**Table S1.** Pharmacokinetic parameters of IRs/α-ARs ligands and CNS drugs related to BBB penetration

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Compounds** | **log PS***a* | **log (PS x *f*u,brain)***b* | ***F*u***c* | **P-gp substrate specificity***d* | **S+P-gp**  ***ADMET****e* |
| **Amiloride** | -5.3 | -5.3 | 0.82 | Non-substrate | No |
| **Brimonidine** | -3 | -3.4 | 0.31 | Probably non-substrate | No |
| **Bromazepam** | -1.6 | -2.2 | 0.21 |  |  |
| **Carbamazepine** | -1.6 | -2.3 | 0.25 |  |  |
| **Citalopram** | -3 | -3.1 | 0.49 |  |  |
| **Clonazepam** | -1.5 | -2.4 | 0.08 |  |  |
| **Clonidine** | -2 | -2.8 | 0.11 | Non-substrate | No |
| **Clozapine** | -1.5 | -2.6 | 0.07 |  |  |
| **Efaroxan** | -2.1 | -3 | 0.26 | Non-substrate | No |
| **Fluoxetine** | -1.5 | -3.2 | 0.02 |  |  |
| **Guanabenz** | -2.1 | -2.9 | 0.26 | Non-substrate | No |
| **Guanfacine** | -2.3 | -2.9 | 0.16 | Non-substrate | No |
| **Harmane** | -1.4 | -2.4 | 0.07 | Non-substrate | No |
| **Harmine** | -1.4 | -2.5 | 0.06 | Non-substrate | No |
| **Idazoxan** | -2.6 | -3 | 0.33 | Non-substrate | No |
| **Lamotrigine** | -2.1 | -2.8 | 0.17 |  |  |
| **Lorazepam** | -1.5 | -2.4 | 0.07 |  |  |
| **Mianserin** | -1.1 | -2.5 | 0.12 |  |  |
| **Moxonidine** | -3.1 | -3.2 | 0.44 | Non-substrate | No |
| **Naphazoline** | -1.6 | -3 | 0.06 | Non-substrate | No |
| **Olanzapine** | -3.6 | -3.7 | 0.51 |  |  |
| **Oxazepam** | -1.7 | -2.4 | 0.04 |  |  |
| **Prazepam** | -1.1 | -2.7 | 0.02 |  |  |
| **Rilmenidine** | -2.1 | -2.6 | 0.77 | Non-substrate | No |
| **Risperidone** | -2.9 | -3.1 | 0.26 |  |  |
| **Tetrahydrozoline** | -1.8 | -2.9 | 0.22 | Non-substrate | No |
| **Tizanidine** | -2.8 | -3.2 | 0.46 | Probably non-substrate | No |
| **Trimazoline** | -1.7 | -3 | 0.40 | Non-substrate | No |
| **Viloxazine** | -2.5 | -2.8 | 0.34 |  |  |
| **Xylometazoline** | -1.5 | -3.2 | 0.17 | Non-substrate | No |
| **Ziprasidone** | -1.2 | -2.9 | 0.01 |  |  |

*a* Rate of brain penetration

*b* Brain/plasma equilibration rate

*c* Fraction unbound in plasma