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Supplementary Material

Identification of Naturally Occurring Antiviral Molecules for SARS-CoV-2 Mitigation

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Abstract:

Aim:

This study aimed to virtually screen the naturally occurring antiviral molecules for SARS-CoV-2 mitigation based on multiple molecular targets using docking and molecular dynamics simulations.

Background:

The coronavirus catastrophe (COVID-19) caused by a novel strain of coronavirus (SARS-CoV-2) has turned the world upside down at an unprecedented level and has been declared a pandemic by the World Health Organization. It has resulted in a huge number of infections as well as fatalities due to severe lower respiratory tract sickness.

Objective:

The objective of this study was the identification of inhibitors against the crucial molecular targets linked with viral infection caused by SARS-CoV-2.

Materials and Methods:

In silico screening of twenty naturally occurring antiviral molecules was performed using the Autodock docking tool. Further, molecular dynamics (MD) simulations were performed on the most stable docked complex between cysteine-like protease or 3CL protease (3CLpro) and the best-identified inhibitor (bilobetin).

Results:

3CLpros is one of the very important molecular targets as it is involved in the replication process of the virus. In the present study, we have initially investigated the inhibitory potential of naturally occurring antiviral molecules against the activity of main viral protease (3CLpro) to put a halt to viral replication. The investigation had been carried out through docking of the molecules with 3CLpro. Based on the results, the three most potential molecules (bilobetin, ginkgetin and sciadopitysin) have been screened. Further, these molecules were subjected to checking their activity on other molecular targets like papain-like protease (PLpro), spike protein S1, RNA dependent RNA polymerase (RdRp), and Angiotensin-Converting Enzyme 2 (ACE2) receptor. In addition to 3CLpro inhibition, ginkgetin was also predicted as an inhibitor of PLpro. However, none of these three compounds was found to be effective on the rest of the molecular targets. Molecular Dynamics (MD) simulations of the most stable docked complex between 3CLpro and its best inhibitor (bilobetin) confirmed notable conformational stability of the docked complex under a dynamic state.

Conclusion:

Bilobetin alone or a combination of bilobetin and ginkgetin may be used to impede viral replication. These observations are solely based on the results from blind docking with protein molecules and need to be further corroborated with experimental results.

Keywords: SARS-Cov-2, Cysteine like protease inhibition, Papain-like protease inhibition, Bilobetin, Ginkgetin, Sciadopitysin.

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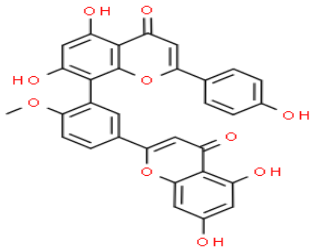
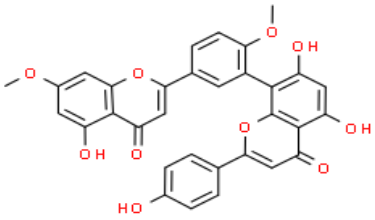
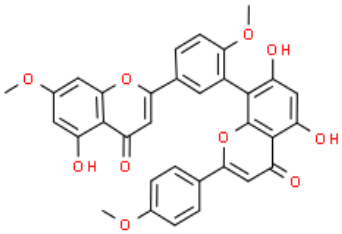
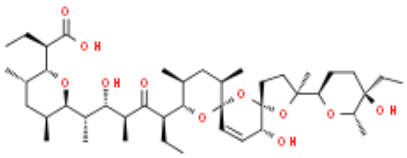
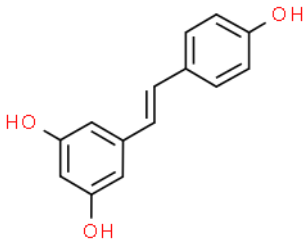
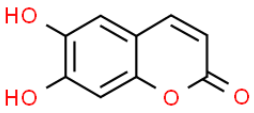
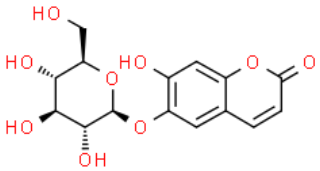
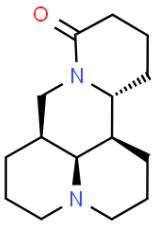
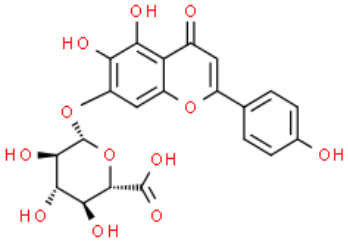
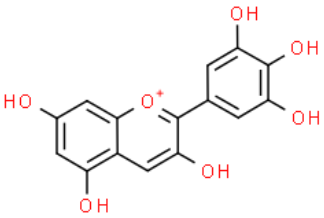
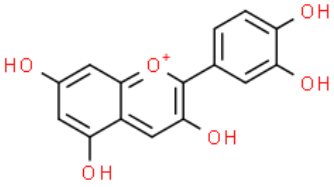
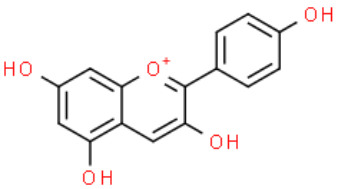
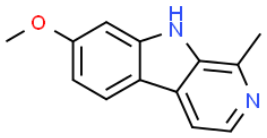
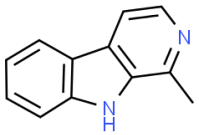
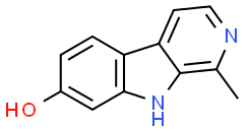
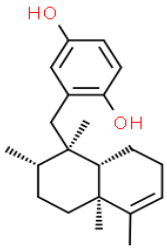
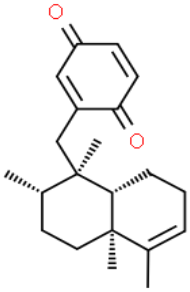
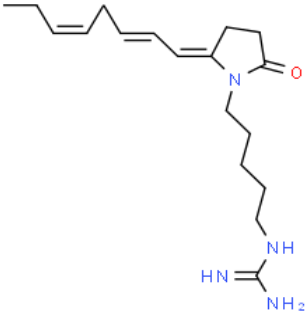
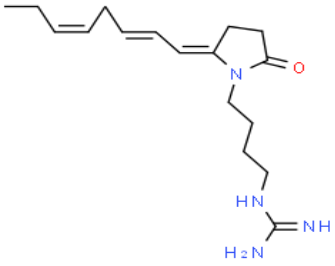
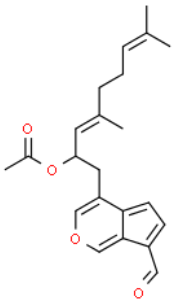
Table S1. Naturally occurring compounds.

S. No.	Compound	Structure	ChemSpider ID	Source	Reported Antiviral Activity Against
1.	Bilobetin		4474758	*Torreya nucifera*	SARS-CoV [1]
2.	Ginkgetin		4436579	*Torreya nucifera*	SARS-CoV [1]
3.	Sciadopitysin		4445013	*Torreya nucifera*	SARS-CoV [1]
4.	Narasin		58911	Ionophores	Dengue virus (DENV-2) [2]
5.	Resveratrol		392875	Blueberries, cranberries *etc*.	Respiratory syncytial virus [3]
6.	Esculetin		4444764	*Lactuca virosa*	Porcine Circovirus Type 2 (PCV2) [4]

S. No.	Compound	Structure	ChemSpider ID	Source	Reported Antiviral Activity Against
7.	Esculin		4444765	*Lactuca virosa*	Porcine Circovirus Type 2 (PCV2) [4]
8.	(+)-Matrine		82591	*Sophora flavescens* and *Sophora tonkinensis*	Human Enterovirus 71 [5]
9.	Scutellarin		161366	*Scutellaria barbata*	Porcine Reproductive and Respiratory Syndrome Virus [6]
10.	Delphinidin		114185	Blueberry	West Nile Virus, Zika Virus, and Dengue Virus [7]
11.	Cyanidin		114193	Bilberry	H1N1 Influenza Virus [8]
12.	Pelargonidin		389676	*Solanum tuberosum*	InfV A and B [9]

S. No.	Compound	Structure	ChemSpider ID	Source	Reported Antiviral Activity Against
13.	Harmine		4444445	*Peganum harmala*	murine cytomegalovirus and Sindbis virus [10]
14.	Harmane		4444755	*Symplocos setchuensis*	HIV [11]
15.	Harmol		10296888	*Peganum harmala*	Dengue Virus [12]
16.	Avarol		65156	*Disidea avara*	HIV [13]
17.	Avarone		65157	*Disidea avara*	HIV [13]
18.	Polyandrocarpidine B		10469701	*Polyandrocarpa sp.*	HSV [14]

S. No.	Compound	Structure	ChemSpider ID	Source	Reported Antiviral Activity Against
19.	Polyandrocarpidine D		10469702	*Polyandrocarpa sp.*	HSV [14]
20.	Halitunal		8513688	*Halimeda tuna*	murine coronavirus A59 [15]

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