Supplementary material

*In silico* receptor-based drug design of X,Y-benzenesulfonamide derivatives as selective COX-2 inhibitors

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Table S1. Descriptors' correlation matrix.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
|  |  | 0.978 | 0.002 | 0.157 | 0.131 |
| 0.978 |  | 0 | 0.124 | 0.088 |
| 0.002 | 0 |  | 0.002 | 0.033 |
| 0.157 | 0.124 | 0.002 |  | 0.035 |
| 0.131 | 0.088 | 0.033 | 0.035 |  |

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Figure S1. Validation of the molecular docking calculation in COX-2. The experimental binding mode of celecoxib was reproduced with a Root Media Square Deviation (RMSD) of 0.52. Legend: experimental binding mode is presented as red colored and the calculated pose in red. The blue dashed lines are the calculated hydrogen bonds which corresponded well with those observed in experimental binding.

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Figure S2. Validation of the molecular docking calculation in COX-1. The experimental binding mode of celecoxib was reproduced with a Root Media Square Deviation (RMSD) of 076. Legend is the same as Figure S1.

Table S2. Interactions energies (kcal/mol) of *proposed inhibitor* **52** with COX-1 residues.

|  |  |
| --- | --- |
| *Residues* | 52 |
| Ala527 | -12.91 |
| Arg120 | --- |
| Arg513 | -4.23 |
| Glu524 | --- |
| His90 | -6.57 |
| Leu531 | -0.63 |
| Ser530 | -6.95 |
| Tyr355 | -5.51 |
| Val349 | -12.61 |
| Val523 | -10.96 |

Table S3. Interactions energies (kcal/mol) of *proposed inhibitor* **52** with COX-2 residues.

|  |  |
| --- | --- |
| *Residues* | 52 |
| Ala527 | -14.76 |
| Arg120 | -0.51 |
| Glu524 | --- |
| Ile523 | -15.36 |
| Leu531 | -0.50 |
| Ser530 | -5.97 |
| Tyr355 | -7.31 |
| Val349 | -7.33 |

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Figure S3. Binding mode of **52** into COX-2. Hydrogen bonds are depicted as blue dashed lines. Legend: residues are colored according to their hydropathy index value; red represent hydrophilic residues, blue hydrophobic and purple amphiphilic.

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Figure S4. Binding mode of **52** into COX-1. Hydrogen bonds are depicted as blue dashed lines. Legend is the same as Figure S3.