Chemical composition of *Agathis robusta* bark essential oil: In silico and in vitro antiviral activities against COVID-19.

Maged E. Mohamed [1, 2,*], Nora Tawfeek [2], Samar S. Elbaramawi [3], Eman Fikry [2]

[1] Department of Pharmaceutical Sciences, College of Clinical Pharmacy, King Faisal University, 31982 Al-Ahsa, Saudi Arabia; memohamed@kfu.edu.sa

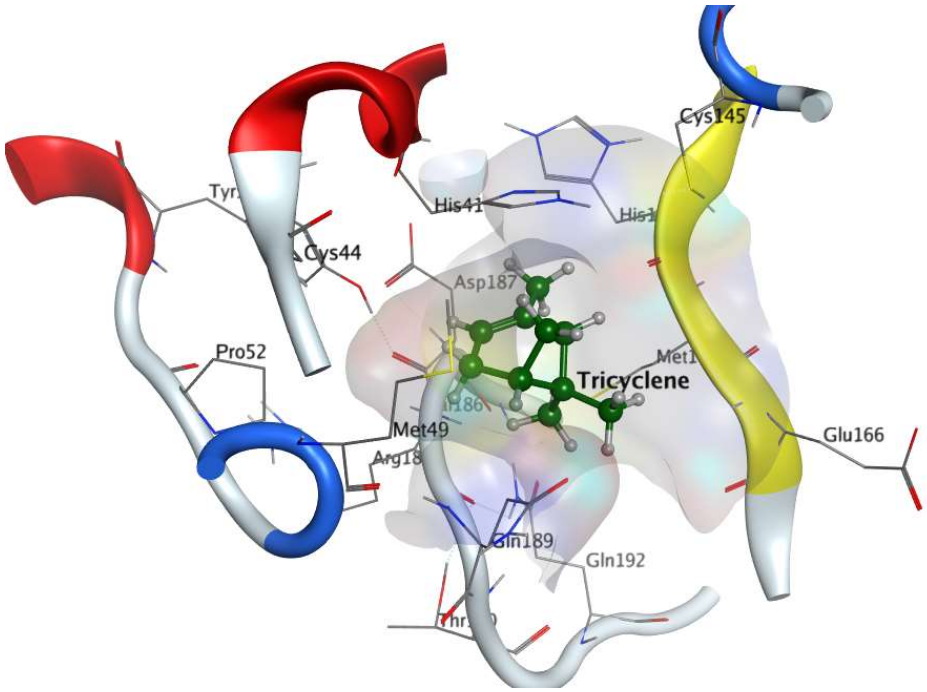
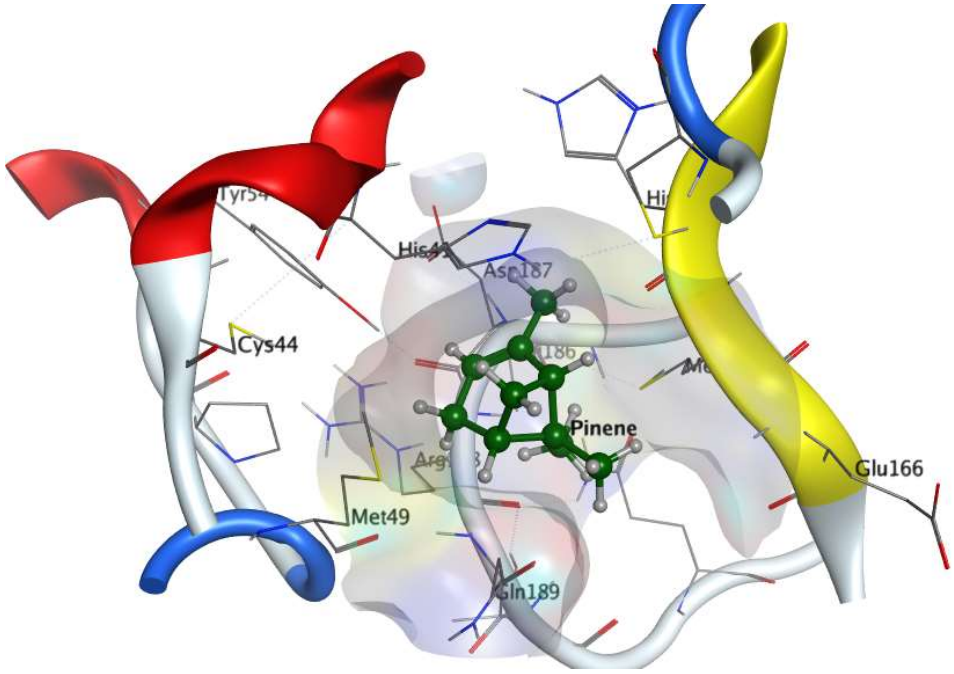
[2] Department of Pharmacognosy, Faculty of Pharmacy, Zagazig University, Zagazig 44519, Egypt; noratawfeek@zu.edu.eg (N.T.); efhassan@zu.edu.eg (E.F.)

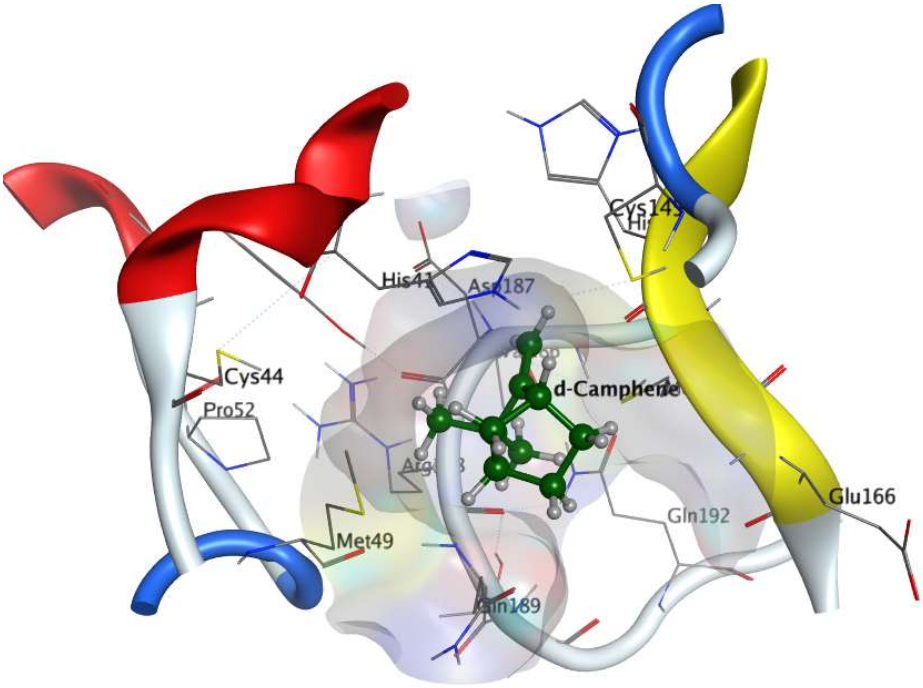
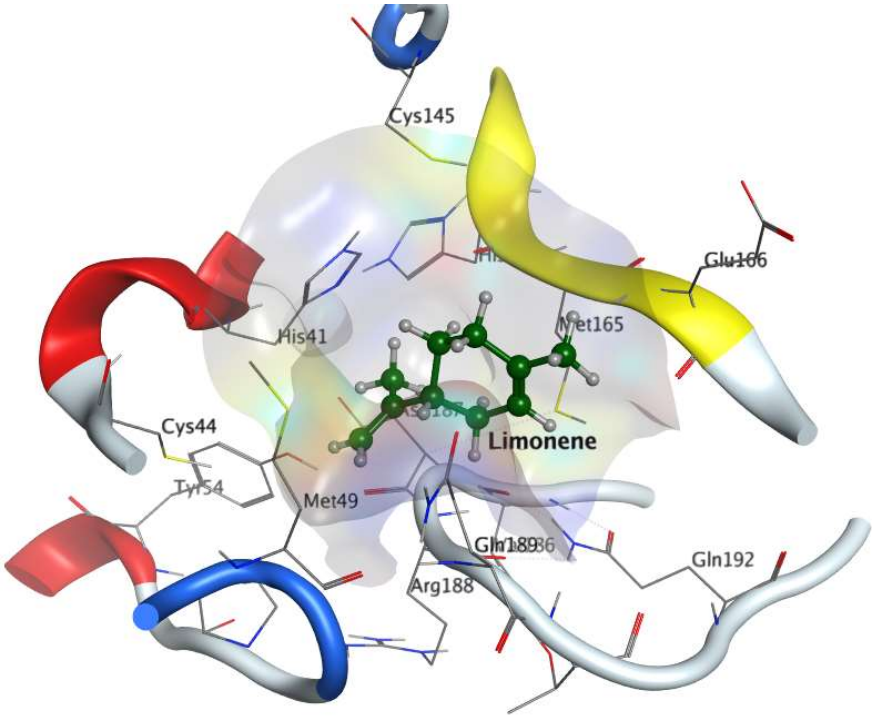
[3] Department of Medicinal Chemistry, Faculty of Pharmacy, Zagazig University, Zagazig 44519, Egypt; sselbaramawy@pharmacy.zu.edu.eg

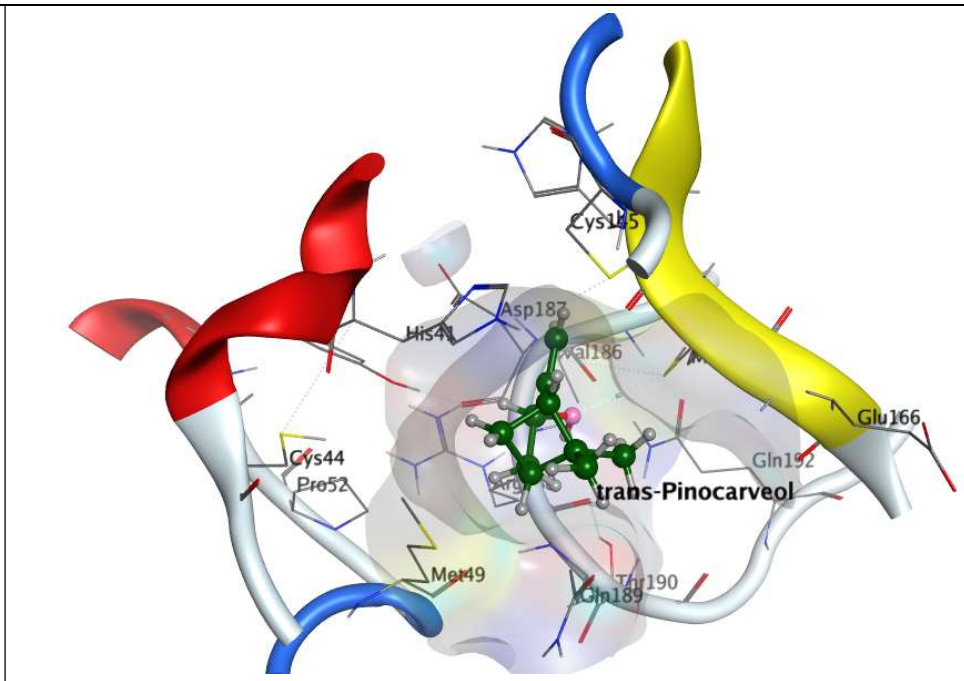
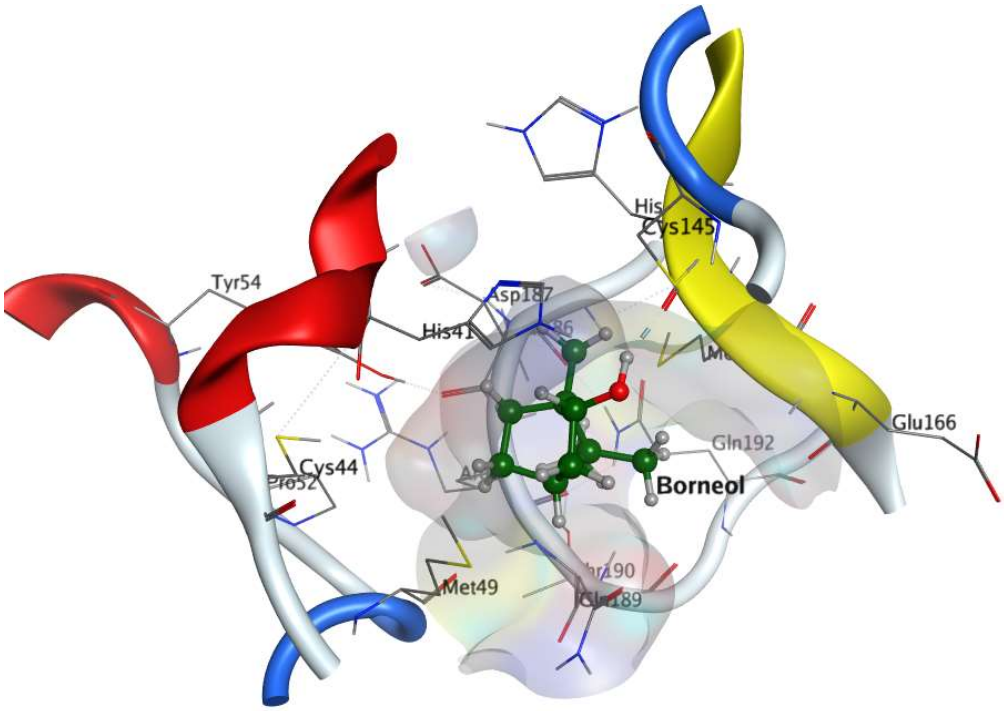
* Correspondence: memohamed@kfu.edu.sa; Tel.: (optional; include country code; if there are multiple corresponding authors, add author initials)

Supplementary material

Table S1. 3D-Binding mode of the major components of *A. robusta* bark EO inside the Mpro active site (PDB code: 6LU7).

Component name	3D Protein- Ligand interaction	Energy score (S) (kcal/mol)/RMSD (Å)
Tricyclene		**-4.6674** **1.4627**
***α*-Pinene**		**-4.7570** **1.2320**

***d*-Camphene**		**-4.4746** **1.7971**
Limonene		**-4.7005** **1.6112**

***trans*-Pinocarveol**		**-4.59218** **2.0991**
Borneol		**-4.1916** **1.1248**

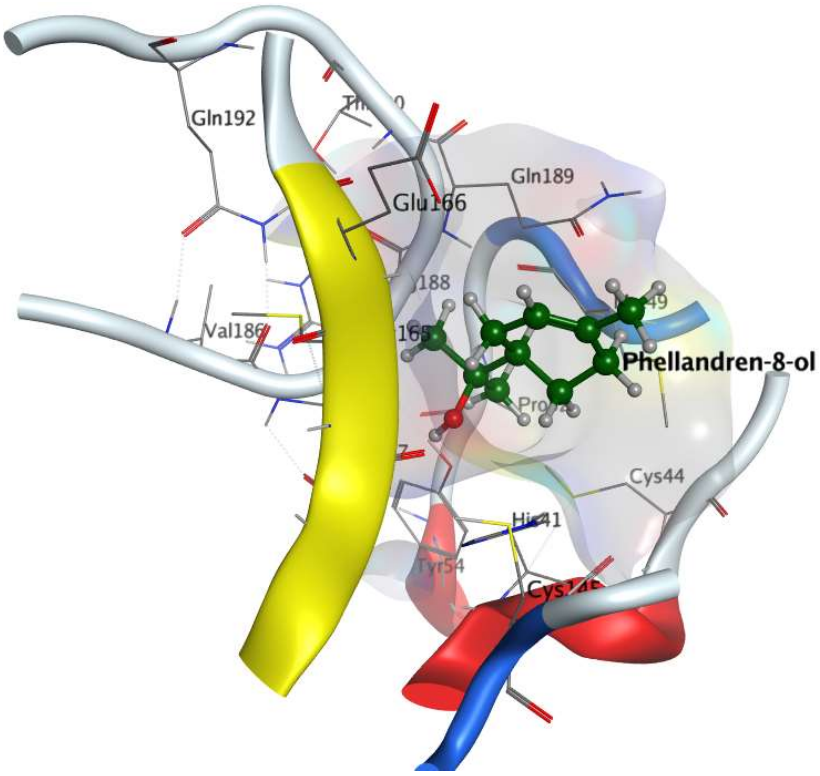
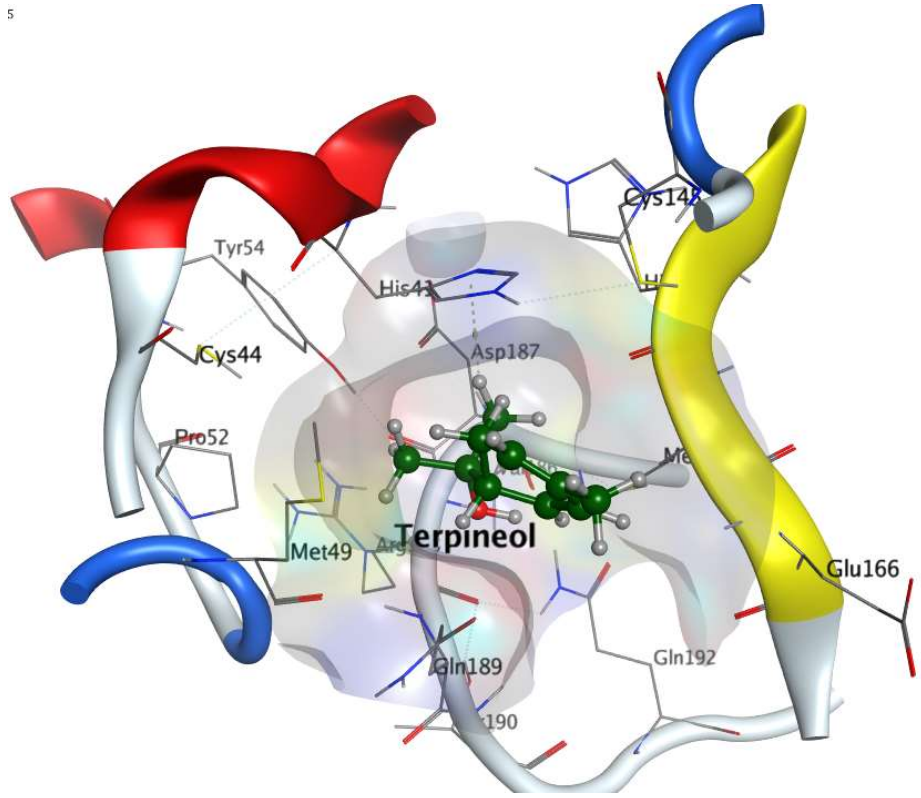
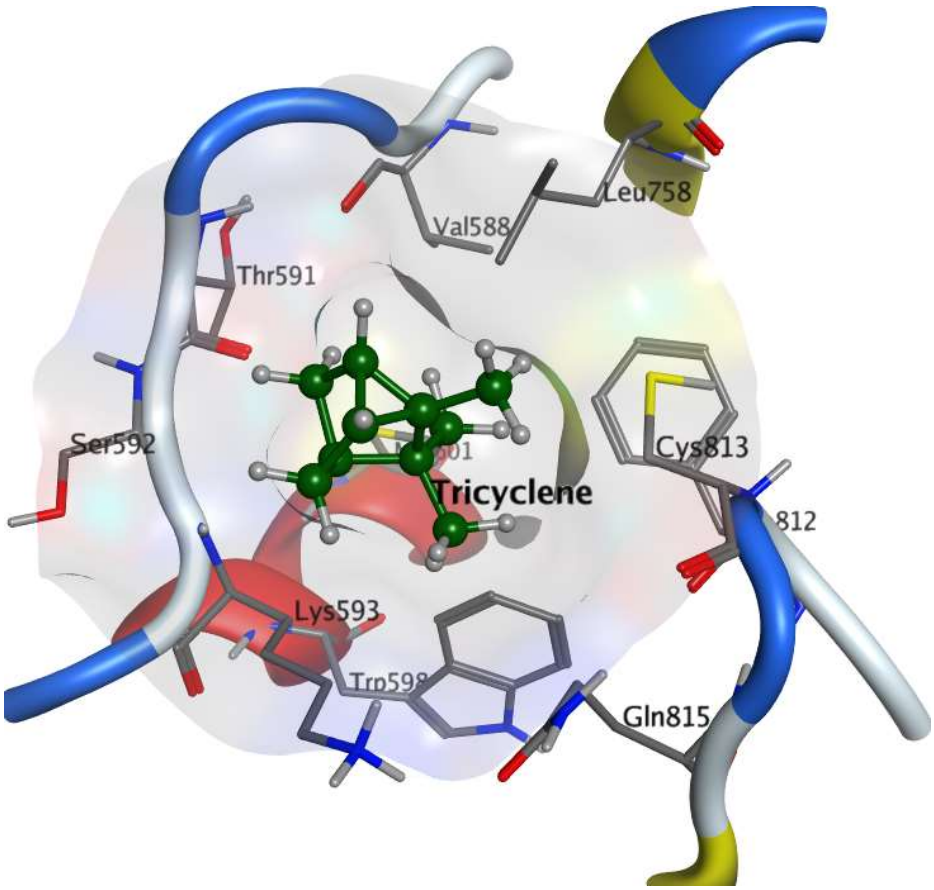
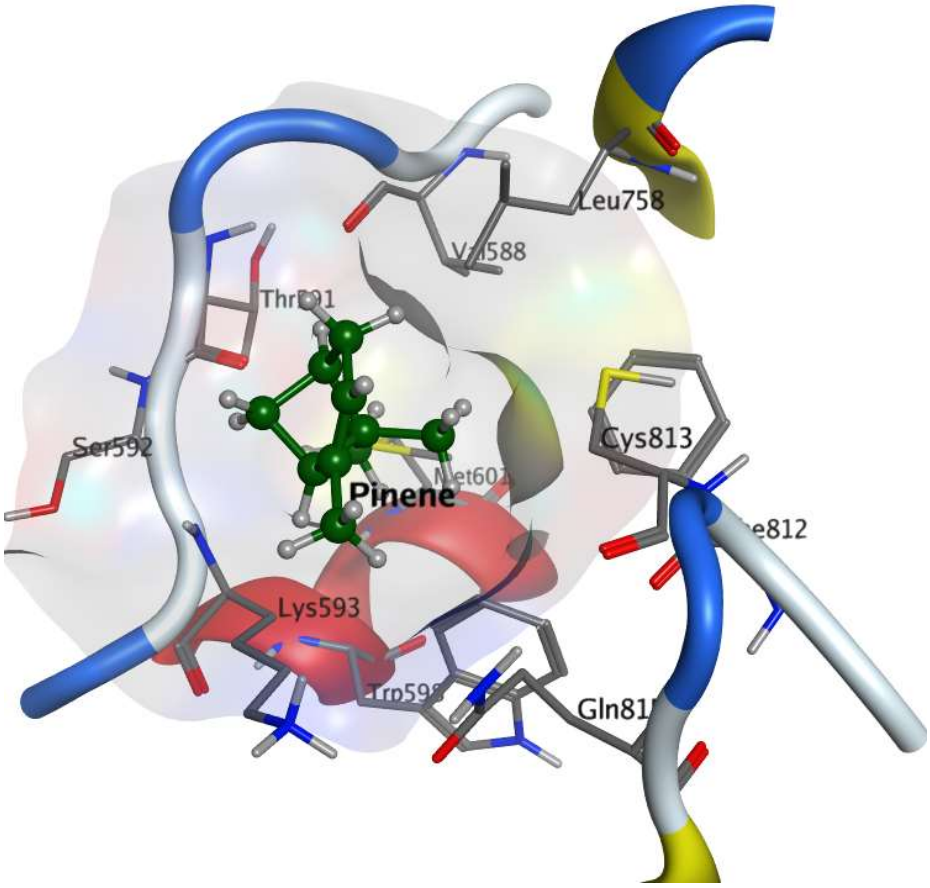
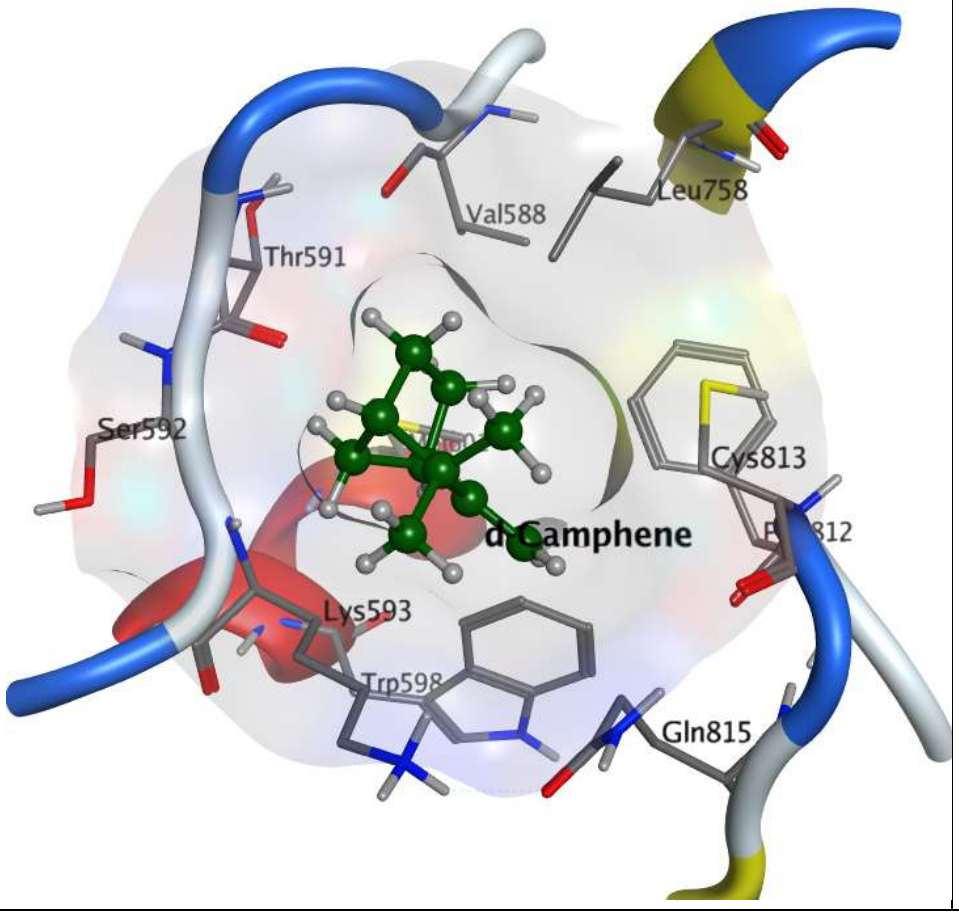
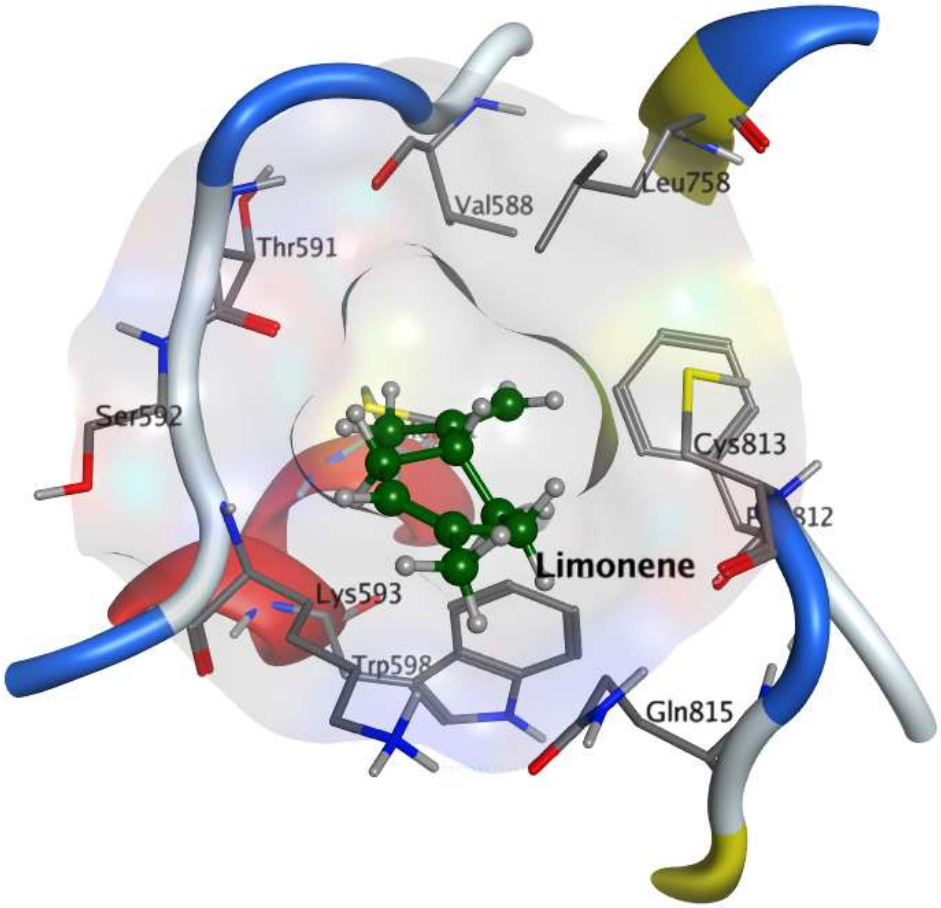
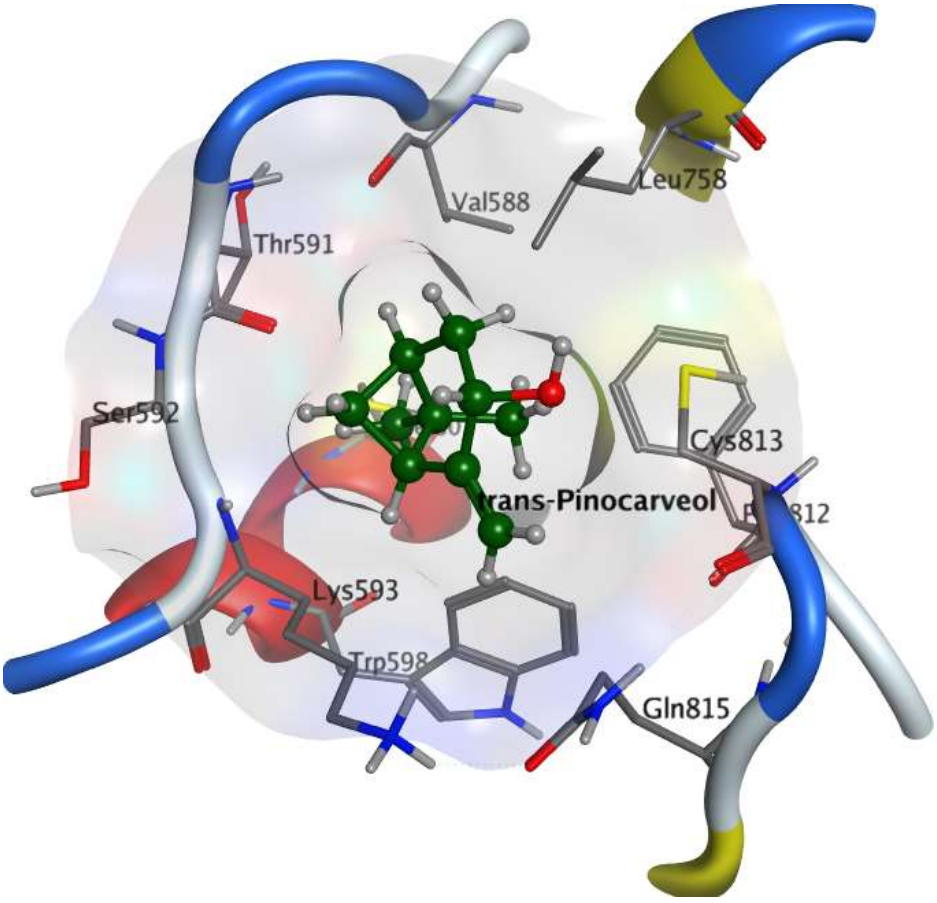
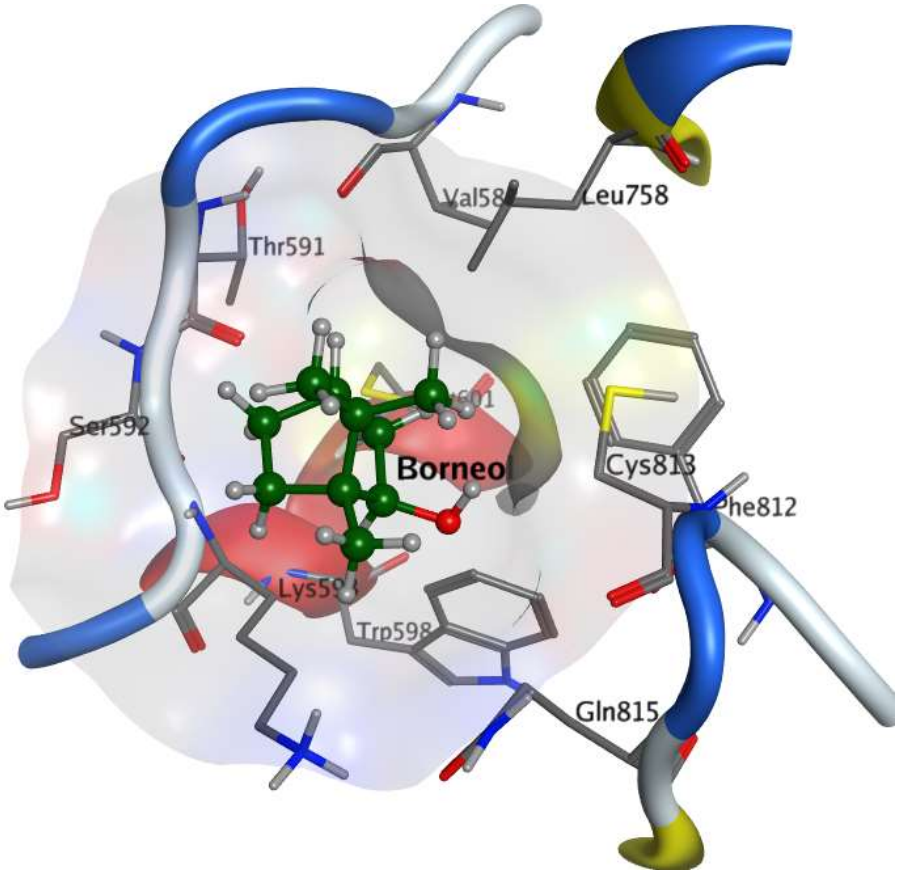
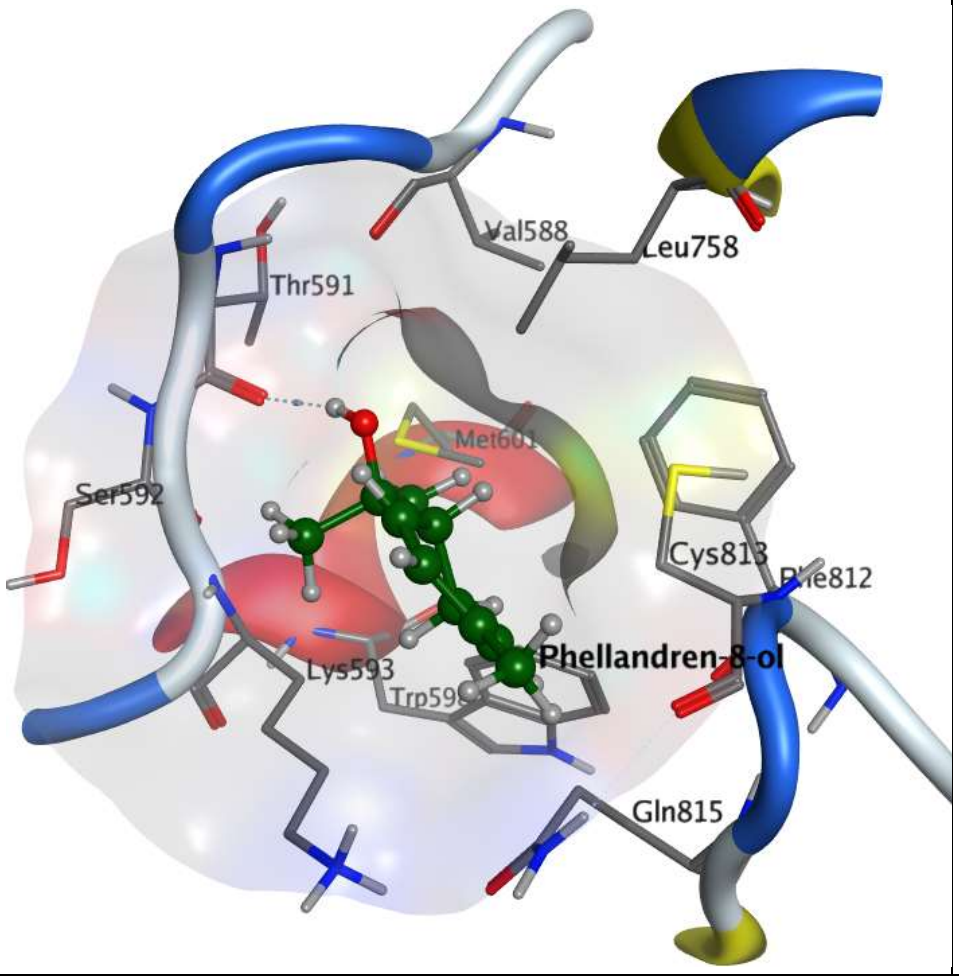
***α*-Phellandren-8-ol**		**-4.9801** **1.1112**
***α*-Terpineol**		**-5.0752** **1.7314**

Table S2. 3D-Binding mode of the major components of *A. robusta* bark EO inside Covid-19 RNA-dependent RNA polymerase (PDB code: 7D4F).

Component name	3D Protein- Ligand interaction	Energy score (S) (kcal/mol) /RMSD (Å)
Tricyclene		**-4.10620** **2.0938**

***α*-Pinene**		**-4.2618** **1.7163**
***d*-Camphene**		**-3.9284** **1.2590**

Limonene		**-4.5654** **0.9815**
***trans*-Pinocarveol**		**-4.2639** **1.3717**

Borneol		**-4.0815** **1.4960**
***α*-Phellandren-8-ol**		**-4.3839** **2.0164**

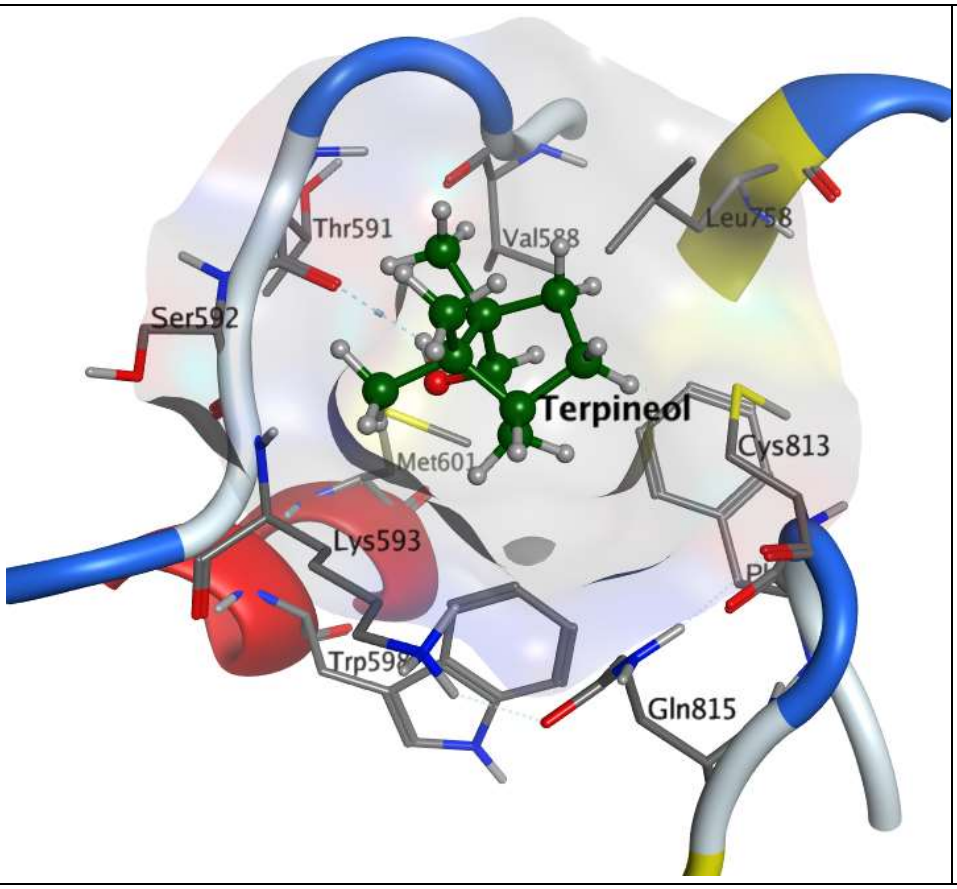
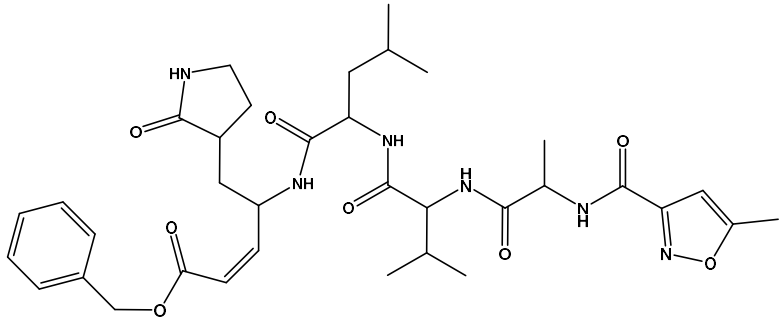
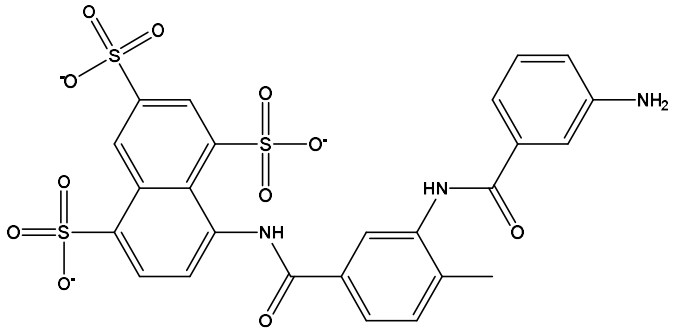
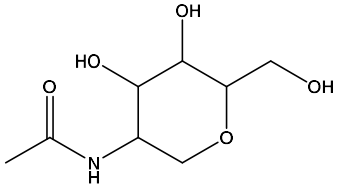
α-Terpineol		**-4.7213** **1.1632**

Table S3. Molecular docking details of *A. robusta* bark EO with RBD.

Component name	Energy score (S) (kcal/mol)	RMSD	Amino acid residues forming	
			H-bond	**H-*pi***
Co-crystallized ligand (NAG)	-4.5304	1.5097	ASN 343	-
Tricyclene	-4.0962	1.4562	-	-
α-Pinene	-3.8556	1.1748	-	-
***d*-Camphene**	-4.0584	1.8286	-	-
Limonene	-3.9563	1.5847	-	-
***trans*-Pinocarveol**	-4.1561	1.5353	VAL 367	-
Borneol	-3.9368	2.1738	ASN 343	-
α-Phellandren-8-ol	-4.0385	1.2068	ASN 343	-
α-Terpineol	-4.2190	1.9985	ASN 343	-
2,4-Thujadiene	-3.9973	1.7303	-	-
L-β-Pinene	-3.9127	1.5637	-	-
***m*-Cymene**	-4.1107	1.1504	-	PHE 338
γ-Terpinene	-4.2683	1.5342	-	-
α-Campholenal	-4.1039	1.3665	-	-
Camphor	-4.0149	1.6277	GLY 339	-
Camphene hydrate	-3.9441	1.4994	--	-
Trans-Pinocamphone	-4.0541	1.8483	-	TRP 436
Pinocarvone	-3.9968	1.4778	-	-
Isoborneol	-3.9323	1.9775	-	-
***cis*-Verbenol**	-4.0902	1.4764	SER 371	-
L-terpinen-4-ol	-4.2719	0.85503		-
Myrtenal	-3.9592	1.7403	LEU 368	-
Verbenone	-4.1378	1.5315	-	-
***trans*-Carveol**	-4.1642	1.2461	-	-
(-)-Carvone	-4.1215	0.9209	-	PHE 342
Bornyl acetate	-4.5766	0.9564	-	TRP 436
α-Terpineol acetate	-4.7246	0.9855	-	-

Table S4. The target enzymes involved for docking of the major components of *A. robusta* bark EO.

Proteins (PDB)	Resolution	Cognate Ligand	Structure of the cognate ligand	RMSD	Energy score (S) (kcal/mol)
COVID-19 main protease in complex with an inhibitor N3(**6LU7**)	**2.16 Å**	**N3**		**1.9061**	**-8.4596**
COVID-19 RNA-dependent RNA polymerase bound to suramin: **(7D4F)**	**2.57 Å**	**H3U**		**1.8239**	**-7.7170**
COVID-19 virus spike receptor-binding domain complexed with a neutralizing antibody: **(7BZ5)**	**1.84 Å**	**NAG**		**1.5097**	**-4.5304**