Supplementary Table S1 | Amino acid substitutions of spike protein of hundred isolates.

Position	Amino acid replaced	GenBank Definition	GenBank ID
28	AY(N)T	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/Yunnan-01/human/2020/CHN, complete genome	MT049951.1
49	LH(Y)S	Severe acute respiratory syndrome coronavirus 2 isolate 2019-nCoV/USA-CA5/2020, complete genome	MT027064.1
157	EL(F)R	Severe acute respiratory syndrome coronavirus 2 isolate 2019-nCoV/USA-CruiseA-18/2020, complete genome	MT159716.1
181	EV(G)K	Severe acute respiratory syndrome coronavirus 2 isolate 2019-nCoV/USA-CruiseA-23/2020, complete genome	MT184910.1
221	FW(S)A	Severe acute respiratory syndrome coronavirus 2 isolate SNU01, complete genome	MT039890.1
247	RR(S)Y	Severe acute respiratory syndrome coronavirus 2 isolate Australia/VIC01/2020, complete genome	MT007544.1
407	VI(R)Q	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/29/human/2020/IND, complete genome	MT012098.1
614	QG(D)V	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/PC00101P/human/2020/USA, complete genome	MT192765.1
930	SV(A)I	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/166/human/2020/IND, complete genome	MT050493.1

Multiple sequence alignment were performed to identify the homology of spike protein with in the hundred isolates. Results revealed that there were nine amino acid substitutions with in the spike protein sequence of hundred isolates. Red colour residue indicates the substituted amino acid in place of the residue shown in brackets.

Supplementary Table S2 | Amino acid substitutions of main protease of hundred isolates.

Position	Amino acid replaced	GenBank Definition	GenBank ID
74	PX(S)G	Severe acute respiratory syndrome coronavirus 2 isolate 2019-nCoV/USA-CruiseA-24/2020, complete genome	MT184911.1
124	IC(R)K	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2/nCoV-19-02S/human/2020/VNM, complete genome	MT192773.1

Multiple sequence alignment were performed to identify the homology of main protease with in the hundred isolates. Results revealed that there were only two amino acid substitutions with in the main protease sequence of hundred isolates. Red colour residue indicates the substituted amino acid in place of the residue shown in brackets.

Supplementary Table S3 | Docking score and binding site residues of TMPRSS2 against 16 protease inhibitors.

Target	Ligand	LibDock Score	Active site residues interacted through H-bond
TMPRSS2	Ritonavir (CID_392622)	195.831	HIS296, SER441
	Atazanavir (CID_148192)	185.41	HIS296, SER441
	Indinavir (CID_5362440)	178.747	SER441,ASP435
	Lopinavir (CID_92727)	177.819	SER441
	Darunavir(CID_213039)	177.313	SER441
	Saquinavir(CID_441243)	170.439	SER441
	Tipranavir(CID_54682461)	168.931	-
	Nelfinavir(CID_64143)	163.876	HIS296
	Amprenavir(CID_65016)	160.613	HIS296, SER441, ASP435
	Fosamprenavir(CID_131536)	159.957	SER441
	Paritaprevir*(CID_45110509)	153.917	HIS296, SER441
	Simeprevir* (CID_24873435)	151.171	SER441, ASP435
	Boceprevir * (CID_10324367)	99.9736	SER441
	Asunaprevir*(CID_16076883)	71.993	SER441
	Grazoprevir* (CID_44603531)	No pose	-
	Telaprevir*(CID_3010818)	No pose	-

Molecular docking studies were done using LibDock protocol in Discovery studio 4.1 and the pose having highest docking score corresponding to each ligand is documented for further analysis. Study revealed that Ritonavir showed highest docking score and favorable interactions with amino acid residues in defined active site. * indicate HCV inhibitors.

Supplementary Table S4 | Docking score and binding site residues of Cathepsin L against 16 protease inhibitors.

Target	Ligand	LibDock Score	Active site residues interacted through H-bond
Cathepsin L	Atazanavir (CID_148192)	166.186	ASP162, GLY68, MET70, MET161, HIS163, GLY67, LEU69
	Ritonavir (CID_392622)	158.542	ASP162, GLN19, GLY68,MET161, TRP26, GLY23, GLY67
	Indinavir (CID_5362440)	157.285	ASP162, GLN19, GLY68
	Tipranavir(CID_54682461)	150.714	ASP162, GLY68, MET161
	Lopinavir (CID_92727)	148.381	ASP162, GLY68, TRP26, HIS163, GLY23, GLY67
	Saquinavir(CID_441243)	140.171	GLY68, MET161
	Darunavir(CID_213039)	137.975	MET70, MET161
	Amprenavir(CID_65016)	136.064	GLY68, MET161, TRP26, GLY67
	Nelfinavir(CID_64143)	134.429	ASP162, CYS25, GLY68, TRP26, GLY67
	Fosamprenavir(CID_131536)	132.857	ASP162, CYS25, GLY68, MET161, LEU69
	Simeprevir* (CID_24873435)	123.044	ASP162, GLY68, MET161, GLY67
	Paritaprevir*(CID_45110509)	118.679	ASP162, MET161
	Boceprevir * (CID_10324367)	109.652	ASP162, GLY68
	Asunaprevir*(CID_16076883)	101.922	ASP162, CYS25, GLY68, HIS163
	Grazoprevir* (CID_44603531)	No pose	-
	Telaprevir*(CID_3010818)	No pose	-

Molecular docking studies were done using LibDock protocol in Discovery studio 2020 and the pose having highest docking score corresponding to each ligand is documented for further analysis. Study revealed that Atazanavir showed highest docking score and favorable interactions with amino acid residues in defined active site. * indicate HCV inhibitors.

Supplementary Table S5: Docking score and binding site residues of Cathepsin B against 16 protease inhibitors.

Target	Ligand	LibDock Score	Active site residues interacted through H-bond
Cathepsin B	Indinavir (CID_5362440)	169.347	GLY27, CYS29, HIS111, GLN23, GLY24, GLY198
	Darunavir(CID_213039)	157.177	GLY27, TRP221, GLY74, GLY73, GLY24
	Amprenavir(CID_65016)	152.165	GLY27, TRP221, GLY74, GLY73, GLY24
	Fosamprenavir(CID_131536)	151.241	GLY27, TRP221, GLY74, HIS199
	Tipranavir(CID_54682461)	151.187	CYS29
	Ritonavir (CID_392622)	150.161	GLN23, GLY74
	Nelfinavir(CID_64143)	149.193	HIS111, GLN23, CYS26
	Boceprevir * (CID_10324367)	137.083	GLY27, TRP221, GLN23, GLY73, GLY198
	Saquinavir(CID_441243)	134.155	GLY27, GLY74
	Lopinavir (CID_92727)	123.733	CYS26
	Atazanavir (CID_148192)	118.746	GLY73
	Grazoprevir* (CID_44603531)	No pose	-
	Simeprevir* (CID_24873435)	No pose	-
	Paritaprevir*(CID_45110509)	No pose	-
	Telaprevir*(CID_3010818)	No pose	-
	Asunaprevir*(CID_16076883)	No pose	-

Molecular docking studies were done using LibDock protocol in Discovery studio 2020 and the pose having highest docking score corresponding to each ligand is documented for further analysis. Study revealed that Indinavir showed highest docking score and favorable interactions with amino acid residues in defined active site. * indicate HCV inhibitors.