Supporting Information

Molecular Descriptors calculations

An approximation for absolute hardness η was developed [1-3] as given below:

$$\eta = \frac{I-A}{2} \quad (1)$$

Where *I* is the vertical ionization energy and *A* is the vertical electron affinity.

As per Koopmans theorem [4] the ionization energy and electron affinity can be specified through HOMO and LUMO orbital energies as:

I = □ E_{HOMO}

A = □ E_{LUMO}

Values of *I* and *A* of calculated are given in Table 4. The higher energy of HOMO is corresponds to the more reactive molecule in the reactions with electrophiles, while lower LUMO energy is essential for molecular reactions with nucleophiles [5].

Hence, the hardness of any material corresponds to the gap between the HOMO and LUMO orbitals. If the energy gap of HOMO-LUMO is larger then the molecule would be harder [2].

$$\eta = \frac{1}{2}\,(E_{LUMO} - E_{HOMO}) \quad (2)$$

The electronic chemical potential (μ) of a molecule is calculated by:

$$\mu = -\left(\frac{I+A}{2}\right) \quad (3)$$

The softness of a molecule is calculated by:

$$S = \frac{I}{2\eta} \quad (4)$$

The electronegativity of the molecule is calculated by:

$$\chi = \left(\frac{I+A}{2}\right) \quad (5)$$

The electrophilicity index of the molecule is calculated by:

$$\omega = \frac{\mu^2}{2\eta} \quad (6)$$

Molecular electrostatic potential

The Molecular Electrostatic Potential (MEP) is an applicable property to explore the reactivity of various compounds and/or species. In fact, MEP is a physical observable property that can be measured experimentally by diffraction approaches [6, 7]. Moreover, it can also be explored by computational means. The MEP illustrates the wide-ranging electronic and nuclear charge distribution which is an appropriate feature to understand the reactivity of various species [8]. The red color specifies the higher negative potential regions which are beneficial for the electrophilic attack, whereas the blue color identifies the higher positive potential regions favorable for nucleophilic attack. The MEP decreases in the order blue > green > yellow > orange > red, the red color shows the strongest repulsion while blue elucidates the sufficient attraction.

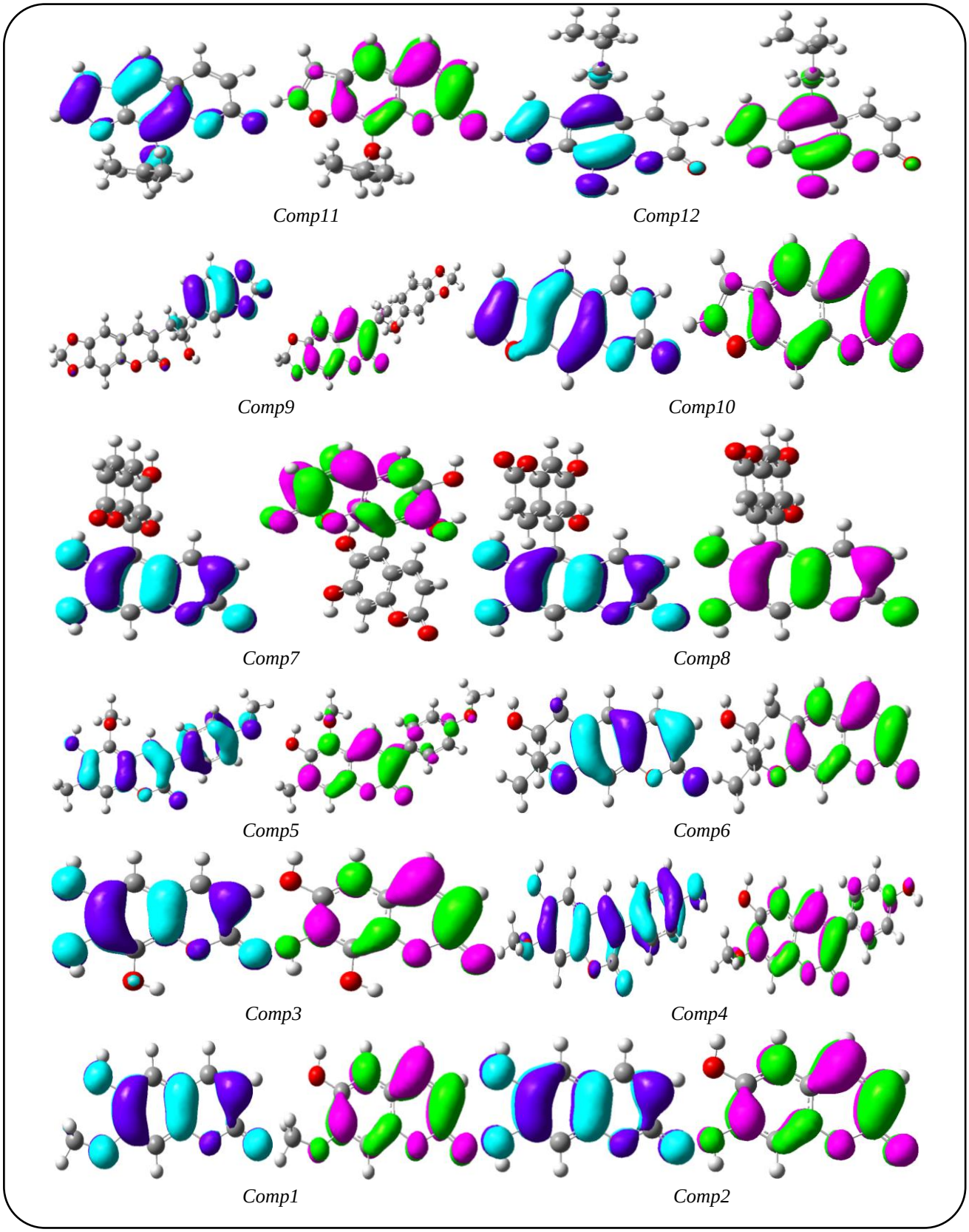


Fig. S1: Ground state charge density of FMOs of isolated compounds and reference drugs (contour value=0.035).

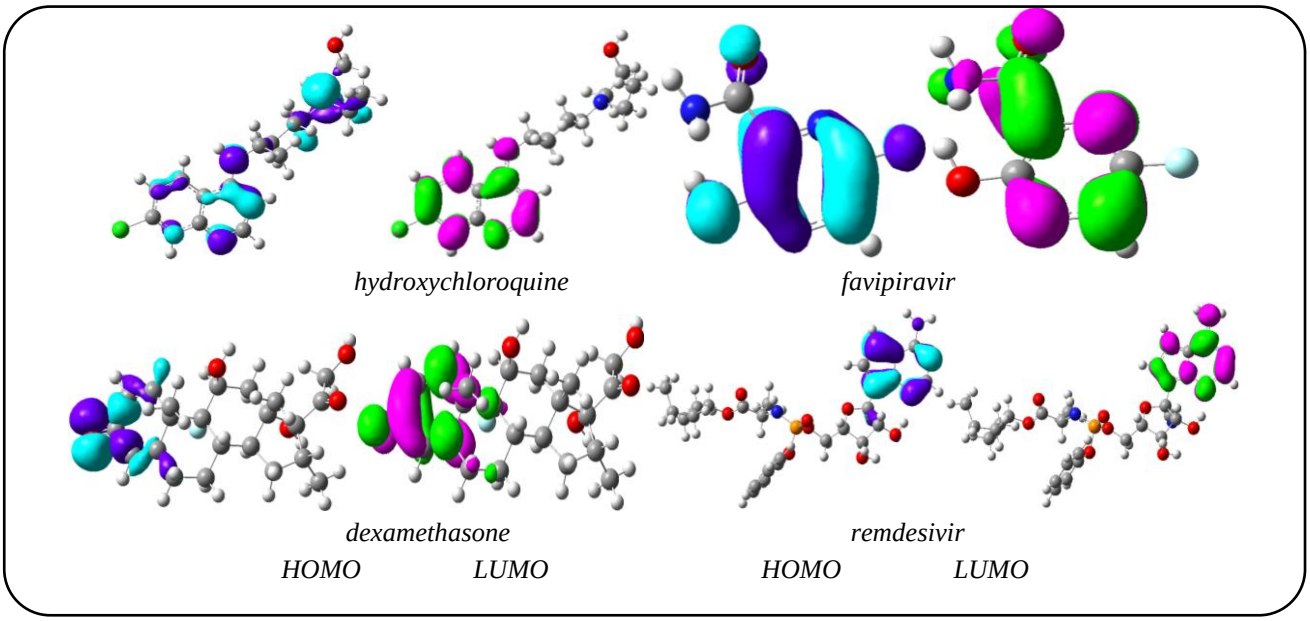


Fig. S1. The ground state charge density of FMOs of isolated compounds and reference drugs (contour value=0.035). (Continuation)

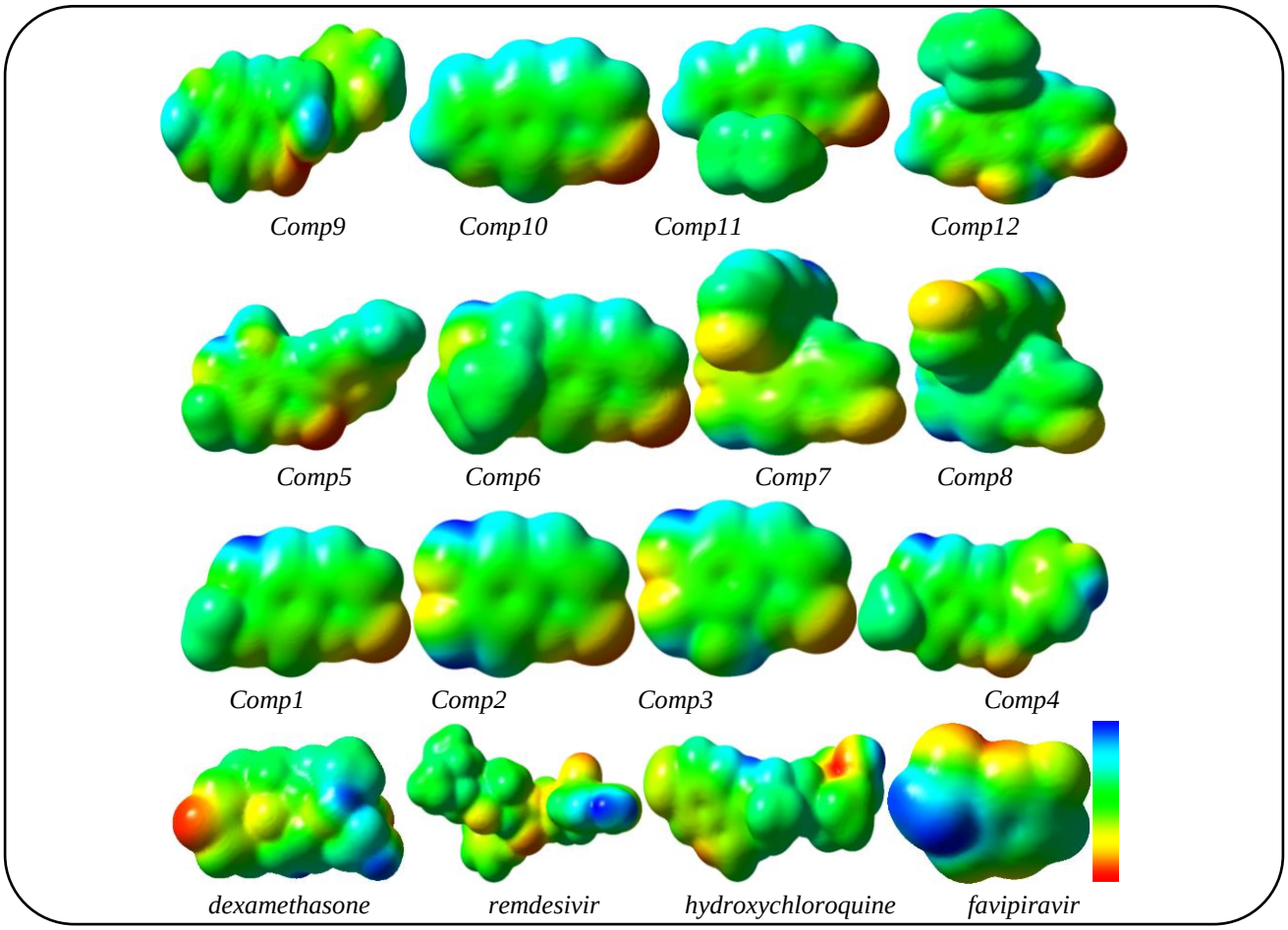
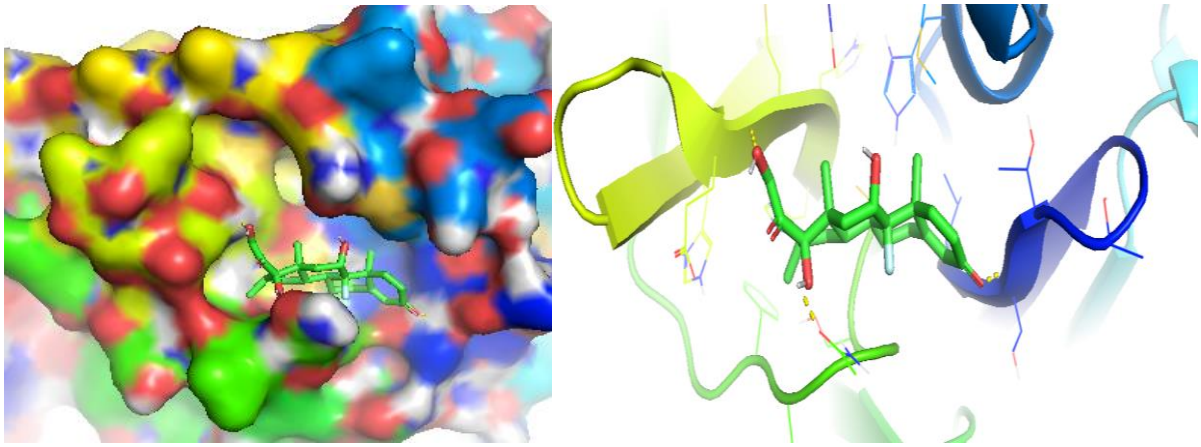
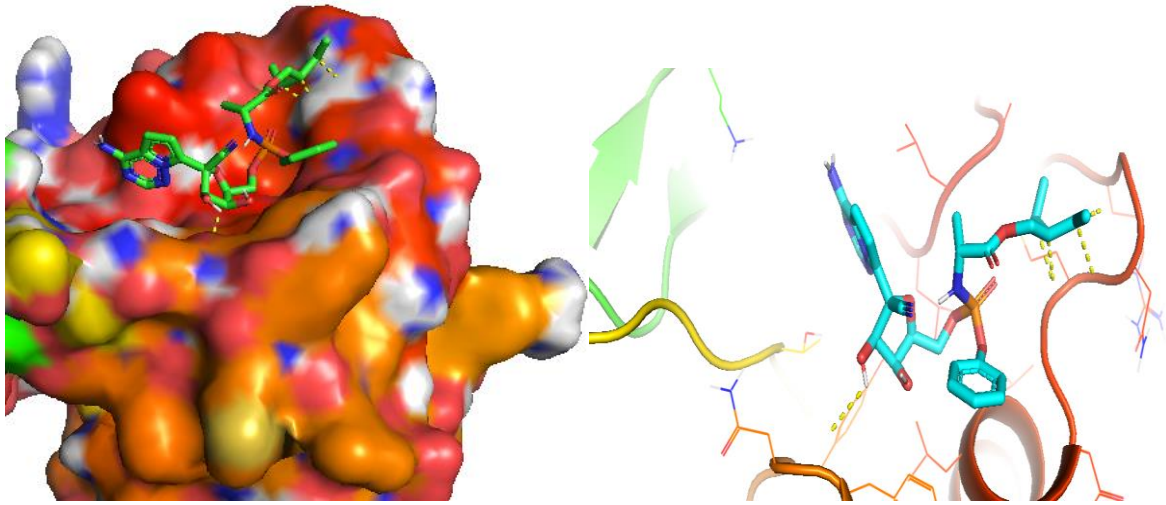


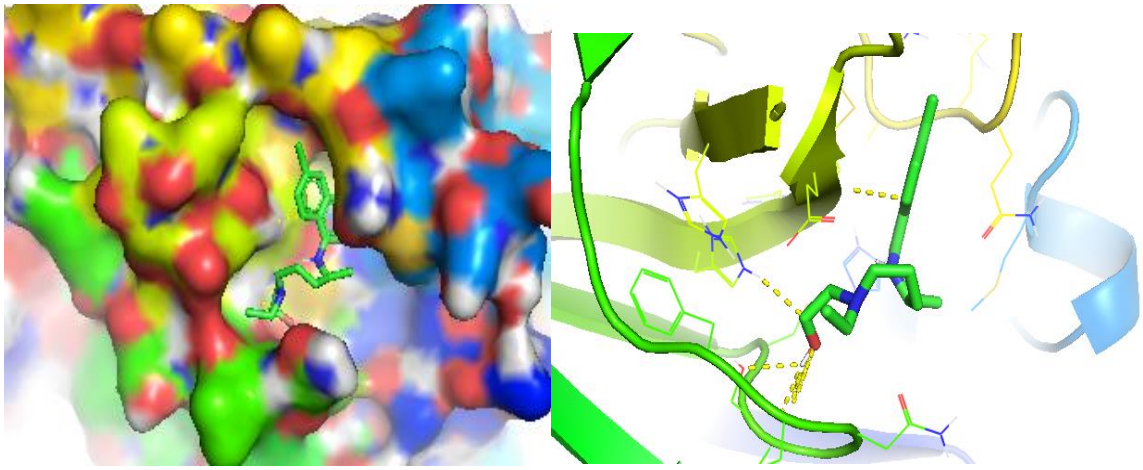
Fig. S2: Molecular electrostatic potential surface views of isolated compounds and reference drugs.



dexamethasone

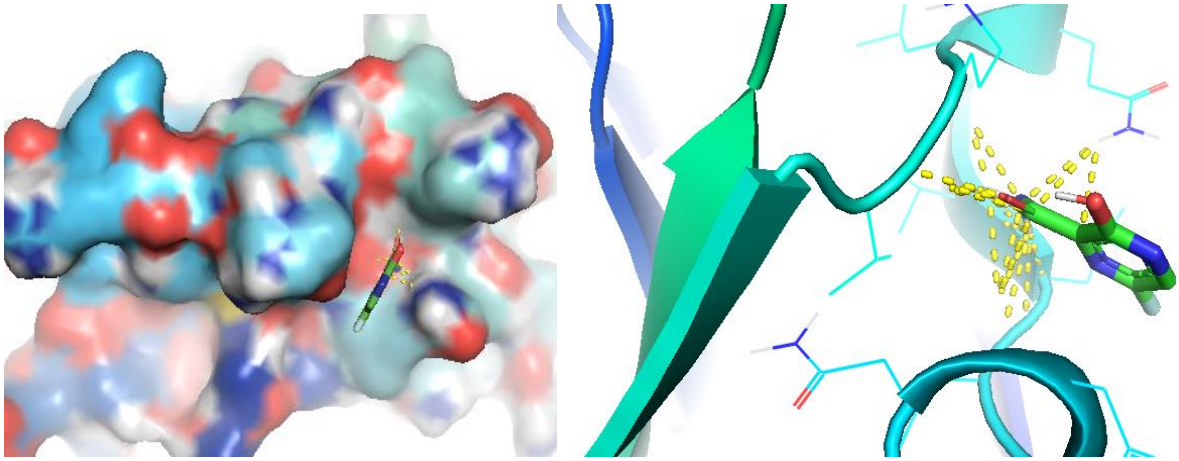


remdesivir

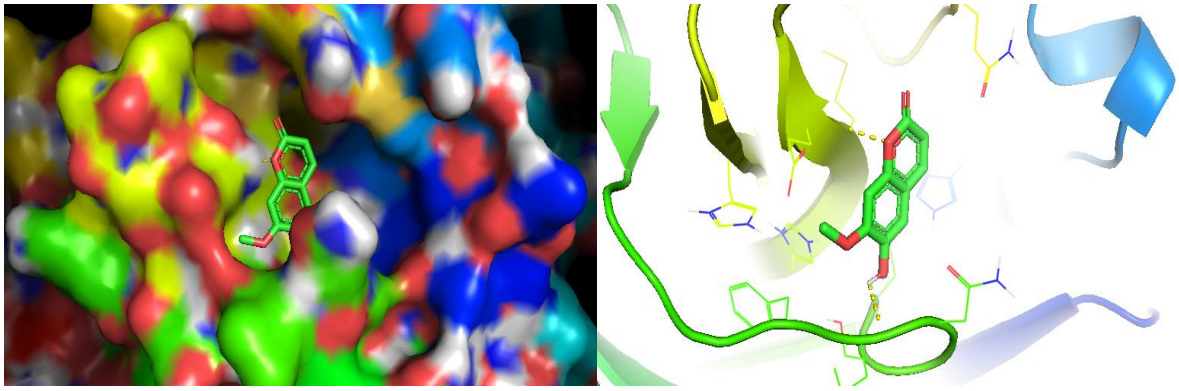


Hydroxychloroquine

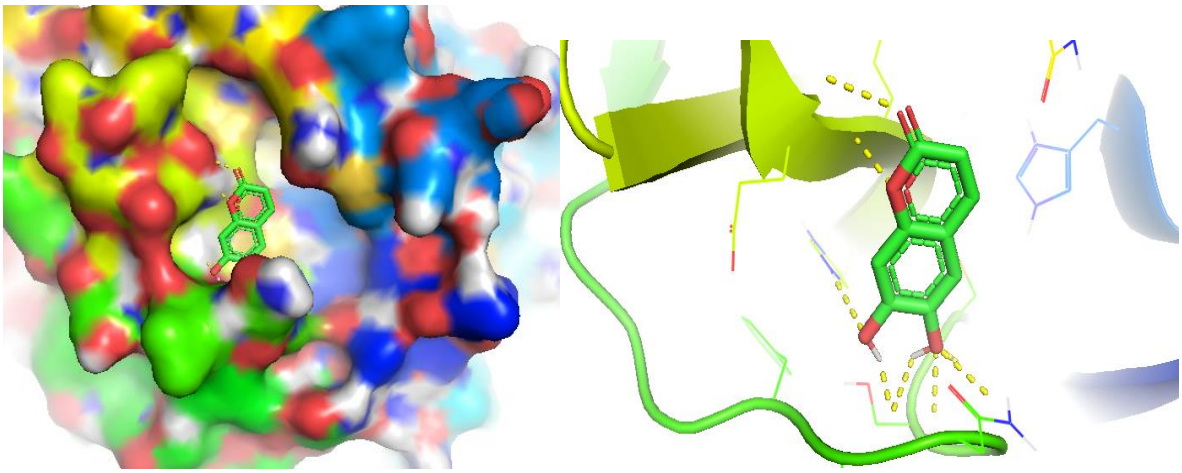
Fig. S3. Docking simulation of the interaction between isolated compounds, reference drugs, and the 6LU7 protein of SARS-CoV-2.



Favipiravir

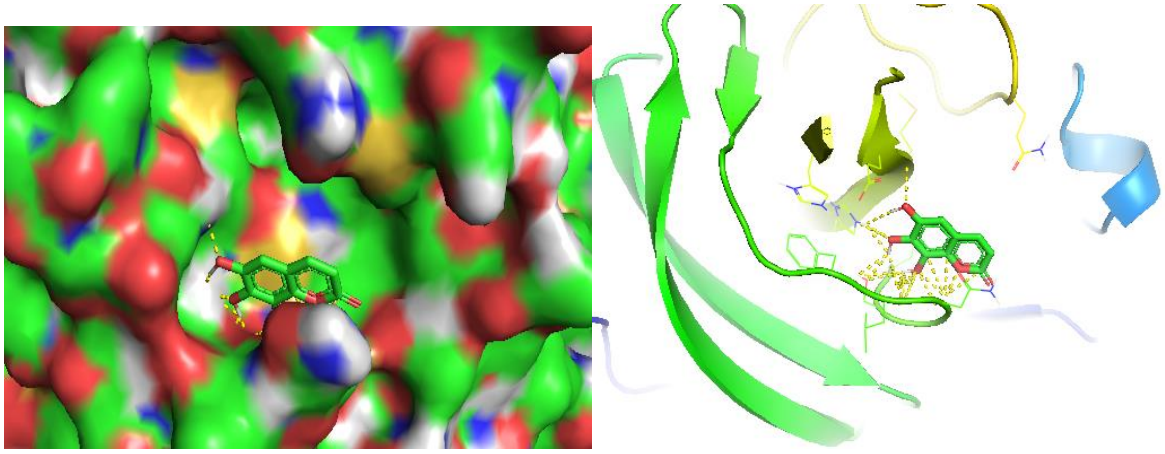


Comp1

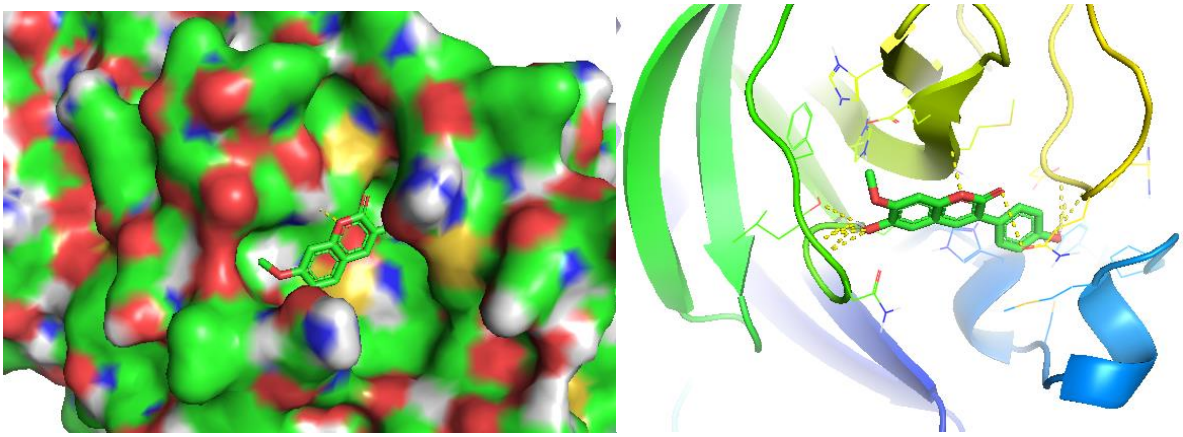


Comp2

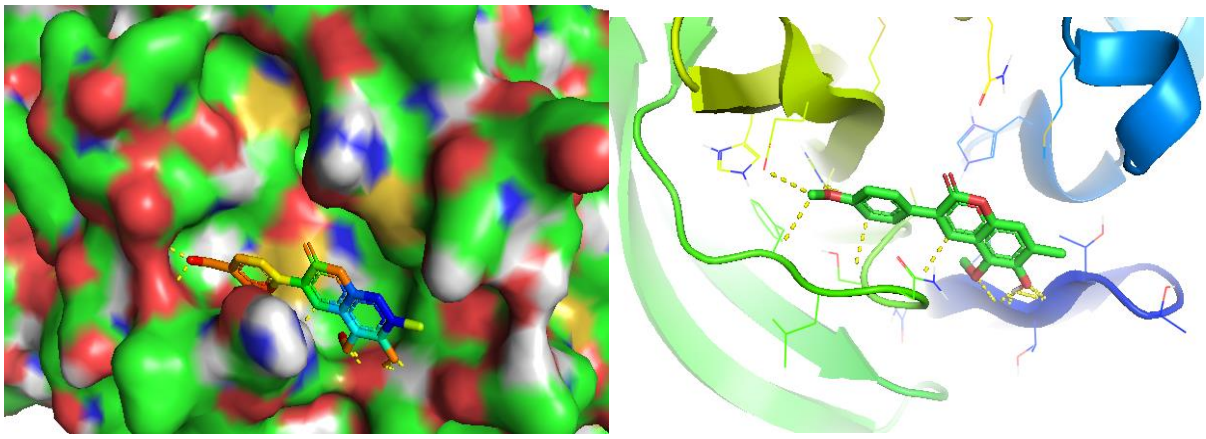
Fig. S3. Docking simulation of the interaction between isolated compounds, reference drugs and the 6LU7 protein of SARS-CoV-2. (Continuation)



Comp3

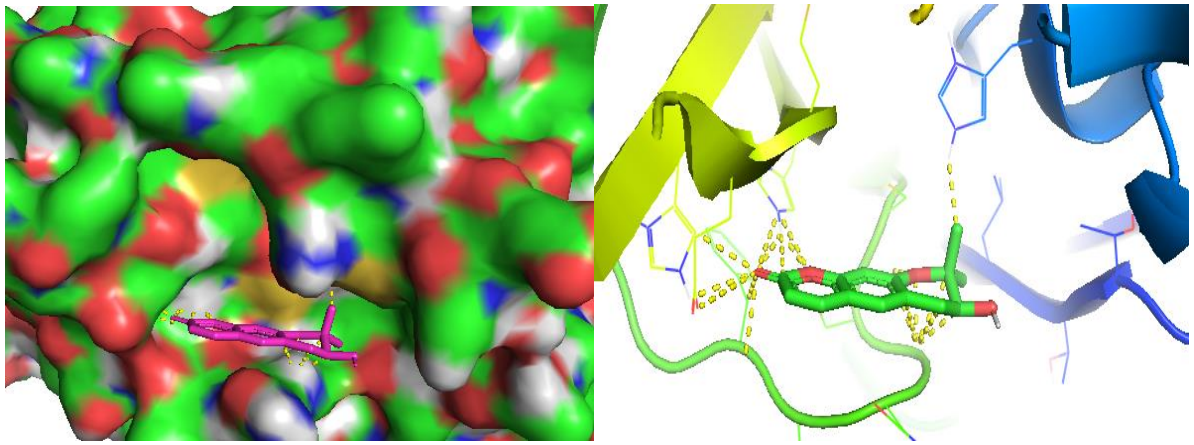


Comp4

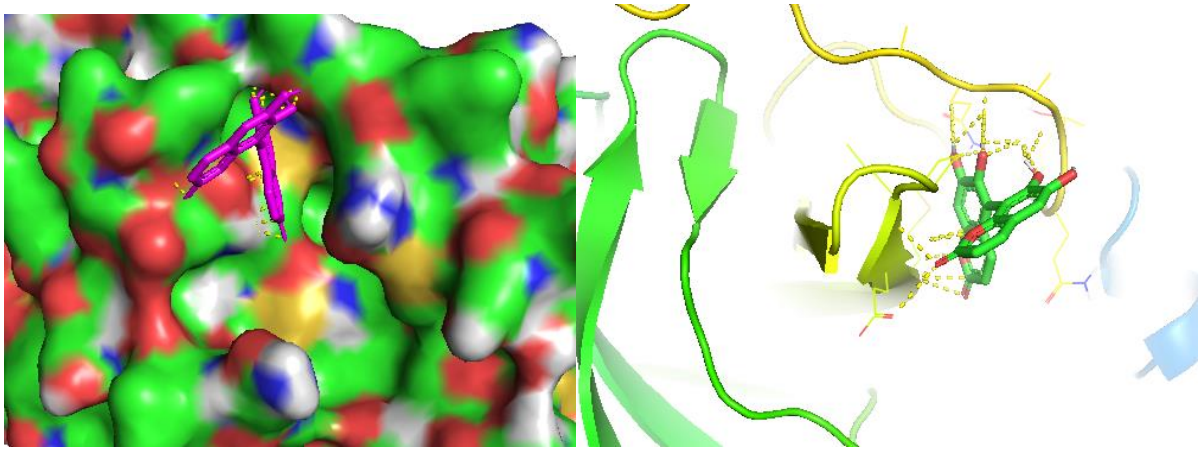


Comp5

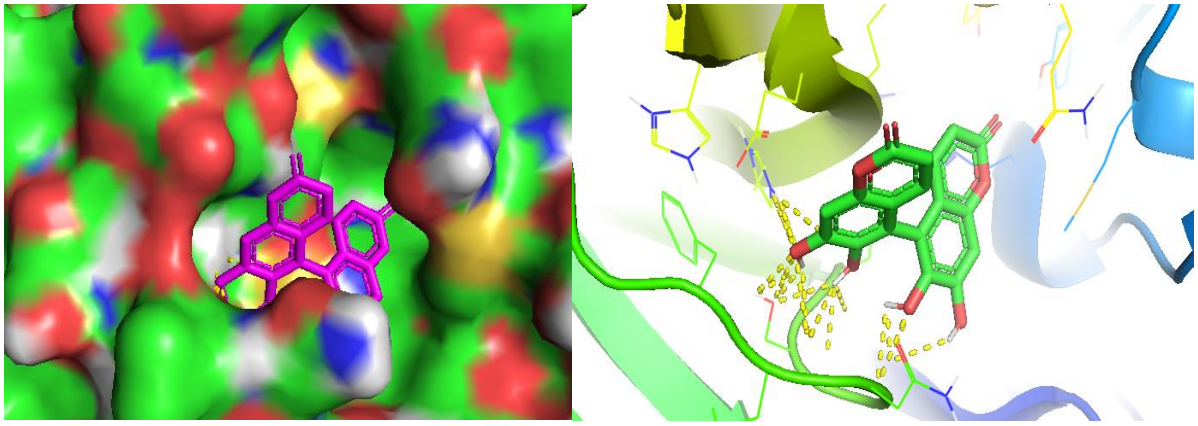
Fig. S3: Docking simulation of the interaction between isolated compounds, reference drugs, and the 6LU7 protein of SARS-CoV-2. (Continuation)



Comp6

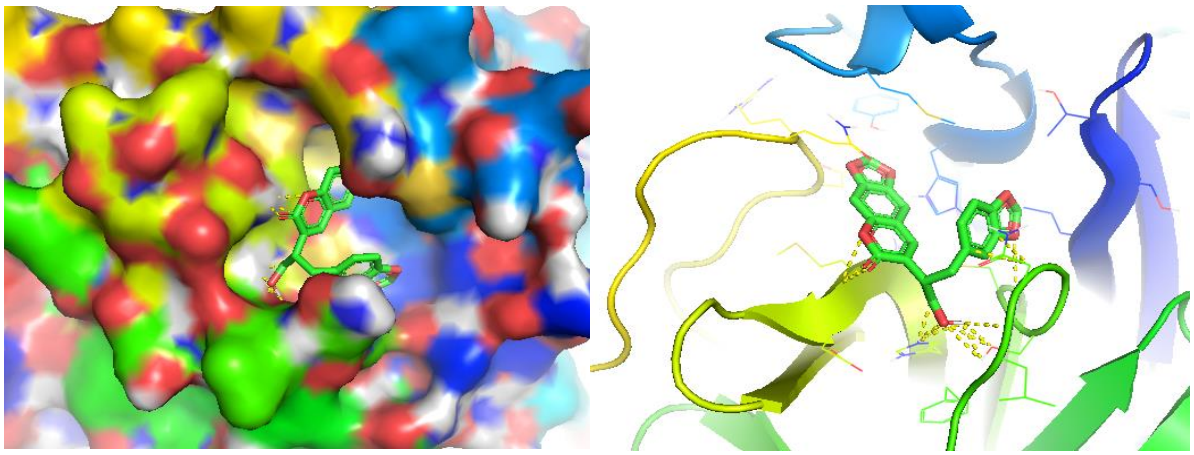


Comp7

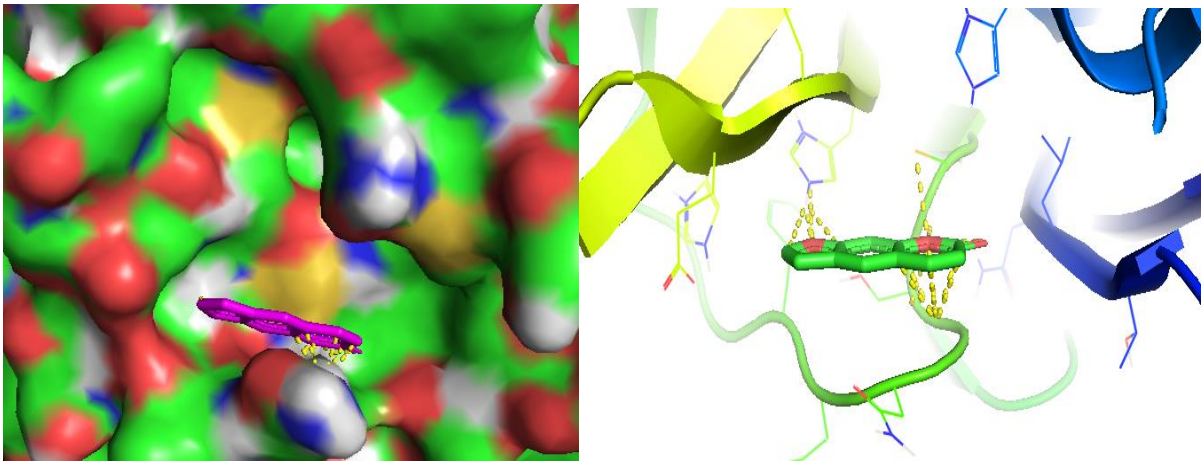


Comp8

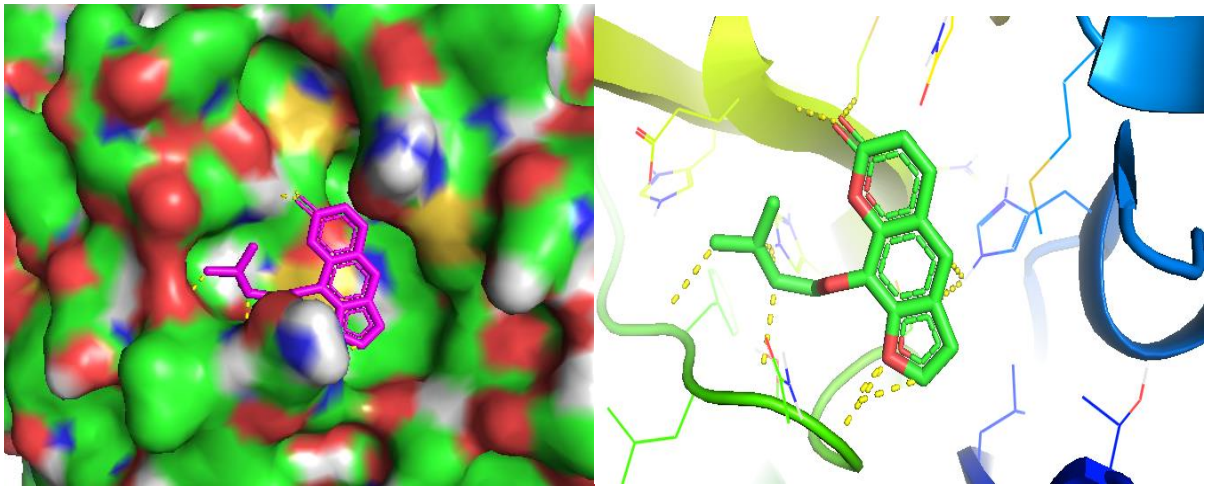
Fig. S3: Docking simulation of the interaction between isolated compounds, reference drugs, and the 6LU7 protein of SARS-CoV-2. (Continuation)



Comp9

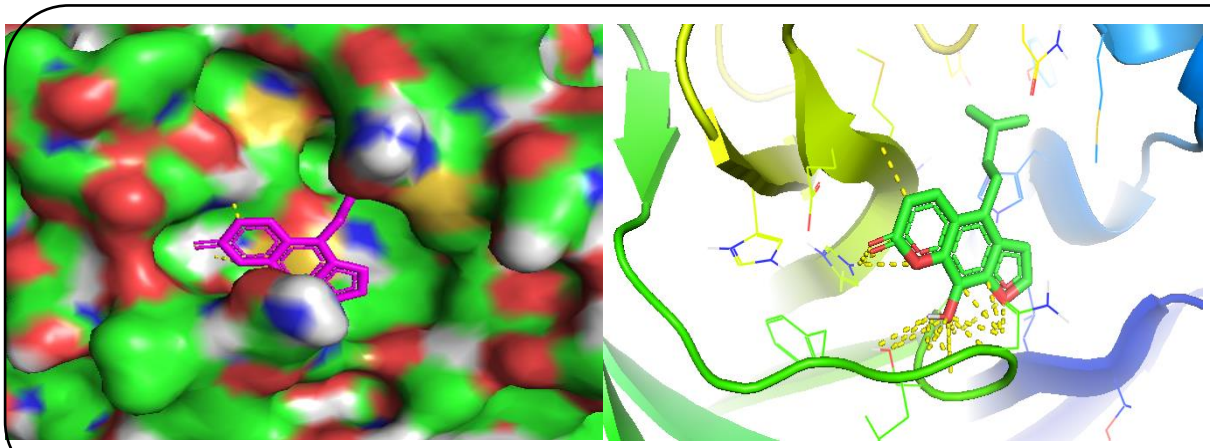


Comp10



Comp11

Fig. S3: Docking simulation of the interaction between isolated compounds, reference drugs, and the 6LU7 protein of SARS-CoV-2. (Continuation)



Comp12

Fig. S3: Docking simulation of the interaction between isolated compounds, reference drugs, and the 6LU7 protein of SARS-CoV-2. (Continuation)

Table S1: The ground state HOMO energies (E_{HOMO}), LUMO energies (E_{LUMO}), energy gaps (E_{gaps}), IP, EA, η, μ, S, χ and ω in eV.

Parameters	dexamethasone	remdesivir	hydroxyl-chloroquine	Favipiravir	Comp1	Comp2
E_{HOMO}	-6.22	-6.20	-5.57	-6.98	-5.74	-5.80
E_{LUMO}	-1.39	-1.36	-1.14	-2.24	-1.66	-1.69
E_{gap}	4.83	4.84	4.43	4.74	4.08	5.11
η	2.41	2.42	2.21	2.37	1.99	2.03
μ	-3.80	-3.78	-3.35	-4.61	-3.75	-3.75
S	1.29	1.28	1.26	1.47	1.44	1.41
χ	3.80	3.78	3.35	4.61	3.75	3.75
ω	3.00	2.95	2.54	4.48	3.53	3.41
IP	6.22	6.20	5.57	6.98	5.74	5.80
EA	1.39	1.36	1.14	2.24	1.66	1.69
Parameters	Comp3	Comp4	Comp5	Comp6	Comp7	Comp8
E_{HOMO}	-5.84	-5.53	-5.53	-5.94	-5.57	-5.83
E_{LUMO}	-1.80	-1.80	-1.79	-1.62	-2.07	-2.12
E_{gap}	4.04	3.73	3.74	4.32	3.50	3.71
η	2.02	1.86	1.87	2.16	1.75	1.86
μ	-3.82	-3.66	-3.78	-3.82	-3.98	-3.49
S	1.44	1.48	1.48	1.37	1.59	1.57
χ	3.82	3.66	3.78	3.82	3.98	3.49
ω	3.61	3.60	3.58	3.31	4.17	4.26
IP	5.84	5.53	5.53	5.94	5.57	5.83
EA	1.80	1.80	1.79	1.62	2.07	2.12
Parameters	Comp9	Comp10	Comp11	Comp12		
E_{HOMO}	-5.39	-6.15	-5.91	-5.74		
E_{LUMO}	-1.58	-1.83	-1.67	-1.83		
E_{gap}	3.81	4.32	4.24	3.91		
η	1.91	2.16	2.12	1.96		
μ	-3.49	-3.99	-3.79	-3.79		
S	1.41	1.42	1.39	1.47		
χ	3.49	3.99	3.79	3.79		
ω	3.19	3.69	3.39	3.66		
IP	5.39	6.15	5.91	5.74		
EA	1.58	1.83	1.67	1.83		

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