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# Interactions of omeprazole-based analogues with cytochrome P450 2C19: a computational study

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**Table S1** The details of the representative poses

| Compound | Number of clusters | Cluster_ID[a] | Cluster_Size[b] | Highest[c] | Average[d] | Mode[e] | $\Delta G_{exp}$ (kcal/mol) |
|---|---|---|---|---|---|---|---|
| **cpd01** | 3 | 1 | 27 | 26.74 | 25.57 | BM2 | -5.96 |
| | | 3 | 72 | 25.73 | 24.97 | BM1 | |
| **cpd02** | 2 | 1 | 31 | 28.74 | 27.66 | BM2 | -7.26 |
| | | 2 | 69 | 28.06 | 27.17 | BM1 | |
| **cpd03** | 2 | 1 | 73 | 30.81 | 29.39 | BM1 | -8.36 |
| | | 2 | 27 | 30.70 | 29.60 | BM2 | |
| **cpd06** | 6 | 1 | 28 | 36.90 | 35.02 | BM1 | -9.96 |
| **cpd11** | 2 | 1 | 84 | 29.76 | 28.24 | BM1 | -5.87 |
| **cpd15** | 5 | 1 | 41 | 40.07 | 38.10 | BM1 | -10.09 |
| **cpd28** | 5 | 1 | 53 | 39.66 | 37.52 | BM1 | -6.77 |
| | | 3 | 21 | 37.02 | 36.20 | BM2 | |
| **cpd30** | 2 | 1 | 34 | 38.01 | 35.61 | BM1 | -10.5 |
| | | 2 | 66 | 37.01 | 36.18 | BM2 | |

[a.] The identity of the selected cluster

[b.] Number of poses in the selected cluster

[c.] The highest docking score (ChemScore) of the selected cluster

[d.] The average docking score of the selected cluster

[e.] The binding mode of the representative pose.

**Table S2** The predicted binding free energies of each system using $GB_{n1}$ model at "D7.0"

| | $\Delta E_{vdw}$ | $\Delta E_{ele}$ | $\Delta G_{pol}$ | $\Delta G_{nonpol}$ | $\Delta G_{GBSA}$ | $-T\Delta S$ | $\Delta G_{bind}$ | $\Delta G_{exp}$ |
|---|---|---|---|---|---|---|---|---|
| **Cpd01**-BM1 | -30.77 ± 2.00 | -14.13 ± 3.36 | 16.54 ± 2.27 | -3.86 ± 0.21 | -32.22 ± 3.03 | 17.14 ± 4.10 | -15.07 | -5.96 |
| **Cpd02**-BM1 | -32.73 ± 2.09 | -11.89 ± 3.63 | 18.09 ± 2.72 | -4.39 ± 0.15 | -30.91 ± 2.73 | 17.00 ± 5.69 | -13.90 | -7.26 |
| **Cpd03**-BM1 | -31.89 ± 2.17 | -8.92 ± 3.01 | 16.43 ± 2.26 | -4.29 ± 0.22 | -28.67 ± 2.39 | 19.07 ± 4.31 | -9.60 | -8.36 |
| **Cpd06**-BM1 | -47.22 ± 2.74 | -13.38 ± 2.61 | 18.75 ± 1.91 | -5.83 ± 0.21 | -47.68 ± 3.25 | 20.47 ± 5.10 | -27.22 | -9.96 |
| **Cpd11**-BM1 | -33.63 ± 2.25 | -17.32 ± 4.92 | 29.12 ± 2.55 | -4.68 ± 0.19 | -26.51 ± 4.25 | 19.41 ± 4.77 | -7.10 | -5.87 |
| **Cpd15**-BM1 | -43.94 ± 2.45 | -14.37 ± 2.89 | 18.58 ± 2.19 | -5.53 ± 0.17 | -45.26 ± 2.75 | 21.90 ± 3.93 | -23.36 | -10.09 |
| **Cpd28**-BM1 | -38.70 ± 2.57 | -9.70 ± 4.61 | 18.85 ± 2.53 | -5.04 ± 0.29 | -34.59 ± 5.25 | 22.40 ± 6.37 | -12.20 | -6.77 |
| **Cpd30**-BM1 | -39.69 ± 1.91 | -11.37 ± 3.62 | 12.87 ± 2.02 | -5.13 ± 0.14 | -43.32 ± 3.58 | 21.54 ± 5.06 | -21.78 | -10.50 |
| | | | | | | | | |
| **Cpd01**-BM2 | -30.08 ± 1.97 | -6.13 ± 3.61 | 13.17 ± 2.95 | -3.95 ± 0.16 | -26.99 ± 2.45 | 16.43 ± 5.77 | -10.56 | -5.96 |
| **Cpd02**-BM2 | -31.41 ± 1.93 | -13.41 ± 2.79 | 17.56 ± 2.64 | -4.28 ± 0.18 | -31.54 ± 2.39 | 16.91 ± 4.88 | -14.63 | -7.26 |
| **Cpd03**-BM2 | -36.81 ± 1.97 | -5.06 ± 2.15 | 14.61 ± 2.33 | -4.77 ± 0.17 | -32.03 ± 3.24 | 18.87 ± 3.59 | -13.17 | -8.36 |
| **Cpd28**-BM2 | -44.84 ± 2.40 | -17.85 ± 4.03 | 28.80 ± 3.99 | -6.03 ± 0.17 | -39.92 ± 3.63 | 19.52 ± 4.36 | -20.40 | -6.77 |
| **Cpd30**-BM2 | -39.62 ± 2.10 | -26.72 ± 2.73 | 29.06 ± 2.09 | -4.90 ± 0.13 | -42.18 ± 2.24 | 17.34 ± 5.65 | -24.84 | -10.50 |

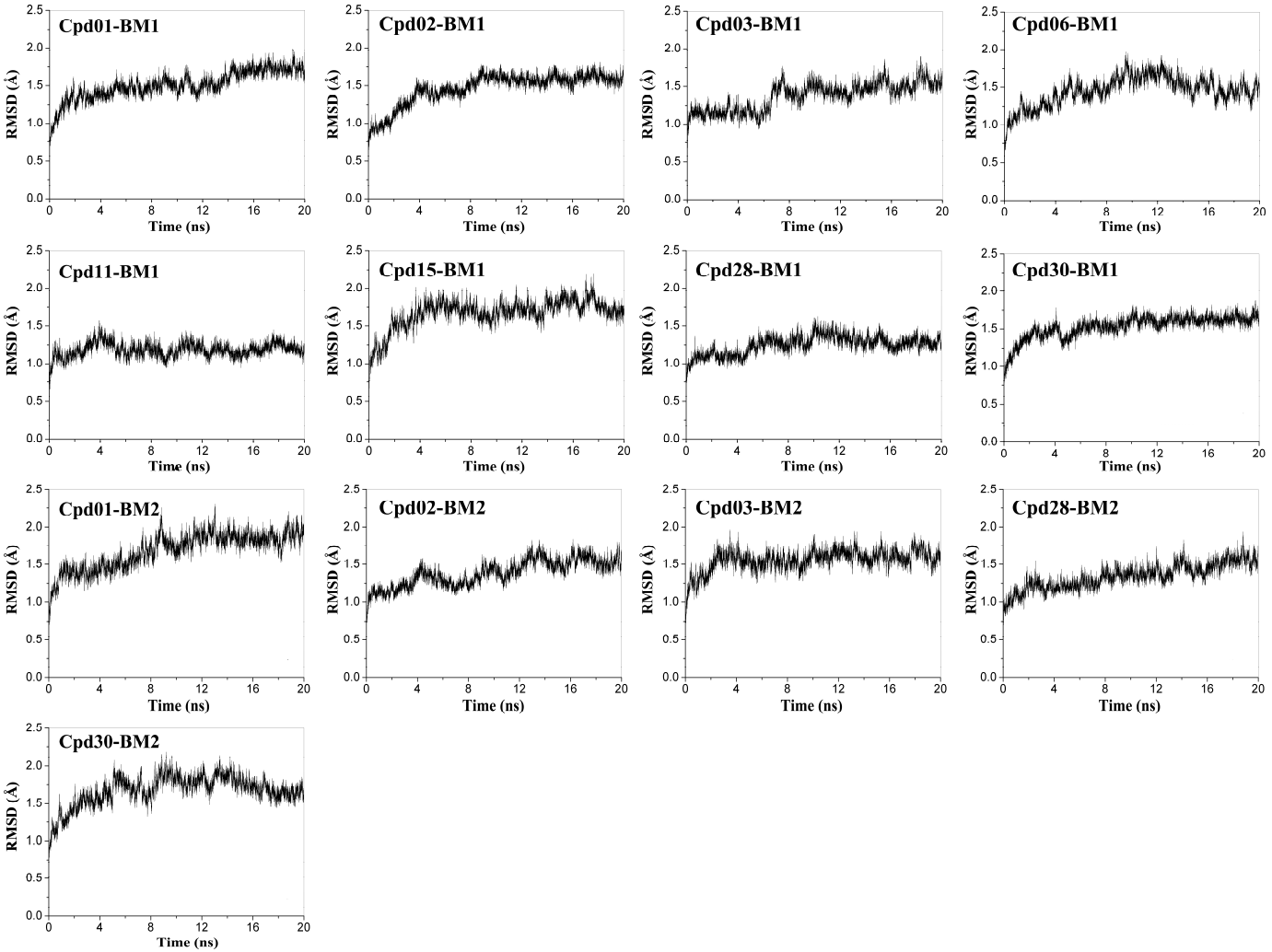


**Fig. S1** The RMSD values of protein backbone atoms for each system

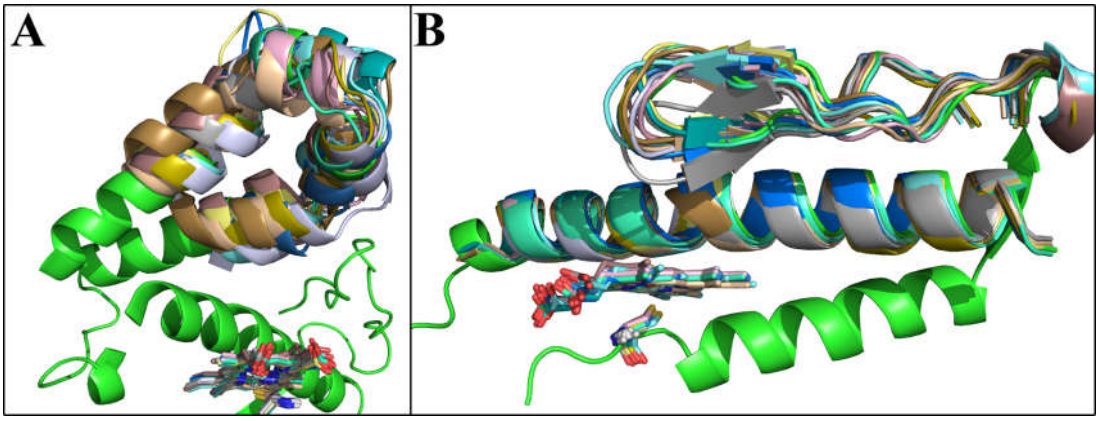


**Fig. S2** Local conformational changes of protein atoms (The crystal structure was represented in green cartoon): F-G loop (A) and C-terminal loop (B)

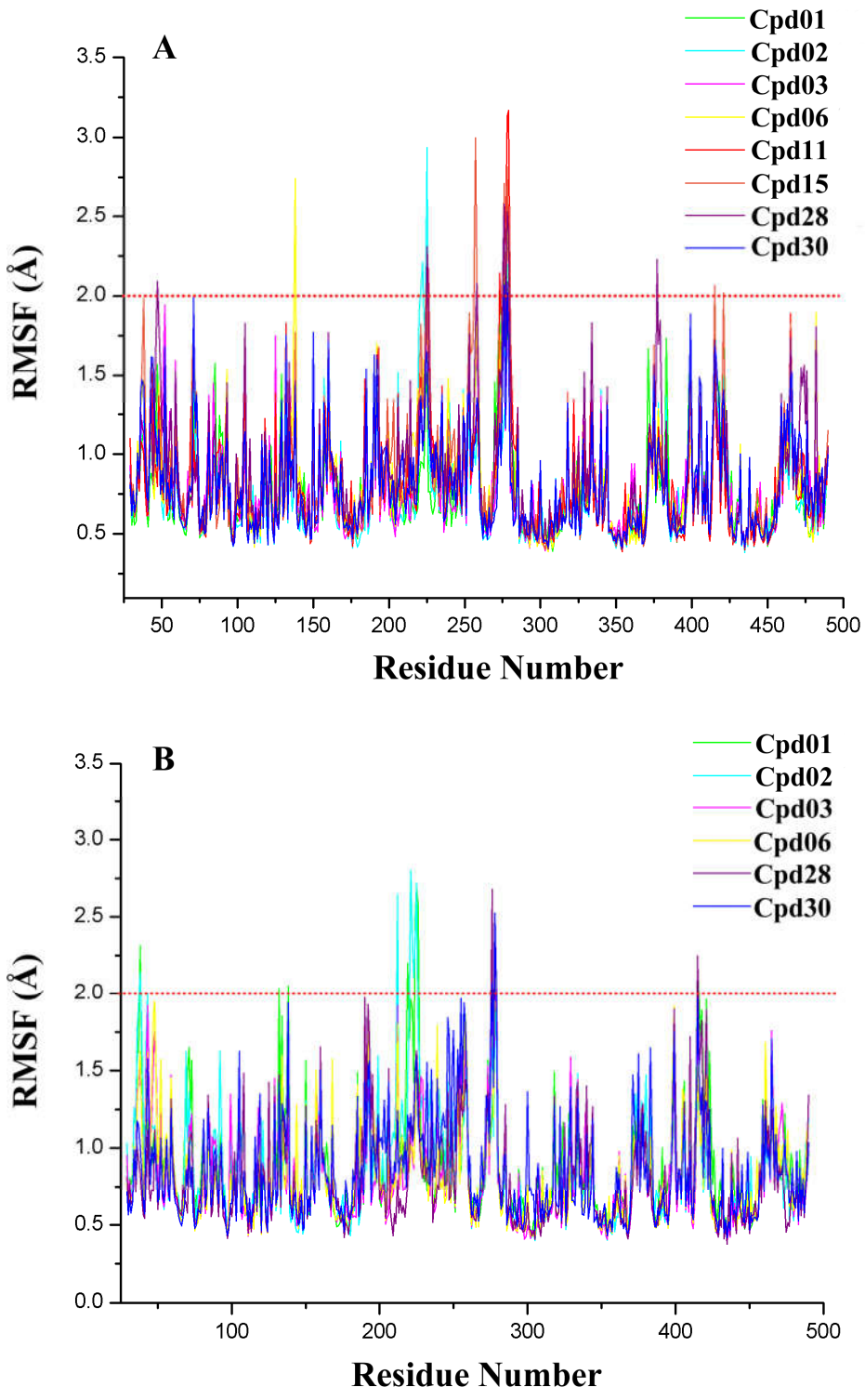


**Fig. S3** The RMSF values of all residues in the equilibrated trajectories. (A. The RMSF values for BM1 systems; B. The RMSF values for all BM2 systems)

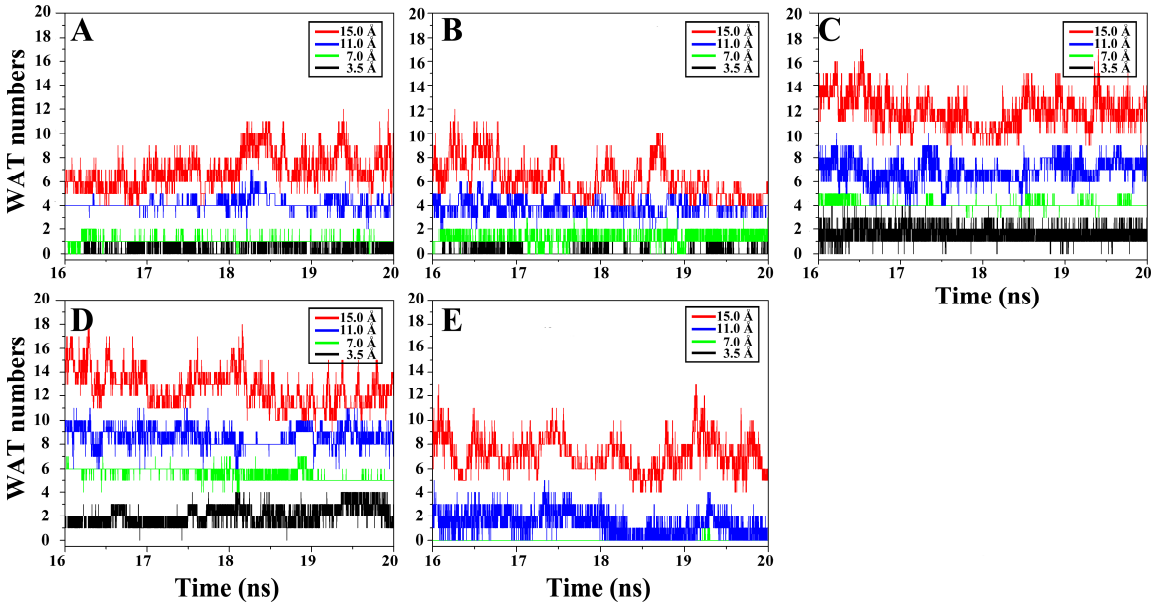


**Fig. S4** Hydration analysis of the BM2 systems: **Cpd01** (A); **Cpd02** (B); **Cpd03** (C); **Cpd28** (D); **Cpd30** (E)

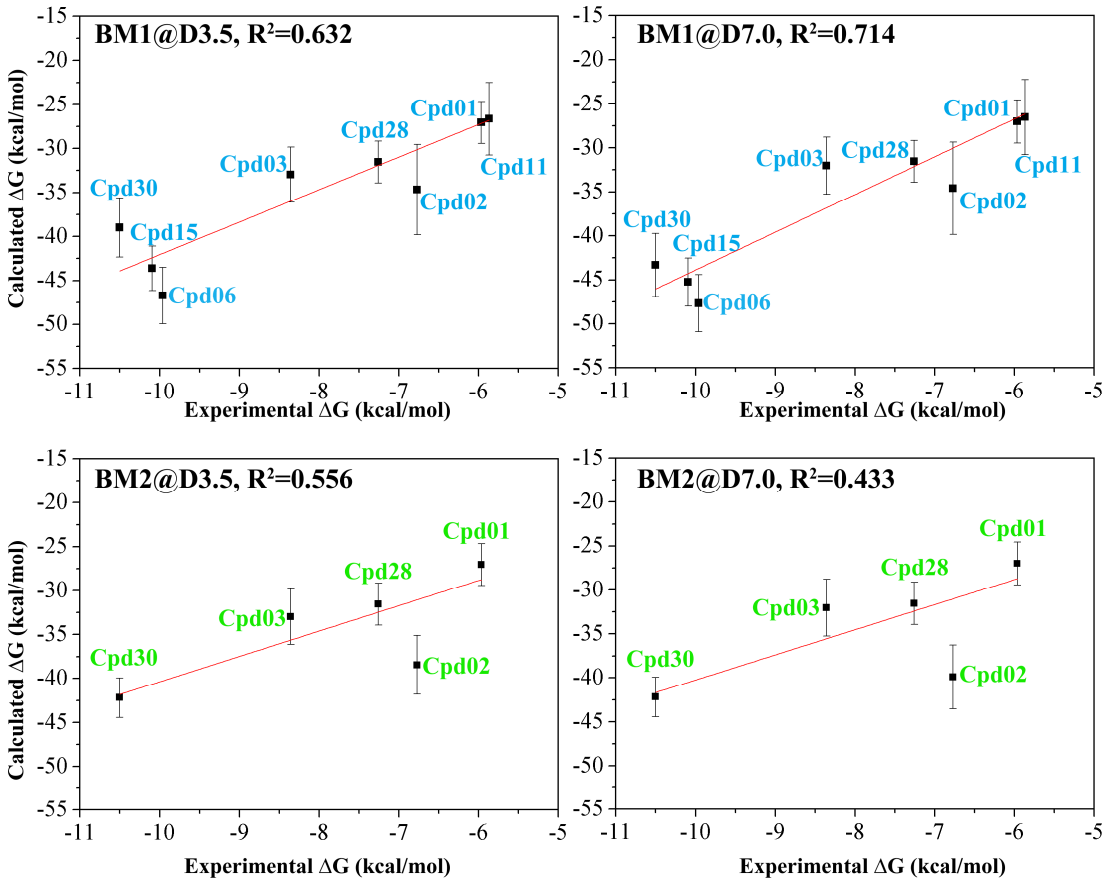


**Fig. S5** The correlation coefficient ($r^2$) between calculated binding energies and those derived from experimental data with explicit hydration shell (showing all BM1 and BM2 compounds at "D3.5" and "D7.0", respectively. The experimental binding free energy was derived from: $\Delta G_{exp} = -RTlnK_i$)