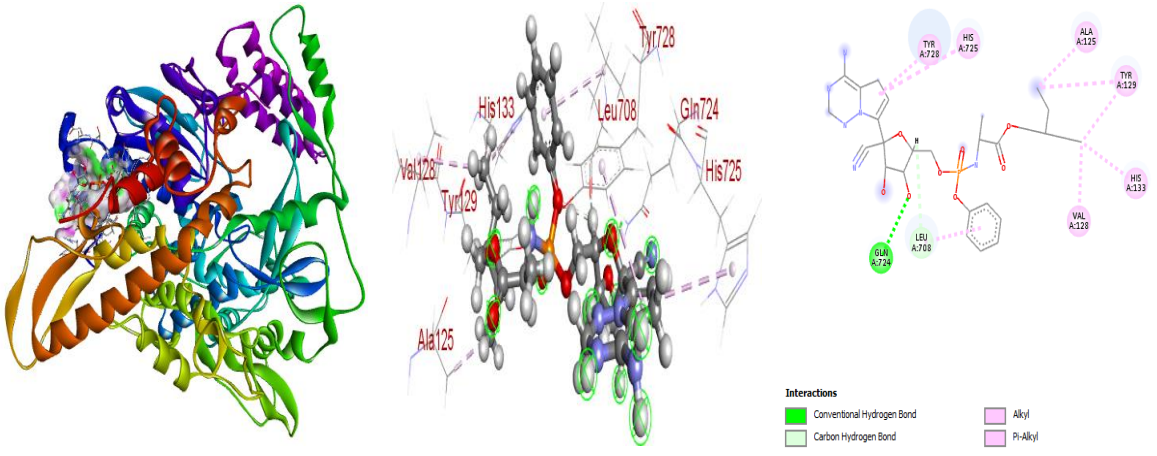
Appendix 4. Interactions of the natural compounds with different structural and non-structural proteins of SARS CoV-2.



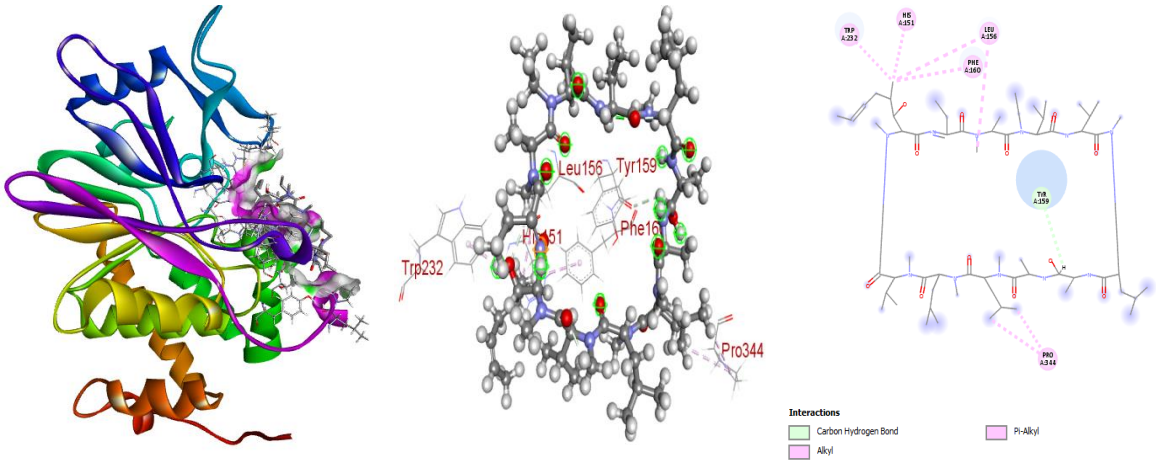
(A) Ritonavir - 3CL^{PRO}



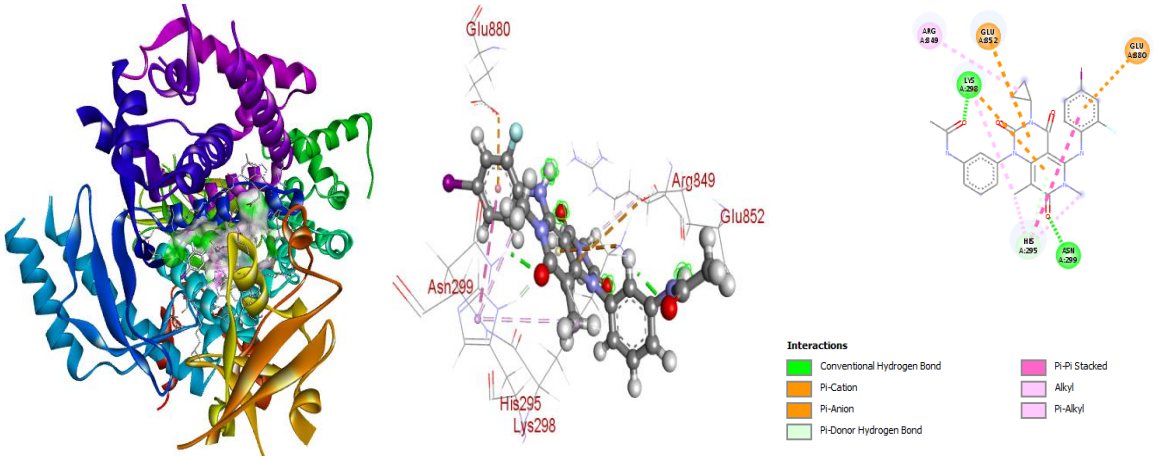
(B) Lopinavir - PL^{PRO}



(C) Remdesivir - RdRp

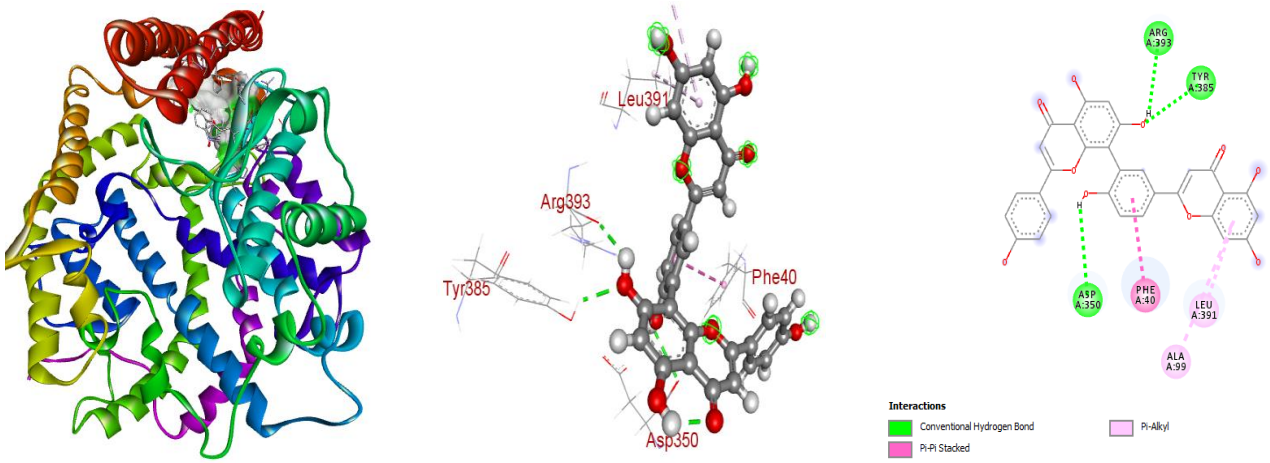


(D) Alisporivir - NFAT

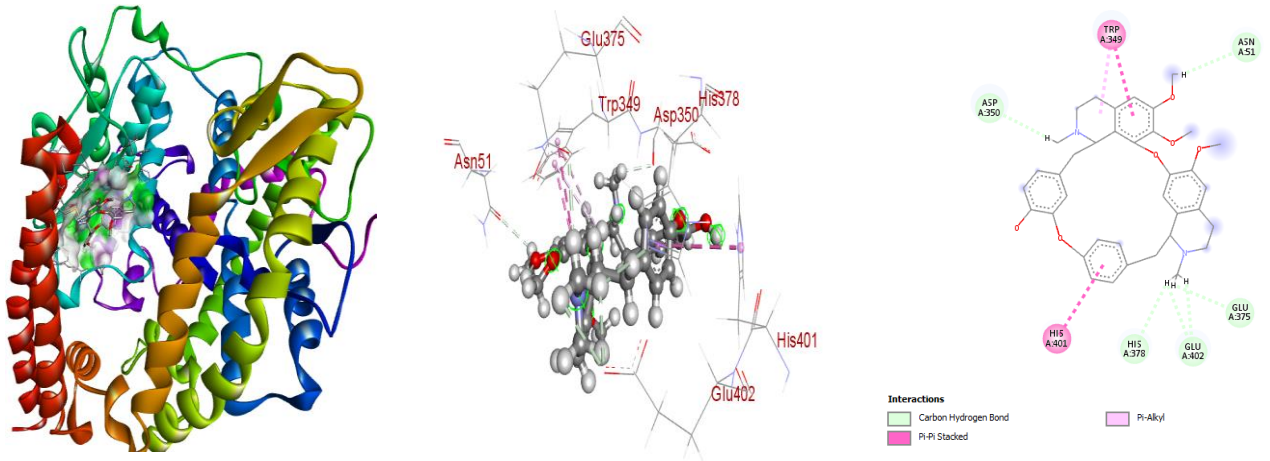


(E) Trametinib - ABL1

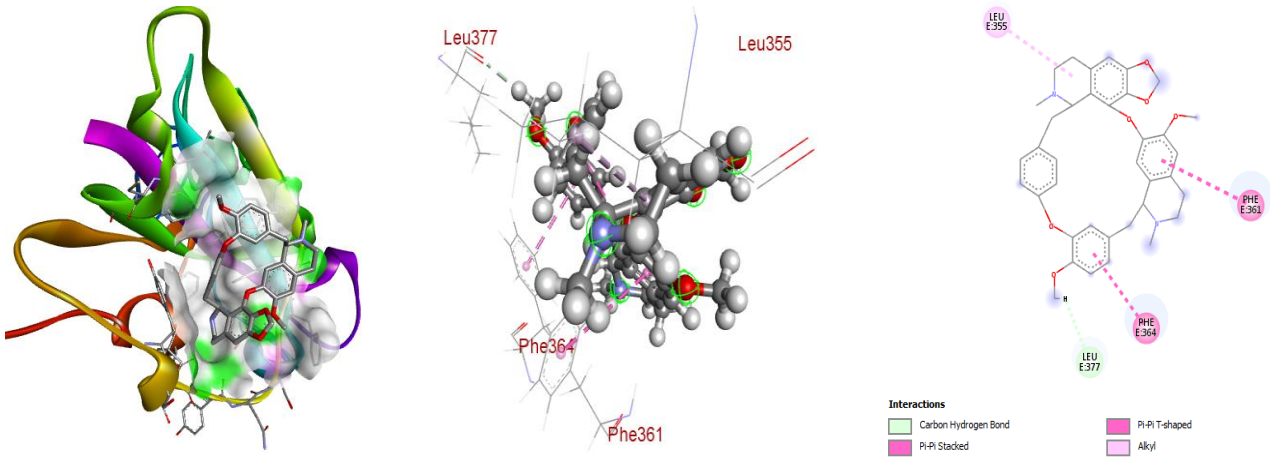
Appendix 5. Interactions of the standard drugs with the structural and non-structural proteins of SARS CoV-2.



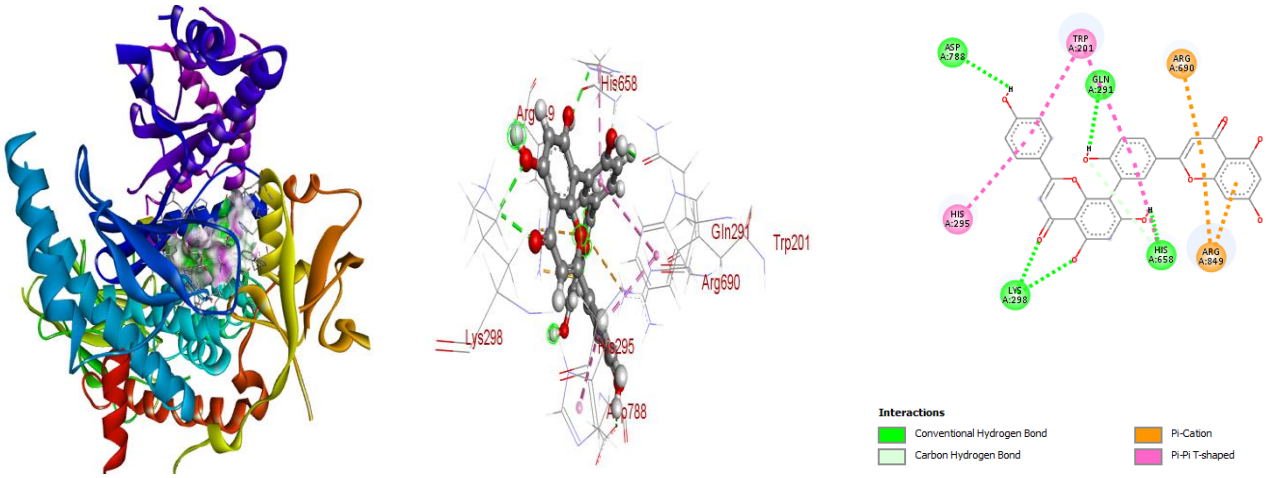
(A) Amentoflavone - hACE2R



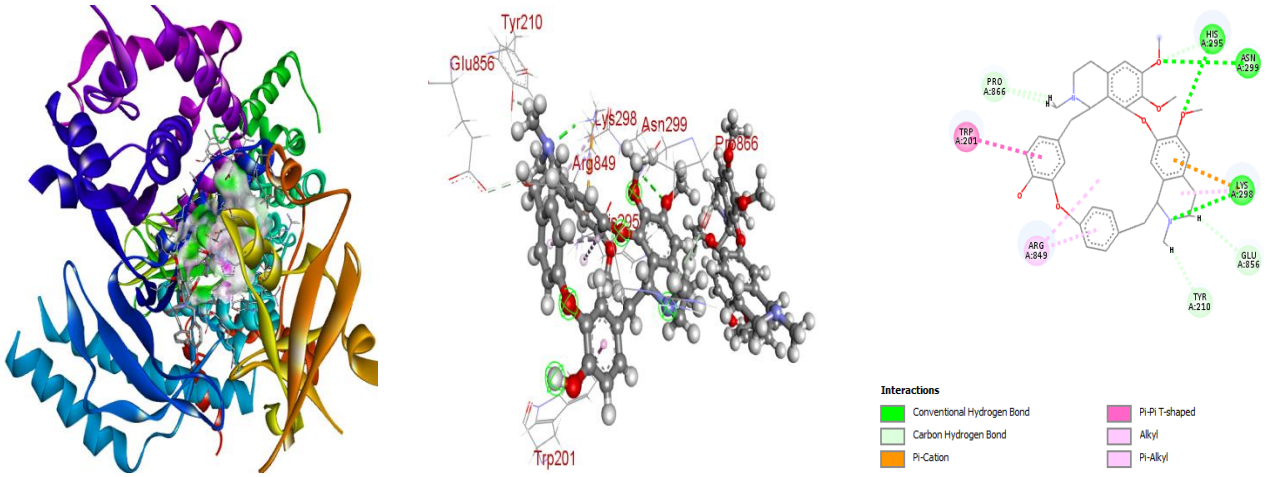
(B) Berbamine - hACE2R



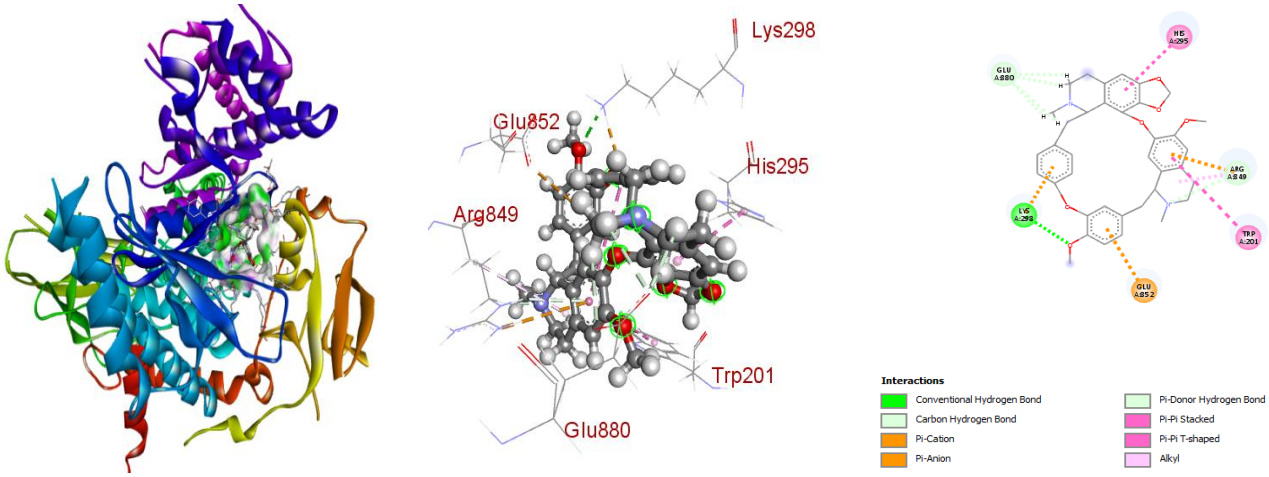
(C) Cepharanthine - S protein



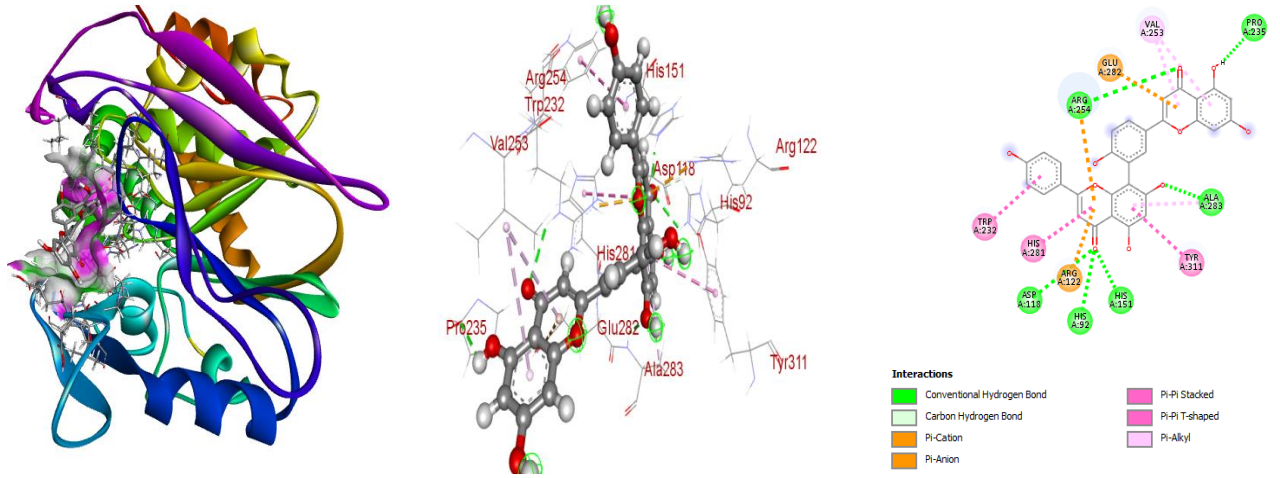
(D) Amentoflavone - ABL1



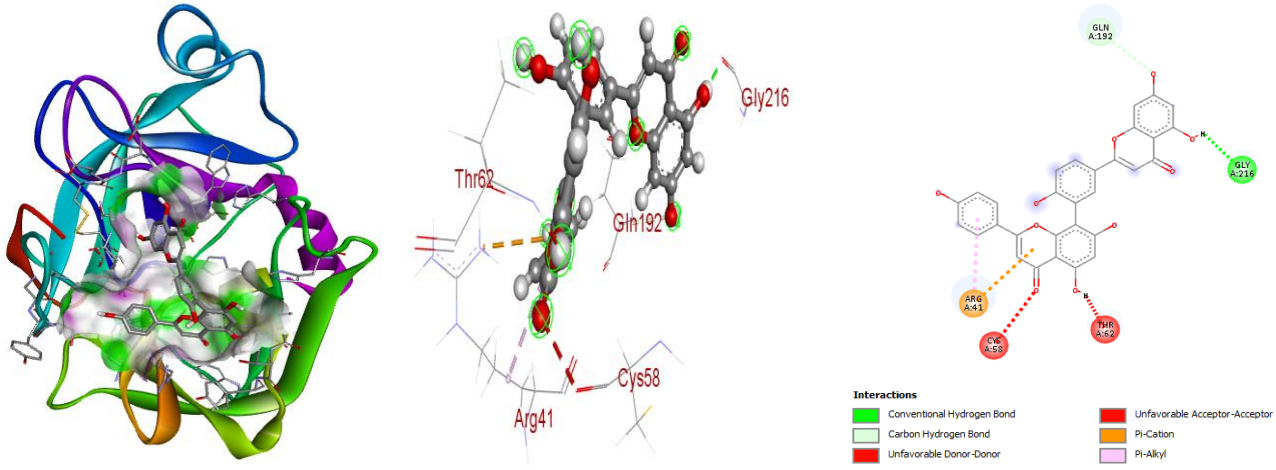
(E) Berbamine - ABL1



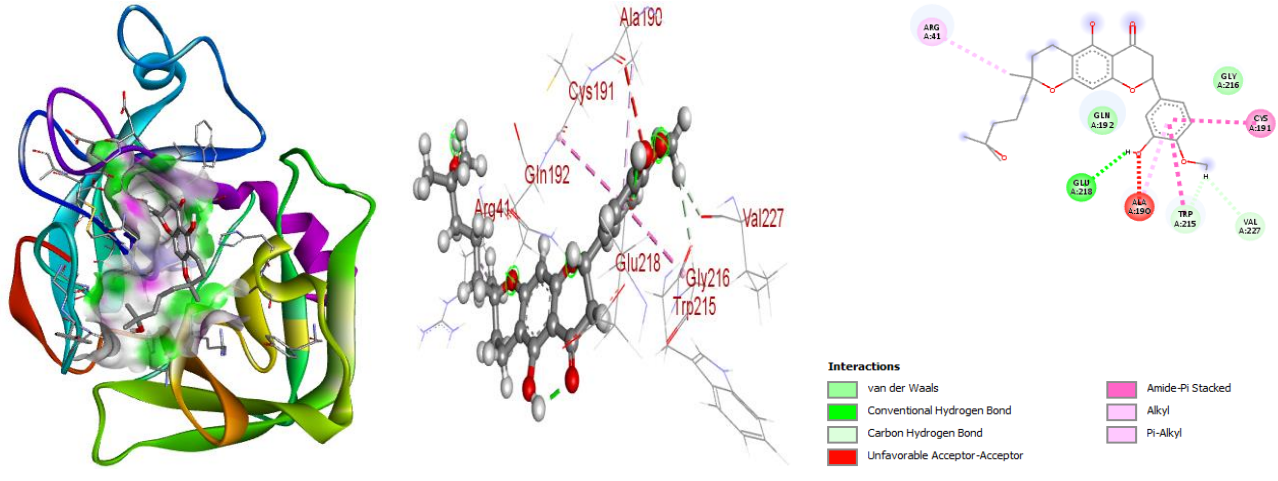
(F) Cepharanthine - ABL1



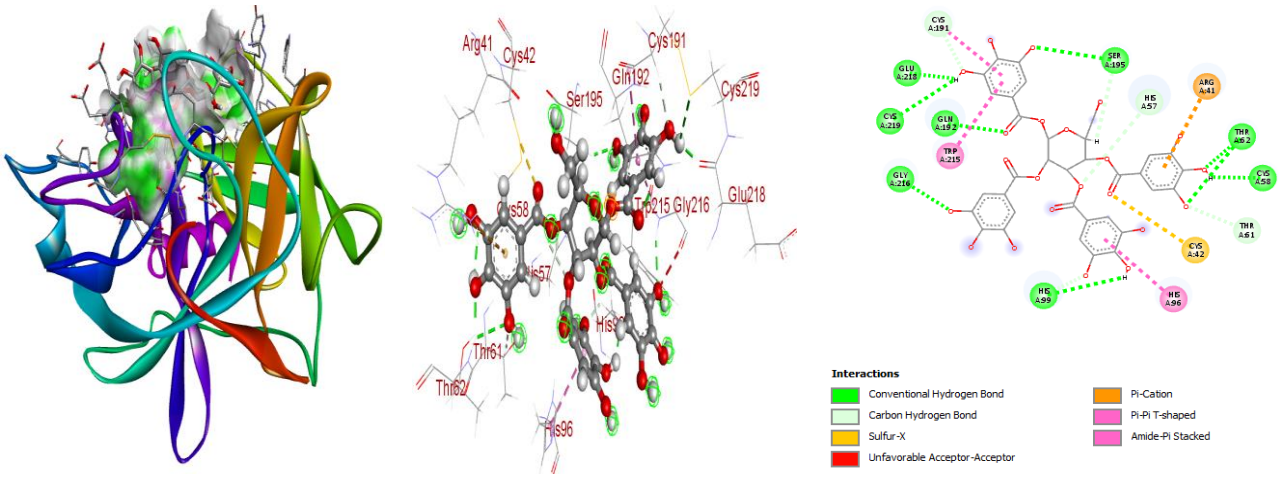
(G) Amentoflavone - calcineurin–NFAT



(E) Amentoflavone - TMPRSS2



(F) Tomentin B - TMPRSS2



(G) Glucogallin - TMPRSS2

Appendix 6. Interactions of the natural compounds with different structural proteins of SARS CoV-2.