Table S1: Preliminary filtering of the newly constructed compounds from DHODH inhibitor fragments

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **NAME** | **DOCKING SCORE** | **Binding free energy** | **ROF** | **PAIN**  | **BRENK**  | **GI** | **P-gp substrate** | **Veber**  | **Solubility****(Log S)** |
| YME001 | -10.741 | 3.792445 | 1 | 0 | 0 | Low | Yes | Yes  | Poorly soluble |
| YME002 | -10.740 | -40.1677 | 1 | 0 | 0 | High  | No | Yes | Moderately soluble |
| YME003 | -9.672 | -35.9761  | 1 | 0 | 0 | High | No | Yes | Soluble |
| YME004 | -9.450 | -31.8628 | 0 | 0 | 0 | High  | Yes | Yes | soluble |
| YME005 | -9.102 | 16.2404 | 1 | 0 | 0 | Low | No | Yes | Soluble |
| YME006 | -8.041 | -33.338 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME007 | -7.906 | -33.6053 | 0 | 0 | 1 | High | No | Yes | Soluble |
| YME008 | -7.822 | -33.9985 | 1 | 0 | 0 | Low | No | Yes | Moderately soluble |
| YME009 | -7.8 | -10.9535 | 0 | 0 | 0 | High | Yes | Yes | Soluble |
| YME010 | -7.78 | -30.5685 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME011 | -7.67 | -35.9723 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME012 | -7.516 | -42.2654 | 1 | 0 | 0 | Low | Yes | Yes  | Poorly soluble |
| YME013 | -7.516 | -20.3283  | 0 | 0 | 0 | High | No | Yes | Moderately soluble |
| YME014 | -7.496 | -32.2986 | 0 | 0 | 1 | Low | No | Yes | Poorly soluble |
| YME015 | -7.489 | -22.986 | 0 | 0 | 1 | Low | Yes  | Yes  | Moderately soluble  |
| YME016 | -7.391 | -34.2975 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME017 | -7.337 | 43.0481 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME018 | -7.217 | -35.7727 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME019 | -7.163 | 19.5816 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME020 | -7.162 | 33.4639 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME021 | -7.111 | -6.70221 | 1 | 0 | 0 | Low | yes | Yes | Poorly soluble |
| YME022 | -7.067 | -26.5476 | 1 | 0 | 0 | Low | Yes  | Yes | Poorly soluble |
| YME023 | -7.059 | -24.2252 | 0 | 0 | 0 | High | Yes | Yes | Soluble |
| YME024 | -7.056 | -35.2961 | 0 | 0 | 0 | High | Yes | Yes | Soluble |
| YME025 | -7.016 | -39.7786  | 0 | 1 | 0 | Low | No | Yes | Poorly soluble |
| YME026 | -6.993 | -33.9426 | 0 | 0 | 0 | High | No | Yes | Moderately soluble |
| YME027 | -6.958 | -41.578 | 0 | 0 | 1 | Low | Yes | Yes | Poorly soluble |
| YME028 | -6.826 | -47.9494 | O | O | O | High | No | Yes | Soluble |
| YME029 | -6.784 | -37.1278 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME030 | -6.762 | -31.2595 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME031 | -6.677 | -45.2476 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME032 | -6.653 | -29.3835 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME033 | -6.631 | -40.3198 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME034 | -6.615 | -34.716 | 0 | 0 | 1 | Low | No | Yes | Moderately soluble  |
| YME035 | -6.599 | -29.6908 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME036 | -6.584 | -30.9336 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME037 | -6.576 | -33.7349 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME038 | -6.542 | -24.5747 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME039 | -6.532 | -40.0985 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME040 | -6.53 | -29.789 | 0 | 0 | 1 | High | No | Yes | Soluble |
| YME041 | -6.507 | -34.3 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME042 | -6.503 | -29.3565 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME043 | -6.49 | -28.3708 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME044 | -6.487 | -37.6199 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME045 | -6.318 | -33.5026 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME046 | -6.312 | -33.3739 | 0 | 0 | 1 | Low | Yes  | Yes | Poorly soluble |
| YME047 | -6.258 | -32.9498 | 0 | 0 | 0 | High | No | Yes | Poory soluble |
| YME048 | -6.092 | -34.8115 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME049 | -6.013 | -30.9511 | 0 | 0 | 0 | High | No | Yes | Soluble |
| YME060 | -6 | -33.2206 | 0 | 0 | 0 | High | No | Yes | Soluble |

**Table S2:** Post-docking and docking analysis of the experimental inhibitors

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Name  | Docking score | Interacting residues | Binding free energy | PAINS | BLENK | ROF | GI  |
| DSM330 | -7.556 | No intermolecular interaction | -35.97 | 0 | 0 | 0 | High |
| DSM74 | -7.459 | No intermolecular interaction | -38.92 | 0 | 0 | 0 | High |
| DSM190 | -7.138 | No intermolecular interaction | -29.48 | 0 | 0 | 0 | High |
| DSM331 | -7.109 | No intermolecular interaction | -28.39 | 0 | 0 | 1 | Low |
| DSM338 | -7.090 | No intermolecular interaction | -26.55 | 0 | 0 | 1 | Low |
| DSM267 | -7.005 | No intermolecular interaction | -34.00 | 0 | 0 | 1 | Low |
| DSM265 | -6.491 | No intermolecular interaction | -23.82 | 0 | 0 | 0 | Low |
| P218 | -6.444 | ARG265 | -48.88 | 0 | 0 | 0 | High |

Table S3: Quantitative parameters used for generating QSAR model

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **S/n** | **Molecule ChEMBL ID** | **Y(Obs)** | **Y(Pred)**  | **residual error** | **set**  |
| 1 | CHEMBL219856 | 4.4 | 4.6954 | 0.2954 | train |
| 2 | CHEMBL218703 | 6.36 | 6.0796 | -0.2805 | train |
| 3 | CHEMBL1784712 | 5.77 | 6.0491 | 0.2791 | test |
| 4 | CHEMBL2172233 | 6.36 | 6.7712 | 0.4112 | train |
| 5 | CHEMBL2012826 | 4.54 | 5.5647 | 1.0247 | train |
| 6 | CHEMBL2012945 | 7.25 | 6.6067 | -0.6433 | train |
| 7 | CHEMBL1956298 | 5.6 | 5.6343 | 0.0343 | test |
| 8 | CHEMBL1956273 | 6.26 | 6.7346 | 0.4746 | train |
| 9 | CHEMBL475814 | 7.25 | 7.0137 | -0.2363 | test |
| 10 | CHEMBL2431503 | 6.43 | 6.628 | 0.198 | test |
| 11 | CHEMBL1956285 | 8 | 7.8717 | 0.3915 | train |
| 12 | CHEMBL1956285 | 7.48 | 7.8715 | 0.3915 | train |
| 13 | CHEMBL2431480 | 5.63 | 5.6949 | 0.0649 | train |
| 14 | CHEMBL2431497 | 6.16 | 6.4722 | 0.3122 | test |
| 15 | CHEMBL2012960 | 7.5 | 6.7912 | -0.7088 | test |
| 16 | CHEMBL2012961 | 7.77 | 6.4862 | -1.2838 | test |
| 17 | CHEMBL2012966 | 7.21 | 6.4033 | -0.8067 | train |
| 18 | CHEMBL2012830 | 6.95 | 6.1863 | -0.7637 | test |
| 19 | CHEMBL1956466 | 7.05 | 6.6386 | -0.4114 | train |
| 20 | CHEMBL1956473 | 7.24 | 6.0724 | -1.1676 | test |
| 21 | CHEMBL1784564 | 5.96 | 6.8203 | 0.8603 | train |
| 22 | CHEMBL1784555 | 6 | 5.7177 | -0.2823 | train |
| 23 | CHEMBL1784717 | 5.85 | 6.5501 | 0.7001 | train |
| 24 | CHEMBL1784589 | 6.3 | 6.6605 | 0.3605 | train |
| 25 | CHEMBL2431518 | 6.41 | 6.902 | 0.492 | train |
| 26 | CHEMBL2431500 | 7.19 | 6.4476 | -0.7424 | test |
| 27 | CHEMBL3218518 | 5.16 | 4.9493 | -0.2107 | test |
| 28 | CHEMBL1784581 | 4.68 | 5.8346 | 1.1546 | train |
| 29 | CHEMBL2431511 | 6.27 | 6.4814 | 0.2114 | train |
| 30 | CHEMBL2431488 | 7.48 | 6.7172 | -0.7628 | train |
| 31 | CHEMBL2234186 | 7 | 6.3507 | -0.6493 | train |
| 32 | CHEMBL3690145 | 5.95 | 6.1027 | 0.1527 | train |
| 33 | CHEMBL1956269 | 7 | 6.71 | -0.29 | train |
| 34 | CHEMBL475813 | 7.19 | 6.9032 | -0.2868 | train |
| 35 | CHEMBL3218528 | 4.33 | 3.756 | -0.574 | train |
| 36 | CHEMBL3694246 | 6.75 | 6.3761 | -0.3739 | train |
| 37 | CHEMBL1956303 | 7.52 | 6.6156 | -0.9044 | train |
| 38 | CHEMBL2172236 | 6.82 | 6.4995 | -0.3205 | train |
| 39 | CHEMBL3690134 | 6.49 | 6.0402 | -0.4498 | train |
| 40 | CHEMBL4457827 | 4.72 | 5.4041 | 0.6841 | train |
| 41 | CHEMBL1784595 | 6.17 | 6.6503 | 0.4803 | train |
| 42 | CHEMBL1784569 | 5.46 | 5.9262 | 0.4662 | test |
| 43 | CHEMBL2012958 | 7.4 | 6.7233 | -0.6767 | train |
| 44 | CHEMBL2431487 | 5.44 | 5.9837 | 0.5437 | train |
| 45 | CHEMBL582694 | 6.09 | 6.3416 | 0.2516 | train |
| 46 | CHEMBL1956497 | 5.28 | 5.5418 | 0.2618 | train |
| 47 | CHEMBL1956278 | 6.85 | 6.4258 | -0.4242 | train |
| 48 | CHEMBL1956287 | 7.52 | 7.014 | -0.506 | train |
| 49 | CHEMBL3694248 | 4.55 | 6.0891 | 1.5391 | train |
| 50 | CHEMBL3218524 | 4.85 | 4.5191 | -0.3309 | train |
| 51 | CHEMBL3218516 | 4.99 | 5.1837 | 0.1937 | train |
| 52 | CHEMBL3218520 | 5 | 5.2666 | 0.2666 | train |
| 53 | CHEMBL3218522 | 4.84 | 4.8113 | -0.0287 | train |
| 54 | CHEMBL2431514 | 6.46 | 6.6535 | 0.1935 | train |
| 55 | CHEMBL2177856 | 5.72 | 5.5917 | -0.1283 | train |
| 56 | CHEMBL2431499 | 7.75 | 6.7342 | -1.0158 | train |
| 57 | CHEMBL3218515 | 4.36 | 4.8665 | 0.5065 | train |
| 58 | CHEMBL1956264 | 7.06 | 6.4504 | -0.6096 | train |
| 59 | CHEMBL973 | 5.41 | 5.6856 | 0.2756 | train |
| 60 | CHEMBL3694253 | 7.16 | 6.8443 | -0.3157 | train |
| 61 | CHEMBL2234182 | 7 | 6.8705 | -0.1295 | test |
| 62 | CHEMBL2012942 | 5.25 | 6.0169 | 0.7669 | train |
| 63 | CHEMBL2012943 | 7.41 | 6.6619 | -0.7481 | train |
| 64 | CHEMBL4517934 | 4.92 | 4.8627 | -0.0573 | test |
| 65 | CHEMBL4436588 | 4.46 | 4.9637 | 0.5037 | test |
| 66 | CHEMBL586157 | 6.66 | 6.5532 | -0.1068 | train |
| 67 | CHEMBL2012829 | 7 | 6.579 | -0.421 | train |
| 68 | CHEMBL3690128 | 6.3 | 6.4116 | 0.1116 | test |
| 69 | CHEMBL2012824 | 7.25 | 6.2618 | -0.9882 | train |
| 70 | CHEMBL2012944 | 7.25 | 6.9791 | -0.2709 | train |
| 71 | CHEMBL2234190 | 6.52 | 6.6404 | 0.1204 | test |
| 72 | CHEMBL199572 | 4.37 | 5.7232 | 1.3532 | train |
| 73 | CHEMBL2178514 | 4.58 | 5.4536 | 0.8736 | test |
| 74 | CHEMBL4451149 | 4.64 | 5.3181 | 0.6781 | train |
| 75 | CHEMBL4458056 | 5.55 | 5.6959 | 0.1459 | train |
| 76 | CHEMBL2012956 | 7.4 | 6.9791 | -0.4209 | test |
| 77 | CHEMBL2234187 | 6.82 | 6.3507 | -0.4693 | train |
| 78 | CHEMBL1956291 | 7.52 | 6.9898 | -0.5302 | train |