Supplementary files

Title

Protocetraric and Salazinic Acids as Potential Inhibitors of SARS-CoV-2 3CL Protease: Biochemical, Cytotoxic, and Computational Characterization of Depsidones as Slow-Binding Inactivators

Authors

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	DOCKING SCORE	INTERACTIONS	DISTANCES		POSES GAINED WITH CovDock
SALAZINIC acid 'CLOSE'	-5.982	2 H-Bond 1 stacking	Leu 141 Gly 143 stacking	2.64 2.69 3.76	52
SALAZINIC acid 'OPEN'	-7.007	3 H-Bond 1 stacking His 41 1 salt bridge His 41	Ser144 Gly 143 Glu166 stacking salt bridge	2.77 2.77 2.01 3.79 4.67	82
PROTOCETRARIC acid 'CLOSE'	-5.531	1 H-Bond 1 stacking	Asn 142 stacking	2.21 3.78	37
PROTOCETRARIC acid 'OPEN'	-6.332	3 H-Bond 1 stacking	Gly143 His 41 Glu 166 stacking	1.82 2.41 2.11 3.90	74

Table S1. A library of 13 ligands, prepared from the closed and the open conformation of inhibitors salazinic and protocetraric acids, as reported in paragraph 1.1, was docked in the active site of SARS-CoV main protease using GLIDE Extra Precision XP (non-covalent docking) and CovDock modes (Schrödinger, LLC, New York, NY, USA). The number of docked conformers for each ligand, generated with LigPrep: Salazinic acid cyclic ester (closed) 4; Salazinic acid (open) 4; Protocetraric acid cyclic ester (closed) 2; Protocetraric acid (open) 3.
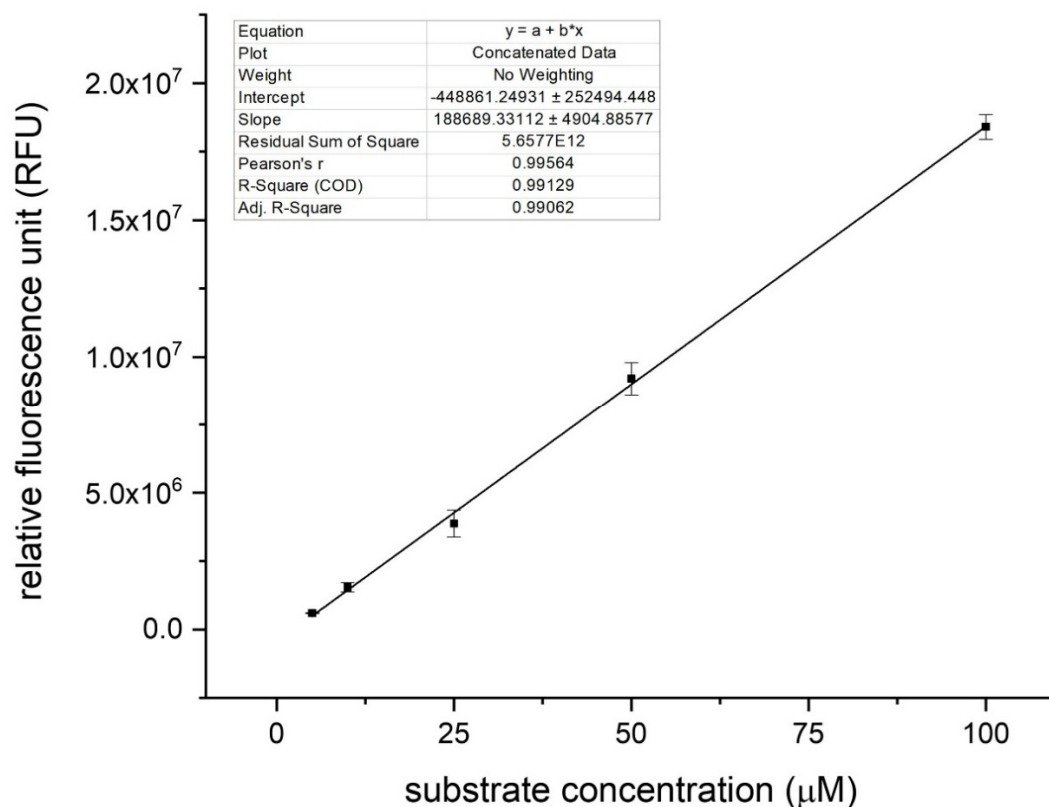
Figure S1. The calibration curve was generated to convert the relative fluorescence unit (RFU) to the amount of the cleaved substrate.
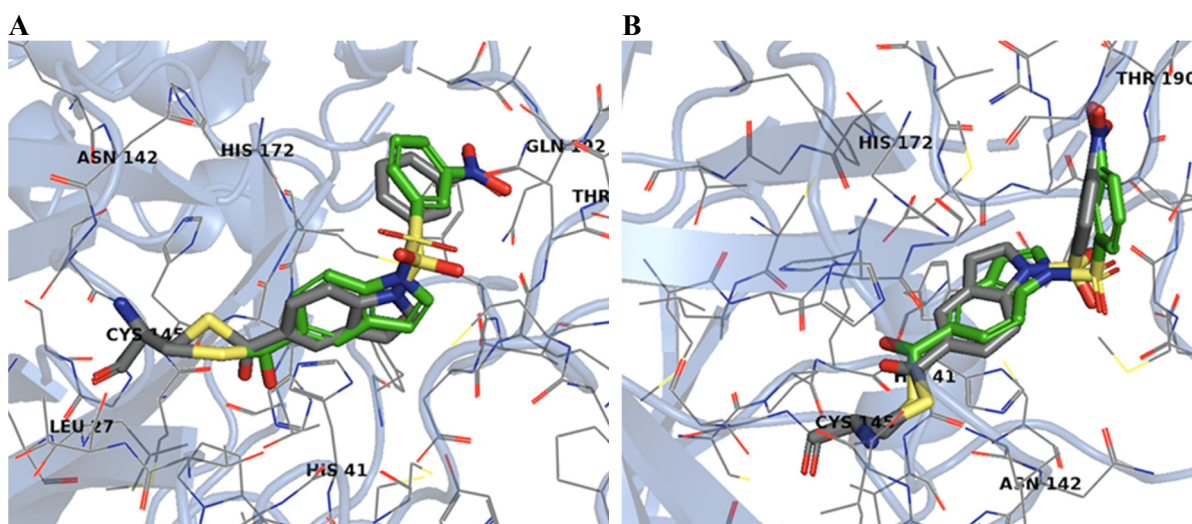

Figure S2. GRL-0686 in SARS-CoV-2 main protease active site: predicted (green) vs crystallographic orientation (gray). Figures were prepared with PyMOL (PyMOL Molecular Graphics System, Version 2.5 Schrödinger).
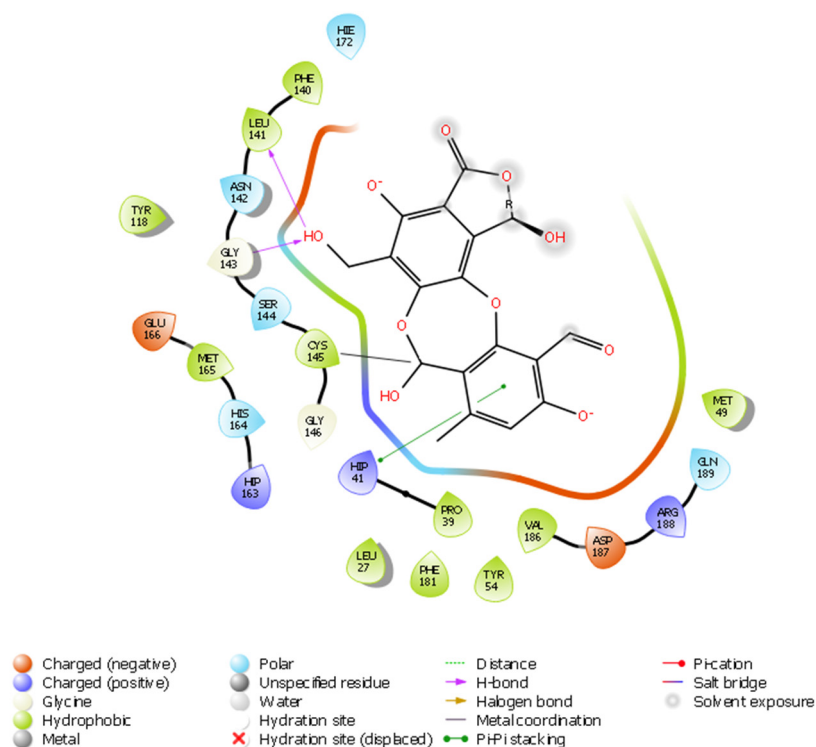
Figure S3. Cyclic ester salazinic acid conformer covalently bound to CoV-2: detailed interactions. Figures were prepared with PyMOL (PyMOL Molecular Graphics System, Version 2.5 Schrödinger, LLC).
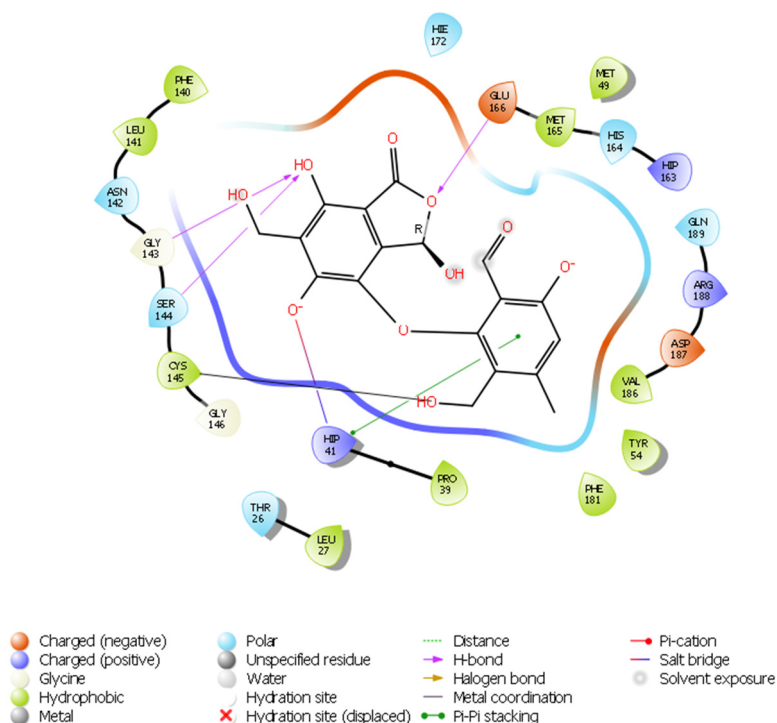

Figure S4. Open salazinic acid conformer covalently bound to CoV-2: detailed interactions. Figures were prepared with PyMOL (PyMOL Molecular Graphics System, Version 2.5 Schrödinger, LLC).
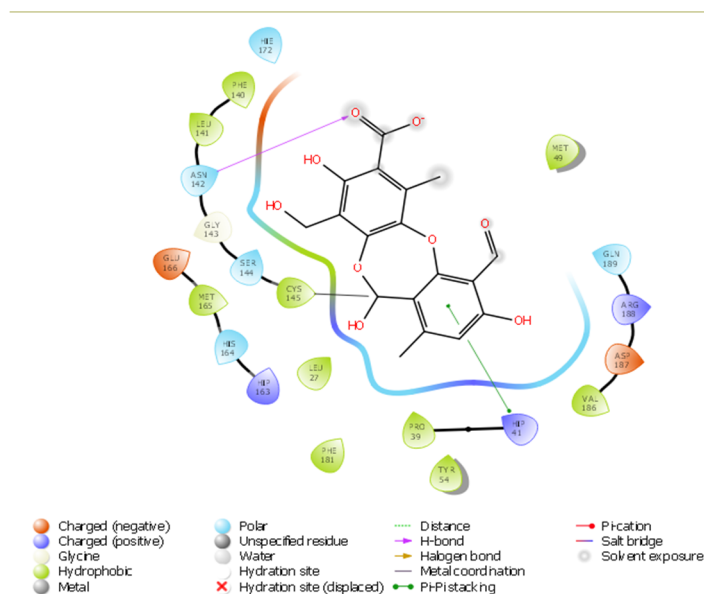
Figure S5. Cyclic ester protocetraric acid conformer covalently bound to CoV-2: detailed interactions. Figures were prepared with PyMOL (PyMOL Molecular Graphics System, Version 2.5 Schrödinger, LLC).
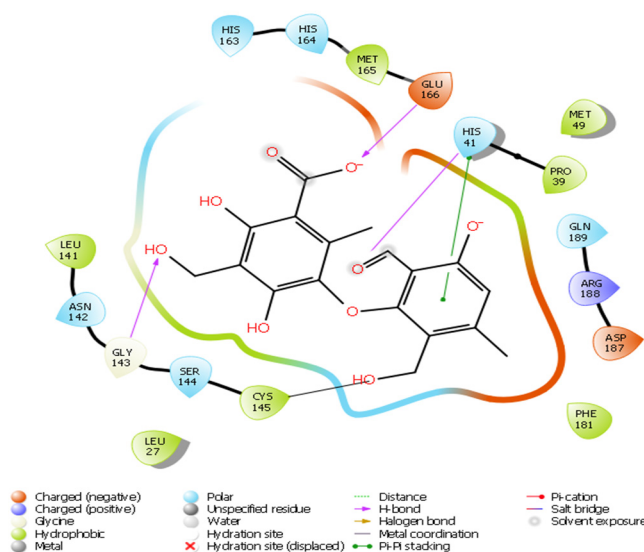

Figure S6. Open protocetraric acid conformer covalently bound to CoV-2: detailed interactions. Figures were prepared with PyMOL (PyMOL Molecular Graphics System, Version 2.5 Schrödinger, LLC).