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The Phytochemical Luteolin Interacts With the SARS-Cov-2 Main Protease

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Abstract
Severe Acute Respiratory Syndrome Corona-Virus 2 (SARS-CoV-2) has put the entire globe into unrest. Unavailability of specific drug against the virus is more imperative. This demanding situation requires development of pharmacophores for efficient treatment against severe acute SARS-CoV-2. The crystal structure of SARS-CoV-2 main protease (M^{pro}) has been released, thus can be used for fast *in silico* molecular docking. This may result into identification of active bio-molecules chiefly phytochemicals. *In silico* molecular docking revealed that the phytochemical, Luteolin 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, Luteolin.

Introduction
The pandemic situation caused due to the 2019-nCoV represents a severe public health calamity across the globe. 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]. About more than 80% of the case that are reported are asymptomatic in nature thus it is one of the main cause of communal spread and it is the period when the infected person affects most of the person and during this time the person also doesn't show any such serious symptoms. 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]. Researchers all around the world are carrying out various examinations and tests to successfully produce a antidote against the corona virus but till date there has been no such significance development. 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 luteolin, 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 Luteolin 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:15864 corresponding to the luteolin (Fig. 2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

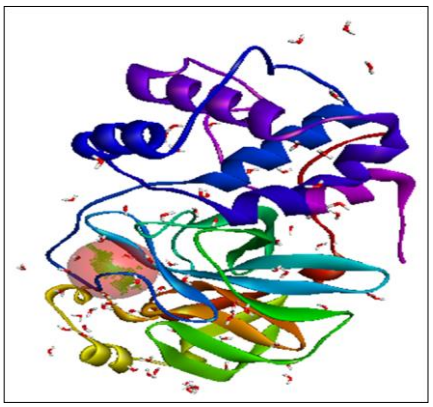

Fig 1: 3-D Structure of the SARS-CoV-2 M^{pro} showing the active site of the protein.

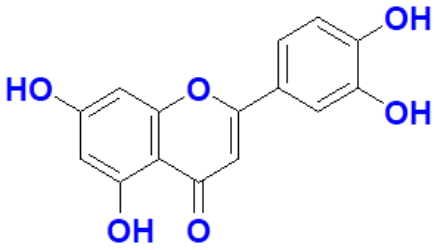

Fig 2: Chemical structure of Luteolin

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 luteolin; 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 luteolin 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 luteolin and eventually can be used in the pharmaceutical sector. Chemical synthesis of luteolin can be cost effective as compared to the isolation process from specific plants.

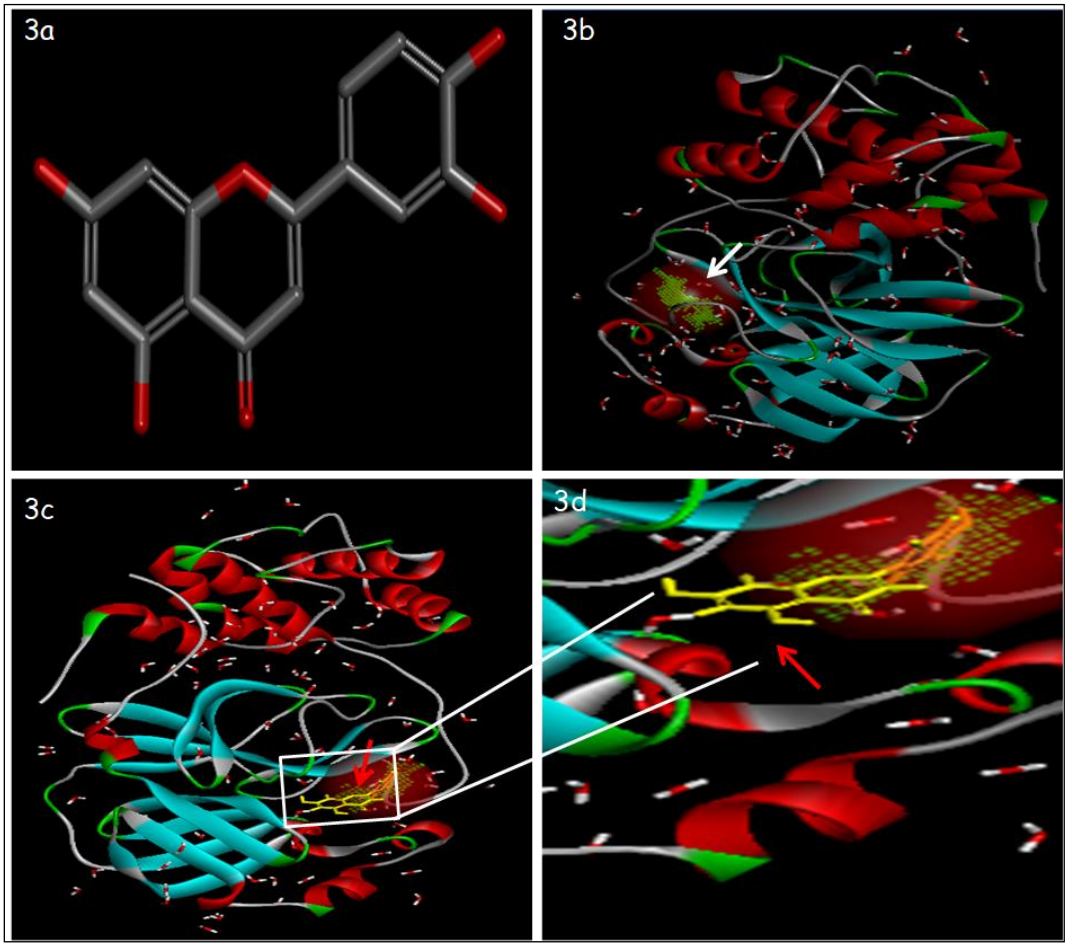

Fig 3: The active site of the SARS-CoV-2 main protease (M^{pro}) interacts with Luteolin. **3a:** Phytochemical, Luteolin. **3b:** Free form of M^{pro}. **3c:** M^{pro} associated with the ligand, Luteolin. **3d:** Magnified image showing the association of the Luteolin with the M^{pro}. (The white colored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

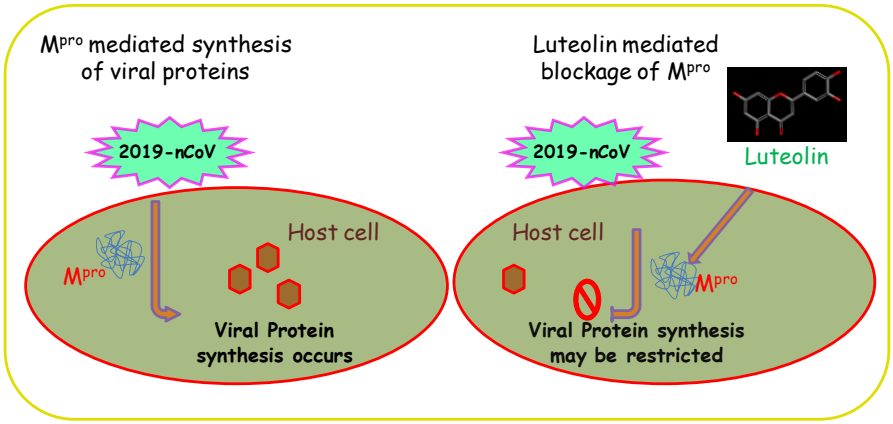

Fig. 4: Luteolin, a phytochemical may inhibit COVID-19 M^{pro} and thus restrict the synthesis of viral proteins.

Table 1: CDocker energy and CDocker interaction energy values generated for the interaction of Luteolin 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: 15864	Luteolin	Covid-19 Main protease	6M03	Positive	-18.31	-21.02

Conclusion and Future perspectives

The current *in silico* molecular docking-based study reveals that luteolin can target the reported SARS-CoV-2 M^{pro} (Fig. 4). It would be extremely noteworthy being confirmed *in vivo*. It is crucial to develop diagnostic tools, potential therapeutics and antibodies selectively for the COVID-19 proteins. Phytochemicals like luteolin is commercially available and thus may be effectively prescribed to circumvent the current global scenario. Essentially, this study makes an attempt to reveal simple phytochemicals like luteolin which can be employed for designing novel therapeutics.

Author contribution statement

GKP conceived the idea. AS, GKP, TD, SKS, PKP performed the experiments. GKP 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.

References

1. Chen N, Zhou M, Dong X, *et al*. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet, 2020; 395:507-513.
2. Huang C, Wang Y, Li X, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet, 2020; 395:497-506. https://doi.org/10.1016/S0140-6736(20)30183-5.
3. Lu R, Zhao X, Li J, *et al*. 2020. Genomic characterisation and epidemiology of novel coronavirus: implications for virus origins and receptor binding. Lancet, 2019; 395:565-574.
4. Wu F, Zhao S, Yu B, *et al*. A new coronavirus associated with human respiratory disease in China. Nature, 2020; 579:265-269.
5. Chan JFW, Yuan S, Kok KH, *et al*. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet, 2020; 395:514-523.
6. Li Q, Guan X, Wu P, *et al*. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. N Engl J Med, 2020, 1-9.
7. Liu W, Morse JS, Lalonde T, Xu S. Learning from the Past: Possible Urgent Prevention and Treatment Options for Severe Acute Respiratory Infections Caused by 2019- nCoV. Chem Bio Chem, 2020, 730-738.
8. Wrapp D, Wang N, Corbett KS, *et al*. 2020. Cryo-EM structure of the -nCoV spike in the prefusion conformation. Science, 2019; 1263:1260-1263.
9. Lung Jrhau, Yu-Shih Lin, Yao-Hsu Yang, *et al*. The potential chemical structure of anti-SARS-CoV-2 RNA-dependent RNA polymerase. J Med Virol, 2020, 0-1.
10. Ton AT, Gentile F, Hsing M, *et al*. Rapid Identification of Potential Inhibitors of SARS- CoV-2 Main Protease by Deep Docking of 1.3 Billion Compounds. Mol Inform, 2020, 1-18.
11. Dassault Systèmes BIOVIA, DISCOVERY STUDIO, San Diego: Dassault Systèmes, 2020.
12. Panigrahi Gagan Kumar, Sahoo Shraban Kumar and Satapathy Kunja Bihari. In silico Molecular Docking-Based Screening of Phytochemicals Targeted against Glypican-1. IJONS. 2020; 59(10):18708-18712.