Supplementary Figures

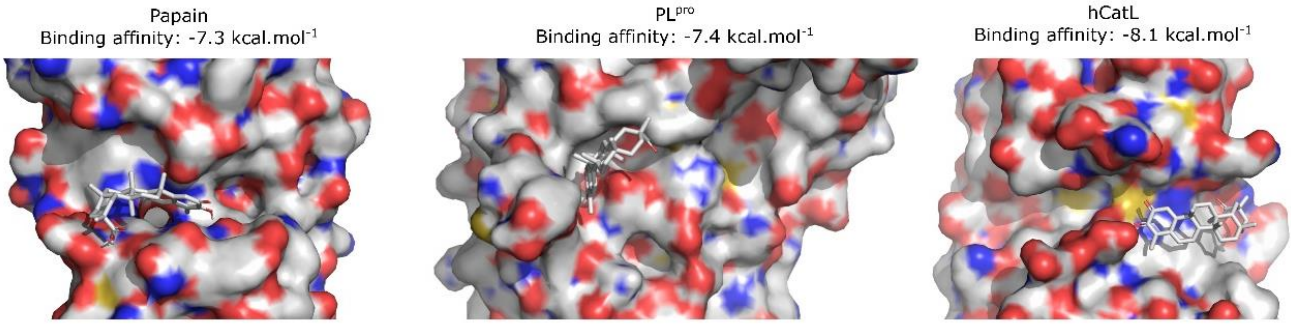

FIGURE S1 Docking of celastrol to the active site of hCatL, PL^{Pro}, and papain proteases. The poses of celastrol with the best-ranked binding affinity at catalytic sites of enzymes are shown. The atoms of celastrol are represented as sticks and the enzymes as surface. The dockings were carried out with the same protocol described in the Models and Methods section. The crystallographic apo structures were obtained from Protein Data Bank (PDB) with the following IDs: 9PAP for papain of Carica papaya, 6WZU for PL^{Pro} of SARS-CoV-2, and 4AXL for hCatL.

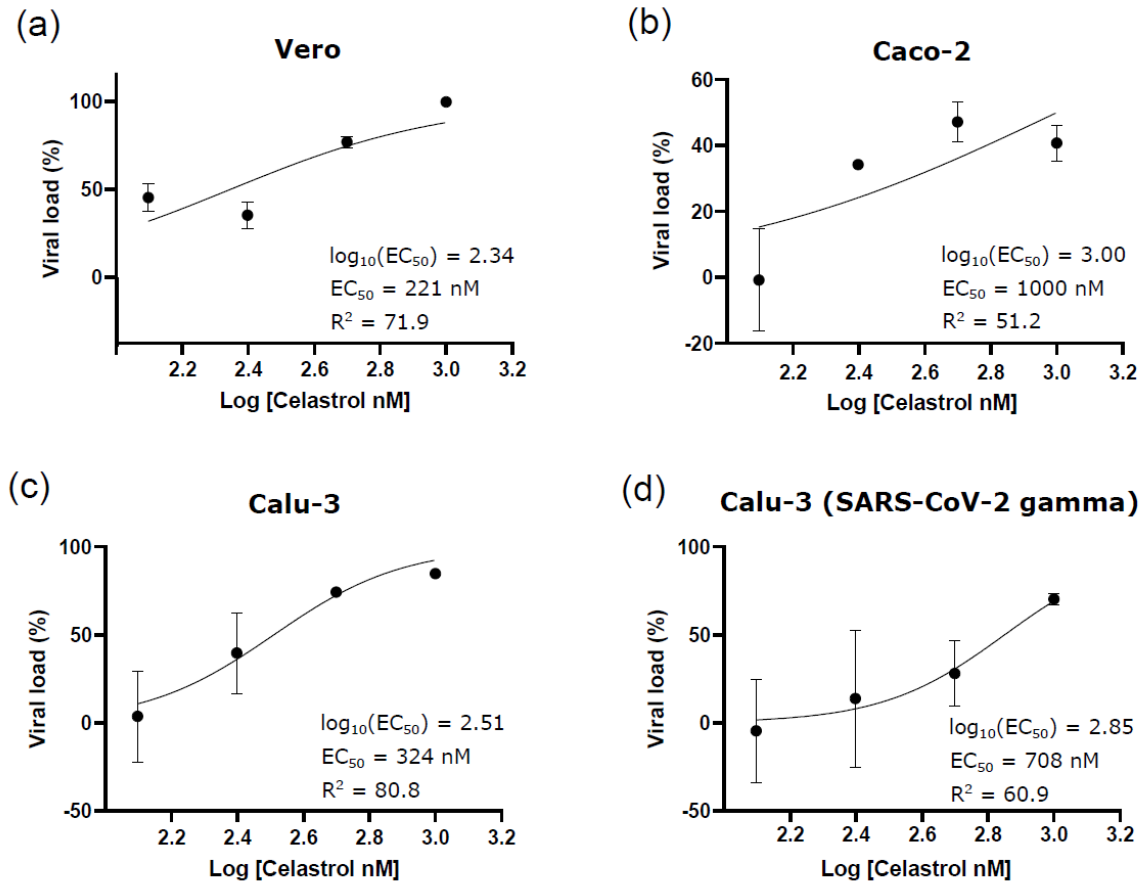

FIGURE S2 EC50 of celastrol to reduce SARS-CoV-2 viral load in different cell lines. EC50 was calculated from the same data described in Figure 5 by fitting the Hill equation to the viral load percentage of (a) Vero CCL-81, (b) Caco-2, and (c) Calu-3 infected with SARS-CoV-2, and (d) Calu-3 infected with SARS-CoV-2 gamma variant treated with celastrol at concentrations of 125, 250, 500, and 1000 nM. The concentration of celastrol was log-10 transformed and was used as an independent variable in regression using GraphPad Prism.

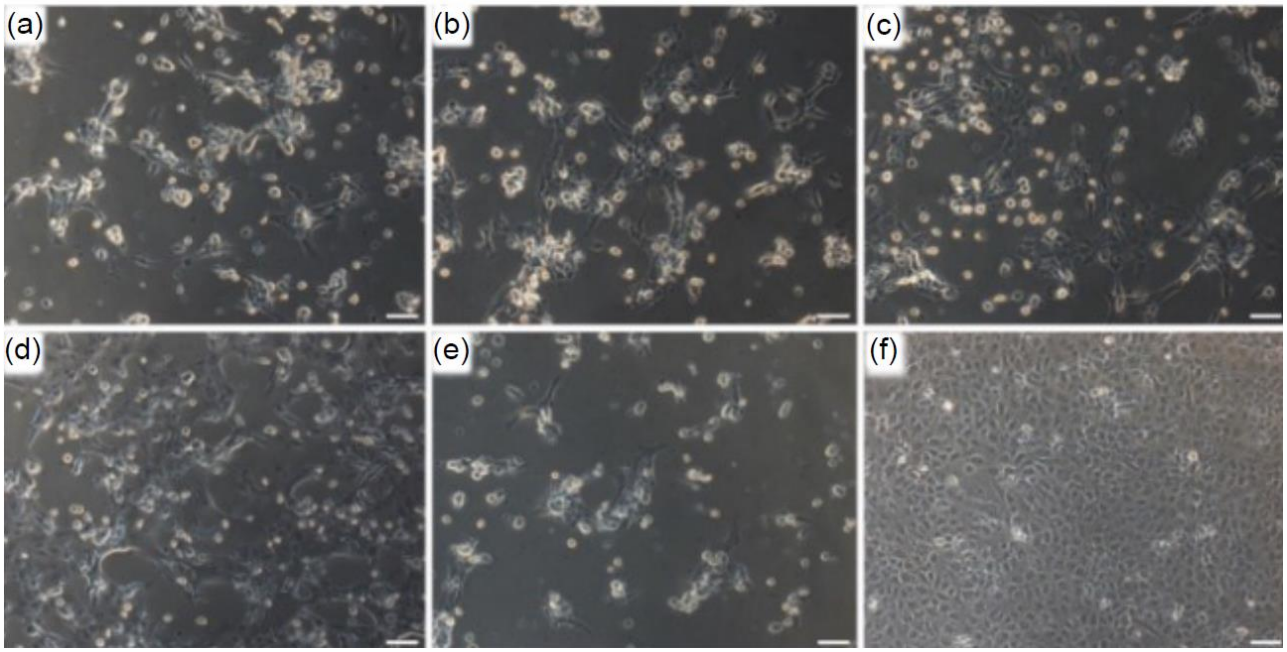

FIGURE S3 Celastrol reduces SARS-CoV-2 cytopathic action. Optical microscopy analysis of Vero CCL-81 cells infected with SARS-CoV-2 (MOI = 1.0) and treated with celastrol at the concentrations of (a) 125, (b) 250, (c) 500, and (d) 1000 nM, for 48 hours. Infected cells not treated with celastrol were used as the positive control (e). Cells incubated only with culture media were used as the negative control (f). Bar = 100 μm.