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In silico Molecular Docking Reveals the Interaction of Sulforaphane with the SARS-Cov-2 Main Protease

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Abstract
2019 Novel corona-virus (2019-nCoV) emerged as a global threat and put the entire globe into unrest. Unavailability of explicit drug against the virus is more essential. This demanding situation requires development of bio-molecules for efficient treatment against severe acute SARS-CoV-2. The crystal structure of SARS-CoV-2 main protease (M^{pro}) is known and thus can be used for fast *in silico* docking. This may lead to identification of active bio-molecules including phytochemicals. *In silico* Molecular Docking revealed that the phytochemical, Sulforaphane effectively binds to the active pocket of the SARS-CoV-2 main protease.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, Docking, Phytochemicals, Sulforaphane.

Introduction
The emerging 2019 Novel coronavirus (2019-nCoV) threatens public health. 2019-nCoV is also referred to as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The city of Wuhan was the epicentre where the outbreak of this human pathogen emerged, and resulted to human ailment, termed as COVID-19 [1, 2]. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [3, 4]. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing to its fast rate of transmission within the humans [1, 5, 6]. Specific drug against the virus is yet to be discovered. But there are certain preventive methods that have been suggested by the healthcare authorities like: quarantining the infected person, rapid examination of the people entering new premises from elsewhere, use of appropriate mask and washing hand regularly. Development of bio-molecules for proficient treatment against severe acute SARS-CoV-2 is challenging. The solved crystal structure of SARS-CoV-2 main protease (M^{pro}) can be used as one of the primary target molecule and possible inhibitory ligands may be screened using *in silico* docking. The spread of SARS-COV-2 is quickest and it spreads at a faster rate than any other flu it's such quick transmission can be catastrophic in nature. Primarily phytochemicals can be screened to detect any potential bio active molecules. Researchers have developed certain drugs which. Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves to be an exceptional ground for screening specific ligands [7]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins are defining features paving the path of virus from entry to infection in the host cell [8, 9, 10]. Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins. The effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear. The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that sulforaphane, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 main protease as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of sulforaphane to be used as COVID-19 therapeutics.

Methods
Viral Protein Structure and Phytochemical dataset collection
The 3D structure of M^{pro} was accessed from Protein Data Bank accession 6M03 (Fig. 1). The SDF accession CHEBI:47807 corresponding to the Sulforaphane (Fig. 2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Fig 1: 3-D Structure of the SARS-CoV-2 M^{pro} showing the active site of the protein.

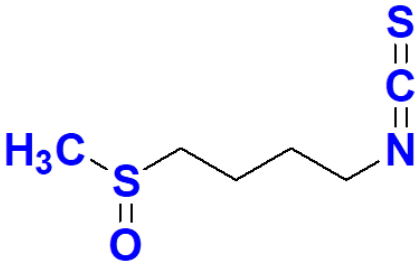

Fig 2: Chemical structure of Sulforaphane

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method was used [11]. The catalytic pocket of the M^{pro} protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

Results and Discussion

It was found that sulforaphane; a common phytochemical specifically binds to the active pocket of the SARS-CoV-2 M^{pro} (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy (Table 1). Since, simple active bio molecule like sulforaphane effectively binds into the active pocket of the M^{pro} under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of sulforaphane and eventually can be used in the pharmaceutical sector. Chemical synthesis of sulforaphane can be cost effective as compared to the isolation process from specific plants.

Table 1: CDocker Energy and CDocker Interaction Energy values generated for the interaction of Sulforaphane with the active site of SARS-CoV-2 main protease (M^{pro}).

Ligand		Receptor			Interaction status	
SDF Accession	Phytochemical	Protein	PDB Accession	Docking Result	CDocker Energy	CDocker Interaction Energy
CHEBI: 47807	Sulforaphane	Covid-19 Main protease	6M03	Positive	-15.37	-16.87

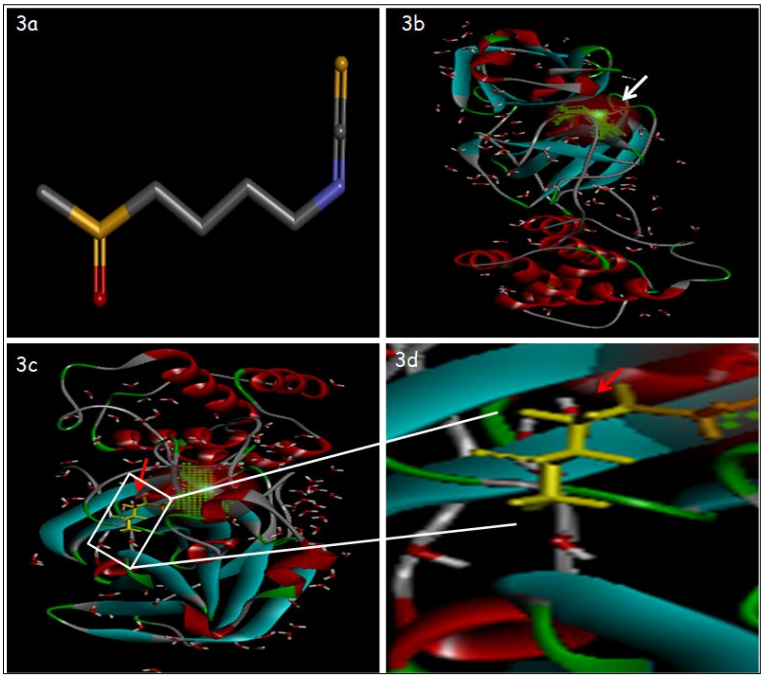

Fig 3: The active site of the SARS-CoV-2 main protease (M^{pro}) interacts with Sulforaphane. **3a:** Phytochemical, Sulforaphane. **3b:** Free form of M^{pro}. **3c:** M^{pro} associated with the ligand, Sulforaphane. **3d:** Magnified image showing the association of the Sulforaphane with the M^{pro}. (The white colored arrow and the red colored arrow indicate the active site of the M^{pro} and binding of Sulforaphane respectively).

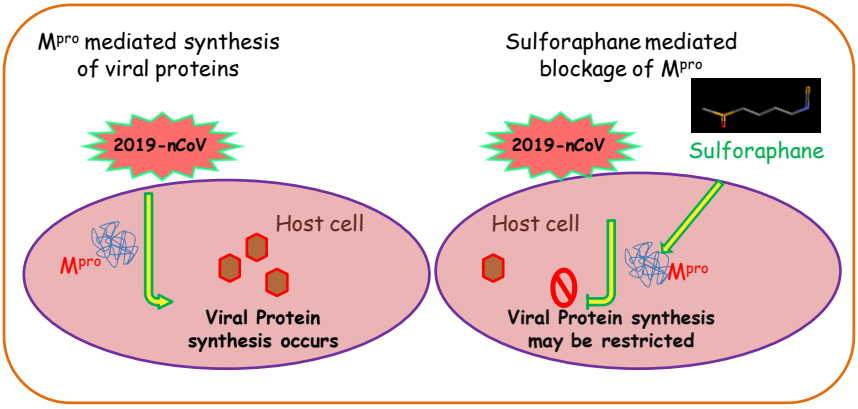

Fig. 4: Sulforaphane, a phytochemical may inhibit COVID-19 M^{pro} and thus restrict the synthesis of viral proteins.

Conclusion and Future perspectives

The current *in silico* molecular docking-based study reveals Sulforaphane can effectively target the SARS-CoV-2 M^{pro} (Fig. 4). It is being difficult for the researchers worldwide to prepare any kind of vaccine because corona virus is a novel virus that means it's contact was not traced anytime before in the history and it is a virus which finds humans as it's suitable hosts and it also changes its structure to defy the action of various photochemical with which it is treated. Various countries like Iran America etc are trying they level best to develop a vaccine which could help fight this pandemic but now due to no such development of vaccines a broad spectrum of antidotes are used which were used to treat asthma pneumonia which are said to be showing certain positive results in helping cure the person. Essentially, this study makes an attempt to reveal simple phytochemicals like sulforaphane which can be employed for designing novel therapeutics.

Author contribution statement

GKP conceived the idea. AS, GKP, TD, SKS, PKP, CR performed the experiments. GKP and CR analyzed the data. All authors have significant contribution in drafting the manuscript.

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Conflict of interest

The authors declare that they have no conflict of interest.

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