**Table S1** Node information associated with CART configured by recursive partitioning for 33anti-Alzheimer agents based on subset 3

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Node | SplittingVariable | SplittingValue | Nodesize | NodeOutput | Role |
| 1 | R3u | 2.23 | 25 | 1.240 | N |
| 2 | Km | 0.428 | 16 | 1.417 | P |
| 3 | Mor15u | 0.401 | 9 | 0.924 | N |
| 4 | MATS1v | 0.000 | 8 | 1.259 | N |
| 5 | TIE | 306.451 | 8 | 1.575 | N |
| 6 | - | - | 3 | 0.651 | - |
| 7 | Ss | 129.25 | 6 | 1.060 | N |
| 8 | - | - | 1 | 0.974 | - |
| 9 | MATS4p | -0.005 | 7 | 1.300 | P |
| 10 | ZM2V | 343.111 | 6 | 1.527 | N |
| 11 | - | - | 2 | 1.721 | - |
| 12 | GNar | 2.249 | 4 | 1.116 | N |
| 13 | - | - | 2 | 0.947 | - |
| 14 | - | - | 4 | 1.261 | - |
| 15 | - | - | 3 | 1.352 | - |
| 16 | - | - | 3 | 1.564 | - |
| 17 | - | - | 3 | 1.491 | - |
| 18 | - | - | 3 | 1.085 | - |
| 19 | - | - | 1 | 1.212 | - |
| Symbol “–” represents the leaf nodes without splitting variables and values. In the last column, “N” represents the negative effect of the corresponding splitting variable on the antimicrobial activity, and vice versa, “P” refers to the positive effect of the corresponding splitting variable on the antimicrobial activity. |

**Table S2**  Symbols and definitions for the selected independent variables and descriptors involved in the CART, MLR and PCA methods

|  |  |  |
| --- | --- | --- |
| Symbols | Type | Description |
| MW | constitutional descriptors | molecular weight |
| AMW | constitutional descriptors | average molecular weight |
| Sv | constitutional descriptors | sum of atomic van der Waals volumes (scaled on Carbon atom) |
| Se | constitutional descriptors | sum of atomic Sanderson electronegativities (scaled on Carbon atom) |
| Sp | constitutional descriptors | sum of atomic polarizabilities (scaled on Carbon atom) |
| Ss | constitutional descriptors | sum of Kier-Hall electrotopological states |
| Mv | constitutional descriptors | mean atomic van der Waals volume (scaled on Carbon atom) |
| Me | constitutional descriptors | mean atomic Sanderson electronegativity (scaled on Carbon atom) |
| Mp | constitutional descriptors | mean atomic polarizability (scaled on Carbon atom) |
| Ms | constitutional descriptors | mean electrotopological state |
| nAT | constitutional descriptors | number of atoms |
| nSK | constitutional descriptors | number of non-H atoms |
| nBT | constitutional descriptors | number of bonds |
| nBO | constitutional descriptors | number of non-H bonds |
| nBM | constitutional descriptors | number of multiple bonds |
| SCBO | constitutional descriptors | sum of conventional bond orders (H-depleted) |
| nCIC | constitutional descriptors | number of rings |
| nCIR | constitutional descriptors | number of circuits |
| RBN | constitutional descriptors | number of rotatable bonds |
| RBF | constitutional descriptors | rotatable bond fraction |
| nDB | constitutional descriptors | number of double bonds |
| nAB | constitutional descriptors | number of aromatic bonds |
| nH | constitutional descriptors | number of Hydrogen atoms |
| nC | constitutional descriptors | number of Carbon atoms |
| Qnmax | charge descriptors | maximum negative charge |
| Qpos | charge descriptors | total positive charge |
| Qneg | charge descriptors | total negative charge |
| Qtot | charge descriptors | total absolute charge (electronic charge index - ECI) |
| Qmean | charge descriptors | mean absolute charge (charge polarization) |
| Q2 | charge descriptors | total squared charge |
| RPCG | charge descriptors | relative positive charge |
| RNCG | charge descriptors | relative negative charge |
| SPP | charge descriptors | subpolarity parameter |
| TE1 | charge descriptors | topographic electronic descriptor |
| TE2 | charge descriptors | topographic electronic descriptor (bond resctricted) |
| PCWTe | charge descriptors | partial charge weighted topological electronic charge |
| LDip | charge descriptors | local dipole index |
| SHP2 | Randic molecular profiles | average shape profile index of order 2 |
| W3D | geometrical descriptors | 3D-Wiener index |
| J3D | geometrical descriptors | 3D-Balaban index |
| H3D | geometrical descriptors | 3D-Harary index |
| AGDD | geometrical descriptors | average geometric distance degree |
| DDI | geometrical descriptors | D/D index |
| ADDD | geometrical descriptors | average distance/distance degree |
| G1 | geometrical descriptors | gravitational index G1 |
| G2 | geometrical descriptors | gravitational index G2 (bond-restricted) |
| RGyr | geometrical descriptors | radius of gyration (mass weighted) |
| SPAN | geometrical descriptors | span R |
| SPAM | geometrical descriptors | average span R |
| MEcc | geometrical descriptors | molecular eccentricity |
| SPH | geometrical descriptors | Spherosity |
| ASP | geometrical descriptors | Asphericity |
| FDI | geometrical descriptors | folding degree index |
| PJI3 | geometrical descriptors | 3D Petijean shape index |
| L/Bw | geometrical descriptors | length-to-breadth ratio by WHIM |
| Hy | empirical descriptors | hydrophilic factor |
| ARR | empirical descriptors | aromatic ratio |
| MR | Properties | Ghose-Crippen molar refractivity |
| PSA | Properties | fragment-based polar surface area |
| MLOGP | Properties | Moriguchioctanol-water partition coeff. (logP) |
| R3e | GETAWAY descriptors | R autocorrelation of lag 3 / weighted by atomic Sanderson electronegativities |
| Km | WHIM descriptors | K global shape index / weighted by atomic masses |
| Mor15u | 3D-MoRSE descriptors | 3D-MoRSE - signal 15 / unweighted |
| Lop | topological descriptors | Lopping centric index |
| GATS5e | 2D autocorrelations | Geary autocorrelation - lag 5 / weighted by atomic Sanderson electronegativities |
| E2m | WHIM descriptors | 2nd component accessibility directional WHIM index / weighted by atomic masses |
| Mor24e | 3D-MoRSE descriptors | 3D-MoRSE - signal 24 / weighted by atomic Sanderson electronegativities |

**Table S3**  Rotated Component Matrix for five PCs

|  |  |  |
| --- | --- | --- |
| Symbols | Component |  |
|  | PC1 | PC2 | PC3 | PC4 | PC5 |
| MW | 0.987 |  |  |  |  |
| AMW |  | -0.675 |  | 0.663 |  |
| Sv | 0.996 |  |  |  |  |
| Se | 0.993 |  |  |  |  |
| Sp | 0.995 |  |  |  |  |
| Ss | 0.975 |  |  |  |  |
| Mv |  | -0.914 |  |  |  |
| Me |  |  |  | 0.949 |  |
| Mp |  | -0.896 |  |  |  |
| Ms | -0.578 |  |  | 0.729 |  |
| nAT | 0.991 |  |  |  |  |
| nSK | 0.999 |  |  |  |  |
| nBT | 0.993 |  |  |  |  |
| nBO | 0.999 |  |  |  |  |
| nBM | 0.988 |  |  |  |  |
| SCBO | 0.997 |  |  |  |  |
| nCIC | 0.993 |  |  |  |  |
| nCIR | 0.988 |  |  |  |  |
| RBN |  | 0.765 |  |  |  |
| RBF | -0.736 | 0.52 |  |  |  |
| nDB |  |  |  |  | 0.774 |
| nAB | 0.988 |  |  |  |  |
| nH | 0.962 |  |  |  |  |
| nC | 0.986 |  |  |  |  |
| Qnmax |  |  | 0.922 |  |  |
| Qpos | 0.985 |  |  |  |  |
| Qneg | 0.985 |  |  |  |  |
| Qtot | 0.985 |  |  |  |  |
| Qmean |  | 0.78 |  |  |  |
| Q2 | 0.976 |  |  |  |  |
| RPCG | -0.957 |  |  |  |  |
| RNCG | -0.955 |  |  |  |  |
| SPP |  |  | 0.932 |  |  |
| TE1 | 0.984 |  |  |  |  |
| TE2 | 0.979 |  |  |  |  |
| PCWTe | 0.978 |  |  |  |  |
| LDip |  | 0.752 |  |  |  |
| SHP2 | -0.989 |  |  |  |  |
| W3D | 0.981 |  |  |  |  |
| J3D | -0.913 |  |  |  |  |
| H3D | 0.986 |  |  |  |  |
| AGDD | 0.987 |  |  |  |  |
| DDI | 0.984 |  |  |  |  |
| ADDD | 0.993 |  |  |  |  |
| G1 | 0.986 |  |  |  |  |
| G2 | 0.998 |  |  |  |  |
| RGyr | 0.969 |  |  |  |  |
| SPAN | 0.81 |  |  |  |  |
| SPAM | -0.96 |  |  |  |  |
| MEcc | -0.8 |  |  |  |  |
| SPH | -0.767 |  | -0.528 |  |  |
| ASP | -0.863 |  |  |  |  |
| FDI | -0.902 |  |  |  |  |
| PJI3 |  |  | 0.815 |  |  |
| L/Bw |  |  | 0.724 |  |  |
| Hy |  |  |  | 0.954 |  |
| MR | 0.993 |  |  |  |  |
| PSA | 0.949 |  |  |  |  |
| MLOGP |  | -0.755 |  |  |  |



**a**



**b**

**Fig. 1s** Different interaction between the less active (5e) and the most active (8e) inhibitors with BuChe enzyme