**Supplementary Material**

**An approach to identify new antihypertensive agents using Thermolysin as model: *in silico* study based on QSARINS and Docking.**

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**Table S1**. Predictions and residuals obtained with the best model for the entire dataset as well as their leverage values.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Comp.** | **Status** | **Exp.**  **endpoint** | **Pred. by**  **model eq.** | **Pred.Mod.**  **Eq.Res.** | **HAT i/i**  **(h\*=0.1353)** | **Std.Pred.Mod.**  **Eq. Res.** | **Reference** |
| 1 | Training | 4.390 | 5.119 | 0.729 | 0.071 | 0.615 | ([Kim, Glekas et al. 2002](#_ENREF_28)) |
| 2 | Prediction | 4.400 | 2.317 | -2.083 | 0.028 | -1.718 | ([Juers, Kim et al. 2005](#_ENREF_25)) |
| 3 | Training | 2.890 | 2.449 | -0.441 | 0.089 | -0.376 | ([Gettins 1988](#_ENREF_15)) |
| 4 | Training | -0.280 | 1.809 | 2.089 | 0.053 | 1.746 | ([Lee and Kim 1998](#_ENREF_33)) |
| 5 | Prediction | 0.110 | 1.676 | 1.566 | 0.062 | 1.315 | ([Lee and Kim 1998](#_ENREF_33)) |
| 6 | Prediction | 0.610 | 3.238 | 2.628 | 0.071 | 2.217 | ([Lee and Kim 1998](#_ENREF_33)) |
| 7 | Training | 1.090 | 2.520 | 1.430 | 0.051 | 1.194 | ([Lee and Kim 1998](#_ENREF_33)) |
| 8 | Training | 1.400 | 2.493 | 1.093 | 0.040 | 0.908 | ([Lee and Kim 1998](#_ENREF_33)) |
| 9 | Prediction | 1.270 | 3.072 | 1.802 | 0.050 | 1.504 | ([Lee and Kim 1998](#_ENREF_33)) |
| 10 | Training | 0.470 | -0.443 | -0.913 | 0.021 | -0.750 | ([Lee and Kim 1998](#_ENREF_33)) |
| 11 | Training | 1.470 | 1.732 | 0.262 | 0.039 | 0.217 | ([Lee and Kim 1998](#_ENREF_33)) |
| 12 | Prediction | 2.740 | 2.901 | 0.161 | 0.106 | 0.139 | ([Beaumont, O’Donohues et al. 1995](#_ENREF_5)) |
| 13 | Training | 2.520 | 3.099 | 0.579 | 0.122 | 0.503 | ([Beaumont, O’Donohues et al. 1995](#_ENREF_5)) |
| 14 | Training | 4.220 | 3.492 | -0.728 | 0.025 | -0.599 | ([Beaumont, O’Donohues et al. 1995](#_ENREF_5)) |
| 15 | Training | 2.450 | 1.342 | -1.108 | 0.036 | -0.917 | ([Beaumont, O’Donohues et al. 1995](#_ENREF_5)) |
| 16 | Prediction | 3.720 | 3.265 | -0.455 | 0.044 | -0.379 | ([Beaumont, O’Donohues et al. 1995](#_ENREF_5)) |
| 17 | Training | 2.660 | 0.824 | -1.836 | 0.035 | -1.520 | ([Beaumont, O’Donohues et al. 1995](#_ENREF_5)) |
| 18 | Training | 4.200 | 3.457 | -0.743 | 0.064 | -0.625 | ([Suda, Aoyagi et al. 1973](#_ENREF_46)) |
| 19 | Training | 3.120 | 2.426 | -0.694 | 0.031 | -0.573 | ([Monzingo and BW 1982](#_ENREF_36)) |
| 20 | Prediction | 5.000 | 3.016 | -1.985 | 0.042 | -1.649 | ([Kim, Glekas et al. 2002](#_ENREF_28)) |
| 21 | Training | 5.040 | 2.930 | -2.110 | 0.027 | -1.740 | ([Holden, Tronrud et al. 1987](#_ENREF_21)) |
| 22 | Training | 2.050 | 0.628 | -1.422 | 0.030 | -1.174 | ([Kim and Sieburth 2004](#_ENREF_29)) |
| 23 | Training | 3.250 | 1.861 | -1.389 | 0.032 | -1.148 | ( [Monzingo and Matthews 1984](#_ENREF_37)) |
| 24 | Training | 2.660 | 2.647 | -0.013 | 0.055 | -0.011 | ([Holland, Barclay et al. 1994](#_ENREF_22)) |
| 25 | Prediction | 3.420 | 3.385 | -0.035 | 0.067 | -0.030 | ([Holland, Barclay et al. 1994](#_ENREF_22)) |
| 26 | Training | -0.580 | -1.331 | -0.751 | 0.033 | -0.621 | ([Bolognesi and Matthews 1979](#_ENREF_9)) |
| 27 | Prediction | 3.700 | 2.360 | -1.340 | 0.035 | -1.109 | ([Gaucher, Selkti et al. 1999](#_ENREF_14)) |
| 28 | Training | 2.920 | 2.881 | -0.039 | 0.061 | -0.033 | ([Gaucher, Selkti et al. 1999](#_ENREF_14)) |
| 29 | Prediction | 4.380 | 2.381 | -1.999 | 0.090 | -1.704 | ([Gaucher, Selkti et al. 1999](#_ENREF_14)) |
| 30 | Training | 4.320 | 2.532 | -1.788 | 0.021 | -1.470 | ([Gaucher, Selkti et al. 1999](#_ENREF_14)) |
| 31 | Training | 4.720 | 2.228 | -2.492 | 0.032 | -2.060 | ([Gaucher, Selkti et al. 1999](#_ENREF_14)) |
| 32 | Prediction | 3.000 | 1.487 | -1.513 | 0.025 | -1.246 | ([Gaucher, Selkti et al. 1999](#_ENREF_14)) |
| 33 | Training | 2.800 | 2.346 | -0.454 | 0.056 | -0.380 | ([Gaucher, Selkti et al. 1999](#_ENREF_14)) |
| 34 | Training | 3.460 | 3.412 | -0.048 | 0.192 | -0.044 | ([Gaucher, Selkti et al. 1999](#_ENREF_14)) |
| 35 | Prediction | 5.110 | 4.510 | -0.600 | 0.085 | -0.510 | ([Bartlett, Yusuff et al. 2002](#_ENREF_4)) |
| 36 | Training | 3.820 | 4.252 | 0.432 | 0.054 | 0.361 | ([Bartlett, Yusuff et al. 2002](#_ENREF_4)) |
| 37 | Training | 2.820 | 4.321 | 1.501 | 0.080 | 1.272 | ([Bartlett, Yusuff et al. 2002](#_ENREF_4)) |
| 38 | Prediction | 0.490 | 1.815 | 1.325 | 0.053 | 1.108 | ([Bartlett and Otake 1995](#_ENREF_3)) |
| 39 | Training | 0.730 | 1.913 | 1.183 | 0.031 | 0.977 | ([Bartlett and Otake 1995](#_ENREF_3)) |
| 40 | Prediction | -0.170 | 0.430 | 0.600 | 0.026 | 0.495 | ([Bartlett and Otake 1995](#_ENREF_3)) |
| 41 | Training | -0.260 | 0.688 | 0.948 | 0.033 | 0.784 | ([Bartlett and Otake 1995](#_ENREF_3)) |
| 42 | Training | 3.050 | 2.206 | -0.844 | 0.034 | -0.698 | ([Gonnella, Bohacek et al. 1995](#_ENREF_16)) |
| 43 | Training | 7.170 | 2.786 | -4.384 | 0.027 | -3.615 | ([Breiman and Friedman 1985](#_ENREF_10)) |
| 44 | Training | -2.630 | -2.388 | 0.242 | 0.112 | 0.209 | ([Muta and Inouye 2002](#_ENREF_38)) |
| 45 | Prediction | -2.000 | -1.845 | 0.156 | 0.100 | 0.133 | ([Muta and Inouye 2002](#_ENREF_38)) |
| 46 | Training | -1.580 | -0.526 | 1.054 | 0.047 | 0.878 | ([Muta and Inouye 2002](#_ENREF_38)) |
| 47 | Training | -1.810 | -1.703 | 0.107 | 0.097 | 0.091 | ([Muta and Inouye 2002](#_ENREF_38)) |
| 48 | Training | -1.700 | -0.940 | 0.760 | 0.034 | 0.629 | ([Muta and Inouye 2002](#_ENREF_38)) |
| 49 | Training | -1.600 | 0.021 | 1.621 | 0.037 | 1.343 | ([Muta and Inouye 2002](#_ENREF_38)) |
| 50 | Prediction | -1.610 | -0.504 | 1.107 | 0.042 | 0.919 | ([Muta and Inouye 2002](#_ENREF_38)) |
| 51 | Training | -2.280 | -1.673 | 0.607 | 0.100 | 0.520 | ([Muta and Inouye 2002](#_ENREF_38)) |

**Table S1**. *Cont.*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Comp.** | **Status** | **Exp.**  **endpoint** | **Pred. by**  **model eq.** | **Pred.Mod.**  **Eq.Res.** | **HAT i/i**  **(h\*=0.1353)** | **Std.Pred.Mod.**  **Eq. Res.** | **Reference** |
| 52 | Training | -1.540 | -1.078 | 0.462 | 0.032 | 0.382 | ([Muta and Inouye 2002](#_ENREF_38)) |
| 53 | Training | -2.040 | -0.483 | 1.557 | 0.038 | 1.291 | ([Muta and Inouye 2002](#_ENREF_38)) |
| 54 | Training | 4.300 | 3.848 | -0.452 | 0.064 | -0.380 | ([Grobelny, Poncz et al. 1992](#_ENREF_18)) |
| 55 | Training | 4.700 | 3.765 | -0.935 | 0.047 | -0.779 | ([Grobelny, Poncz et al. 1992](#_ENREF_18)) |
| 56 | Training | 5.150 | 4.776 | -0.374 | 0.070 | -0.315 | ([Grobelny, Poncz et al. 1992](#_ENREF_18)) |
| 57 | Prediction | 1.800 | 1.276 | -0.524 | 0.046 | -0.436 | ([Grobelny, Poncz et al. 1992](#_ENREF_18)) |
| 58 | Training | 0.300 | 1.932 | 1.632 | 0.053 | 1.364 | ([Grobelny, Poncz et al. 1992](#_ENREF_18)) |
| 59 | Training | 1.520 | 1.750 | 0.230 | 0.031 | 0.190 | ([Grobelny, Poncz et al. 1992](#_ENREF_18)) |
| 60 | Training | 2.520 | 2.123 | -0.397 | 0.034 | -0.329 | ([Grobelny, Poncz et al. 1992](#_ENREF_18)) |
| 61 | Training | 1.280 | 0.894 | -0.386 | 0.052 | -0.323 | ([Park and Kim 2003](#_ENREF_41)) |
| 62 | Prediction | 1.830 | 1.477 | -0.353 | 0.043 | -0.293 | ([Park and Kim 2003](#_ENREF_41)) |
| 63 | Training | 2.600 | 2.342 | -0.258 | 0.062 | -0.216 | ([Park and Kim 2003](#_ENREF_41)) |
| 64 | Training | 0.420 | 1.805 | 1.385 | 0.060 | 1.162 | ([Park and Kim 2003](#_ENREF_41)) |
| 65 | Training | 2.740 | 3.529 | 0.789 | 0.048 | 0.658 | ([Park and Kim 2003](#_ENREF_41)) |
| 66 | Training | 4.780 | 3.066 | -1.715 | 0.026 | -1.413 | ([Bartlett and Marlowe 1987](#_ENREF_2)) |
| 67 | Prediction | 1.890 | 1.680 | -0.210 | 0.024 | -0.173 | ([Bartlett and Marlowe 1987](#_ENREF_2)) |
| 68 | Training | 2.740 | 2.319 | -0.421 | 0.019 | -0.346 | ([Bartlett and Marlowe 1987](#_ENREF_2)) |
| 69 | Training | 3.170 | 2.507 | -0.664 | 0.029 | -0.548 | ([Bartlett and Marlowe 1987](#_ENREF_2)) |
| 70 | Training | 4.350 | 1.909 | -2.441 | 0.037 | -2.022 | ([Bartlett and Marlowe 1987](#_ENREF_2)) |
| 71 | Training | 0.720 | 0.864 | 0.144 | 0.042 | 0.119 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 72 | Training | 2.000 | 0.211 | -1.789 | 0.043 | -1.487 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 73 | Training | -1.320 | -0.687 | 0.634 | 0.027 | 0.522 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 74 | Prediction | 1.890 | 1.065 | -0.826 | 0.042 | -0.686 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 75 | Training | -0.350 | 1.577 | 1.927 | 0.051 | 1.609 | ([Nishino and Powers 1978](#_ENREF_39); ) |
| 76 | Training | 2.570 | 1.259 | -1.311 | 0.037 | -1.086 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 77 | Prediction | 0.030 | -0.093 | -0.123 | 0.057 | -0.103 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 78 | Training | 1.410 | 1.976 | 0.566 | 0.047 | 0.472 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 79 | Training | 1.700 | 1.331 | -0.369 | 0.035 | -0.305 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 80 | Training | 3.180 | 2.291 | -0.889 | 0.036 | -0.737 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 81 | Training | 3.370 | 2.407 | -0.964 | 0.046 | -0.802 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 82 | Prediction | -0.830 | -0.771 | 0.059 | 0.017 | 0.049 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 83 | Training | 0.420 | -1.031 | -1.451 | 0.020 | -1.192 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 84 | Training | -0.040 | -0.880 | -0.840 | 0.018 | -0.690 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 85 | Training | -0.810 | 0.301 | 1.111 | 0.024 | 0.915 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 86 | Prediction | -0.900 | 0.187 | 1.087 | 0.018 | 0.892 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 87 | Prediction | -1.190 | -1.321 | -0.131 | 0.028 | -0.108 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 88 | Training | -0.700 | -1.324 | -0.624 | 0.028 | -0.515 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 89 | Training | 0.080 | -0.987 | -1.067 | 0.062 | -0.896 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 90 | Training | -0.330 | 0.419 | 0.749 | 0.018 | 0.615 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 91 | Training | -1.270 | 0.298 | 1.568 | 0.015 | 1.285 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 92 | Training | -1.070 | -0.693 | 0.377 | 0.028 | 0.311 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 93 | Training | -2.400 | -0.928 | 1.472 | 0.048 | 1.227 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 94 | Training | -1.070 | -1.237 | -0.167 | 0.038 | -0.138 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 95 | Prediction | -1.740 | 0.387 | 2.127 | 0.024 | 1.750 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 96 | Prediction | -1.900 | -0.493 | 1.408 | 0.016 | 1.154 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 97 | Prediction | -1.590 | -0.925 | 0.665 | 0.020 | 0.546 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 98 | Training | -0.880 | -1.777 | -0.897 | 0.046 | -0.747 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 99 | Training | -1.280 | -0.449 | 0.831 | 0.055 | 0.695 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 100 | Training | -0.680 | 0.105 | 0.785 | 0.082 | 0.666 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 101 | Training | -0.200 | 0.186 | 0.386 | 0.019 | 0.317 | ([Kester and Matthews 1977](#_ENREF_27)) |
| 102 | Training | -1.590 | 0.690 | 2.280 | 0.025 | 1.877 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 103 | Training | -2.150 | -1.216 | 0.934 | 0.034 | 0.773 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |

**Table S1**. *Cont.*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Comp.** | **Status** | **Exp.**  **endpoint** | **Pred. by**  **model eq.** | **Pred.Mod.**  **Eq.Res.** | **HAT i/i**  **(h\*=0.1353)** | **Std.Pred.Mod.**  **Eq. Res.** | **Reference** |
| 104 | Prediction | -1.440 | -0.404 | 1.036 | 0.018 | 0.850 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 105 | Training | -1.040 | -1.215 | -0.175 | 0.028 | -0.144 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 106 | Training | -1.170 | -1.129 | 0.041 | 0.060 | 0.034 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 107 | Training | -0.600 | -0.453 | 0.148 | 0.016 | 0.121 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 108 | Training | 0.460 | -0.001 | -0.461 | 0.030 | -0.380 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 109 | Training | -1.680 | -2.210 | -0.530 | 0.050 | -0.443 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 110 | Training | -1.060 | -1.535 | -0.475 | 0.057 | -0.398 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 111 | Training | -1.720 | -1.487 | 0.233 | 0.055 | 0.195 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 112 | Training | -1.370 | -1.260 | 0.111 | 0.031 | 0.091 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 113 | Prediction | -0.920 | 0.011 | 0.931 | 0.030 | 0.769 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 114 | Training | -1.010 | -1.934 | -0.924 | 0.032 | -0.764 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 115 | Training | -0.750 | -0.639 | 0.111 | 0.017 | 0.091 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 116 | Training | -0.490 | -1.440 | -0.950 | 0.027 | -0.783 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 117 | Training | -0.650 | -0.200 | 0.450 | 0.034 | 0.372 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 118 | Prediction | -0.840 | -0.487 | 0.353 | 0.054 | 0.295 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 119 | Training | 0.660 | -0.014 | -0.674 | 0.028 | -0.556 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 120 | Prediction | 3.030 | 2.824 | -0.206 | 0.038 | -0.171 | ([Selkti, Tomas et al. 2003](#_ENREF_44)) |
| 121 | Training | 3.110 | 2.130 | -0.980 | 0.020 | -0.805 | ([Selkti, Tomas et al. 2003](#_ENREF_44)) |
| 122 | Training | 4.530 | 2.566 | -1.964 | 0.058 | -1.646 | ([Selkti, Tomas et al. 2003](#_ENREF_44)) |
| 123 | Training | 2.040 | 2.749 | 0.709 | 0.041 | 0.589 | ([SHEN and WENDOLOSKI 1995](#_ENREF_45)) |
| 124 | Training | 4.970 | 4.688 | -0.282 | 0.046 | -0.235 | ([SHEN and WENDOLOSKI 1995](#_ENREF_45)) |
| 125 | Training | 3.570 | 2.567 | -1.003 | 0.034 | -0.830 | ([SHEN and WENDOLOSKI 1995](#_ENREF_45)) |
| 126 | Training | 0.640 | 1.535 | 0.895 | 0.030 | 0.739 | ([SHEN and WENDOLOSKI 1995](#_ENREF_45)) |
| 127 | Prediction | 3.120 | 2.521 | -0.599 | 0.042 | -0.498 | ([SHEN and WENDOLOSKI 1995](#_ENREF_45)) |
| 128 | Training | 0.180 | 0.860 | 0.680 | 0.017 | 0.558 | ([SHEN and WENDOLOSKI 1995](#_ENREF_45)) |
| 129 | Training | 4.110 | 3.037 | -1.073 | 0.028 | -0.885 | ([SHEN and WENDOLOSKI 1995](#_ENREF_45)) |
| 130 | Training | 1.280 | 1.362 | 0.082 | 0.042 | 0.068 | ([SHEN and WENDOLOSKI 1995](#_ENREF_45)) |
| 131 | Prediction | 1.820 | 1.373 | -0.447 | 0.077 | -0.378 | ([Mock and Aksamawati 1994](#_ENREF_35)) |
| 132 | Training | 1.590 | 2.287 | 0.697 | 0.021 | 0.573 | ([Mock and Aksamawati 1994](#_ENREF_35)) |
| 133 | Training | 1.000 | 4.116 | 3.116 | 0.090 | 2.655 | ([Mock and Aksamawati 1994](#_ENREF_35)) |
| 134 | Training | 2.000 | 0.146 | -1.855 | 0.135 | -1.621 | ([Pfuetzner and Chan 1993](#_ENREF_42)) |
| 135 | Training | 2.310 | 1.763 | -0.547 | 0.090 | -0.467 | ([Pfuetzner and Chan 1993](#_ENREF_42)) |
| 136 | Prediction | 1.850 | 0.869 | -0.981 | 0.060 | -0.823 | ([Pfuetzner and Chan 1993](#_ENREF_42)) |
| 137 | Training | 3.190 | 2.325 | -0.865 | 0.041 | -0.718 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 138 | Training | 3.320 | 1.754 | -1.566 | 0.037 | -1.297 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 139 | Training | -0.040 | 0.909 | 0.949 | 0.041 | 0.788 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 140 | Training | 2.420 | 1.753 | -0.667 | 0.054 | -0.557 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 141 | Training | -0.530 | 1.164 | 1.694 | 0.047 | 1.411 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 142 | Prediction | 3.180 | 0.133 | -3.047 | 0.024 | -2.508 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 143 | Training | 3.120 | 2.514 | -0.606 | 0.028 | -0.500 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 144 | Training | 2.590 | 1.288 | -1.302 | 0.033 | -1.077 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 145 | Training | 2.150 | 1.467 | -0.683 | 0.040 | -0.567 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 146 | Training | -0.630 | 1.171 | 1.801 | 0.028 | 1.485 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 147 | Training | -0.460 | -1.402 | -0.942 | 0.029 | -0.777 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 148 | Prediction | -0.490 | -0.617 | -0.127 | 0.024 | -0.105 | ([Nishino and Powers 1979](#_ENREF_40)) |
| 149 | Training | -2.320 | -2.920 | -0.600 | 0.052 | -0.501 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 150 | Training | 0.290 | 0.133 | -0.158 | 0.040 | -0.131 | ([Kester and Matthews 1977](#_ENREF_27)) |
| 151 | Training | -2.000 | -0.846 | 1.154 | 0.027 | 0.951 | ([Kester and Matthews 1977](#_ENREF_27)) |
| 152 | Prediction | -0.300 | 0.459 | 0.759 | 0.016 | 0.622 | ([Kester and Matthews 1977](#_ENREF_27)) |
| 153 | Training | -2.480 | -1.427 | 1.054 | 0.035 | 0.872 | ([Klopman and Bendale 1989](#_ENREF_30)) |
| 154 | Prediction | 1.140 | 2.194 | 1.054 | 0.021 | 0.866 | ([Klopman and Bendale 1989](#_ENREF_30)) |
| 155 | Training | 1.060 | -1.205 | -2.265 | 0.030 | -1.870 | ([Klopman and Bendale 1989](#_ENREF_30)) |

**Table S1**. *Cont.*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Comp.** | **Status** | **Exp.**  **endpoint** | **Pred. by**  **model eq.** | **Pred.Mod.**  **Eq.Res.** | **HAT i/i**  **(h\*=0.1353)** | **Std.Pred.Mod.**  **Eq. Res.** | **Reference** |
| 156 | Training | 3.440 | 3.218 | -0.222 | 0.076 | -0.188 | ([Klopman and Bendale 1989](#_ENREF_30)) |
| 157 | Training | 4.720 | 3.034 | -1.686 | 0.044 | -1.402 | ([Klopman and Bendale 1989](#_ENREF_30)) |
| 158 | Training | -2.480 | -1.366 | 1.114 | 0.042 | 0.926 | ([Klopman and Bendale 1989](#_ENREF_30)) |
| 159 | Training | -2.030 | -1.069 | 0.961 | 0.040 | 0.798 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 160 | Prediction | -1.200 | -0.926 | 0.274 | 0.032 | 0.227 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 161 | Training | 2.640 | 2.070 | -0.571 | 0.081 | -0.484 | ([Feder, Brougham et al. 1974](#_ENREF_12)) |
| 162 | Training | 0.600 | 2.699 | 2.099 | 0.052 | 1.754 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 163 | Training | 1.230 | 1.980 | 0.750 | 0.036 | 0.621 | ([Nishino and Powers 1978](#_ENREF_39)) |
| 164 | Prediction | 2.770 | 2.383 | -0.387 | 0.025 | -0.319 | ([Bartlett and Marlowe 1983](#_ENREF_1)) |
| 165 | Prediction | 4.820 | 3.107 | -1.713 | 0.032 | -1.416 | ([Kam, Nishino et al. 1979](#_ENREF_26)) |
| 166 | Training | -1.760 | -0.427 | 1.333 | 0.024 | 1.097 | ([McLachlan 1992](#_ENREF_34)) |
| 167 | Prediction | -1.530 | -1.510 | 0.020 | 0.026 | 0.016 | ([McLachlan 1992](#_ENREF_34)) |
| 168 | Training | -1.280 | -0.241 | 1.039 | 0.024 | 0.855 | ([McLachlan 1992](#_ENREF_34)) |
| 169 | Training | -2.210 | -1.207 | 1.003 | 0.071 | 0.846 | ([McLachlan 1992](#_ENREF_34)) |
| 170 | Training | 1.620 | 2.824 | 1.204 | 0.030 | 0.994 | ([Bartlett and Marlowe 1987](#_ENREF_2)) |
| 171 | Training | 3.320 | 3.741 | 0.421 | 0.030 | 0.348 | ([Bartlett and Marlowe 1987](#_ENREF_2)) |
| 172 | Training | 1.520 | 4.239 | 2.719 | 0.060 | 2.281 | ([Bartlett and Marlowe 1987](#_ENREF_2)) |
| 173 | Training | 1.380 | 3.573 | 2.193 | 0.040 | 1.820 | ([Bartlett and Marlowe 1987](#_ENREF_2)) |
| 174 | Training | 5.820 | 5.610 | -0.210 | 0.109 | -0.181 | ([Grobelny, Goli et al. 1989](#_ENREF_17)) |
| 175 | Training | 2.840 | 4.471 | 1.631 | 0.045 | 1.358 | ([Grobelny, Goli et al. 1989](#_ENREF_17)) |
| 176 | Prediction | 4.280 | 4.605 | 0.325 | 0.117 | 0.282 | ([Grobelny, Goli et al. 1989](#_ENREF_17)) |

**Table S2**. Compounds predicted by the model in Group 2 (2.5<pKi<3.5).

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Drug Bank\_ID** | **Pred. by model eq.** | **HAT i/i**  **(h\*=0.1353)** | **LAI** | **Drug Bank\_ID** | **red. by model eq.** | **HAT i/i**  **(h\*=0.1353)** | **LAI** |
| DB01548 | 2.88 | 0.07 | 0 | DB00950 | 3.08 | 0.07 | 0 |
| DB00178 | 2.74 | 0.05 | 0 | DB00995 | 2.50 | 0.05 | 0 |
| DB00180 | 2.60 | 0.09 | 0 | DB01015 | 3.06 | 0.10 | 0 |
| DB00185 | 3.03 | 0.05 | 0 | DB01047 | 2.64 | 0.09 | 0 |
| DB00220 | 3.48 | 0.08 | 0 | DB01049 | 3.12 | 0.11 | 0 |
| DB00222 | 3.11 | 0.06 | 0 | DB01116 | 3.47 | 0.07 | 0 |
| DB00248 | 2.99 | 0.08 | 0 | DB01120 | 3.28 | 0.04 | 0 |
| DB00263 | 2.86 | 0.09 | 0 | DB01132 | 3.43 | 0.04 | 0 |
| DB00287 | 2.82 | 0.06 | 0 | DB01244 | 3.17 | 0.06 | 0 |
| DB00288 | 3.07 | 0.08 | 0 | DB01287 | 3.14 | 0.05 | 0 |
| DB00301 | 3.49 | 0.06 | 0 | DB01340 | 2.65 | 0.05 | 0 |
| DB00320 | 3.14 | 0.05 | 0 | DB01409 | 3.46 | 0.08 | 0 |
| DB00342 | 3.23 | 0.09 | 0 | DB01622 | 3.22 | 0.04 | 0 |
| DB00374 | 2.51 | 0.12 | 0 | DB01623 | 3.38 | 0.13 | 0 |
| DB00376 | 2.70 | 0.11 | 0 | DB01624 | 2.93 | 0.08 | 0 |
| DB00409 | 2.51 | 0.05 | 0 | DB04839 | 2.75 | 0.09 | 0 |
| DB00433 | 3.47 | 0.06 | 0 | DB04930 | 2.65 | 0.05 | 0 |
| DB00485 | 3.03 | 0.05 | 0 | DB06255 | 2.74 | 0.06 | 0 |
| DB00490 | 3.13 | 0.06 | 0 | DB06267 | 2.93 | 0.03 | 0 |
| DB00519 | 2.98 | 0.06 | 0 | DB01640 | 3.00 | 0.03 | 0 |
| DB00588 | 3.00 | 0.05 | 0 | DB01658 | 3.47 | 0.07 | 0 |
| DB00596 | 2.68 | 0.09 | 0 | DB01732 | 2.90 | 0.06 | 0 |
| DB00616 | 3.04 | 0.12 | 0 | DB01800 | 3.29 | 0.13 | 0 |
| DB00663 | 2.82 | 0.09 | 0 | DB01820 | 3.09 | 0.06 | 0 |
| DB00679 | 3.45 | 0.07 | 0 | DB01871 | 2.90 | 0.05 | 0 |
| DB00713 | 3.18 | 0.04 | 0 | DB01891 | 3.32 | 0.07 | 0 |
| DB00769 | 2.91 | 0.12 | 0 | DB01899 | 2.76 | 0.06 | 0 |
| DB00771 | 2.53 | 0.05 | 0 | DB01943 | 2.86 | 0.04 | 0 |
| DB00775 | 3.27 | 0.10 | 0 | DB01963 | 2.73 | 0.06 | 0 |
| DB00810 | 2.87 | 0.10 | 0 | DB01974 | 3.16 | 0.06 | 0 |
| DB00838 | 3.21 | 0.09 | 0 | DB02046 | 2.93 | 0.03 | 0 |
| DB00846 | 3.01 | 0.13 | 0 | DB02071 | 3.10 | 0.09 | 0 |
| DB00905 | 2.58 | 0.08 | 0 | DB02128 | 3.46 | 0.06 | 0 |
| DB00906 | 2.80 | 0.05 | 0 | DB02177 | 2.89 | 0.05 | 0 |
| DB00911 | 3.07 | 0.07 | 0 | DB02255 | 3.24 | 0.05 | 0 |
| DB00912 | 2.57 | 0.06 | 0 | DB02285 | 3.20 | 0.06 | 0 |
| DB02341 | 2.73 | 0.05 | 0 | DB03890 | 2.94 | 0.06 | 0 |
| DB02347 | 3.36 | 0.06 | 0 | DB03945 | 2.53 | 0.10 | 0 |
| DB02465 | 2.73 | 0.07 | 0 | DB03949 | 3.41 | 0.03 | 0 |
| DB02468 | 3.21 | 0.06 | 0 | DB03984 | 2.52 | 0.04 | 0 |

**Table S2**. *Cont.*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Drug Bank\_ID | Pred. by model eq. | HAT i/i (h\*=0.1353) | LAI | Drug Bank\_ID | Pred. by model eq. | HAT i/i (h\*=0.1353) | LAI |
| DB02558 | 2.62 | 0.02 | 0 | DB04032 | 3.04 | 0.09 | 0 |
| DB02565 | 2.60 | 0.06 | 0 | DB04107 | 3.44 | 0.06 | 0 |
| DB02597 | 3.26 | 0.03 | 0 | DB04140 | 3.27 | 0.05 | 0 |
| DB02615 | 3.07 | 0.04 | 0 | DB04152 | 2.98 | 0.05 | 0 |
| DB02634 | 2.86 | 0.04 | 0 | DB04195 | 2.65 | 0.08 | 0 |
| DB02669 | 2.59 | 0.04 | 0 | DB04199 | 2.69 | 0.08 | 0 |
| DB02715 | 3.07 | 0.04 | 0 | DB04199 | 3.17 | 0.05 | 0 |
| DB02731 | 2.95 | 0.12 | 0 | DB04280 | 2.71 | 0.03 | 0 |
| DB02753 | 2.68 | 0.05 | 0 | DB04288 | 2.88 | 0.05 | 0 |
| DB02782 | 2.65 | 0.12 | 0 | DB04373 | 3.28 | 0.07 | 0 |
| DB02790 | 2.67 | 0.02 | 0 | DB04378 | 3.47 | 0.07 | 0 |
| DB02804 | 2.64 | 0.12 | 0 | DB04496 | 2.95 | 0.08 | 0 |
| DB02808 | 3.02 | 0.06 | 0 | DB04513 | 3.14 | 0.08 | 0 |
| DB02894 | 2.72 | 0.06 | 0 | DB04623 | 2.99 | 0.11 | 0 |
| DB02927 | 2.51 | 0.06 | 0 | DB04653 | 2.96 | 0.08 | 0 |
| DB02929 | 3.25 | 0.10 | 0 | DB04695 | 2.71 | 0.05 | 0 |
| DB02968 | 2.70 | 0.03 | 0 | DB04708 | 3.13 | 0.08 | 0 |
| DB03097 | 2.88 | 0.07 | 0 | DB04796 | 2.80 | 0.13 | 0 |
| DB03101 | 2.55 | 0.05 | 0 | DB04850 | 2.79 | 0.07 | 0 |
| DB03139 | 3.26 | 0.11 | 0 | DB04857 | 2.79 | 0.05 | 0 |
| DB03160 | 2.83 | 0.06 | 0 | DB04859 | 2.59 | 0.06 | 0 |
| DB03188 | 2.98 | 0.12 | 0 | DB04865 | 2.79 | 0.09 | 0 |
| DB03268 | 3.24 | 0.08 | 0 | DB04946 | 3.40 | 0.04 | 0 |
| DB03471 | 2.56 | 0.08 | 0 | DB05251 | 3.48 | 0.08 | 0 |
| DB03536 | 2.71 | 0.07 | 0 | DB06191 | 3.28 | 0.10 | 0 |
| DB03573 | 2.50 | 0.08 | 0 | DB06199 | 2.74 | 0.05 | 0 |
| DB03584 | 2.98 | 0.12 | 0 | DB06200 | 2.91 | 0.11 | 0 |
| DB03599 | 2.98 | 0.12 | 0 | DB06446 | 2.60 | 0.05 | 0 |
| DB03691 | 2.50 | 0.08 | 0 | DB06635 | 2.67 | 0.04 | 0 |
| DB03742 | 2.90 | 0.02 | 0 | DB03855 | 3.30 | 0.09 | 0 |
| DB03748 | 3.14 | 0.07 | 0 |  |  |  |  |

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comp 1 | | | | | Comp 2 | | | | |
| Comp 3 | | | Comp 4 | | | | Comp 5 | | |
| Comp 6 | | | Comp 7 | | | | | | Comp 8 |
| Comp 9 | | | | Comp 10 | | | | | Comp 11 |
| Comp 12 | Comp 13 | | | | | Comp 14 | | | |
| Comp 15 | | Comp 16 | | | | | | Comp 17 | |
|  | | | | | | | | | |

**Figure S1:** Molecular structure of the entire database.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Comp 18 | | | Comp 19 | |
| Comp 20 | | Comp 21 | | |
| Comp 22 | | Comp 23 | | |
| Comp 24 | | Comp 25 | | |
| Comp 26 | Comp 27 | | | Comp 28 |

**Figure S1:** *Cont…*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Comp 29 | | | Comp 30 | | | |
| Comp 31 | | Comp 32 | | | | Comp 33 |
| Comp 34 | Comp 35 | | | | Comp 36 | Comp 37 |
| Comp 38 | | | | Comp 39 | | |
|  | | | |  | | |

**Figure S1:** *Cont…*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comp 40 | | | | Comp 41 | | | | |
| Comp 42 | | | Comp 43 | | | | Comp 44 | |
| Comp 45 | |
| Comp 46 | Comp 47 | | Comp 48 | | Comp 49 | Comp 50 | | Comp 51 |
| Comp 52 | | Comp 53 | | | Comp 54 | | | |
| Comp 55 | | | | | Comp 56 | | | |
| Comp 57 | | | | | Comp 58 | | | |

**Figure S1:** *Cont…*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Comp 59 | | | | | Comp 60 | | |
| Comp 61 | Comp 62 | | | | | Comp 63 | |
| Comp 64 | |  | | Comp 65 | | | |
| Comp 66 | | | | | Comp 67 | | |
| Comp 68 | | | | | Comp 69 | | |
|  | | |  | | | |  |
|  | | |  | | | | |

**Figure S1:** *Cont…*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Comp 70 | | Comp 71 | | Comp 72 |
|  | |  | | |
| Comp 73 | | Comp 74 | | |
| Comp 75 | | Comp 76 | | |
| Comp 77 | | Comp 78 | | |
| Comp 79 | Comp 80 | | Comp 81 | |

**Figure S1:** *Cont…*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Comp 82 | | | Comp 83 | | | |
| Comp 84 | | | Comp 85 | | | |
| Comp 86 | | | Comp 87  Comp 88 | | Comp 89 | |
| Comp 90 | Comp 91 | | | Comp 92    Comp 93 | | |
| Comp 94 | | Comp 95 | | | |  |

**Figure S1:** *Cont…*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Comp 96 | | Comp 97 | | |
| Comp 98 | | Comp 99 | | |
| Comp 100 | | Comp 101    Comp 102 | | |
| Comp 103 | Comp 104 | | | Comp 105 |
| Comp 106 | | | Comp 107 | |

**Figure S1:** *Cont…*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Comp 108 | | | Comp 109 | | | | Comp 110 |
| Comp 111 | | Comp 112 | | | Comp 113 | | |
| Comp 114 | Comp 115 | | | | | Comp 116 | |
| Comp 117    Comp 119 | | | | Comp 118 | | | |
| Comp 120 | | | |

**Figure S1:** *Cont…*

|  |  |
| --- | --- |
| Comp 121 | Comp 122 |
| Comp 123 | Comp 124 |
| Comp 125 | Comp 126 |
| Comp 127 | Comp 128 |
| Comp 129 | Comp 130 |

**Figure S1:** *Cont…*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Comp 131 | | Comp 132 | | | |
| Comp 133 | | Comp 134 | Comp 135 | | Comp 136 |
| Comp 137 | Comp 138 | | | Comp 139 | |
| Comp 140 | | Comp 141 | | | |

**Figure S1:** *Cont…*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comp 142 | | | Comp 143 | | | | Comp 144 | |
| Comp 145 | | | | | Comp 146 | | | |
| Comp 147 | | | | | Comp 148 | | | |
| Comp 149 | Comp 150 | | | | | Comp 151 | | |
| Comp 152 | | Comp 153 | | Comp 154 | | | | Comp 155 |

**Figure S1:** *Cont…*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Comp 156 | | Comp 157 | | | Comp 158 | |
| Comp 159 | | Comp 160 | | Comp 161 | | |
| Comp 162 | | | Comp 163 | | | |
| Comp 164 | | | Comp 165 | | | |
| Comp 166 | Comp 167 | | Comp 168 | | | Comp 169 |
| Comp 170 | | | Comp 171 | | | |

**Figure S1:** *Cont…*

|  |  |
| --- | --- |
| Comp 172 | Comp 173 |
| Comp 174 | Comp 175 |
| Comp 176 | |

**Figure S1:** *Cont…*

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