**Table-S1.** Summary of conventional (or) non-covalent docking of ligands into the ligand-binding pocket of SARS-CoV-2 Mpro.

*(a) Allicin*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **SR. No** | **PDB** | **Interaction with amino acids** | **(S-S) distance in A°** | **Glide score** |
| 1 | 6LU7 | His 41, Met 49, His 164, Met 165, Glu 166, Val 186, Asp 187, Arg 188, Gln 189, Gln 192 | 6.0 | -2.568 |
| 2 | 6Y2F | Cys 44, His 41, Met 49, Pro 52, Tyr 54, Cys 145, Asp 187, Arg 188, Gln 189 | 6.6 | -2.011 |
| 3 | 5RFV | Thr 25, Thr 26, Leu 27, His41, Val 42, Leu 141, Asn 142, Gly 143, Ser 144, Cys 145, Glu 166, His 163, His 172 | 3.5 | -2.963 |
| 4 | 5RFW | His 41, Met 49, Phe 140, Leu 141, Asn 142, Gly 143, Ser 144, Cys 145, His 163, His 164, Met 165, Glu 166, Asp 187, Arg 188, Gln 189 | 7.3 | -1.608 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **SR. No** | **PDB** | **Interaction with amino acids** | **(S-S) distance in A°** | **Glide score** |
| 1 | 6LU7 | His 41, Cys 44, Pro 52, Tyr 54, Met 49,Cys 145, His 164, Met 165, Glu 166, Val 186, Asp 187, Arg 188, Gln 189 | 5.7 | -3.778 |
| 2 | 6Y2F | Thr 25, His 41, Val 42, Cys 44, Met 49, Tyr 54, His 164, Met 165, Phe 181, Val 186, Asp 187, Arg 188, Gln 189, Gln 192 | 7.2 | -3.527 |
| 3 | 5RFV | Met 49, Phe 140, Leu 141, Asn 142, Ser 144, Cys 145, His 163, His 164, Met 165, Glu 166, His 172 | 5.1 | -3.090 |
| 4 | 5RFW | Met 165, Glu 166, Leu 167, Pro 168, Gln 189, Thr 190, Ala 192, | 11.5 | -4.016 |

*(b) PX-12*

**Table-S2** The summary of covalent docking of PX-12/allicin/allyl sulfenic acid at the cysteine thiols of crystal structures of SARS-CoV-2 Mpro.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **SL.NO** | **PDB ID** | **cDock affinity (kcal/mol)** | | | |
| **CYS-145** | | **CYS-85** | **CYS-156** |
| **PX-12** | **Allicin** | **Allyl sulfenic acid** | |
| 1 | 6LU7 | 0.410 | -0.077 | -1.433 | -0.650 |
| 2 | 6Y2F | -3.663 | -2.265 | -1.334 | -0.934 |
| 3 | 5RFV | -2.218 | -1.231 | -1.585 | -0.649 |
| 4 | 5RFW | -1.658 | -2.036 | -0.896 | -1.398 |



**Scheme-S1.** The reaction schemes used for generation of custom-made covalent reaction type by Schrödinger for covalent docking on Glide, Maestro of Schrödinger software.



**Figure-S1.** The homodimer structure of SARS-CoV-2 Mpro. The active site residues and exposed cysteine residues are indicated.



**Figure-S2.** Structures of covalent inhibitors of SARS-CoV-2 Mpro. (a) Peptidomimetic and (b) small molecules. These inhibitors are covalently bound at Cys-145 residue in the co-crystal structures of SARS-CoV-2 Mpro.

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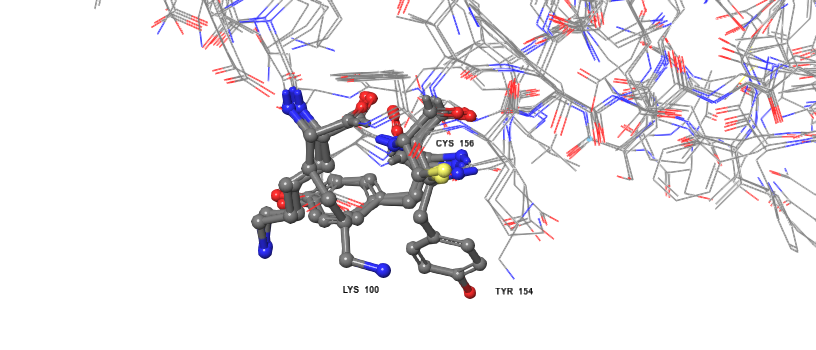
**Figure-S3.** The interacting residues derived from the conventional (or) non-covalent docking of allicin into the active site of SARS-CoV-2 Mpro. PDB ID (a) 6LU7 and (b) 5RFV of SARS-CoV-2 Mpro were used as templates for conventional docking of allicin.



**Figure-S4.** (a) Conventional (or) non-covalent docking and (b) interacting residues of PX-12 at the active site of SARS-CoV-2 Mpro. PDB ID: 6LU7 of SARS-CoV-2 Mpro was used for docking of PX-12.



**Figure-S5.** Covalent docking of PX-12 at the active site of SARS-CoV-2 Mpro. PDB ID: 6LU7 of SARS-CoV-2 Mpro was used for docking of PX-12.



**Figure-S6.** The residues in the vicinity of Cys-156 in the unbound and inhibitor bound form of SARS-CoV-2 Mpro. Distortion of Lys-100/Tyr-154 residue in 6LU7 with N3 inhibitor.



**Figure-S7.** Superposition of crystal structures of apo-form and inhibitor bound form of SARS-CoV-2 Mpro.



**Figure-S8** The pKa of cysteine residues around the binding pocket of allicin in the SARS-CoV-2 Mpro. Structures of SARS-CoV-2 Mpro (PDB ID) are indicated. PDB ID: 6Y2E is unbound form and that of PDB ID: 6LU7, 5RFV, and 5RFW are a ligand-bound form of SARS-CoV-2 Mpro.



**Figure-S9.** The optimized structures of reactants, intermediates, and products of reactions between *N*-acetylcysteine amide and allicin deduced by density functional theory (DFT). Structures were indicated as they appear in the putative reactions shown in Figure-5a.