Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information for: Structure-Based Lead Optimization of Herbal Medicine Rutin for Inhibiting SARS-CoV-2's Main Protease

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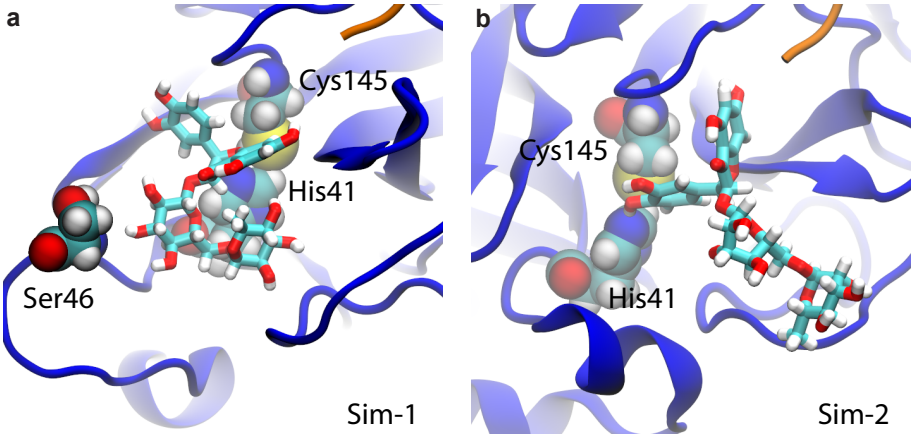

Figure S1: Illustrations of rutin around the active site (Cys145 and His41) in the Mpro's pocket. a) Sim-1; b) Sim-2. The proximity of hydroxyl groups on rutin to Ser46 and Cys145 could allow the design of an irreversible binding (see main text).

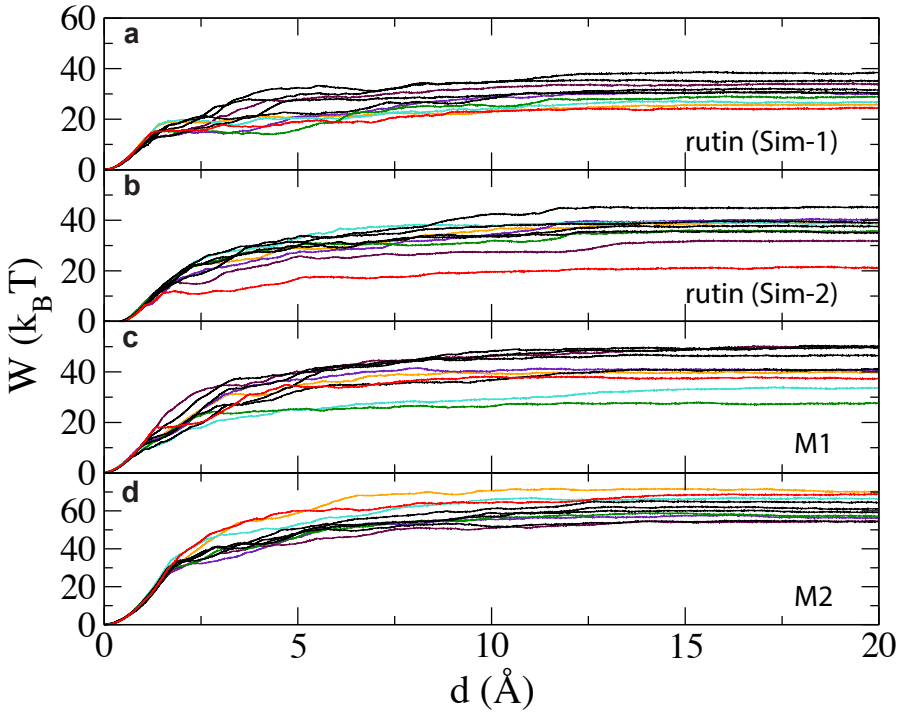

Figure S2: Works along the path way to pull the drug molecule from its binding site (in the Mpro's pocket) to the solution (bulk water). a) Rutin in Sim-1. b) Rutin in Sim-2. c) M1. d) M2.

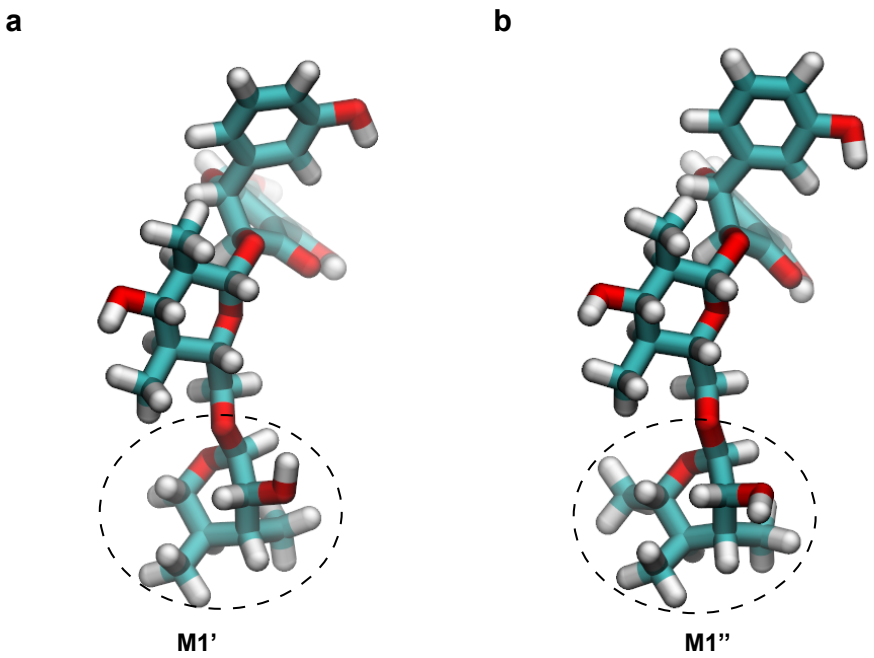

Figure S3: Molecular structures of M1' (a) and M1" (b) designed based on M1. The structural difference between M1'/M1" and M1 are highlighted by dashed ellipses (i.e. the second sugar ring). Note that in M1, M1' and M1" the modified second sugar ring failed to stay inside the Mpro's pocket.

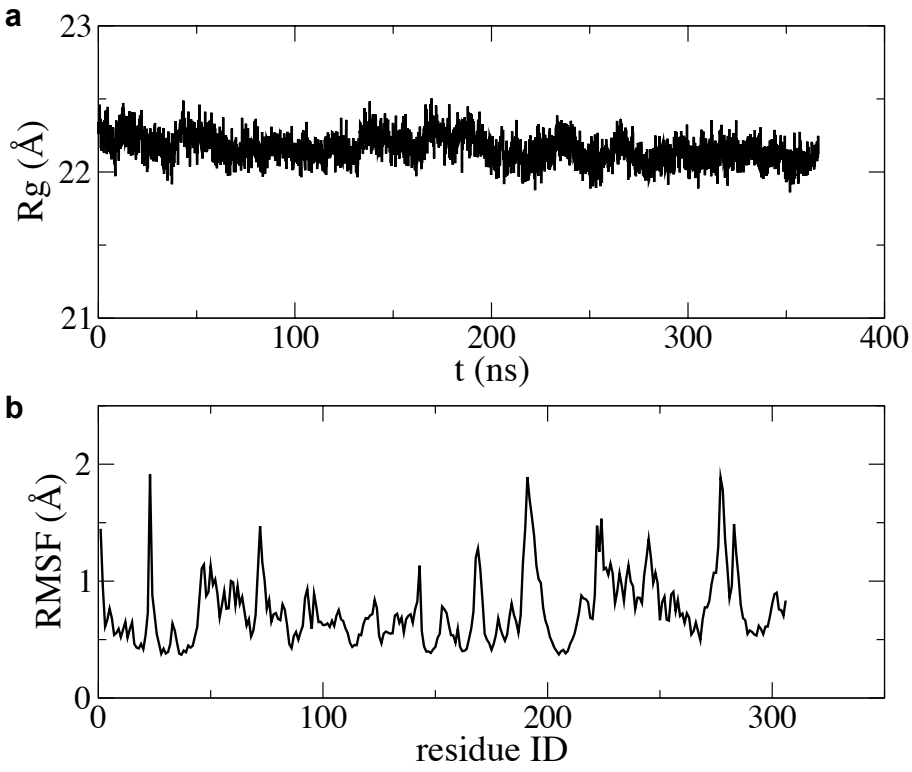

Figure S4: Analyses of Mpro's structure equilibrated in MD simulation. a) Radius of gyration for the monomer (in Mpro) harboring the M2 molecule. b) Root mean square fluctuations (RMSF) of C_α atoms in the monomer with the bound M2 molecule. Peaks correspond well with flexible cords in Mpro.

Supplementary Movies

Supplementary Movie 1 (rutin-Sim1.mpg): showing the simulation trajectory of rutin (Sim-1).

Supplementary Movie 2 (rutin-Sim2.mpg): showing the simulation trajectory of rutin (Sim-2).

Supplementary Movie 3 (M2.mpg): showing the simulation trajectory of M2.