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Molecular Docking of Phytochemical compounds against Sars-Cov-2 Surface Glycoprotein and Envelope Protein

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Abstract: **In December 2019 Wuhan city, the capital of Hubei province in China became the epicenter of an outbreak of pneumonia of unknown cause. Chinese scientists had isolated a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-COV-2): previously known as 2019 (COVID-19). In this work we have taken Covid 19's Surface glycoprotein and Envelope protein. Using homology modeling the 3d structure of the proteins are modeled. Phytochemical compounds from the established medicinal herbs are selected and ADME studies are done. Further virtual screening was done and as per the screening results it is seen that the phyto-compounds Withanolide A and Withaferine A has very good docking score with the viral proteins selected.**

Keywords: SARS-COV-2, phytocompounds, modeling, ADME, docking

I. INTRODUCTION

Immune resoponses induced by COVID-19 infection.

Clinically the immune response induced by SARS-COV-2 infection is two phased [1]. During the incubation and non-seven stages, a specific adaptive immune response is required to eliminate the virus and to preclude disese progression to severe stages [1]. Therefore, strategies to boost immune responses at this stage are certainly important [1].

Protiens

Coronaviruses are a recently characterized group of enveloped viruses which contain large single – stranded RNA genomes of messenger polarity [2]. In corona virus it has spikes protein on its surface, these spike proteins are glycoproteins which are responsible for initial binding of previous SARS corona viruses to lung cells and their activation of the spike protein by a proteolytic cleavage [3, 4].

The spike glycoprotein (spike protein) is the familiar spike that studs the surface of the corona viruses, giving it the appearance of a crown to electron microscopy, hence "corona" (latin: crown) [4].

Spike Protien (S Protein)

The corona virus spike protein is a class-1 fusion protein [5]. The formation of an alpha helical coiled-coil structure is characteristic of this class of fusion protein, which contain in their C-terminal part regions predict to have an alpha helical secondary structure and to form coiled coils [5, 6]. The S2 subunits are the most conserved region of the protein, where as S1 subunit diverge in sequence even among species of a single corona virus [4]. S1 contains two subdomains, a N-terminal domain (NTD) and a C-terminal domain (CTD) [7, 8]. Both are able to function as receptor binding domain (RBDs). And bind variety of proteins and sugars [8].

Envelop Protein (E Protein)

Corona virus (CoV) envelope (E) proteins play manifold functions during infection, including virus morphogenesis [9, 10]. In the case of severe acute respiratory syndrome (SARS) CoV, pathogenesis the E proteins are small (74-109 amino acids) hydrophobic viroporins [11, 12]. The proteins consist of two distinct structural domains, a longer typical hydrophobic domain and a charged cytoplasmic tail; E proteins from across the virus family exhibit amino acid sequence variability [11]. The role of E proteins in assembly and egress is not fully understood but the absolute requirement for E during virus morphogenesis varies depending on the virus genus [10].

Effect Of The Phytochemical Compounds Against The Sars-Cov-2

Phytocompounds are plant compounds having biological activity [13, 14]. In the pharmaceutical industry, phytocompounds are the active ingredients who exhibit pharmacological effects applicable to the treatment of various diseases [13, 14]. There are various established anti-viral compounds and hence in this work we can claim that medicinal plants can give the strong base towards developing a novel treatment of corona virus [13, 14]. We are selecting few phytocompounds in this work (Table 1) like curcumin, anaferine, anahygrine, wihaferine, withnolides, causcohygrine and isopelletierine.

Table 1: Phytocompound used with their plant source

Phytocompound	Plant source
Curcumin	*Curcuma longa*
Anaferine	*Piper longum/ Withania somnifera*
Anahygrine	*Withania somnifera*
Wihaferine	*Withania somnifera*
Withnolides	*Withania somnifera*
Causcohygrine	*Erythroxylon coca*
Isopelletierine	*Punica granatum*

II. METHODOLOGY

Target Selction And Homology Modeling

The protein sequences of SARS-CoV-2 are downloaded from genbank (Table 2) and using swiss model server [15] their 3D structures are modeled (Fig. 1).

Table 2: SARS-CoV-2 protein with their genebank accession number

Protein name	Accession number
Surface glycoprotein (severe acute respiratory syndrome coronavirus 2)	GenBank: QJX59866.1
Envelope protein (severe acute respiratory syndrome coronavirus 2)	GenBank: YP_009724392.1

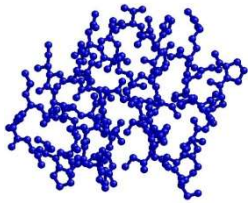
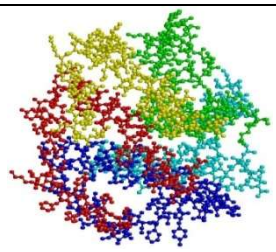
Protein name	Model
Surface glycoprotein model	
E protein model	

Fig. 1: 3D structure of modeled SARS-CoV-2 receptor proteins

Phytocompounds used in this work curcumin, anaferine, anahygrine, wihaferine, withnolides, causcohygrine and isopelletierine are downloaded from pubchem (Fig. 2)

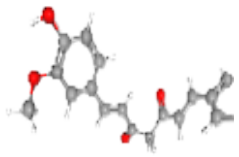
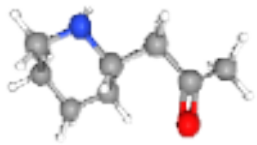
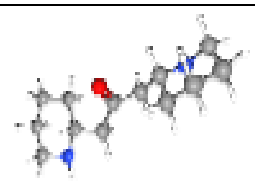
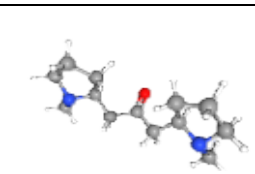
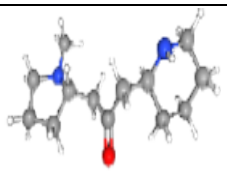
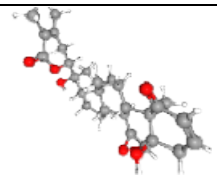
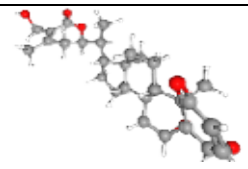
Compound name	3D Structure	Molecular formula
Curcumin		$C_{21}H_{20}O_6$
Isopelletierine		$C_8H_{15}NO$
Anaferine		$C_{13}H_{24}N_2O$
Cuscohygrine		$C_{13}H_{24}N_2O$
Anahygrine		$C_{13}H_{24}N_2O$
Withanolide A		$C_{28}H_{38}O_6$
Withaferine A		$C_{28}H_{38}O_6$

Fig. 2: Phytocompounds and Structures (From Pubchem)

Further the SARS-CoV-2 receptor proteins are docked with the above phycompounds. Using OPEN BABEL online server [16] the phytocompounds in sdf format are converted to pdb format. The ADME properties of the phytocompounds are predicted using molinspiration software.

III. RESULTS AND DISCUSSION

The ADME properties of the phytocompounds in table 2 are predicted using MOLINSPIRATION server (Table 3)

Table 3: ADME studies for the phytocompounds

Compound Name	miLogP	TPSA	natoms	MW	nON	nOHNH	nrotb	volume	nviolations
Curcumin	2.30	93.07	27	368.38	6	2	8	332.18	0
Isopelletierine	0.18	29.10	10	141.21	2	1	2	150.58	0
Anaferine	1.38	41.12	16	224.35	3	2	4	236.41	0
Cuscohygrine	0.86	23.55	16	224.35	3	0	4	236.69	0
Anahygrine	1.12	32.34	16	224.35	3	1	4	236.55	0
Withanolide A	4.15	96.36	34	470.61	6	2	2	441.81	0
Withaferine A	3.86	96.36	34	470.61	6	2	3	442.38	0

The SARS-CoV-2 receptor proteins (in *pdb format) in table 1 are docked with the phytocompounds in table 1 (converted in *pdb format using OPEN BABEL online server [17]) using PATCH DOCK server [18] (Table 4 and 5).

Table 4: Docking score of surface glycoprotein (SARS2) with phytocompounds

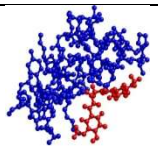
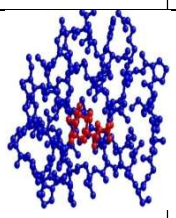
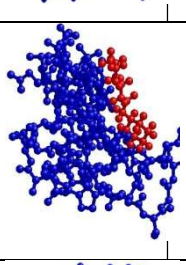
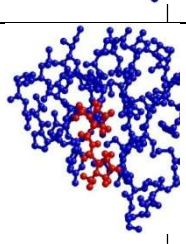
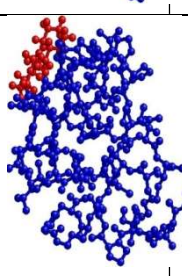
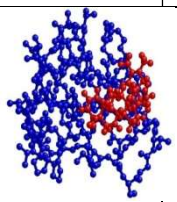
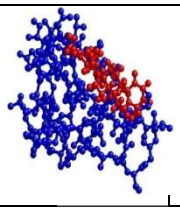
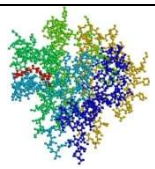
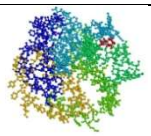
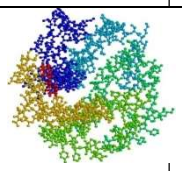
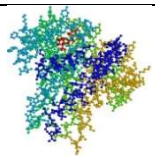
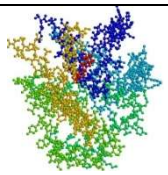
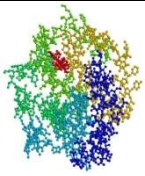
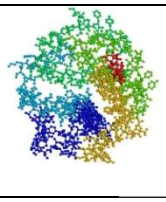
Protein	ligand	Docking scores (-kcal/mol)	Docking Interaction	
Surface glycoprotein (SARS 2)	Curcumin	3548		
Surface glycoprotein(SARS2)	Isopeletierine	1966		
Surface glycoprotein(SARS2)	Anaferine	2692		
Surface glycoprotein(SARS2)	Cuscohygrine	2726		
Surface glycoprotein(SARS2)	Anahygrine	2720		
Surface glycoprotein(SARS2)	Withanolide A	3672		Selected
Surface glycoprotein(SARS2)	Withaferine A	3854		Selected

Table 5: Docking score of E protein (SARS coronavirus2) with phytocompounds

Protein	Ligand	Docking scores (-kcal/mol)	Docking interactions	
E protein (SARS corona virus2)	Curcumin	5512		
E protein (SARS corona virus2)	Isopeletierine	2810		
E protein (SARS corona virus2)	Anaferine	3778		
E protein (SARS corona virus2)	Cuscohygrine	3826		
E protein (SARS corona virus2)	Anahygrine	4022		
E protein (SARS corona virus2)	Withanolide A	5814		Selected

E protein (SARS corona virus2)	Witha ferine A	5596		Selected

IV. CONCLUSION

As per the docking report it is seen that the phyto-compounds Withanolide A and Withaferine A has very good docking score with the viral proteins selected. Also, both the phyto-compounds shows no violations in the ADME profile. Hence, the phytocompounds Withanolide A and Withaferine A can be successfully used as ligands on SARS-CoV-2 Surface glycoprotein (severe acute respiratory syndrome coronavirus 2) and Envelope protein (severe acute respiratory syndrome coronavirus 2).

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