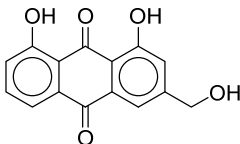
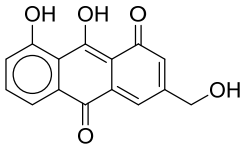
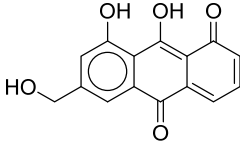
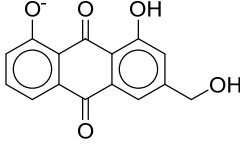
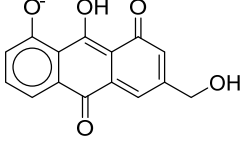
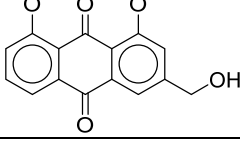
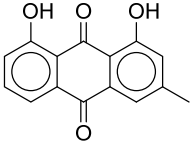
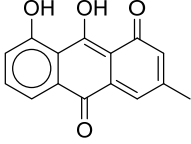
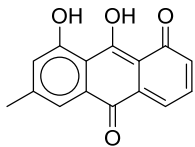
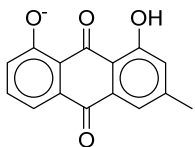
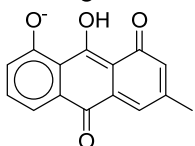
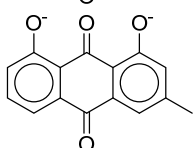
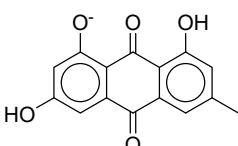
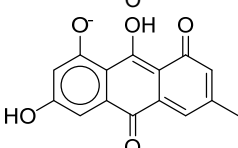
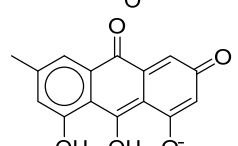
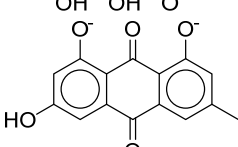
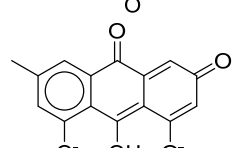
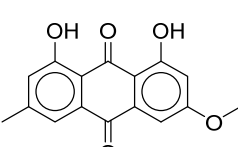


Supplementary Material for “In Silico Neuroprotective Effects of Specific *Rheum palmatum* Metabolites on Parkinson’s Disease Targets”

Table S1. List of *R. palmatum* major metabolites and generated ligand forms.

Ligand	Exact Molecular Weight	Ionization pH	Structure
<i>Aloe-emodin</i> (CID: 10207)			
Form 1	254.058	6.84	
Form 2	254.058	6.84	
Form 3	254.058	6.84	
Form 4	253.05	6.84	
Form 5	253.05	6.84	
Form 6	252.042	7.17	
<i>Chrysophanol</i> (CID: 10208)			
Form 1	254.058	6.84	
Form 2	254.058	6.84	

Form 3	254.058	6.84	
Form 4	253.05	6.84	
Form 5	253.05	6.84	
Form 6	252.042	7.17	
<hr/> <i>Emodin (CID: 3220)</i>			
Form 1	269.045	7.17	
Form 2	269.045	7.17	
Form 3	269.045	7.17	
Form 4	268.037	7.17	
Form 5	268.037	7.17	
<hr/> <i>Physcion (CID: 10639)</i>			
Form 1	284.068	6.91	

Form 2	284.068	6.91	
Form 3	284.068	6.91	
Form 4	283.061	6.91	
Form 5	283.061	6.91	
Form 6	282.053	7.17	
<i>Rhein (CID: 10168)</i>			
Form 1	283.024	6.93	
Form 2	283.024	6.93	
Form 3	283.024	6.93	
Form 4	282.016	6.93	
Form 5	282.016	6.93	
Form 6	281.009	7.7	

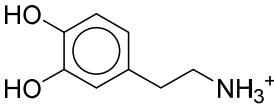
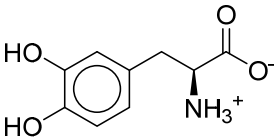
<i>Dopamine</i>	154.087	—	
<i>Levodopa</i>	197.069	—	

Table S2. Parkinson's disease target proteins and binding sites.

Protein	PDB ID	RMSD (Å)	Binding spheres (x y z r)	Reference
ASN	1XQ8	1.0192	235.761238 87.098921 -11.467784 12.834573	[1,2]
MAOB	2C65	0.6723	AS1: 56.169204 140.800776 16.387916 13.400000 AS2: 50.646075 154.441830 28.109744 8.900000 AS3: 28.564668 124.319410 9.517245 13.200000 AS4: 16.683806 129.076451 23.305674 8.500000	PDB site records [3,4]
COMT	3BWM	0.6887	AS1: -3.065429 -9.775358 -12.231862 5.000000 AS2: 9.521219 -3.947800 -3.317792 6.000000 AS3: -8.323370 -4.020339 -16.877004 10.400000 AS4: -4.031587 -11.005142 -16.061175 9.100000	PDB site records [5]
A _{2A} AR	3EML	0.7421	ASA1: -8.619491 -4.022831 53.851527 9.700000 ASA2: -5.753475 -21.755505 44.032696 5.000000 ASA3: -3.104069 -15.067314 28.427817 5.000000 ASA4: -6.152340 -20.745973 46.934776 5.100000 ASA5: -1.261143 -18.640946 55.134056 5.000000 ASA6: -15.100131 -17.313670 26.230558 5.000000 ASA7: -6.194983 15.030722 8.292277 15.300000 ASA8: -19.087429 -14.862891 18.906995 5.500000 ASA9: -2.195901 11.933315 16.502750 7.100000 ASB1: 5.283943 -17.175302 60.435534 5.000000 ASB2: -4.298667 4.042169 -1.331465 5.600000 ASB3: -10.197447 12.413895 -15.647710 5.700000 ASB4: 3.681484 28.326672 -7.840765 5.000000	PDB site records [6]

AS = active site

Table S3. 3D QSAR dataset of known ASN inhibitors.

Ligand No.	Canonical SMILES	IC ₅₀ (nM)
<i>Training Set</i>		
1	<chem>C\C=C(CO)\C=C\C=C(C)\C=C\C1=C(C)CCCC1(C)C</chem>	190
2	<chem>COc1cc(\C=C\C(=O)[CH-]C(=O)\C=C\c2ccc(O)c(OC)c2)ccc1O</chem>	220
3	<chem>[O-][N+](=O)c1ccc2Nc3ccc(Br)cc3Sc2c1</chem>	313.8
4	<chem>[O-][N+](=O)c1ccc2Nc3ccc(I)cc3Sc2c1</chem>	441.5
5	<chem>[O-][N+](=O)c1ccc2Nc3ccccc3Sc2c1</chem>	485
6	<chem>COc1ccc2Nc3ccc(OC)cc3Sc2c1</chem>	507.1
7	<chem>O[C@@H]1Cc2c(O)cc(O)cc2O[C@@H]1c3ccc(O)c(O)c3</chem>	800
8	<chem>Oc1cc(cc(O)c1O)C(=O)Nc2ccc(NC(=O)c3ccc([O-])cc3)cc2</chem>	980
9	<chem>[O-][N+](=O)c1ccc2[nH]c(\C=C\C=C\c3ccccc3)nc2c1</chem>	1,090
10	<chem>Nc1ccc(NC(=O)c2cc(O)c(O)c(O)c2)cc1</chem>	1,340
11	<chem>COc1ccc2Nc3ccc(cc3Sc2c1)C#N</chem>	1,440
12	<chem>o1c(\C=C\C=C\c2ccncc2)nc3ccccc13</chem>	1,850
13	<chem>Clc1ccc2nc(oc2c1)\C=C\C=C\c3ccncc3</chem>	2,190

14	<chem>C\ C(=C/C=C/C(=O)[O-])/C)\ C=C\ C1=C(C)CCCC1(C)C</chem>	3,000
15	<chem>CNc1ccc2[N@H+](C)c3ccc(OC)cc3Sc2c1</chem>	3,329
16	<chem>COc1ccc2N(C)c3ccc(N)cc3Sc2c1</chem>	3,928
17	<chem>Oc1cc(cc(O)c1[O-])C(=O)[O-]</chem>	4,430
18	<chem>Cc1ccc2oc(\ C=C\ C=C\ c3ccncc3)nc2c1</chem>	4,430
19	<chem>Oc1cc(O)c2cc(O)c([o+])c2c1)c3cc(O)c(O)c(O)c3</chem>	6,500
20	<chem>CCC[N@@H+][C][C@H](CSC)C[C@H]2[C@H]1Cc3c[nH]c4cccc2c34</chem>	7,900
21	<chem>Oc1c([O-])cc2OC(=CC(=O)c2c1O)c3ccccc3</chem>	8,200
22	<chem>O[C@H]1Cc2c(O)cc(O)cc2O[C@@H]1c3cc(O)c(O)c(O)c3</chem>	8,900
23	<chem>Oc1cc(O)c2cc(O)c([o+])c2c1)c3ccc(O)c(O)c3</chem>	10,300
24	<chem>O[C@@H]1Cc2c(O)cc(O)cc2O[C@H]1c3cc(O)c(O)c(O)c3</chem>	10,600
25	<chem>COc1ccc2[N@@H+](C)c3ccc(cc3Sc2c1)N(C)C</chem>	10,736
26	<chem>OC1=CC=Cc2cc(O)c(O)c(O)c2C1=O</chem>	12,900
27	<chem>CC1=CC(=O)c2ccccc2C1=O</chem>	15,000
28	<chem>O=C1C=CC(=O)c2ccccc2C1=O</chem>	15,000
29	<chem>Oc1cc(ccc1[O-])C2=C([O-])C(=O)c3c(O)cc([O-])cc3O2</chem>	20,000
30	<chem>CC(=O)N1c2ccccc2Sc3cc(ccc13)[N+](=O)[O-]</chem>	23,491
31	<chem>Oc1cc(ccc1[O-])C2=CC(=O)c3c(O)cc([O-])cc3O2</chem>	28,000
32	<chem>CC(=O)N1c2ccc(O)cc2Sc3cc(ccc13)[N+](=O)[O-]</chem>	32,074
33	<chem>C[C@]12CC[C@H]3[C@@H](CCC4=CC(=O)CC[C@]34C)[C@@H]1CCC2=O</chem>	85,900
34	<chem>C[C@]12CC[C@H]3[C@@H](CCc4cc(O)ccc34)[C@@H]1CCC2=O</chem>	93,100
35	<chem>C[C@]12CC[C@H]3[C@@H](CCC4=CC(=O)CC[C@]34C)[C@@H]1CC[C@@H]2O</chem>	96,800
36	<chem>COc1cc(\ C=C\ c2cc(\ C=C\ c3ccc(O)c(OC)c3)[nH][nH+])2)ccc1O</chem>	126,800
Test Set		
1	<chem>Oc1ccc(C[C@@H](OC(=O)\ C=C\ c2ccc(O)c(O)c2)C(=O)[O-])cc1O</chem>	210
2	<chem>C[C@H](Cc1ccc(O)c(O)c1)[C@H](C)Cc2ccc(O)c(O)c2</chem>	210
3	<chem>C[C@H](Cc1ccccc1)[N@H+](C)CC#C</chem>	270
4	<chem>[NH3+][C]Cc1ccc(O)c(O)c1</chem>	530
5	<chem>Oc1cc(cc(O)c1O)C(=O)Nc2ccc(NC(=O)c3ccc(F)cc3)cc2</chem>	1,700
6	<chem>Clc1ccc(NC(=O)c2ccc(cc2)C(=O)\ C=C\ C=C\ c3ccncc3)cc1</chem>	2,050
7	<chem>COc1ccc2N(C(=O)C)c3ccc(cc3Sc2c1)[N+](=O)[O-]</chem>	14,031
8	<chem>C[NH+]1CCN(CC1)[NH2+][C][NH+]2c3ccccc3Sc4ccccc24</chem>	16,000
9	<chem>C[C@]12CC[C@H]3[C@@H](CCc4cc(O)ccc34)[C@@H]1CC[C@@H]2O</chem>	60,000

Table S4. 3D QSAR dataset of known MAOB inhibitors.

Ligand No.	Canonical SMILES	IC ₅₀ (nM)
Training Set		
1	<chem>C[C@H](Cc1ccccc1)[N@H+](C)CC#C</chem>	19
2	<chem>FC(F)(F)c1ccc(\ C=C\ C2CC[NH+](CC#C)CC2)cc1</chem>	18.6
3	<chem>CN(CC#C)CC(=C)c1ccc(Cl)cc1</chem>	120
4	<chem>CN(CC#C)CC(=C)c1ccc(F)c(C)c1</chem>	230
5	<chem>CN(CC#C)[C@H](CF)CC(=C)C</chem>	664
6	<chem>Fc1cc(F)c(\ C=C\ C2CC[NH+](CC#C)CC2)cc1F</chem>	436.2
7	<chem>Fc1ccc(\ C=C\ [C@@H]2CCC[N@H+](CC#C)C2)cc1</chem>	1,469.50
8	<chem>FC(F)(F)c1ccc(\ C=C/C2CC[NH+](CC#C)CC2)cc1</chem>	1,506.60
9	<chem>CC(C)c1ccc(\ C=C/C2CC[NH+](CC#C)CC2)cc1</chem>	1,883.90
10	<chem>Fc1ccccc1\ C=C\ C2CC[NH+](CC#C)CC2</chem>	11,830.40
11	<chem>Fc1ccccc1CCC2CCN(CC#C)CC2</chem>	14,159.50
12	<chem>Cc1ccc(\ C=C/C2CC[NH+](CC#C)CC2)cc1</chem>	19,162.80
13	<chem>Fc1cccc(\ C=C/C2CC[NH+](CC#C)CC2)c1</chem>	48,912
14	<chem>[NH3+][C@H]1C[C@H]1c2ccccc2</chem>	33

15	<chem>COc1cccc(c1)C(=C)CN(C)CC#C</chem>	200
16	<chem>[NH3+]C[C@@]1(C[C@@H]1F)c2ccccc2</chem>	12
17	<chem>Cc1cccc(COc2cccc(Br)c2)c1</chem>	1,980
18	<chem>BrC1cccc(OCc2ccccc2)c1</chem>	2,730
19	<chem>CN1N=C(C[C@@H]1c2cccc(F)c2)c3ccccc3</chem>	60
20	<chem>Cc1ccc2oc(cc2c1)c3ccccc3Br</chem>	200
21	<chem>CN1N=C(C[C@H]1c2ccccc2C)c3ccccc3</chem>	110
22	<chem>Cc1ccc(cc1)C2=Cc3cc(C)ccc3OC2=O</chem>	0.3085
23	<chem>CN1N=C(C[C@@H]1c2ccc(F)cc2)c3ccccc3</chem>	140
24	<chem>CCC(C)(C)c1ccc(OC[C@H]1N2CCC[C@@H](C)C2)cc1</chem>	428
25	<chem>CN(CC#C)CC(=C)c1ccc(COc2ccccc2)cc1</chem>	620
26	<chem>CC[C@@]1([NH3+])C[C@@H]1c2ccccc2</chem>	190
27	<chem>CN1N=C(C[C@@H]1c2ccccc2F)c3ccccc3</chem>	280
28	<chem>BrC1cccc1c2oc3ccccc3c2</chem>	1,130
29	<chem>BrC1cccc(c1)c2oc3ccccc3c2</chem>	1,170
30	<chem>COc1ccc2C(=O)\C(=C\c3ccccc3)\C2c1</chem>	9.2
31	<chem>CC(=O)c1ccc(OCc2ccc(F)cc2)cc1</chem>	12.9
32	<chem>Cc1ccc(cc1)C2=CC(=S)c3ccc(F)cc3O2</chem>	1,610
33	<chem>CCC(C)(C)c1ccc(OC[C@H]1N2CCC(C)CC2)cc1</chem>	2,070
34	<chem>CC(=O)c1cccc(OCc2ccc(Cl)cc2)c1</chem>	10.52
35	<chem>Cc1ccc(COc2ccc3C(=O)CCCc3c2)cc1</chem>	11
36	<chem>CCC[C@@]1([NH3+])C[C@H]1c2ccccc2</chem>	600
37	<chem>CC(=O)c1ccc(OCc2cccc(Cl)c2)cc1</chem>	21.5
38	<chem>Fc1cccc(COc2ccc3C(=O)CCCc3c2)c1</chem>	17
39	<chem>Cc1cccc2cc(oc12)c3ccccc3</chem>	10,730
40	<chem>CC(=O)c1ccc(OCc2ccc(F)cc2F)cc1</chem>	27.3
41	<chem>Fc1ccc(\C=C\C2=COc3ccccc3C2=O)cc1</chem>	8.6
42	<chem>CC(=O)c1ccc(OCc2ccccc2F)cc1</chem>	56.9
43	<chem>COc1ccc2OC(=O)C(=Cc2c1)c3ccc(C)cc3</chem>	1.52
44	<chem>Clc1cccc(COc2ccc3C(=O)CCCc3c2)c1</chem>	15
45	<chem>CN(CC#C)CC(=C)c1cccc(CNc2ccccc2)c1</chem>	1,400
46	<chem>Clc1ccc(COc2ccc3COC(=O)c3c2)cc1</chem>	2.8
47	<chem>Fc1ccc(COc2ccc3COC(=O)c3c2)cc1</chem>	6.4
48	<chem>Clc1ccc(CN[C@H]2C[C@@H]2c3ccccc3)cc1</chem>	14,100
49	<chem>CC(=O)c1ccc(OCc2cccc(C)c2)cc1</chem>	86.3
50	<chem>COc1ccc(cc1)C(=O)\C=C\c2ccccc2F</chem>	56
51	<chem>CC(=O)c1cccc(OCc2ccc(F)cc2)c1</chem>	86.4
52	<chem>Cc1ccc2C(=O)C[C@H](Oc2c1)c3ccccc3</chem>	110
53	<chem>CC(=O)c1ccc(OCc2ccc(C)cc2)cc1</chem>	102
54	<chem>Cc1ccc2CC(=O)C(=Cc2c1)C(=O)[O-]</chem>	19.05
55	<chem>CC(=O)c1cccc(OCc2cccc(c2)C(F)(F)F)c1</chem>	21.2
56	<chem>CC1=C(C)c2ccc(OCc3ccccc(F)c3)cc2OC1=O</chem>	0.912
57	<chem>CC(=O)c1ccc(OCc2ccc(Cl)cc2)cc1</chem>	63.2
58	<chem>Cc1ccc2C(=O)C[C@@H](Oc2c1)c3ccccc3</chem>	140
59	<chem>CC(=O)c1cccc(OCc2ccc(C)cc2)c1</chem>	140
60	<chem>COc1ccc(cc1)C(=O)\C=C\c2ccc(Cl)cc2</chem>	54
61	<chem>CN(CC#C)Cc1ccc(O)c2ncccc12</chem>	57
62	<chem>Clc1ccc(COc2ccc3OC=CC(=O)c3c2)cc1</chem>	2
63	<chem>Fc1ccc(COc2ccc3C(=O)CCOc3c2)cc1</chem>	8.6
64	<chem>Cc1ccc(COc2ccc3OC=CC(=O)c3c2)cc1</chem>	6
65	<chem>Cc1ccc(COc2ccc3SC(=O)Oc3c2)cc1</chem>	5
66	<chem>CN1N=C(C[C@H]1c2ccccc2Cl)c3ccccc3</chem>	3,650
67	<chem>Clc1cccc(COc2ccc3OCCOc3c2)c1</chem>	57

68	<chem>CC(=O)c1cccc(OCc2ccc(cc2)C(F)(F)F)c1</chem>	43.2
69	<chem>Fc1cccc(COc2cccc3[C@@H](CCc23)NCC#C)c1</chem>	280
70	<chem>Cc1ccc(cc1)[C@H]2CC(=O)c3ccc(F)cc3O2</chem>	150
71	<chem>Cc1ccc(cc1)[C@@H]2CC(=O)c3ccc(F)cc3O2</chem>	150
72	<chem>Fc1ccc(cc1)c2csc(NN=C3CCCCC3)n2</chem>	3.802
73	<chem>[NH3+][C@H]1C[C@]1(F)c2ccc(F)cc2</chem>	4,900
74	<chem>Cc1cccc2cc(oc12)c3ccccc3Br</chem>	9,680
75	<chem>Clc1cccc(COc2ccc3OC=CC(=O)c3c2)c1</chem>	3.6
76	<chem>Cc1ccc(cc1)[C@H]2CC(=O)c3ccc(F)cc3O2</chem>	160
77	<chem>Fc1ccc(cc1)[C@H]2CC(=O)c3ccc(F)cc3O2</chem>	150
78	<chem>CC1=C(Cl)C(=O)Oc2cc(OCc3ccccc3)ccc12</chem>	2.1
79	<chem>Clc1ccc(COc2ccc3C(=O)OCc3c2)cc1</chem>	13.87
80	<chem>Fc1ccc(COc2ccc3OC=CC(=O)c3c2)cc1</chem>	8.4
81	<chem>Fc1ccc(cc1)[C@@H]2CC(=O)c3ccc(F)cc3O2</chem>	170
82	<chem>COc1ccc2C(=O)C(=COc2c1)\C=C\c3ccc(F)cc3</chem>	3.1
83	<chem>Cc1ccc(cc1)[C@@]2(F)C[C@H]2[NH3+]</chem>	6,700
84	<chem>Oc1ccc2C(=O)\C(=C\c3ccc(Cl)cc3)\Cc2c1</chem>	13
85	<chem>Clc1ccc(\C=C\2/COc3ccccc3C2=O)cc1</chem>	154.23
86	<chem>CC(=O)c1ccc(OCc2ccc(cc2)C(F)(F)F)cc1</chem>	77.8
87	<chem>COc1ccc(cc1)C2=Cc3cc(C)ccc3OC2=O</chem>	13.05
88	<chem>CN(C)c1ccc(\C=C\2/Oc3ccccc3C2=O)cc1</chem>	99
89	<chem>[NH3+][C@H]1C[C@]1(F)c2ccc(Cl)cc2</chem>	3,700
90	<chem>Fc1cc(NC(=O)c2ccc3[nH]ncc3c2)ccc1Cl</chem>	0.6607
91	<chem>O=C1CCOc2cc(OCc3ccccc3)ccc12</chem>	57.37
92	<chem>Cc1cccc(COc2ccc3OC=CC(=O)c3c2)c1</chem>	19
93	<chem>Cc1ccc(NC(=O)C2=COc3ccccc3C2=O)cc1C</chem>	0.67
94	<chem>CC(=O)c1ccc(OCc2ccccc2Cl)cc1</chem>	311
95	<chem>Fc1ccc(COc2cccc(C=O)c2)cc1</chem>	930
96	<chem>Fc1ccc2C(=O)C[C@@H](Oc2c1)c3ccccc3</chem>	650
97	<chem>COc1ccc2C(=O)C(=COc2c1)\C=C\c3ccccc3</chem>	16
98	<chem>BrC1ccc(COc2cccc(C=O)c2)cc1</chem>	190
99	<chem>Fc1ccc(COc2ccc3C(=O)C=COc3c2)cc1</chem>	25
100	<chem>Cc1ccc(cc1)[C@@]2(F)C[C@@H]2[NH3+]</chem>	13,000
101	<chem>COc1ccc(\C=C\2/COc3ccccc3C2=O)cc1</chem>	58.9
102	<chem>O=C1C=COc2ccc(OCc3ccccc3)cc12</chem>	53
103	<chem>Cc1ccc(cc1)[C@@H]2CC(=O)c3ccc(C)cc3O2</chem>	500
104	<chem>Cc1ccc(cc1)[C@H]2CC(=O)c3ccc(C)cc3O2</chem>	530
105	<chem>CC(=O)c1ccc(OCc2ccccc2C(F)(F)F)cc1</chem>	183
106	<chem>Clc1cccc(COc2ccc3C(=O)C=COc3c2)c1</chem>	17
107	<chem>O=C1Oc2cc(COc3ccccc3)ccc2C=C1</chem>	64.57
108	<chem>Clc1ccc(COc2ccc3C(=O)CCOc3c2)cc1</chem>	33.45
109	<chem>Oc1ccc2C(=O)\C(=C\c3ccc(F)c3)\Cc2c1</chem>	84
110	<chem>Cc1ccc(cc1)[C@@H]2CC(=O)c3ccc(C)cc3O2</chem>	590
111	<chem>Fc1ccc(CCOc2ccc3COC(=O)c3c2)cc1</chem>	68
112	<chem>CC(=O)c1cccc(OCc2cccc(C)c2)c1</chem>	893
<hr/>		
<i>Test Set</i>		
1	<chem>CN(CC#C)Cc1ccccc1</chem>	8.2
2	<chem>CN(CC#C)CC(=C)c1ccc(Cl)c(C)c1</chem>	100
3	<chem>Cc1ccc(\C=C\C2CC[NH+](CC#C)CC2)cc1</chem>	147
4	<chem>C#CC[NH+]1CCC(CC1)\C=C/c2ccc(cc2)C3CC3</chem>	2,640.10
5	<chem>FC(F)(F)c1cccc(\C=C/C2CC[NH+](CC#C)CC2)c1</chem>	9,352.50
6	<chem>F[C@H]1Cc2ccccc2[C@H]1[NH2+][C]#C</chem>	27
7	<chem>CCC(C)(C)c1ccc(OCCC[N@H+]2CCCC[C@@H]2C)cc1</chem>	20

8	<chem>Cc1ccc(COc2cccc(Br)c2)cc1</chem>	1,530
9	<chem>Cn1ncc2cc(\C=N\c3ccc(Cl)c(Cl)c3)ccc12</chem>	1.023
10	<chem>[NH3+]C\C=C(\F)/COc1cccc(Cl)c1</chem>	30
11	<chem>Cc1cccc2cc(oc12)c3cccc(Br)c3</chem>	3,980
12	<chem>[O-]C(=O)C1=Cc2cccc2OC1=O</chem>	17.38
13	<chem>Fc1cc(ccc1Cl)\N=C\c2ccc3[nH]ncc3c2</chem>	1.905
14	<chem>CC(=O)c1ccc(OCc2cccc(F)c2)cc1O</chem>	2.8
15	<chem>CC1=CC(=O)Oc2cc(OCCCC#C)ccc12</chem>	18.2
16	<chem>O=C1CCc2cccc(OCCCCC#C)cc2N1</chem>	52.6
17	<chem>Fc1ccc(NC(=O)c2ccc3[nH]ncc3c2)cc1Cl</chem>	0.6761
18	<chem>CC(=O)c1ccc(OCc2ccc(Br)cc2)cc1</chem>	85.6
19	<chem>C[C@@H]1CCC/C/1=N\Ne2nc(cs2)c3ccc(F)cc3</chem>	9.13
20	<chem>COc1ccc2OC(=O)C(=Cc2c1)c3cccc(C)c3</chem>	17.05
21	<chem>Oc1ccc(cc1)C(=O)\C=C\c2ccc(Cl)cc2</chem>	31
22	<chem>COc1ccc2C(=O)\C(=C\c3ccc(cc3)N(C)C)\Cc2c1</chem>	60
23	<chem>[NH3+][C@@H]1C[C@]1(F)c2ccc(Cl)cc2</chem>	4,800
24	<chem>Fc1ccc(cc1F)c2cc3C(=O)c4cccc4c3nn2</chem>	5.012
25	<chem>Fc1ccc2C(=O)C[C@H](Oc2c1)c3cccc3</chem>	620
26	<chem>[NH3+]C\C=C(\F)/COc1ccc(cc1)C(F)(F)F</chem>	130
27	<chem>Fc1cccc(COc2cccc(C=O)c2)c1</chem>	1,210
28	<chem>[NH3+]CCc1ccc(OCc2cccc(F)c2)cc1</chem>	193

Table S5. 3D QSAR dataset of known COMT inhibitors.

Ligand No.	Canonical SMILES	IC ₅₀ (nM)
<i>Training Set</i>		
1	<chem>[O-]c1c(F)cc(c2ccncc12)S(=O)(=O)C3CCCC3</chem>	1.995
2	<chem>[O-]c1c(F)cc(c2ccncc12)S(=O)(=O)N3CCCC3</chem>	3.981
3	<chem>Cc1cccc(C)c1CN2CCN3C=C([O-])C(=O)C=C3C2</chem>	6.3
4	<chem>Oc1ccc(c2ccncc12)S(=O)(=O)C3CCCC3</chem>	6.31
5	<chem>Cc1ccc(cc1)S(=O)(=O)c2cc(F)c([O-])c3ncccc23</chem>	6.31
6	<chem>Oc1ccc(c2ccncc12)S(=O)(=O)N3CCCC3</chem>	7.943
7	<chem>Oc1c(Cl)cc(c2ccncc12)S(=O)(=O)N3CCCC3</chem>	10
8	<chem>[O-]C1=CN2CCN(Cc3ccc(Cl)cc3Cl)CC2=CC1=O</chem>	10
9	<chem>[O-]C1=CN2CCN(Cc3c(Cl)cccc3Cl)CC2=CC1=O</chem>	10
10	<chem>Cc1ccc(C[N@@H+]2CCN3C=C([O-])C(=O)C=C3C2)c(C)c1</chem>	13
11	<chem>[O-]C1=CN2CCN(Cc3c(F)cccc3Cl)CC2=CC1=O</chem>	16
12	<chem>Oc1c(Cl)cc(c2ccncc12)S(=O)(=O)C3CCCC3</chem>	19.95
13	<chem>Cc1cc(c2ccncc2c1O)S(=O)(=O)N3CCCC3</chem>	19.95
14	<chem>Cc1ccc(cc1)S(=O)(=O)c2ccc(O)c3ncccc23</chem>	19.95
15	<chem>Oc1cc(\C=C(/C#N)\C(=O)N2CCC2)cc(c1[O-])[N+](=O)[O-]</chem>	33
16	<chem>[O-]C1=CN2CCN(Cc3c(F)cccc3F)CC2=CC1=O</chem>	38
17	<chem>[O-]C1=CN(C=CC1=O)c2cc(cc[nH+]2)c3cccc3</chem>	40
18	<chem>[O-]C1=CN2CCN(Cc3ccc(F)cc3Cl)CC2=CC1=O</chem>	40
19	<chem>[O-]C1=CN2CCN(Cc3cccc3Cl)CC2=CC1=O</chem>	40
20	<chem>Cc1cccc(CN2CCN3C=C([O-])C(=O)C=C3C2)c1C</chem>	40
21	<chem>[O-]C1=CN(C=CC1=O)c2cccc(c2)c3cccc3</chem>	47
22	<chem>[O-]C1=CN2CCN(Cc3cccc3F)CC2=CC1=O</chem>	50
23	<chem>Cc1cccc1CN2CCN3C=C([O-])C(=O)C=C3C2</chem>	50
24	<chem>CCS(=O)(=O)c1ccc(O)c2ncccc12</chem>	50.12
25	<chem>CC1=CC(=O)C(=CN1c2cccc(c2)c3cccc3)O</chem>	53
26	<chem>[O-]C1=CN(C=CC1=O)c2nccc(c2F)c3cccc3</chem>	55

27	<chem>C[C@@H](O)C1=CC(=O)C(=CN1c2cccc(c2)c3ccccc3)O</chem>	61
28	<chem>Cc1ccc(C)c(CN2CCN3C=C([O-])C(=O)C=C3C2)c1</chem>	63
29	<chem>COc1ccc(cc1)C2(CC2)c3cc([nH]n3)c4sc(C)nc4C</chem>	75
30	<chem>[O-]C1=CN2CCN(Cc3ccccc3C#N)CC2=CC1=O</chem>	100
31	<chem>Oc1cc(\C=C(/C#N)\c2cnccn2)cc(c1O)[N+](=O)[O-]</chem>	108
32	<chem>[O-]C1=CN(C=CC1=O)c2cccc(n2)c3ccccc3</chem>	128
33	<chem>OCC1=CC(=O)C(=CN1c2cccc(c2)c3ccccc3)O</chem>	140
34	<chem>OCC1=CC(=O)C(=CN1c2ccc(cc2)c3ccccc3)O</chem>	140
35	<chem>CN1C(=O)C(=CN=C1c2cccc(c2)c3ccccc3)O</chem>	170
36	<chem>CCN1C(=O)S\C=C\c2cc(O)c([O-])c(c2)[N+](=O)[O-]\C1=O</chem>	179
37	<chem>OB(O)C1=CN(C=C([O-])C1=O)c2cccc(c2)c3ccccc3</chem>	200
38	<chem>OC1=CN=C([N-]C1=O)c2ccc(cc2)C(F)(F)F</chem>	210
39	<chem>CCN(CC)C(=O)\C=C(/N)\c1cc([O-])c(O)c(c1)[N+](=O)[O-]\C#N</chem>	214
40	<chem>[O-]C1=CN2CCN(Cc3ccccc3)CC2=CC1=O</chem>	220
41	<chem>COc1ccccc1CN2CCN3C=C([O-])C(=O)C=C3C2</chem>	250
42	<chem>Cc1ccc(cc1)c2ccc(O)c3nccccc23</chem>	251.19
43	<chem>COc1ccc(CN2CCN3C=C([O-])C(=O)C=C3C2)cc1</chem>	400
44	<chem>[O-]C1=CN2CC[N@H+](Cc3ccc(cc3)C(F)(F)F)CC2=CC1=O</chem>	450
45	<chem>OC1=CN(C=CC1=O)c2cc([nH+])c(c2)c3ccccc3</chem>	456
46	<chem>COc1ccc(cc1)[C@@H](C)c2cc([nH]n2)c3sc(C)nc3C</chem>	470
47	<chem>CCN(CC)C(=O)\C=C(/[O-])\c1cc([O-])c(O)c(c1)[N+](=O)[O-]\C#N</chem>	551
48	<chem>[O-]C1=CN(C=CC1=O)c2cc(ccn2)c3ccccc3</chem>	574
49	<chem>OC1=CN=C([N-]C1=O)c2cccc(c2)C#Cc3ccccc3</chem>	590
50	<chem>[O-]C1=CN(C=CC1=O)c2cc(ccn2)c3ccccc3</chem>	672
51	<chem>Cc1cc(C)cc(c1)N2C=C(O)C(=O)C=C2CO</chem>	680
52	<chem>C[C@H](c1ccccc1)c2cc([nH]n2)c3sc(C)nc3C</chem>	700
53	<chem>[O-]C1=CN(C=CC1=O)c2cc(ccn2)c3ccccc3</chem>	826
54	<chem>OC1=CN=C([N-]C1=O)c2cccs2</chem>	860
55	<chem>COc1ccc(cc1)[C@H](C)c2cc([nH]n2)c3sc(C)nc3C</chem>	860
56	<chem>C[C@H](c1ccccc1)c2cc([nH]n2)c3sc(C)nc3C</chem>	900
57	<chem>[O-]C1=CN(C=CC1=O)c2nccc3ccccc23</chem>	962
58	<chem>COc1ccc(Cc2cc([nH]n2)c3sc(C)nc3C)cc1</chem>	1,000
59	<chem>C[C@@H](c1ccccc1)c2cc([nH]n2)c3sc(C)nc3C</chem>	1,100
60	<chem>Cc1nc(C)c(s1)c2cc([nH]n2)C(C)(C)c3ccccc3</chem>	1,100
61	<chem>Cc1ccc(cc1)S(=O)(=O)c2cc(O)c3nccccc3c2</chem>	1,584.89
62	<chem>CC(C)C[N@H+]1CCN2C=C([O-])C(=O)C=C2C1</chem>	1,600
63	<chem>Cc1cn2nc(ccc2n1)N3C=CC(=O)C(=C3)[O-]</chem>	1,667
64	<chem>Cc1ccc(cc1)N2C=C(O)C(=O)C=C2CO</chem>	1,700
65	<chem>[O-]C1=CN2CC[N@H+](Cc3ccc(cc3)C#N)CC2=CC1=O</chem>	2,000
66	<chem>Cc1nc(C)c(s1)c2cc(Cc3ccccc3)[nH]n2</chem>	2,000
67	<chem>[O-]C1=CN2CCN(CCc3ccccc3)CC2=CC1=O</chem>	2,000
68	<chem>COc1ccc(cc1)C2=C(N(C)C(=O)C(=C2)O)c3ccccc3</chem>	2,100
69	<chem>Cc1ccc(cc1)C(=O)c2ccc(O)c3nccccc23</chem>	3,981.07
70	<chem>OCC1=CC(=O)C(=CN1CCCc2ccccc2)[O-]</chem>	4,500
71	<chem>CC1=C(O)C(=O)C=CN1c2cc(C)cc(C)c2</chem>	5,500
72	<chem>Cc1ccc(N2C=C(O)C(=O)C=C2CO)c(C)c1</chem>	5,800
73	<chem>[O-]C1=CN2CCN(Cc3ccccc3)CC2=CC1=O</chem>	6,300
74	<chem>Cc1nc(C)c(s1)c2cc(CCc3ccccc3)[nH]n2</chem>	8,000
75	<chem>Cc1ccc(cc1)c2nc(C)c(s2)c3cc[nH]n3</chem>	11,000
76	<chem>Cc1nc(C)c(s1)c2cc[nH]n2</chem>	16,000
77	<chem>CC1=C(O)C(=O)C=CN1c2ccccc2</chem>	18,000
78	<chem>CCc1cc([nH]n1)c2sc(C)nc2C</chem>	20,000
79	<chem>CCc1nc(C)c(s1)c2cc[nH]n2</chem>	21,000

80	<chem>CC[C@H](c1ccccc1)c2cc([nH+][nH]2)c3sc(C)nc3C</chem>	21,000
81	<chem>Cc1nc(sc1c2cc[nH]n2)c3ccccc3</chem>	24,000
82	<chem>CCn1cc(c(C)n1)c2cc[nH]n2</chem>	69,000
83	<chem>Cc1ccn2c(c(C)[nH+])c2c1)c3cc[nH]n3</chem>	85,000
84	<chem>Cc1nc(C)c(s1)c2cc([nH]n2)c3ccccc3</chem>	130,000
Test Set		
1	<chem>[O-]c1c(F)cc(c2ccnc12)S(=O)(=O)c3ccc(F)cc3</chem>	3,981
2	<chem>[O-]C1=CN2CCN(Cc3ccccc3C(F)(F)F)CC2=CC1=O</chem>	60
3	<chem>CCN(CC)C(=O)\C(=C\c1cc(O)c([O-])c(c1)[N+](=O)[O-])\C#N</chem>	60
4	<chem>COc1cccc(\C=C\C(=O)c2cc(O)c(O)c(c2)[N+](=O)[O-])c1</chem>	70
5	<chem>COc1ccc(Oc2cccc(c2)C3=NC=C(O)C(=O)N3C)cc1</chem>	93
6	<chem>Cc1ccc(cc1)C(=O)c2cc(O)c(O)c(c2)[N+](=O)[O-]</chem>	127
7	<chem>CCCCc1ccc(cc1)N2C=C(O)C(=O)C=C2CO</chem>	160
8	<chem>CN1C(=O)C(=CN=C1c2ccc(Cl)c(c2)C(F)(F)F)O</chem>	180
9	<chem>Cc1nc(C)c(s1)c2cc([nH]n2)C3(CC3)c4ccccc4</chem>	210
10	<chem>[O-]C1=CN2C(=CC1=O)CSc3ccccc23</chem>	400
11	<chem>CC(C)C1=CC(=O)C(=CN1c2cccc(c2)c3ccccc3)O</chem>	410
12	<chem>CCC(CC)C[N@H+]1CCN2C=C([O-])C(=O)C=C2C1</chem>	630
13	<chem>[O-]C1=CN(C=CC1=O)c2ccnc([nH+])c3ccccc3</chem>	706
14	<chem>Oc1cccc2ccnc12</chem>	1,584.89
15	<chem>[O-]C1=CN(C=CC1=O)c2ccccc2</chem>	2,400
16	<chem>OCC1=CC(=O)C(=CN1c2ccccc2)O</chem>	3,400
17	<chem>Oc1c([O-])cc(cc1[N+](=O)[O-])\C(=C(/C#N)\C(=O)N2CCC2)\[O-]</chem>	3,560
18	<chem>Oc1ccc(c2ccnc12)S(=O)(=O)[O-]</chem>	6,309.57
19	<chem>[NH3+]CCCC1=CC(=O)C(=CN1c2cccc(c2)c3ccccc3)O</chem>	13,000
20	<chem>Cc1nc(C)c(s1)c2cc(CCCc3ccccc3)[nH][nH+]2</chem>	34,000
21	<chem>Cc1ccc2[nH+]c(C)c(c3cc[nH]n3)n2c1</chem>	80,000

Table S6. 3D QSAR dataset of known A_{2A}AR inhibitors.

Ligand No.	Canonical SMILES	IC ₅₀ (nM)
Training Set		
1	<chem>Nc1nc(c2ccc(F)cc2)c(c3ccc(O)nc3)c4nc(Cc5ccc(F)cn5)nn14</chem>	0.3
2	<chem>Nc1nc(NCc2ccsc2)nc3sc([nH+]c13)c4occc4</chem>	0.36
3	<chem>CN1C=C(C=CC1=O)c2c(nc(N)n3nc(nc23)[C@H](O)c4ncccc4F)c5ccccc5</chem>	0.52
4	<chem>Nc1nc(NCc2cccn2)nc3sc([nH+]c13)c4occc4</chem>	0.68
5	<chem>Nc1nc(NCCc2occc2)nc3sc([nH+]c13)c4occc4</chem>	2.93
6	<chem>COc1cccc1CNc2nc(N)c3nc(sc3n2)c4ccccc4</chem>	5.34
7	<chem>COc1cccc1Cn2cc3nc(nc(N)c3n2)c4occc4</chem>	6.21
8	<chem>COc1ccc(Cc2nc3c(C4=CN(C)C(=O)C=C4)c(nc(N)n3n2)c5ccccc5)nc1</chem>	7.72
9	<chem>Nc1nc(cn2c3ccccc3nc12)c4cccc(Br)c4</chem>	10.1
10	<chem>COc1cccc(c1)c2cn3c4ccccc4nc3c(N)n2</chem>	10.1
11	<chem>Cc1oc(cc1)c2nc(N)c3nn(Cc4ccccc4)cc3n2</chem>	10.91
12	<chem>Cc1oc(cc1)c2nc(N)nc3N(CCN4CCN(CC4)c5ccccc5F)C(=O)C=Nc23</chem>	11.7
13	<chem>Nc1nc2ccc(Cl)cc2c3[nH+]c(nn13)c4occc4</chem>	12
14	<chem>CC(=O)Nc1cc(nc(n1)n2nc(C)cc2C)c3cccc(n3)N4CCOCC4</chem>	13
15	<chem>Nc1nc2c(cnn2CCc3ccc(O)cc3)c4nc(nn14)c5occc5</chem>	14
16	<chem>Nc1nc(NCc2ccncc2)nc3sc([nH+]c13)c4occc4</chem>	15.3
17	<chem>COc1cc(OC)cc(c1)c2cc(NC(=O)C)nc(n2)n3nc(C)cc3C</chem>	17
18	<chem>COC1CN(C1)c2cccc(n2)c3cc(NC(=O)C)nc(n3)n4nc(C)cc4C</chem>	18
19	<chem>CCCCc1nc2[nH]c[nH+]c2c3nc(nn13)c4ccccc4Cl</chem>	18
20	<chem>COc1cccc(c1)c2cn3c4cc(F)c(F)cc4nc3c(N)n2</chem>	27

21	<chem>CCC(=O)Nc1cc(nc([nH+])1)n2nc(C)cc2C)c3cncc(OC)c3</chem>	31
22	<chem>Nc1nc(cn2c3cccc3nc12)c4occc4</chem>	32.6
23	<chem>Nc1nc(cn2c3cccc3nc12)c4ccc(F)cc4F</chem>	33.7
24	<chem>Nc1nc(cn2c3cccc3nc12)c4ccc(Cl)cc4</chem>	35.4
25	<chem>Nc1nc(cn2c3cccc3nc12)c4ccc(Br)cc4</chem>	38.4
26	<chem>Nc1nc(cn2c3cccc3nc12)c4ccccc4</chem>	46.5
27	<chem>CCCCc1nc2[nH]c[nH+]c2c3nc(Cc4ccccc4)nn13</chem>	47
28	<chem>COc1cccc(CNc2nc(N)c3nc(sc3n2)c4ccccc4)c1</chem>	48
29	<chem>CCNc1c2c(nc(N)n3nc(nc23)c4occc4)nn1C</chem>	48
30	<chem>Cc1oc(cc1)c2nc(N)nc3N(CCN4CCN(CC4)c5ccccc5)C(=O)C=Nc23</chem>	49.2
31	<chem>COc1ccc(cc1)c2cn3c4ccccc4nc3c(N)n2</chem>	51.2
32	<chem>CCCCc1nc2[nH]c[nH+]c2c3nc(nn13)c4cccc(Cl)c4</chem>	56
33	<chem>CCCCc1nc2[nH]c[nH+]c2c3nc(nn13)c4ccc(O)cc4</chem>	58
34	<chem>Cc1oc(cc1)c2nc(N)nc3N(CCN4CCN(CC4)c5ccc(F)cc5)C(=O)C=Nc23</chem>	58.8
35	<chem>Clc1cc2nc(NCc3ccnc3)nc(C(=O)c4cccs4)c2s1</chem>	62
36	<chem>Nc1cc(c2occc2)c3oc(nc3c1)c4occc4</chem>	70.6
37	<chem>CCCCc1nc2[nH]c[nH+]c2c3nc(nn13)c4ccccc4</chem>	71
38	<chem>COc1ccccc1c2cn3c4ccccc4nc3c(N)n2</chem>	83.1
39	<chem>CCOc1ccc(cc1)C2=CN3C(=O)N(N=C3C(=N2)N)c4ccccc4</chem>	98
40	<chem>C[C@@H](Nc1nc(C(=O)c2ccc(C)s2)c3scnc3n1)c4ccnc4</chem>	99
41	<chem>Cc1c(nc(N)c2nc3ccccc3n12)c4ccccc4</chem>	113.7
42	<chem>Cc1ccc(s1)C(=O)c2nc(NCc3cncn3)nc4ccsc24</chem>	116
43	<chem>C[C@@H](Nc1nc(C(=O)c2ccc(C)s2)c3scnc3n1)c4ccccc4</chem>	118
44	<chem>COc1ccc(CNc2nc(N)c3[nH+]c(sc3n2)c4occc4)cc1</chem>	123
45	<chem>CCNc1nc(C(=O)c2ccc(C)s2)c3scnc3n1</chem>	126
46	<chem>CCCCc1nc2[nH]ncc2c3nc(nn13)c4ccccc4Cl</chem>	130
47	<chem>Nc1nc(nc2sc(nc12)c3ccccc3)c4occc4</chem>	163
48	<chem>COC(=O)Nc1cc(nc(n1)n2nc(C)cc2C)c3cncc(OC)c3</chem>	167
49	<chem>CCCCc1nc2[nH]c[nH+]c2c3nc(nn13)c4ccc(C)cc4</chem>	180
50	<chem>Cc1ccc(s1)C(=O)c2nc(NCc3ccnc3)nc4ccsc24</chem>	186
51	<chem>CCCCc1nc2[nH]c[nH+]c2c3nc(nn13)c4ccc(C)c4</chem>	188
52	<chem>CCCCC1nc2[nH]c[nH+]c2c3nc(nn13)c4ccccc4</chem>	200
53	<chem>Cc1oc(cc1)c2nc(N)nc3N(CCc4ccccc4)C(=O)C=Nc23</chem>	208
54	<chem>CCCCc1nc2[nH]c[nH+]c2c3nc(nn13)c4occc4</chem>	210
55	<chem>Nc1cc(NC(=O)CN2CCCC2)cc3nc(oc13)c4occc4</chem>	250
56	<chem>C[C@H](O)CCc1nc(N)c2nc(n(C)c2n1)n3ncn3</chem>	260
57	<chem>CNc1cc2nc(NCc3ccnc3)nc(C(=O)c4cccs4)c2s1</chem>	276.8
58	<chem>Nc1nc(nc2sc(nc12)c3occc3)c4occc4</chem>	301
59	<chem>CN(C)c1cc2nc(NCc3ccnc3)nc(C(=O)c4cccs4)c2s1</chem>	318.3
60	<chem>Cc1ccc(s1)C(=O)c2nc(NCCc3ccnc3)nc4ccsc24</chem>	351
61	<chem>CCc1nc2[nH]c[nH+]c2c3nc(nn13)c4ccccc4</chem>	360
62	<chem>O=C(c1ccsc1)c2nc(NCc3ccnc3)nc4ccsc24</chem>	405
63	<chem>[O-]C(=O)C[C@@H]1CC[C@@H](CC1)Oc2ccc(en2)c3ccc(en3)c4nc5cc(ccc5[nH]4)C#N</chem>	430
64	<chem>Cc1ccc(cc1)C(=O)c2nc(NCc3ccnc3)nc4ccsc24</chem>	442
65	<chem>C[C@H](O)CCc1nc(N)c2nc(n(C)c2n1)n3ncn3</chem>	450
66	<chem>C[C@H](Nc1nc(C(=O)N2CCCC2)c3scnc3n1)c4ccnc4</chem>	468
67	<chem>Cc1oc(cc1)c2nc(N)nc3N(Cc4ccccc4)C(=O)C=Nc23</chem>	481.7
68	<chem>CCCCc1nc2[nH]c[nH+]c2c3nc(nn13)c4ccc(F)cc4</chem>	510
69	<chem>Cc1oc(cc1)c2nc(N)nc3N(CCCc4ccccc4)C(=O)C=Nc23</chem>	712
70	<chem>O=C(c1nccs1)c2nc(NCc3ccnc3)nc4ccsc24</chem>	732
71	<chem>CCCCc1nc2[nH]ncc2c3nc(nn13)c4cccc(Cl)c4</chem>	760
72	<chem>[O-]C(=O)CC1CCC(CC1)OC2CCN(CC2)c3ccc(en3)c4nc5c(F)cccc5[nH]4</chem>	910
73	<chem>Cc1ccc(s1)C(=O)c2nc(NCc3ccnc3)nc4ccsc24</chem>	990

74	<chem>Cc1oc(cc1)c2nc(N)nc3N(CC4CC4)C(=O)C=Nc23</chem>	1,010
75	<chem>COc1cccc1CN2C(=O)C=Nc3c2nc(N)nc3c4oc(C)cc4</chem>	1,016
76	<chem>Cc1oc(cc1)c2nc(N)nc3c2nc(O)n3Cc4cccc4</chem>	1,030
77	<chem>O=C(c1ccnc1)c2nc(NCc3ccnc3)nc4ccsc24</chem>	1,168
78	<chem>Cc1oc(cc1)C(=O)c2nc(NCc3ccnc3)nc4ccsc24</chem>	1,252
79	<chem>COC(=O)Nc1nc2cc(ccc2[nH]1)S(=O)c3cccc3</chem>	1,504
80	<chem>Clc1ccc(s1)C(=O)c2nc(NCc3ccnc3)nc4ccsc24</chem>	1,541
81	<chem>CCCCc1nc2[nH]c[nH+]c2c3[nH+]c(n13)c4ccc(OC)cc4</chem>	1,600
82	<chem>O=C(c1cccc1)c2nc(NCc3ccnc3)nc4ccsc24</chem>	1,619
83	<chem>Cc1[nH]c2nc(nc(NCc3ccnc3)c2c1C)c4cccc4</chem>	1,711
84	<chem>O=C(c1ccnc1)c2nc(NCc3ccnc3)nc4ccsc24</chem>	1,942
85	<chem>Cn1c(nc2c(N)nc(CCCCO)nc12)n3ncn3</chem>	2,100
86	<chem>C[C@@H](Nc1nc(C(=O)N2CCCC2)c3sccc3n1)c4ccnc4</chem>	2,347
87	<chem>CCCCc1nc2[nH]nc2c3[nH+]c(n13)c4ccc(OC)cc4</chem>	2,600
88	<chem>CC(C)NC(=O)c1nc(NCc2ccnc2)nc3ccsc13</chem>	2,610
89	<chem>CCc1cc2nc(NCc3ccnc3)nc(C(=O)c4ccsc4)c2s1</chem>	3,750
90	<chem>COc1cccc1N2CCN(CCN3C(=O)C=Nc4c3nc(N)nc4c5oc(C)cc5)CC2</chem>	3,810.50
91	<chem>CCCCc1nc2cccc2c3[nH+]c(n13)c4ccc(O)cc4</chem>	5,300
92	<chem>O=C(N1CCCC1)c2nc(NCc3ccnc3)nc4ccsc24</chem>	6,136
93	<chem>Cc1ccc(s1)C(=O)c2ncnc3ccsc23</chem>	6,685
94	<chem>CNC(=O)c1nc(NCc2ccnc2)nc3ccsc13</chem>	7,107
95	<chem>CCCC(=O)Oc1ccc(CCNc2nc(N)c3nc(n(C)c3n2)n4ncn4)cc1</chem>	9,770
96	<chem>CNC(=O)[C@H]1O[C@H]([C@H](O)[C@H]1O)n2cnc3c(NCCCCc4cccc4)ncnc23</chem>	14,600

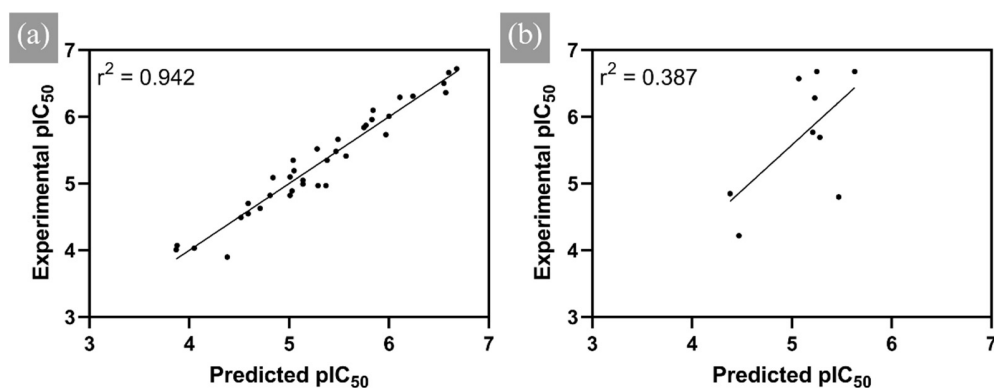
Test Set

1	<chem>Nc1nc2c(cnn2CCc3cccc3)c4nc(n14)c5occc5</chem>	12
2	<chem>Nc1nc(SCc2cccc(CO)c2)c(C#N)c(c3occc3)c1C#N</chem>	22
3	<chem>CC(=O)Nc1cc(nc(n1)n2nc(C)cc2C)c3cccc(n3)N4CCC(O)CC4</chem>	22
4	<chem>CC(C)(C)c1ccc(cc1)c2cn3c4cccc4nc3c(N)n2</chem>	33
5	<chem>CC(=O)Oc1ccc(CCNc2nc(N)n3nc(nc3n2)c4occc4)cc1</chem>	38.9
6	<chem>CCOC(=O)CCCOc1ccc(CCNc2nc(N)n3nc(nc3n2)c4occc4)cc1</chem>	50
7	<chem>COc1ncnc(c1)c2cc(NC(=O)C)nc(n2)n3nc(C)cc3C</chem>	57
8	<chem>COCCN(C)c1cccc(n1)c2cc(NC(=O)C)nc(n2)n3nc(C)cc3C</chem>	70
9	<chem>Nc1nc(cn2c3cccc3nc12)c4ccc(O)cc4</chem>	81.3
10	<chem>Cc1oc(cc1)c2nc(N)nc3N(CCC4CCN(CC4)c5cccc5)C(=O)C=Nc23</chem>	279
11	<chem>C[C@@H](O)CCc1nc(N)c2nc(n(C)c2n1)n3ncn3</chem>	420
12	<chem>Cc1ccc2[nH]c(nc2n1)c3ccc(nc3)c4ccc(O[C@H]5CC[C@H](CC(=O)[O-])CC5)nc4</chem>	490
13	<chem>Nc1nc2c(cnn2Cc3ccc(OCc4cccc4)cc3)c5nc(n15)c6occc6</chem>	500
14	<chem>Nc1nc(nc2nc(n12)c3occc3)N4CCCN(CCC5cccc6NC(=O)Cc56)CC4</chem>	1,479
15	<chem>O=C(c1cnsc1)c2nc(NCc3ccnc3)nc4ccsc24</chem>	1,715
16	<chem>Cc1[nH]c2nc(nc(N[C@@H]3CCCCNC3=O)c2c1C)c4cccc4</chem>	2,060
17	<chem>CCNC(=O)c1nc(NCc2ccnc2)nc3ccsc13</chem>	2,516
18	<chem>CCCCc1nc2[nH]nc2c3[nH+]c(n13)c4ccc(OCC)cc4</chem>	2,700
19	<chem>CCOc1ccc(CCNc2nc(N)c(nc2Cl)C(=O)[NH+]=C(N)N)cc1</chem>	3,400
20	<chem>C=Cc1cc2nc(NCc3ccnc3)nc(C(=O)c4ccsc4)c2s1</chem>	3,750
21	<chem>C[C@@H](Nc1nc(C(=O)N2CCCC2)c3sccc3n1)c4ccnc4</chem>	6,760
22	<chem>Cc1ccc(s1)C(=O)c2nc(C)nc3ccsc23</chem>	7,847
23	<chem>Clc1ccc(CO[C@H](Cn2ccnc2)c3ccc(Cl)cc3Cl)c(Cl)c1</chem>	14,253
24	<chem>CCNC(=O)[C@H]1O[C@H]([C@H](O)[C@H]1O)n2cnc3c(NCCCCc4cccc4)ncnc23</chem>	26,500

Table S7. Electronic properties of ligand forms of *R. palmatum* major metabolites (in eV).

Ligand	Form	ϵ_{HOMO}	ϵ_{LUMO}	$\Delta\epsilon$	η	μ	ω
Aloe-emodin	1	-6.8537	-3.1767	3.6770	1.8385	-5.0152	6.8403
	2	-6.4134	-3.4512	2.9622	1.4811	-4.9323	8.2128
	3	-6.2245	-3.2879	2.9365	1.4683	-4.7562	7.7035
	4	-5.1081	-2.5442	2.5639	1.2820	-3.8261	5.7097
	5	-5.3011	-2.8360	2.4651	1.2326	-4.0686	6.7149
	6	-4.6440	-1.9205	2.7235	1.3617	-3.2822	3.9557
Chrysophanol	1	-6.8255	-3.1426	3.6829	1.8415	-4.9840	6.7448
	2	-6.3779	-3.3847	2.9933	1.4966	-4.8813	7.9602
	3	-6.2081	-3.2660	2.9421	1.4710	-4.7371	7.6271
	4	-5.0816	-2.4914	2.5902	1.2951	-3.7865	5.5353
	5	-5.0780	-2.8130	2.2650	1.1325	-3.9455	6.8729
	6	-4.5940	-1.8685	2.7255	1.3627	-3.2312	3.8308
Emodin	1	-5.1484	-2.5171	2.6313	1.3157	-3.8328	5.5829
	2	-5.1222	-2.8273	2.2949	1.1475	-3.9747	6.8842
	3	-4.9383	-2.8029	2.1354	1.0677	-3.8706	7.0159
	4	-4.6185	-1.8930	2.7255	1.3627	-3.2558	3.8892
	5	-4.6926	-2.3628	2.3298	1.1649	-3.5277	5.3416
Physcion	1	-6.7375	-3.1065	3.6310	1.8155	-4.9220	6.6719
	2	-6.1298	-3.2090	2.9208	1.4604	-4.6694	7.4648
	3	-6.3698	-3.4146	2.9551	1.4776	-4.8922	8.0989
	4	-5.1309	-2.4979	2.6329	1.3165	-3.8144	5.5260
	5	-5.2727	-2.7692	2.5034	1.2517	-4.0210	6.4584
	6	-4.6005	-1.8755	2.7250	1.3625	-3.2380	3.8475
Rhein	1	-6.1419	-3.1308	3.0111	1.5055	-4.6363	7.1387
	2	-6.1363	-3.3761	2.7601	1.3801	-4.7562	8.1958
	3	-6.1499	-3.2503	2.8997	1.4498	-4.7001	7.6185
	4	-4.9859	-2.4559	2.5300	1.2650	-3.7209	5.4723
	5	-5.1946	-2.7709	2.4237	1.2119	-3.9828	6.5447
	6	-4.5353	-1.8210	2.7143	1.3571	-3.1782	3.7213
Dopamine *		-6.2276	-0.4518	5.7758	2.8879	-5.0152	1.9310
Levodopa *		-6.2883	-0.5905	5.6979	2.8489	-4.9323	2.0761

* Standard drugs.

**Figure S1.** Experimental and predicted IC_{50} correlation of (a) training dataset and (b) test dataset for a 3D-QSAR model of ASN.

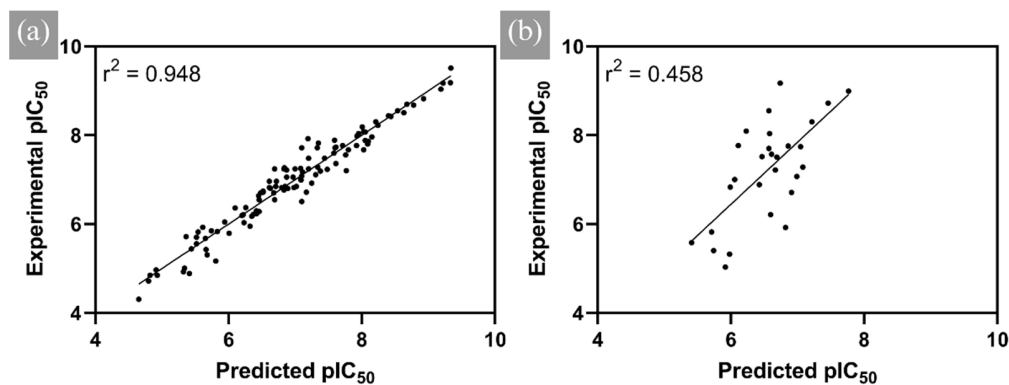


Figure S2. Experimental and predicted IC_{50} correlation of (a) training dataset and (b) test dataset for a 3D-QSAR model of MAOB.

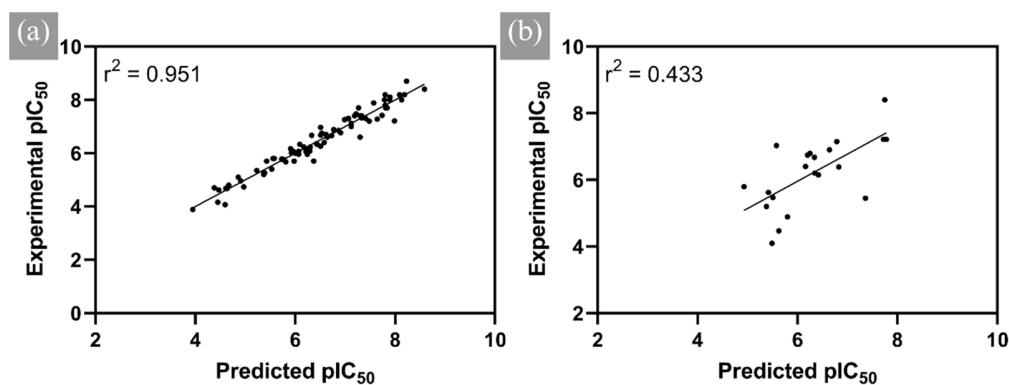


Figure S3. Experimental and predicted IC_{50} correlation of (a) training dataset and (b) test dataset for a 3D-QSAR model of COMT.

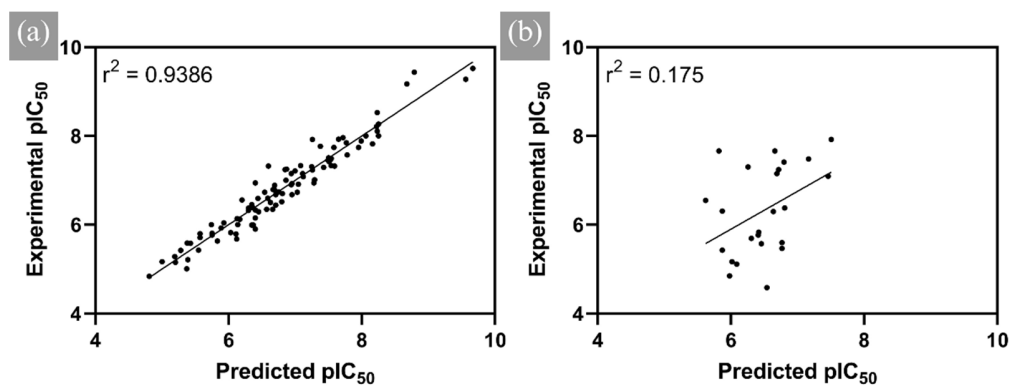


Figure S4. Experimental and predicted IC_{50} correlation of (a) training dataset and (b) test dataset for a 3D-QSAR model of A_{2A}AR.

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