**Table S1:** The molecular structures and their true pIC50 and predicted values of the training and testing data

|  |  |  |  |
| --- | --- | --- | --- |
| No. | Structures | True pIC50 | Rank-Bridge |
|  |
| 4 |  | 8.744 | 7.0386 |
| 59 |  | 5.667 | |  | | --- | | 6.572073 | |
| 87 |  | 6.619 | |  |  | | --- | --- | | |  | | --- | | 8.59524 | | |
| 31 |  | 8.522 | |  |  | | --- | --- | | |  | | --- | | 7.6553 | | |
| 107 |  | 7.397 | |  |  | | --- | --- | | |  | | --- | | 7.151181 | | |
| 73 |  | 7.187 | |  | | --- | | 6.562639 | |
| 75 |  | 8.221 | |  | | --- | | 7.44348 | |
| 5 |  | 5.698 | |  | | --- | | 6.664141 | |
| 89 |  | 7.958 | |  | | --- | | 7.091435 | |
| 49 |  | 9.301 | |  | | --- | | 6.572073 | |
| 90 |  | 7.000 | |  | | --- | | 7.93053 | |
| 12 |  | 6.853 | |  | | --- | | 6.855565 | |
| 44 |  | 7.154 | |  | | --- | | 7.082946 | |
| 100 |  | 6.853 | |  | | --- | | 7.170494 | |
| 27 |  | 6.744 | |  | | --- | | 7.441697 | |
| 98 |  | 5.221 | |  | | --- | | 5.355169 | |
| 26 |  | 6.568 | |  | | --- | | 6.550507 | |
| 24 |  | 6.823 | |  | | --- | | 5.590257 | |
| 101 |  | 4.657 | |  | | --- | | 7.185922 | |
| 67 |  | 6.657 | |  | | --- | | 8.046511 | |
| 11 |  | 4.602 | |  | | --- | | 6.079803 | |
| 32 |  | 7.619 | |  | | --- | | 6.644477 | |
| 68 |  | 5.508 | |  | | --- | | 5.590257 | |
| 35 |  | 9.000 | |  | | --- | | 6.587866 | |
| 83 |  | 6.756 | |  | | --- | | 9.207422 | |
| 82 |  | 7.070 | |  | | --- | | 8.84006 | |
| 106 |  | 7.070 | |  | | --- | | 5.476285 | |
| 93 |  | 5.193 | |  | | --- | | 8.837088 | |
| 7 |  | 5.657 | |  | | --- | | 7.4542 | |
| 47 |  | 8.698 | |  | | --- | | 6.685834 | |
| 96 |  | 5.494 | |  | | --- | | 5.709908 | |
| 20 |  | 8.045 | |  | | --- | | 6.68348 | |
| 36 |  | 8.397 | |  | | --- | | 7.753592 | |
| 25 |  | 5.838 | |  | | --- | | 5.63003 | |
| 56 |  | 7.795 | |  | | --- | | 5.63003 | |
| 53 |  | 7.045 | |  | | --- | | 5.698703 | |
| 15 |  | 6.667 | |  | | --- | | 7.365269 | |
| 77 |  | 7.000 | |  | | --- | | 5.94228 | |
| 38 |  | 6.920 | |  | | --- | | 7.196599 | |
| 103 |  | 5.939 | |  | | --- | | 7.977521 | |
| 74 |  | 6.744 | |  | | --- | | 7.722197 | |
| 85 |  | 7.221 | |  | | --- | | 5.1315 | |
| 40 |  | 6.207 | |  | | --- | | 5.694928 | |
| 69 |  | 5.468 | |  | | --- | | 4.16413 | |
| 29 |  | 6.677 | |  | | --- | | 8.349018 | |
| 3 |  | 6.275 | |  | | --- | | 7.451178 | |
| 10 |  | 5.823 | |  | | --- | | 6.792858 | |
| 52 |  | 8.522 | |  | | --- | | 7.242265 | |
| 50 |  | 9.301 | |  | | --- | | 8.667572 | |
| 79 |  | 6.698 | |  | | --- | | 6.304909 | |
| 34 |  | 8.522 | |  | | --- | | 7.032521 | |
| 92 |  | 6.301 | |  | | --- | | 8.582388 | |
| 33 |  | 9.000 | |  | | --- | | 6.664141 | |
| 54 |  | 5.823 | |  | | --- | | 5.648557 | |
| 63 |  | 6.744 | |  | | --- | | 5.396266 | |
| 17 |  | 8.000 | |  | | --- | | 6.562639 | |
| 16 |  | 6.698 | |  | | --- | | 7.951112 | |
| 104 |  | 6.346 | |  | | --- | | 6.267521 | |
| 41 |  | 7.920 | |  | | --- | | 6.46479 | |
| 21 |  | 8.698 | |  | | --- | | 6.307903 | |
| 22 |  | 9.301 | |  | | --- | | 7.0386 | |
| 45 |  | 7.045 | |  | | --- | | 6.68348 | |
| 46 |  | 7.000 | |  | | --- | | 7.082946 | |
| 48 |  | 8.522 | |  | | --- | | 6.587866 | |
| 84 |  | 7.920 | |  | | --- | | 7.1315 | |
| 64 |  | 6.522 | |  | | --- | | 7.465269 | |
| 6 |  | 6.647 | |  | | --- | | 6.550507 | |
| 43 |  | 9.522 | |  | | --- | | 8.197607 | |
| 9 |  | 7.000 | |  | | --- | | 4.7946209 | |
| 94 |  | 5.769 | |  | | --- | | 5.355169 | |
| 14 |  | 9.000 | |  | | --- | | 7.251896 | |
| 102 |  | 3.795 | |  | | --- | | 6.565764 | |
| 71 |  | 7.187 | |  | | --- | | 7.441697 | |
| 91 |  | 5.568 | |  | | --- | | 8.349916 | |
| 19 |  | 5.200 | |  | | --- | | 3.743679 | |
| 1T |  | 6.886 | |  | | --- | | 6.550507 | |
| 2 T |  | 7.221 | |  | | --- | | 6.027996 | |
| 8 T |  | 7.657 | |  | | --- | | 7.302796 | |
| 13 T |  | 8.337 | |  | | --- | | 8.288356 | |
| 18 T |  | 8.154 | |  | | --- | | 7.6553 | |
| 23 T |  | 6.698 | |  | | --- | | 6.667138 | |
| 28 T |  | 5.455 | |  | | --- | | 5.698703 | |
| 30 T |  | 6.221 | |  | | --- | | 8.33146 | |
| 37 T |  | 7.221 | |  | | --- | | 6.198234 | |
| 39 T |  | 6.275 | |  | | --- | | 7.951112 | |
| 42 T |  | 7.455 | |  | | --- | | 7.33146 | |
| 51 T |  | 5.638 | |  | | --- | | 7.600782 | |
| 55 T |  | 4.443 | |  | | --- | | 4.743679 | |
| 57 T |  | 5.187 | |  | | --- | | 9.259626 | |
| 58 T |  | 9.000 | |  | | --- | | 6.570956 | |
| 60 T |  | 5.4317 | |  | | --- | | 5.963939 | |
| 61 T |  | 5.698 | |  | | --- | | 6.75174 | |
| 62 T |  | 6.732 | |  | | --- | | 8.525536 | |
| 65 T |  | 5.638 | |  | | --- | | 8.197607 | |
| 66 T |  | 6.673 | |  | | --- | | 6.488956 | |
| 70 T |  | 5.468 | |  | | --- | | 6.612533 | |
| 72 T |  | 7.187 | |  | | --- | | 6.716666 | |
| 76 T |  | 7.221 | |  | | --- | | 6.777641 | |
| 78 T |  | 6.247 | |  | | --- | | 5.348098 | |
| 80 T |  | 6.698 | |  | | --- | | 5.598727 | |
| 81 T |  | 7.045 | |  | | --- | | 6.603102 | |
| 86 T |  | 6.698 | |  | | --- | | 6.48578 | |
| 88 T |  | 6.619 | |  | | --- | | 8.867225 | |
| 95 T |  | 5.397 | |  | | --- | | 5.983694 | |
| 97 T |  | 5.494 | |  | | --- | | 5.709908 | |
| 99 T |  | 4.207 | |  | | --- | | 5.637924 | |
| 105 T |  | 7.522 | |  | | --- | | 5.257801 | |
| 108 T |  | 6.397 | |  | | --- | | 6.293347 | |

T The molecule belongs to test data.

Table S2: The correlation between each of the selected descriptors using the Rank-Bridge the bioactivity (pIC50)

|  |  |
| --- | --- |
| Descriptors | pIC50 |
| GATS5m | 0.941 |
| MATS5e | 0.922 |
| RDF025e | 0.893 |
| Mor11s | 0.918 |
| P\_VSA\_MR\_2 | 0.885 |

**Table S3:** The molecular structures and their true pIC50 and predicted values of the validation dataset

|  |  |  |  |
| --- | --- | --- | --- |
| n | compound | pIC50 | Rank-Bridge |
| 1 | S(C)C=1C(OC(CC)CC)C(NC(=O)C)C(N)CC=1C(O)=O | 5.471 | 5.689 |
| 2 | O(C(CC)CC)C1C(NC(=O)C)C(N)CC(C(O)=O)=C1C | 7.162 | 7.652 |
| 3 | OC(=O)C=1CC(N)C(NC(=O)C)C(NC(=O)CC)C=1 | 5.407 | 6.1407 |
| 4 | OC(=O)C=1CC(N)C(NC(=O)C)C(NC(=O)C(C)C)C=1 | 8.207 | 8.823 |
| 5 | OC(=O)C=1CC(N)C(NC(=O)C)C(NC(=O)C(CC)CC)C=1 | 7.221 | 8.065 |
| 6 | O(C(CC)CC)C1C=C(C(O)=O)C(C)C(N)C1NC(=O)C | 6.418 | 6.952 |
| 7 | OC(=O)C1=NN(C(=O)C(CC)CC)C(NC(=O)C)C(N)C1 | 7.257 | 7.101 |
| 8 | O1c2c(c(O)c(O)c(O)c2CN2CCCC2C)C(=O)C=C1c1ccccc1 | 9.011 | 8.247 |
| 9 | O1c2c(c(O)c(O)c(O)c2CN2C(COC2C)C)C(=O)C=C1c1ccccc1 | 6.628 | 6.532 |
| 10 | O1c2c(C(=O)C=C1c1cc(O)c(O)cc1)c(O)cc(O)c2CN1CC(COC1C)C | 6.354 | 6.815 |
| 11 | O1c2c(C(=O)C=C1c1ccc(O)cc1)c(O)cc(O)c2CN1CCC(CC1)CO | 5.741 | 5.547 |
| 12 | S(=O)(=O)(NC1C(N)CC(=CC1OCCC)C(O)=O)C | 5.225 | 6.065 |
| 13 | O1C(CO)C(O)C(O)C(O)C1Oc1cc(cc(O)c1)\C=C\c1ccc(O)cc1 | 4.255 | 4.237 |
| 14 | O1c2c(C(C1c1ccc(O)cc1)c1cc(O)cc(O)c1)c(cc(O)c2)\C=C\c1ccc(O)cc1 | 8.594 | 7.194 |
| 15 | O(CC)C1C=C(CC(N)C1NOC(=O)C)C(O)=O | 6.317 | 6.602 |
| 16 | O(CCC)C1C=C(CC(N)C1NOC(=O)C)C(O)=O | 6.334 | 6.924 |
| 17 | O(CCCC)C1C=C(CC(N)C1NOC(=O)C)C(O)=O | 5.841 | 6.711 |
| 18 | O(CCCCCC)C1C=C(CC(N)C1NOC(=O)C)C(O)=O | 4.659 | 4.463 |
| 19 | O(CCCCCCC)C1C=C(CC(N)C1NOC(=O)C)C(O)=O | 4.587 | 5.103 |
| 20 | O(CCCCCCCC)C1C=C(CC(N)C1NOC(=O)C)C(O)=O | 6.351 | 6.957 |
| 21 | O(CCCCCCCCC)C1C=C(CC(N)C1NOC(=O)C)C(O)=O | 5.094 | 6.421 |
| 22 | O(CCCCCCCCCC)C1C=C(CC(N)C1NOC(=O)C)C(O)=O | 8.621 | 8.552 |
| 23 | OC(=O)C=1CC(N)C(NC(=O)C)C(N(C(CC)CC)C)C=1 | 7.361 | 7.231 |
| 24 | OC(=O)C=1CC(N)C(NC(=O)C)C(N(CCc2ccccc2)C)C=1 | 5.668 | 5.718 |
| 25 | OC(=O)C=1CC(N)C(NC(=O)C)C(N(C)C2CCCCC2)C=1 | 8.619 | 8.041 |

**Prediction evaluation criteria**

To provide a satisfactory evaluation of the compared modeling methods in constructing an efficient QSAR model, the following criteria were performed. The used criteria for the training dataset were mean-squared error of the training dataset () and leave-one-out internal validation (), which are defined by



and



respectively.

Furthermore, the test dataset was used to validate the model by computing the following criteria, i.e., mean-squared error of the test dataset () and external validation   
(). These criteria are defined by



and



respectively, where  and  represent the training and test sample sizes, the , , , and  stand for the pIC50 values of the training dataset, test dataset, and their corresponding predicted values. While  and  represent the mean of all the pIC50 values and the mean of the training pIC50 values, respectively.