1The impact of natural polyphenol on the structure and flexibility COVID-19

2main protease binding pocket: a molecular dynamics simulation study

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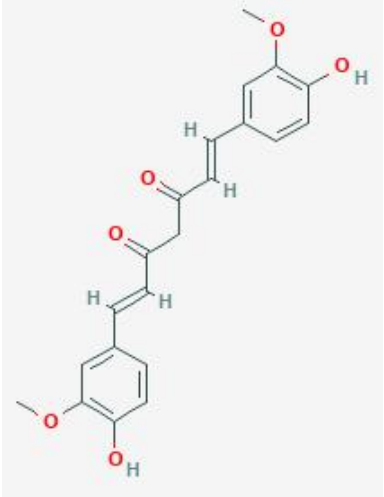
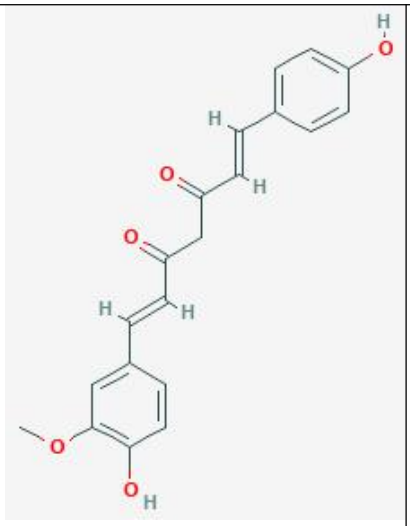
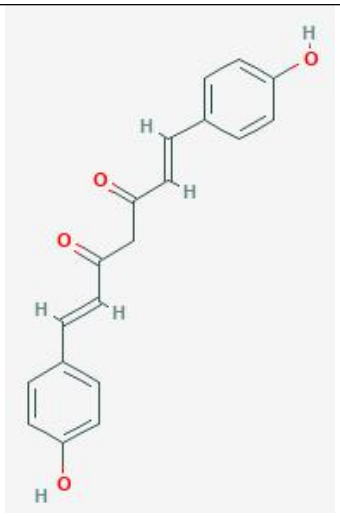
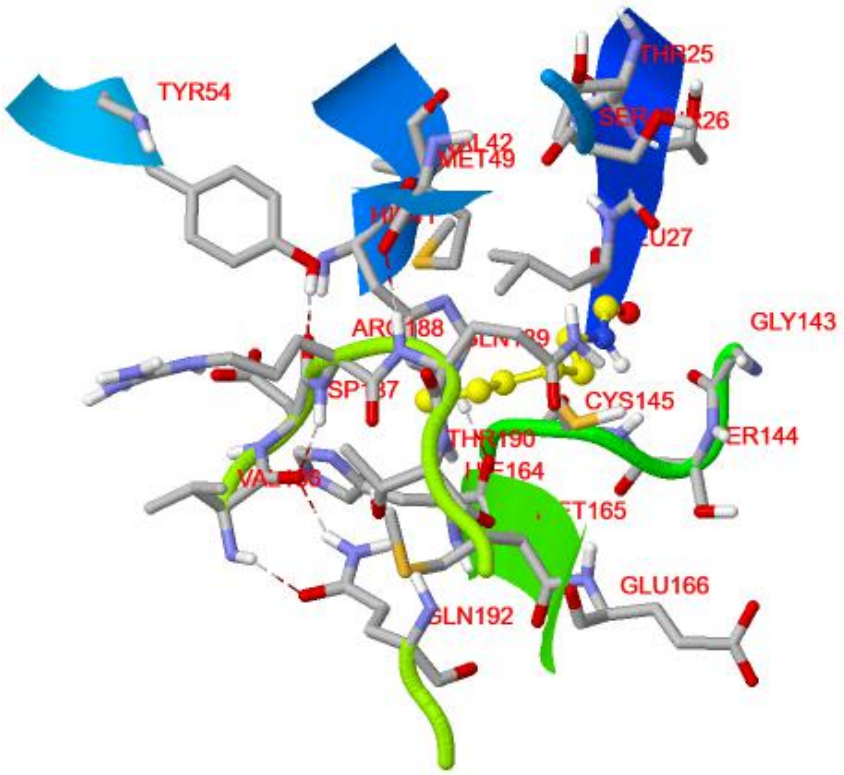
15 Table 1. Details of the selected hits. Open BABEL structure and docking energies

16 obtained after virtual screening and refinement by molecular docking are shown.

Compound	Structure	Autodock (Kcal.mol^{-1})	Autodock Vina (Kcal.mol^{-1})
Diferuloylmethane		-7.98	−202.476 kcal/mol

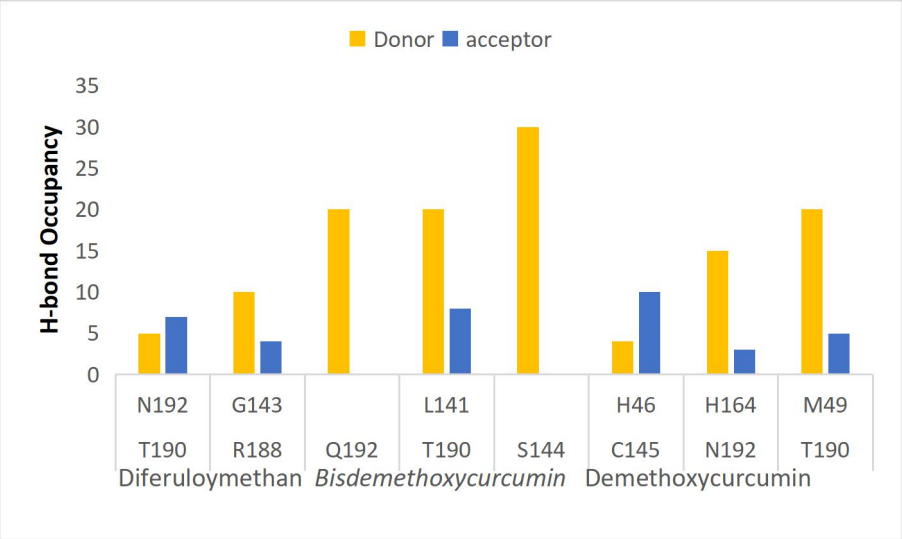
demethoxycurcumin		-8.17	103.901 Kcal/mol
Bisdemethoxycurcumin		-8.30	-151.545 Kcal/mol



17 Figure 1. The potential binding position for the Carmfur-Mpro complex of binding
18 modes in the active site (residues are shown in sticks). The red dotted line
19 represents intermolecular hydrogen bond interactions.

20 Table 2. Table showing the Van der Waal, electrostatic, polar salvation and
21 binding energy in kJ mol^{-1} for Mpro and its Ligands in complex with Carmfur.

Ligand - enzyme complex	Electrostatic energy (kJ/mol)	Van der Waal energy (kJ/mol)	Polar solvation energy (kJ/mol)	Binding free energy (kJ/mol)
Enzyme - bisdemethoxycurcumin complex	−282.1 ± 1.1	−125.1 ± 1.4	264.8 ± 2.4	−169.7 ± 2.5
Enzyme-demethoxycurcumin complex	-118.4 ± 3.7	-108.1 ± 2.2	162.8 ± 5.9	-89.0 ± 45.3
Enzyme-diferuloylmethane	-339.1 ± 15.6	-364.2 ± 18	492.6 ± 15.2	-39.0 ± 1.5



22 **Figure 2**. Hydrogen bond occupancy analysis for Bisdemethoxycurcumin,
23 Demethoxycurcumin and diferuloylmethane.