Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Materials

Searching Phytochemical based Medication for SARS-CoV-2 infection by Molecular docking models towards Spike glycoprotein and Main Protease

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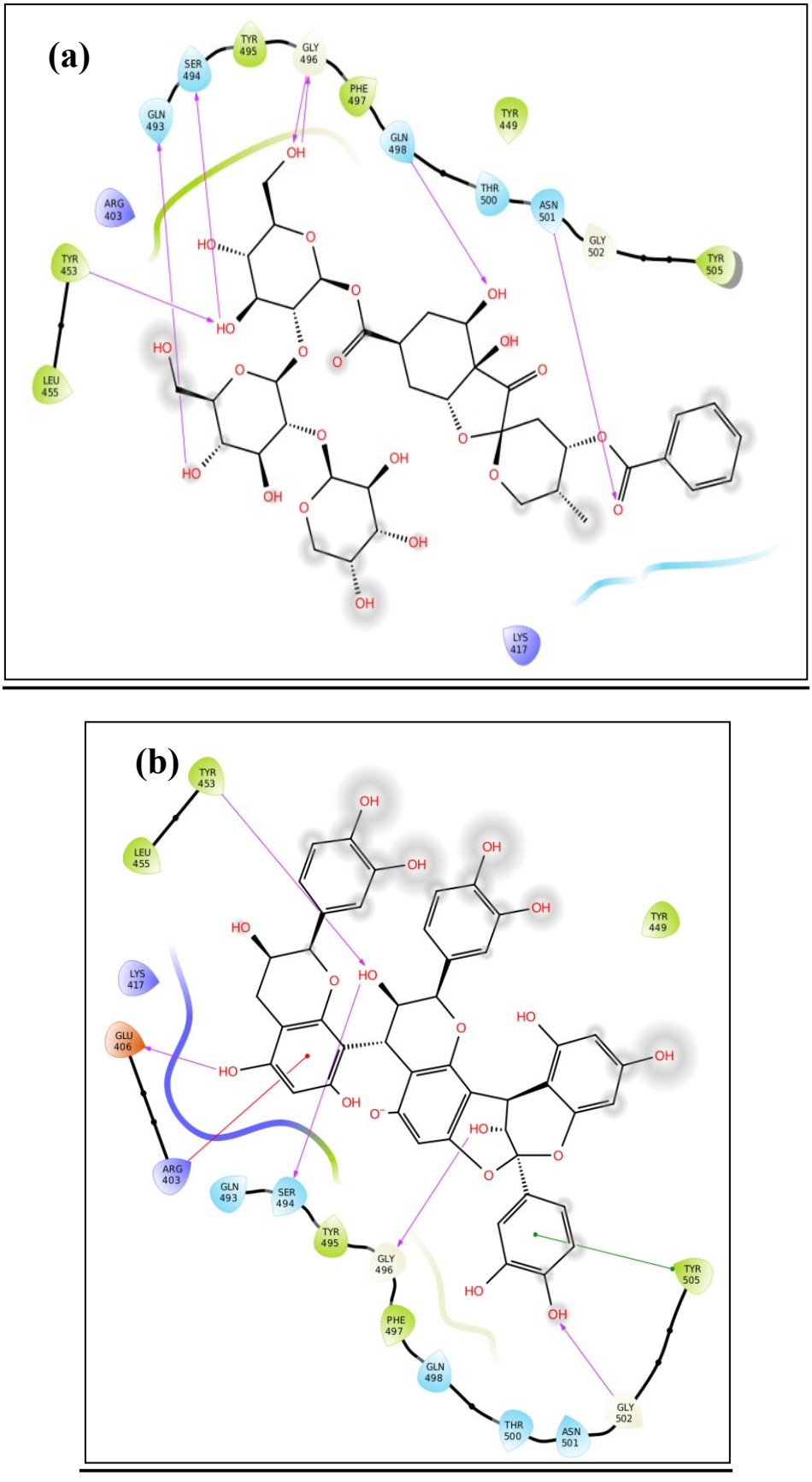

Figure S1. 2D interaction plot of (a) Phyllaemblicin C compound with the RBD domain of spike protein (b) Cinnamtannin B1 compound with the RBD domain of spike protein.

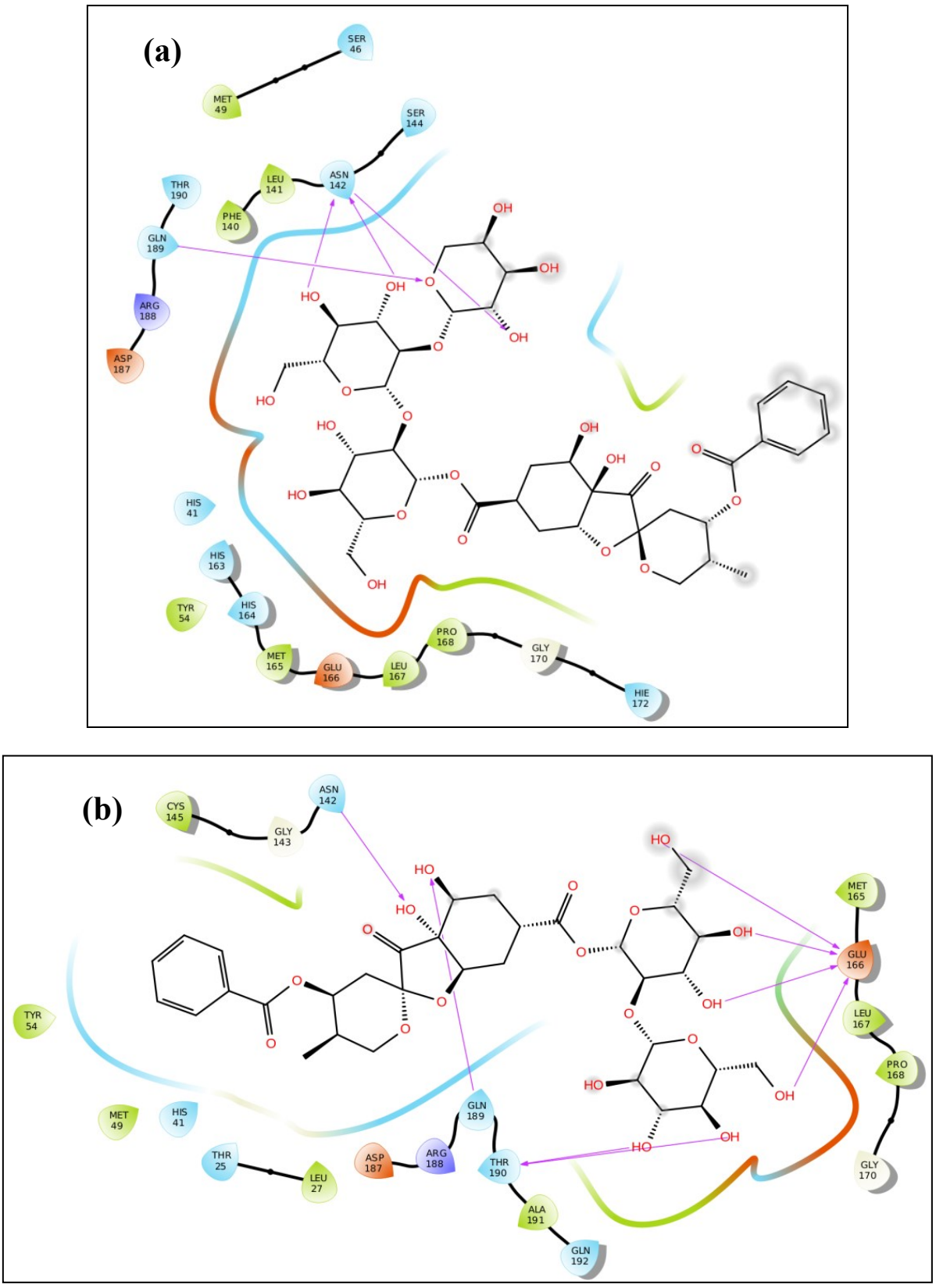

Figure S2. 2D interaction plot of (a) Phyllaemblicin C with the M^{pro} protein and (b) Phyllaemblicin B with the M^{pro} protein.

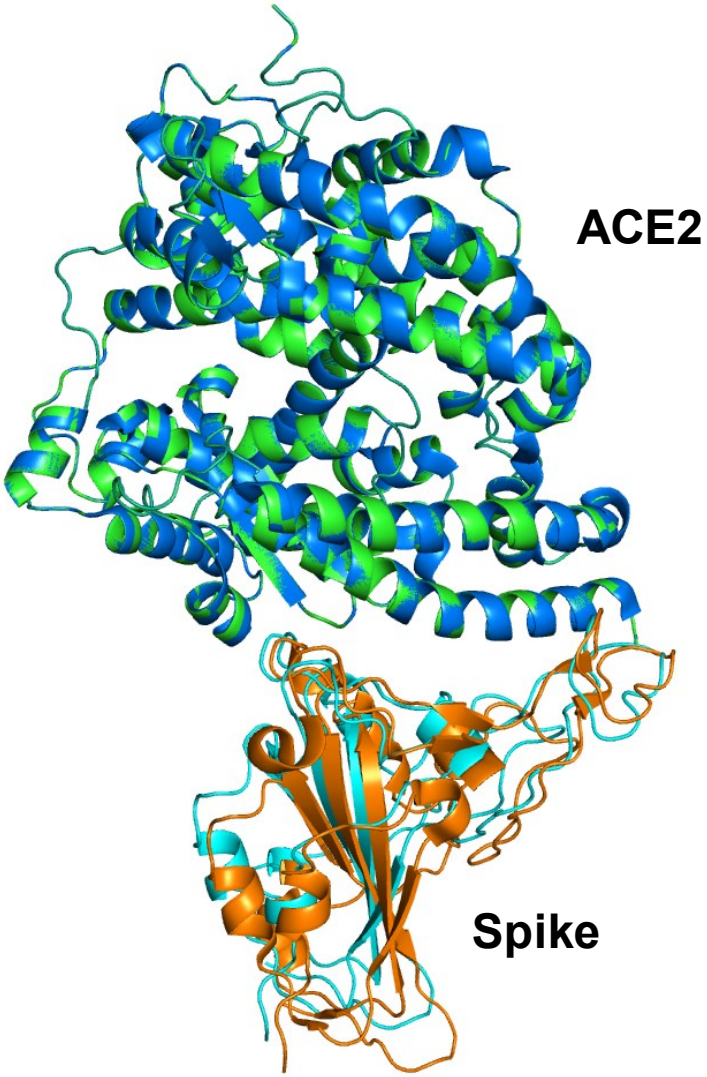

Figure S3. Three dimensional structure alignment of the docked pose of the RBD domain of SARS-CoV-2 Spike protein and human ACE2 receptor from ZDOCK software with the corresponding crystal structure complex (PDB id: 6M0J). The RBD of spike protein in the docked pose and crystal structure is shown as cyan and orange cartoon respectively. Human ACE2 receptor protein is shown in green and blue color respectively.

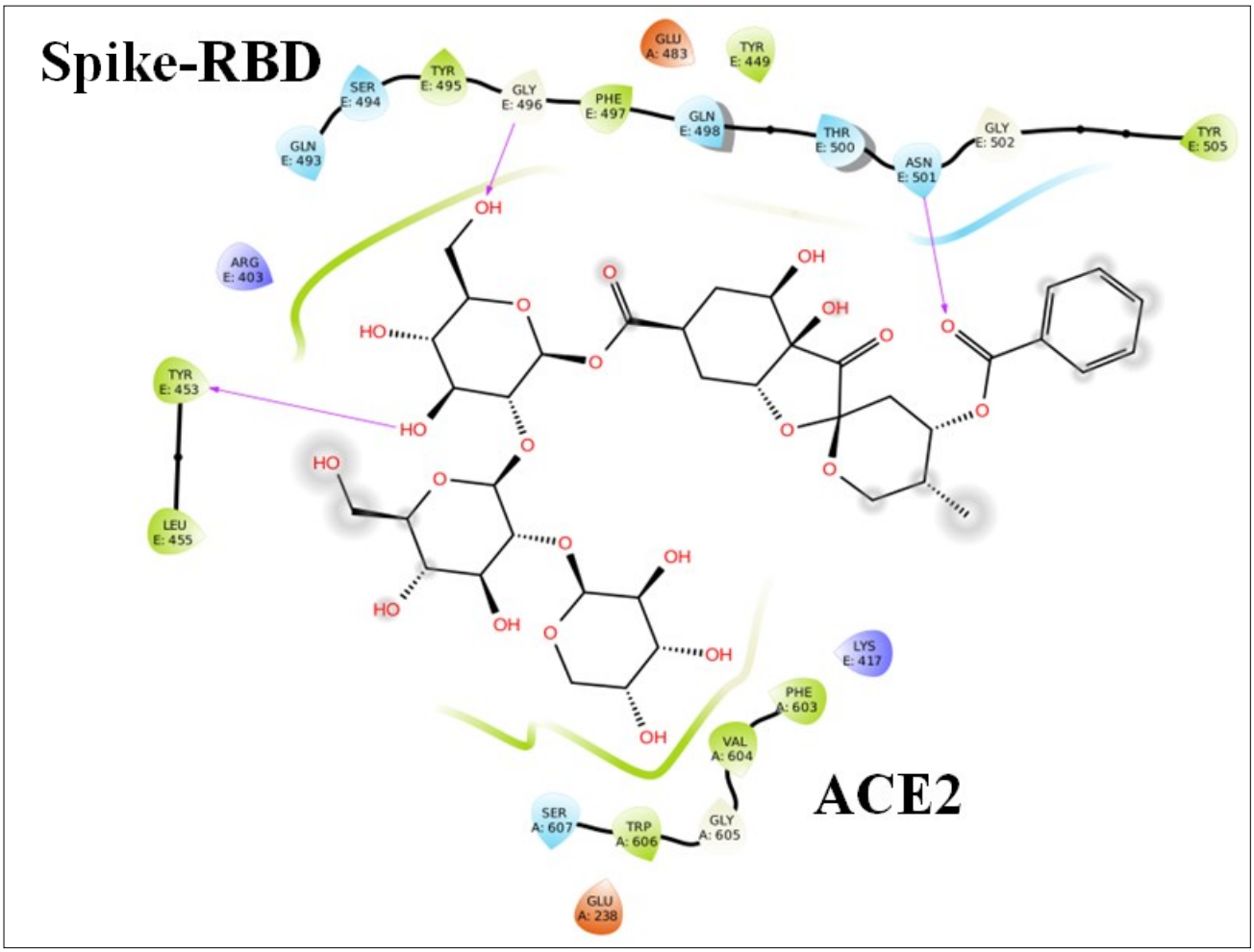

Figure S4: 2D interaction diagram of human ACE2 receptor in complex with RBD spike protein with bound phytochemical Phyllaemblicin C.

Table S1: The binding affinity of the phytochemical compounds towards the SARS-CoV-2 spike protein and M protease.

Protein target	Compounds	Binding affinity (kcal/mol)
Spike protein	Phyllaemblicin C	-9.131
	Cinnamtannin B1	-9.008
	Phyllaemblicins B	-7.381
	Procyanidine B1	-6.275
	Procyanidine A2	-5.023
	Embelin	-4.200
	Vasicine	-3.867
	Germacron	-3.095
Main protease	Phyllaemblicin C	-9.723
	Phyllaemblicins B	-9.151
	Procyanidine B1	-9.151
	Cinnamtannin B1	-8.385
	Procyanidine A2	-7.105
	Vasicine	-3.220
	Embelin	-3.187
	Germacron	-2.143

Table S2: Interacting distance of the three best phytochemical compounds towards SARS-CoV-2 active site residues of spike protein (RBD) and Main protease.

SARS-CoV-2 target	Phytochemicals	Distance (Å)	Interacting amino acid residues
Spike protein (RBD)	Phyllaemblicin C	1.89	**Y453**
		1.93	**G496**
		1.81	**Q498**
		2.05	**N501**
		2.79	**Y449**
		2.17	S494
		1.86	**Q493**
		3.90	**T500**
		5.00	**Y505**
		5.63	F497
		4.58	R403
		4.79	Y495
		4.23	**L455**
		2.80	**Q493**
		6.30	**K417**
	Cinnamtannin B1	4.71	R403
		1.90	**Y453**
		2.13	**G502**
		1.94	**G496**
		2.60	**Q498**
		2.36	S494
		1.86	Q406
		2.87	**Q493**
		3.07	**Y505**
		4.52	**N501**
		4.76	Y495
		5.48	Y449
		5.10	**K417**
		5.14	F497
	Phyllaemblicin B	2.16	R403
		1.81	Q409
		2.10	**K417**
		2.17	**Y453**
		2.00	**Y505**
		2.98	D405

		1.59	Q406
		4.94	Y495
Main protease (M^{pro})	Phyllaemblicin C	2.18	N142
		1.73	**Q189**
		2.69	E166
		2.69	**H164**
		2.66	**H163**
		2.76	**P168**
		2.44	**H41**
		4.92	**L167**
		4.89	**Q192**
		3.10	**M165**
		4.71	**C145**
		4.90	**Y54**
		3.72	**M49**
		2.74	**Q189**
	Phyllaemblicin B	2.22	N142
		2.19	**Q189**
		2.86	E166
		3.07	**L167**
		1.82	**T190**
		2.68	**P168**
		3.18	**C145**
		2.5	**H41**
		5.06	**M49**
		5.34	**M165**
	Procyanidine B1	1.98	E166
		2.15	N142
		1.80	**T190**
		2.19	**H164**
		1.85	F140
		3.25	**Q189**
		2.42	**H41**
		4.80	**P168**
		4.46	**M165**

Table S3: Interaction between amino acid of the docked complexes of RBD of SARS-CoV-2 spike protein and human ACE2 receptor and RBD of SARS-CoV-2 spike protein in complex with Phyllaemblicin C phytochemical with human ACE2 receptor.

Interacting amino acid pairs in the docked complex of Spike protein – human ACE2		Interacting amino acid pairs in the docked complex of Spike protein:Phyllaemblicin C – human ACE2	
RBD of Spike protein	Human ACE2	RBD of Spike protein	Human ACE2[a]
Y 489	**Q 24**	N 487	M 249
G 476	S 19	D 420	F 592
V 503	G 354	T 415	P 235
L 455	**D 30**	T 415	K 596
F 486	M 82	Y 505	E 231
F 456	K 26	K 458	D 597
Q 498	**Y 41**	Y 489	S 257
Y 473	T 27	F 456	S 602
Y 449	**D 38**	R 408	H 228
N 487	**Y 83**	G 504	E 231
Y 505	D 355	K 417	H 239
F 456	**D 30**	S 459	K 600
V 503	T 324	G 485	I 259
Y 505	**R 393**	Y 489	S 602
T 500	G 326	Y 473	N 601
N 487	F 28	Y 473	F 603
N 501	G 354	D 420	K 596
N 501	D 355	F 456	G 605
A 475	F 28	R 408	E 231
T 500	**Y 41**	Y 421	V 604
G 502	G 326	Y 489	I 259
L 455	H 34	K 417	E 238
N 487	**Q 24**	L 455	E 238
Y 449	**K 353**	L 455	G 605
F 486	**Y 83**	A 475	N 601
R 403	**E 37**	G 476	N 601
V 503	**Q 325**	R 457	N 599
Y 449	**Q 42**	R 457	K 596
F 486	L 79	F 486	M 249
N 487	T 27	K 417	P 235
G 446	**Q 42**	R 408	E 232
F 486	**Q 24**	G 413	E 589
N 501	G 352	T 415	F 592
T 500	D 355	G 416	F 592

P 499	**N 330**	A 475	K 600
A 475	E 23	Y 421	K 600
F 456	H 34	Y 473	S 602
T 500	R 357	D 405	E 231
N 501	**K 353**	Y 421	N 599
N 501	G 326	N 460	T 593
G 502	G 354	F 456	F 603
T 500	L 45	N 487	P 258
N 487	A 25	Q 474	N 601
Y 489	T 27	G 485	P 258
G 504	G 354	Y 473	N 599
T 505	G 354	T 415	T 593
Y 421	**D 30**	F 486	I 256
Q 498	**Q 42**	G 476	S 602
G 502	**K 353**	R 403	E 231
Y 489	**Y 83**	D 405	K 234
Y 505	A 386	Q 474	K 600
G 496	**D 38**	Q 406	E 231
Y 505	G 352	Q 409	P 235
A 475	**Q 24**	K 417	G 605
Q 506	G 326	D 405	E 227
Y 489	F 28	Y 473	K 600
P 499	**Q 329**	G 416	K 596
Q 493	K 31	L 455	F 603
Y 495	**K 353**	K 458	N 601
F 456	L 29	F 486	S 257
Q 493	H 34	Y 505	K 234
Q 506	**Q 329**	A 475	F 603
E 484	K 31	R 403	K 234
V 503	G 326	L 455	V 604
Q 474	T 27	Y 421	H 239
F 456	K 31	K 417	V 604
A 475	T 20	D 405	H 228
Y 505	**E 37**	N 487	N 601
S 477	S 19	F 456	V 604
Q 498	**D 38**	Q 474	S 602
K 417	H 34	G 493	F 603
A 475	S 19	R 457	K 600
Q 498	L 45	F 486	P 253
G 502	D 355	A 475	S 602
L 455	K 31	N 487	I 259
F 456	T 27	Y 489	V 604

G 476	**Q 24**	T 415	E 589
Y 453	H 34	K 458	K 600
F 497	**K 353**	Y 489	F 603
Y 505	**K 353**	Y 421	K 596
A 475	T 27	K 458	K 596
G 504	**K 353**	S 459	D 597
Q 493	**E 35**	F 490	F 603
N 501	**Y 41**	Y 489	P 258
Y 489	K 31	F 486	P 258
Q 498	**K 353**	Y 473	V 604
G 502	F 356	R 457	N 601
T 500	**N 330**	G 416	P 235
Q 506	**K 353**	Y 473	Q 598
S 477	**Q 24**	D 420	H 239
Y 489	L 29		
G 496	**K 353**		
K 417	**D 30**		
N 501	**N 330**		
G 502	T 324		

Human ACE2 bold residues are experimentally known to interact directly with the Spike protein of RBD domain[26], and was in good agreement with present protein-protein docking results.

[a]Human ACE2 protein interacting residues was highly distorted due to Phyllaemblicin C binding at the active site of Spike protein RBD domain. There is a major change in the three dimensional binding regions between Spike-ACE2 natural binding interface showing negligible interactions with the experimentally known active sites[26].