Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Data

Table S1. Docking results of SARS-CoV PLpro and SARS-CoV-2 PLpro inhibitors

compounds	BUDE binding Energy KJ/mol	Binding efficacy	target
B004	-60.93	-0.44	SARS-CoV PLpro
B005	-84.75	-0.32	SARS-CoV PLpro
B009	-84.58	-0.34	SARS-CoV PLpro
B010	-75.92	-0.36	SARS-CoV PLpro
B013	-80.75	-0.36	SARS-CoV PLpro
Vaniprevir (VAN)	-76.55	-0.18	SARS-CoV-2 PLpro HCV protease
Simeprevir (SIM)	-84.27	-0.19	SARS-CoV-2 PLpro HCV protease
VIR250	-83.72	-0.24	SARS-CoV-2 PLpro
VIR251	-83.45	-0.23	SARS-CoV-2 PLpro
Rac5C	-84.75	-0.37	SARS-CoV-2 PLpro
Compound 2	-70.86	-0.38	SARS-CoV-2 PLpro
Compound 3	-72.24	-0.39	SARS-CoV-2 PLpro
Compound 6	-68.81	-0.32	SARS-CoV-2 PLpro

Table S2: Average of RMSD, RMSF, BL2 RMSD, Rg, SASA, number of H-bonds and % of H-bonds over 100 ns simulations for SARS-CoV-2 PLpro lead 1, lead 2 and reported SARS-CoV-2 inhibitors.

	Protein	GRL0617	Lead 1	Lead 2	CP2	CP3	CP6	SIM	VAN
RMSD(nm)	0.24	0.20	0.20	0.27	0.21	0.22	0.22	0.31	0.26
RMSF(nm)	0.14	0.13	0.13	0.14	0.13	0.13	0.13	0.14	0.14
BL2 RMSD(nm)	0.11	0.11	0.11	0.13	0.12	0.12	0.12	013	013
Rg (nm)	2.4	2.4	2.3	2.3	2.3	2.3	2.3	2.4	2.4
SASA (A^2)	163.0	161.9	163.2	164.4	163.4	161.5	163.7	167.2	167.3
H-bonds number		3	2	2	2	2	2	1	1
% H-bonds		99.8	91.8	75.9	99	99	98.8	10%	17.1

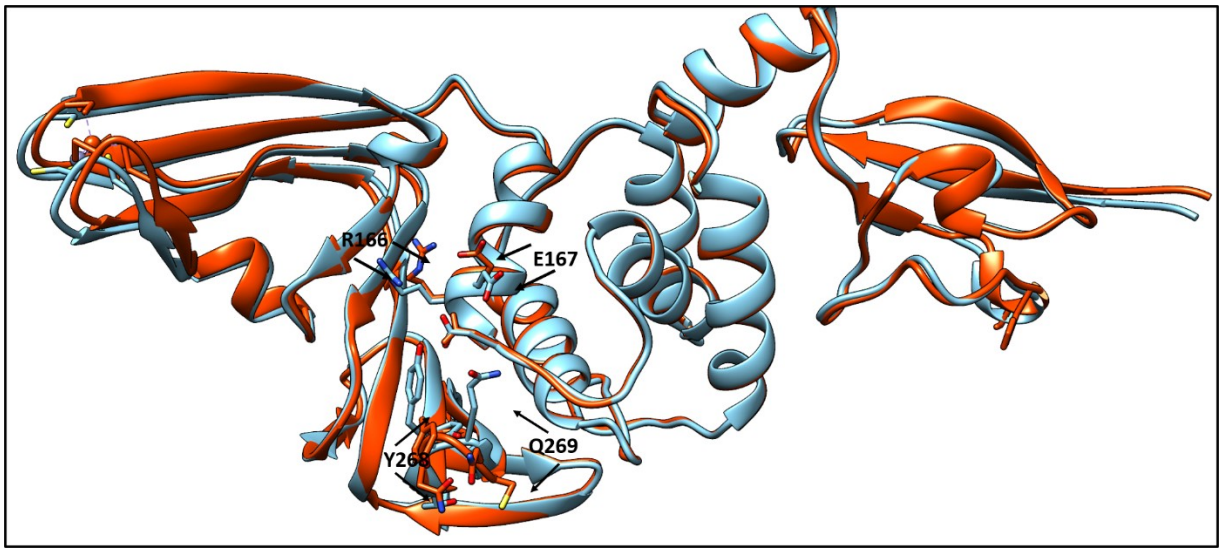

Figure S1. Represented structure superposition of APO PLpro protein (PDB: 6WZU) orange red ribbon, and PLpro protein complexes with GRL0617 (PDB: 7JRN) (sick, blue). BL2 loop residues (Y268, Q269) and R166, E167 in case Apo protein oriented outward while when the PLpro complexes with GRL0617 the residues moved inside. Which indicate the BL2 residues and R166-E167 play role in colsing and opening the putative pocket.

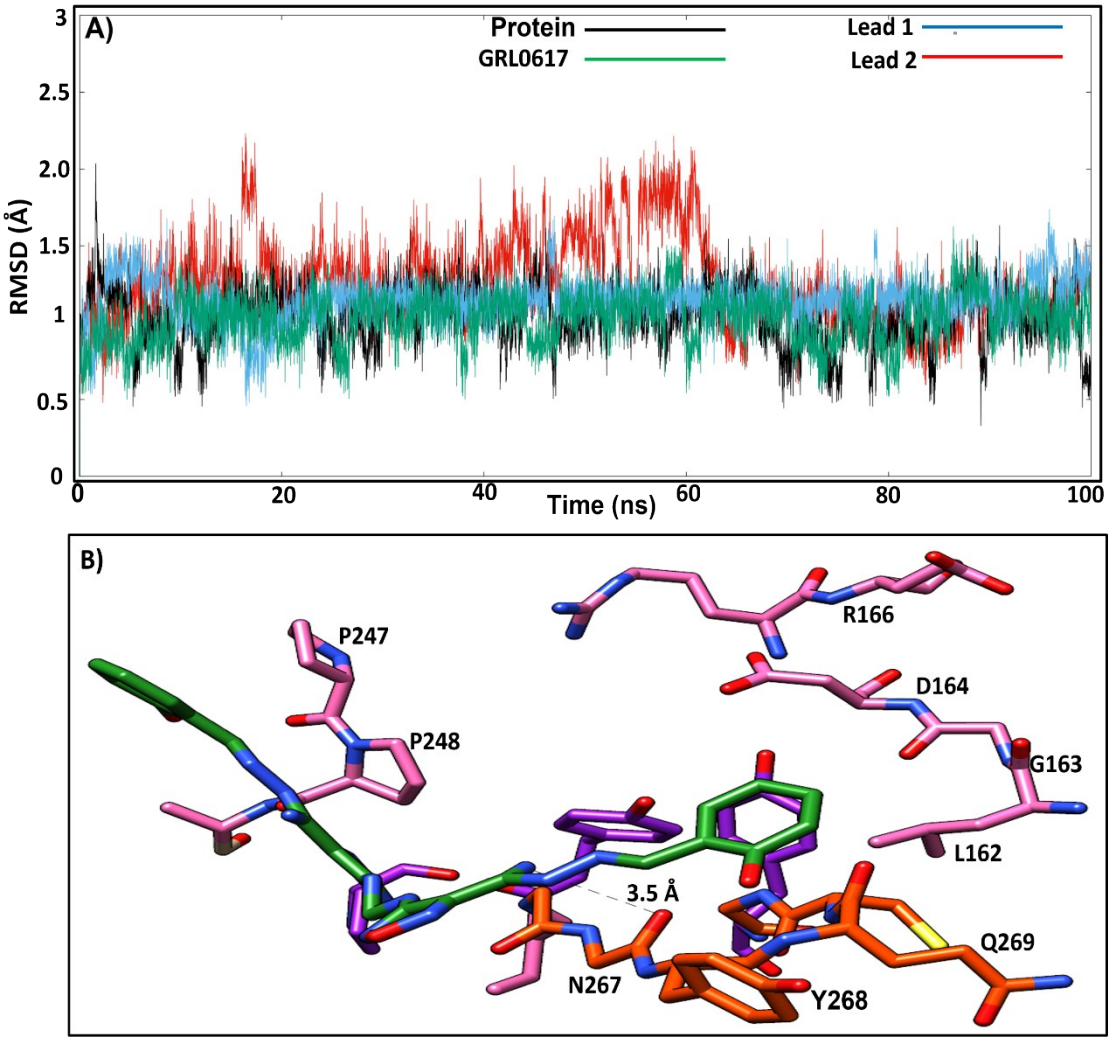

Figure S2: A) RMSD of the BL2 loop complexed with free-ligand protein (black), GRL0617 (green), lead 1 (blue) and lead 2 (red). B) interaction of lead 2 (green) with BL2 loop residues (orange) in the period 50-60 ns, N267, Y268 and Q269 moved outward to give space to accommodate lead 2.

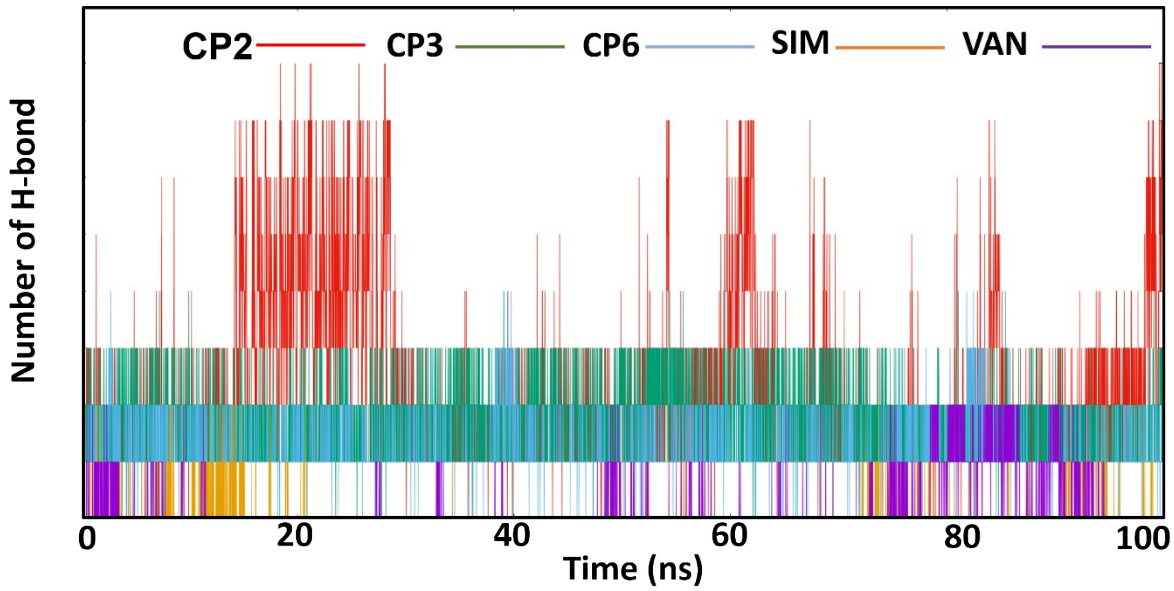

Figure S3: Number of H-bonds of Compounds 2,3,6, SIM and VAN,

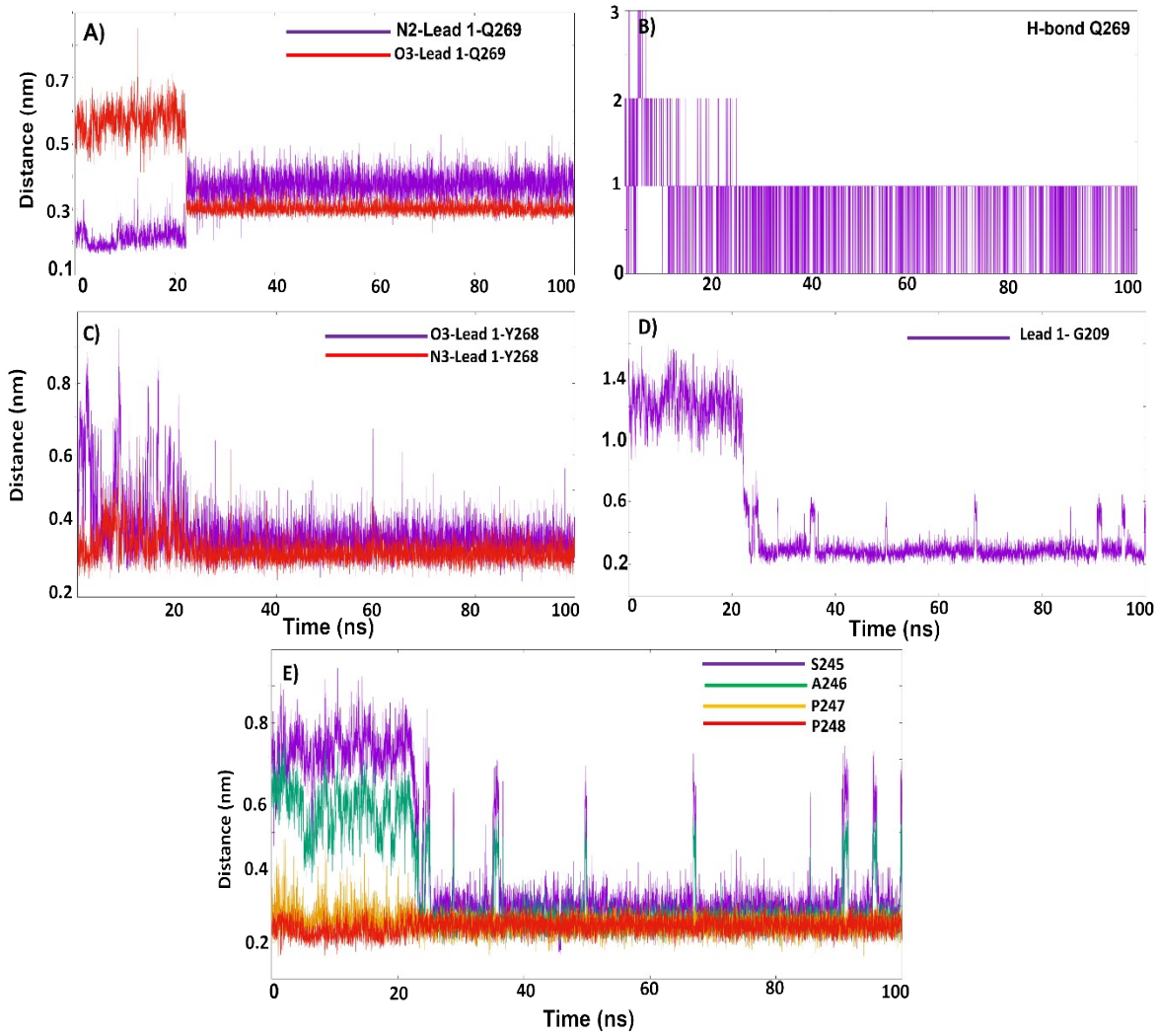

Figure S4: Represented the distance between the key residues and lead 1 A) distance with Q269 B) H-bond with Q269.C) distance with Y268. D) distance with G209. E) distance with S245, A246, P247 and P248.

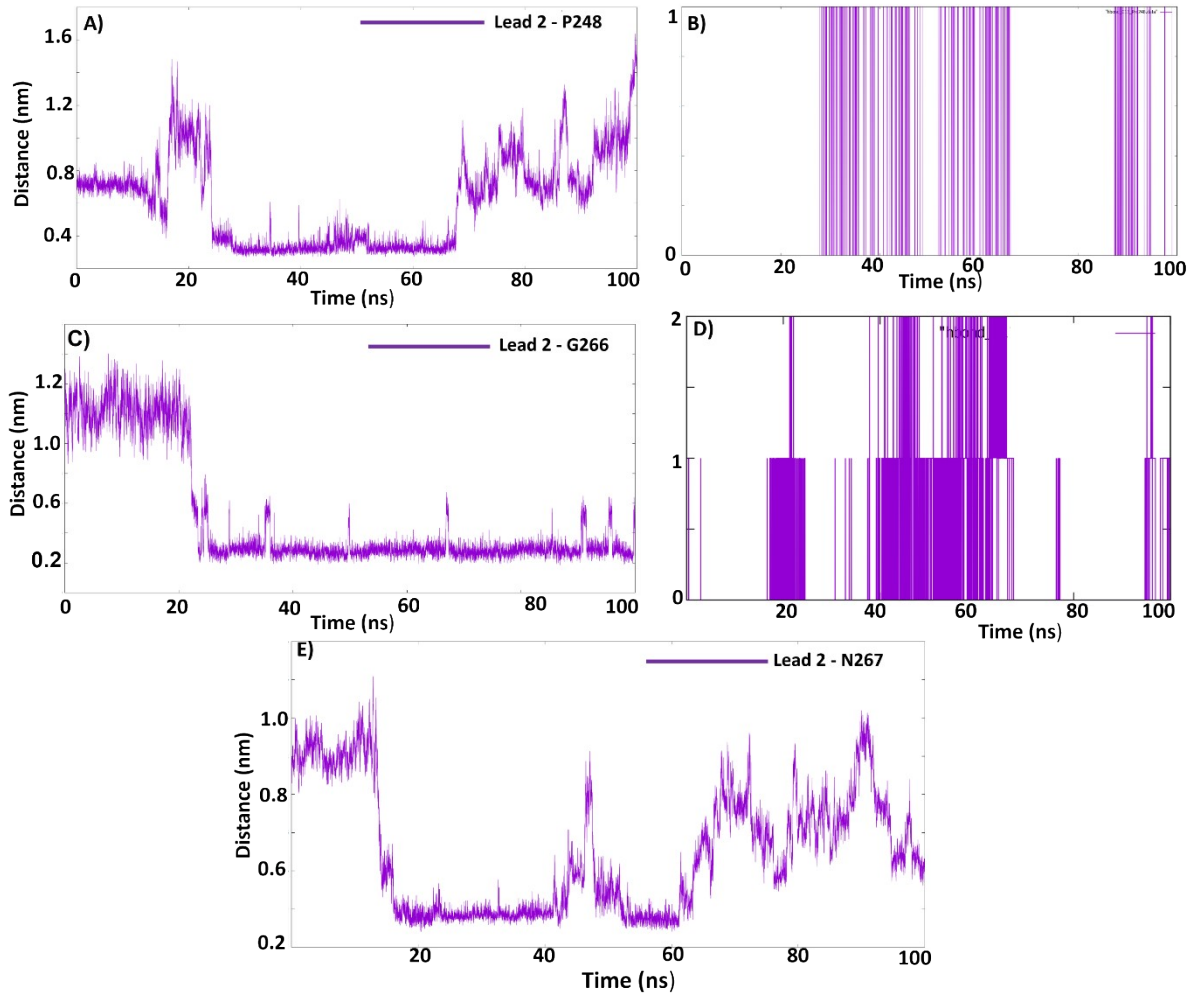

Figure S5: Represented the distance between the key residues and lead 2 A) distance with P248 B) H-bond with P248. C) distance with G266. D) H-bond with G266. E) distance with N267.