

Antiviral activity of chitosan nanoparticles encapsulating silymarin (Sil-CNPs) against SARS- CoV-2 (*in silico* and *in vitro* study).

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Table S1. Residues interacting with ligands (Chitosan nanoparticles, Silymarin, and Remdesivir) in the predicted Hexon, ACE2, and Spike protein binding pockets, respectively.

Hexon								
Chitosan nanoparticles			Silymarin			Remdesivir		
Hydrogen bonding								
Resid.	H-A	D-A	Resid.	H-A	D-A	Resid.	H-A	D-A
117 SER	2.09	2.75	127 LYS	2.19	3.13	644 ASN	2.83	3.27
117 SER	2.17	2.75	463 ASN	2.00	2.87	645 ASP	2.16	3.08
117 SER	2.08	3.00	467 ASN	2.24	3.18	646 TYR	2.54	3.14
127 LYS	3.21	3.90	470 ARG	3.02	3.43	648 SER	3.48	3.96
234 TYR	3.21	3.92	837 ARG	2.77	3.28	676 ARG	2.54	3.41
467 ASN	2.68	3.53				676 ARG	2.22	3.11
470 ARG	3.23	4.04						
470 ARG	3.13	3.95						
475 SER	2.30	3.06						
476 ASN	2.42	3.40						
539 ARG	2.93	3.28						
539 ARG	2.49	3.28						
828 PHE	2.04	3.01						
Salt Bridges								
Resid.	Distance							
127 LYS	3.77							
470 ARG	3.45							
538 HIS	5.18							
Hydrophobic Interactions								
			Resid.	Distance		Resid.	Distance	
			462 ILE	3.74		372 LEU	3.50	
			470 ARG	3.74		646 TYR	3.87	
			471 ASN	3.52		646 TYR	3.47	
			828 PHE	3.82		788 LYS	3.81	
						788 LYS	3.57	
						870 LEU	3.74	
π-Cation Interactions								
			Resid.	Distance	offset	Resid.	Distance	offset
			470 ARG	3.69	0.87	676 ARG	3.89	1.66

ACE2								
Chitosan nanoparticles			Silymarin			Remdesivir		
Hydrogen bonding								
Resid.	H-A	D-A	Resid.	H-A	D-A	Resid.	H-A	D-A
166 GLU	2.32	3.02	479 GLU	3.10	3.42	482 ARG	2.46	2.92
174 LYS	3.45	3.87	644 ARG	3.31	3.88	482 ARG	2.80	3.24
492 PRO	2.54	3.17	668 GLU	2.08	2.86	489 GLU	2.36	3.20
493 HIS	2.47	3.18	672 VAL	2.98	3.79	613 TYR	3.34	3.84
493 HIS	2.48	3.01	675 LEU	2.19	3.18	674 ASN	2.54	3.21
494 ASP	2.40	3.25				675 LEU	2.17	3.18
494 ASP	3.20	4.04						
671 ARG	3.39	4.07						
672 VAL	2.01	2.87						
672 VAL	2.03	2.86						
674 ASN	3.28	3.90						
674 ASN	3.24	3.79						
675 LEU	2.07	3.03						
Salt Bridges								
Resid.	Distance							
174 LYS	5.49							
644 ARG	4.99							
644 ARG	5.42							
671 ARG	4.22							
π -Cation Interactions								
Resid.	Distance	offset	Resid.	Distance	offset	Resid.	Distance	offset
			644 ARG	4.10	1.84			
Hydrophobic Interactions								
			Resid.	Distance	Resid.	Distance		
			475 LYS	3.74	475 LYS	3.84		
			494 ASP	3.36	479 GLU	3.85		
			672 VAL	3.77	492 PRO	3.76		
			675 LEU	3.62	494 ASP	3.50		
					495 GLU	3.68		
					640 MET	3.81		
					672 VAL	3.46		
					672 VAL	3.99		
					675 LEU	3.68		

Spike protein								
Chitosan nanoparticles			Silymarin			Remdesivir		
Hydrogen bonding								
Resid.	H-A	D-A	Resid.	H-A	D-A	Resid.	H-A	D-A

355 ARG	2.31	3.06	336 CYS	2.86	3.73	371 SER	2.22	2.87
428 ASP	2.38	2.92	371 SER	1.87	2.71	371 SER	2.14	2.87
430 THR	2.78	3.73	373 SER	3.60	3.94	373 SER	2.80	3.69
430 THR	1.89	2.84	373 SER	2.91	3.51	436 TRP	2.99	3.78
430 THR	1.98	2.96	436 TRP	2.23	3.03	509 ARG	2.18	2.97
463 PRO	2.30	2.90						
463 PRO	3.26	3.85						
466 ARG	3.12	4.06						
466 ARG	3.25	3.99						
514 SER	2.72	3.11						
515 PHE	2.05	2.97						
516 GLU	1.97	2.87						
517 LEU	1.92	2.89						
517 LEU	1.89	2.74						
Salt Bridges								
Resid.	Distance		Resid.	Distance		Resid.	Distance	
466 ARG	3.78							
Hydrophobic Interactions								
Resid.	Distance		Resid.	Distance		Resid.	Distance	
			338 PHE	3.71		338 PHE	3.72	
			342 PHE	3.96		342 PHE	3.58	
			367 VAL	3.90		342 PHE	3.84	
			368 LEU	3.75		368 LEU	3.69	

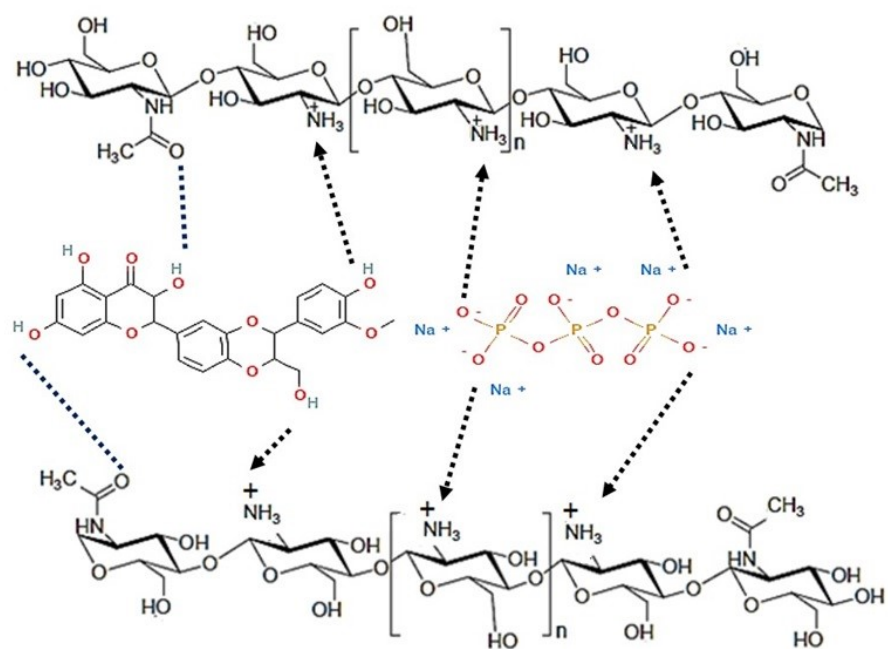


Figure S1. A schematic diagram of the chemical interaction of Sil @ CNPs nanocomposite.