IN Silico Evaluation of Some Flavonoids Honeybee Constituents as SARS-CoV-2 Main Protease (COVID-19) Inhibitors

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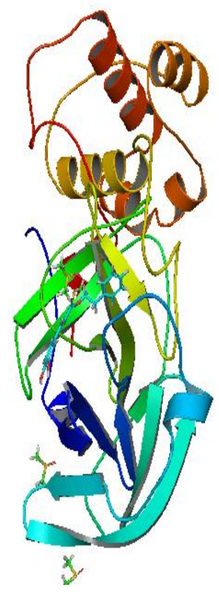
Introduction

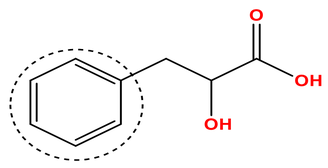


The huge attack of coronavirus disease 2019 (COVID-19) over all the world forces the researcher around the world to study the crystal structure of the main protease M^{pro} (3-chymotrypsin-like cysteine enzyme) which is the essential enzyme for coronavirus processing the polyproteins and its life cycles.

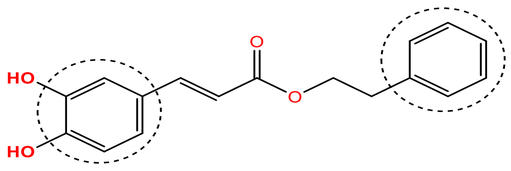
Bee's productions have been used in medicine for several diseases included tumor treatment and immune-related diseases

In this study, we have used the molecular modeling approach to evaluate the activity of different active compounds from honeybee and propolis to inhibit the presented sars-cov-2 main protease *via Schrödinger Maestro v10.1*.

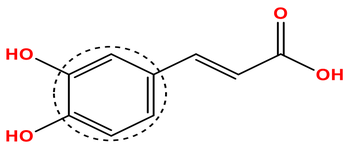
The presented study resulted in six main compounds possess *high binding energy* with the receptor active site of COVID-19 main protease.



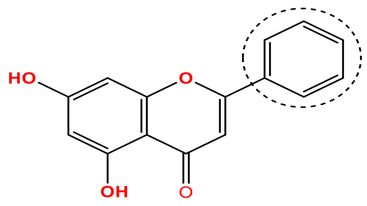
3-Phenyllactic acid
Pubchem CID: 3848



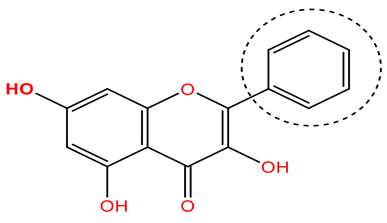
Caffeic acid phenylethyl ester
PubChem CID: 5281787



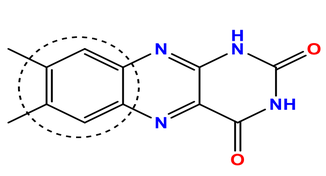
Caffeic acid
Pubchem CID: 689043



Chrysin
Pubchem CID:5281607



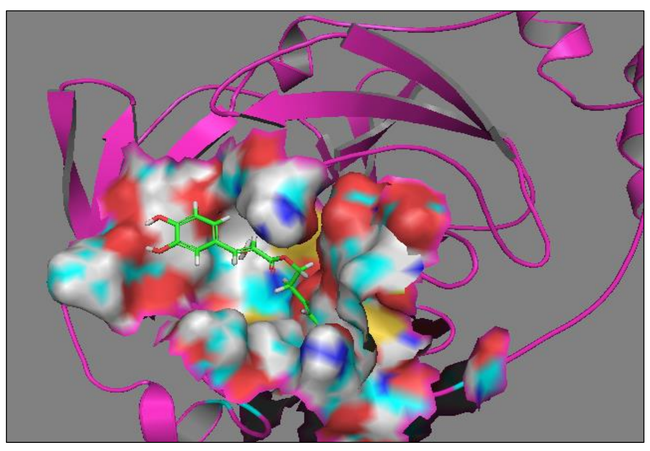
Galangin
PubChem CID: 5281616

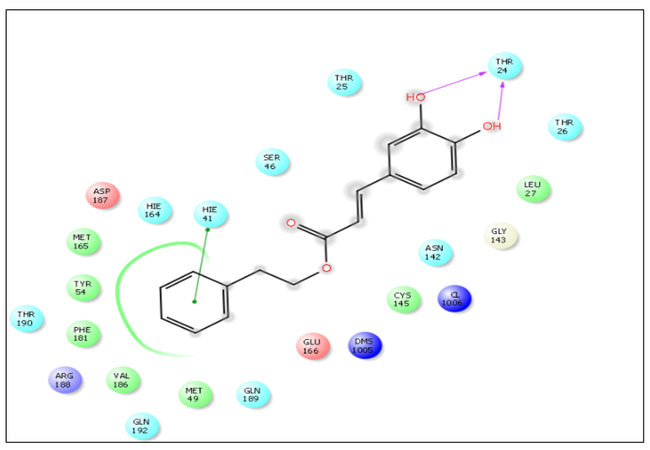


Lumichrome
PubChem CID: 5326566

Two dimensional 2D structures of six selected honeybee constituent.

*The most active compound **CAPE** residue was stabilized within the receptor by interacting through electrostatic (pi-pi stacking) with (HIE-41) with 4.2 Aº, and strong hydrogen bond with (THR-24) and (THR-26)*



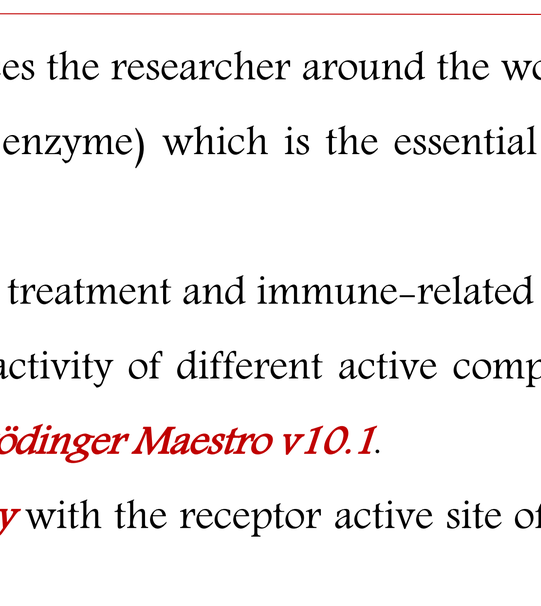


Number	Ligands	Potential energy	Docking Score	Glide score	RMSD
1	3-phenyllactic acid	34.546	-5.867	-5.868	0.049
2	Caffeic acid phenylethyl ester (CAPE)	46.07	-6.383	-6.386	0.048
3	Caffeic acid	14.22	-4.387	-4.387	0.035
4	Chrysin	63.126	-6.097	-6.103	0.047
5	Galangin	74.258	-6.295	-6.307	0.044
6	Lumichrome	94.141	-5.205	-5.205	0.040

- **Docking results for ligands 1-6 with COVID-19 main protease**

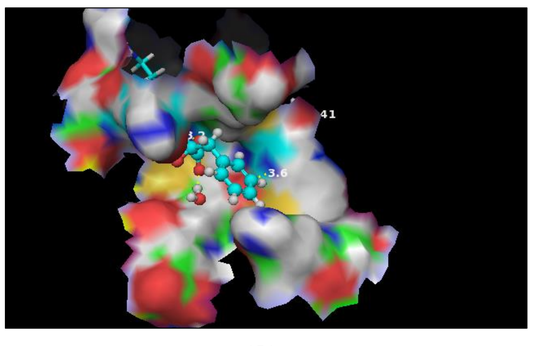
(1)

3-phenyllactic acid



(3)

Caffeic acid



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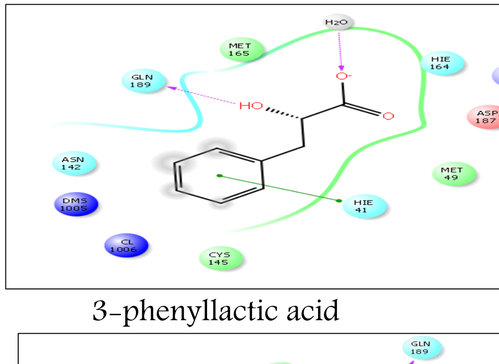
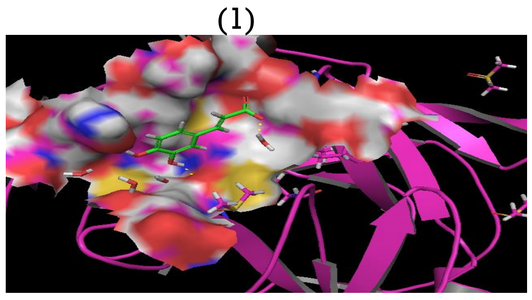


Chrysin



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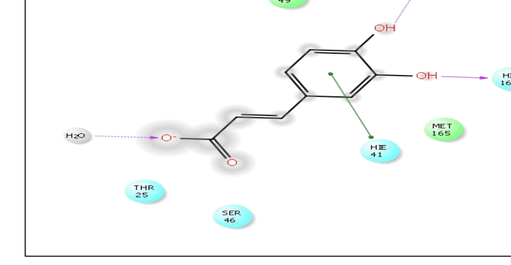
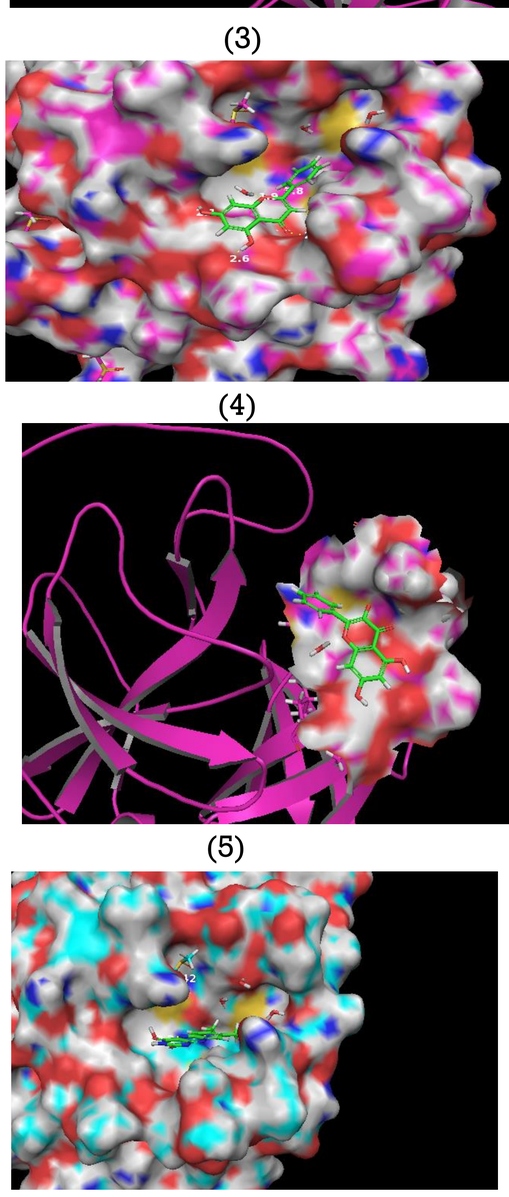
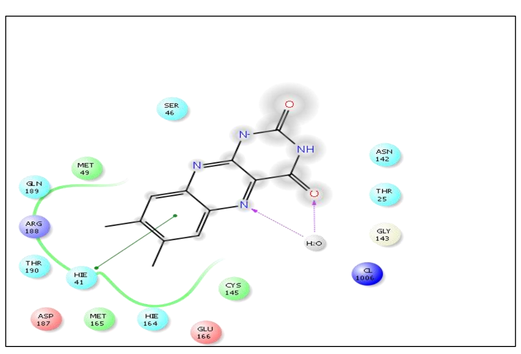


Galangin



(6)

- **Three-dimensional *3D* interaction diagrams of *six tested compounds* docked in the active site of COVID-19 protease using *PyMOL* software;** red color reflects the high polar area; blue color reflects the mild polar area and grey color reflects the hydrophobic area.



Lumichrome

- Ligand interaction diagram of *six tested compounds* with COVID-19 main protease.

Conclusion:

Honeybee and propolis include a wide range of flavonoid compounds with several biological activities. The presented study screened *in silico* the biological activity of six compounds present in honeybee and propolis as antiviral components against the COVID-19 main protease. The study revealed that four compounds have strong binding affinity with good glide score and may inhibit the COVID-19 main proteas and virus replication. The study aimed for further *in-vivo* study in order to produce novel natural anti-COVID-19 drugs without any harmful side effect.