Discovery of New Acetyl- and Butyrylcholinesterase Inhibitors through Structure-Based Virtual Screening

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Supporting information

Table S1. The SMILES format of all the 24 potential hits, and they were validated by Pan Assay Interference Compounds (PAINS) filter.

Chemdiv ID	SMILES string	PAINS filter
C749-0087	CO/C1=C/C=C(C=C1)C=2N=C(ON=2)N3CCN(CC3)C/C5=C/C=C4OCOC4=C5	pass
8003-0197	C/C1=C/C(=NN1CC(=O)N3CCN(C/C2=C/C=CC=C2)CC3)[N+](=O)[O-]	pass
C611-0434	CO/C5=C/C=C(/NC(=O)C=3[S]C2=NC=1CCN(CC=1C=C2C=3N)C/C4=C/C=CC=C4)C(=C5)OC	pass
C629-0196	CC=2N=C1C=CC=CC1=C3OC(=CC=23)C(=O)NC4([H])CCN(CC4)C/C5=C/C=CC=C5	pass
C437-0121	[O-]/[N+]3=C(\NC1([H])CCN(CC1)C/C2=C/C=CC=C2)C(=NN3/C5=C/C=C4OCCOC4=C5)[N+](=O)[O-]	pass
4964-1479	CO/C1=C/C=C(C=C1)OCC(=O)N3CCN(C/C2=C/C=CC([F])=C2)CC3	pass
5905-2743	CO/C1=C/C=C(/C=C1/OC)NC(=O)C2=CC=C(C=C2)CN4CC3=CC=CC=C3CC4	pass
C590-0093	C/C1=C/C=C(C=C1)C=2C=C(NN=2)C(=O)N4CCN(C/C3=C/C=CC=C3)CC4	pass
K284-5464	CO/C1=C/C4=C(/C=C1/OC)N=C([S]CC(=O)NCC/C2=C/C=CC=C2)N(C/C3=C/C=CO3)C4=O	pass

6048-0476	O=C(/C2=C/C(=NC1=CC=CC=C12)C4=CC=C3OCOC3=C4)N7CCN(C/C6=C/C=C5OCOC5=C6)CC7	pass
G070-1566	CN1C=C(/C=C1/C(=O)OC)[S](=O)(=O)NCC2([H])CCN(CC2)C/C3=C/C=C/C=C3/[F]	pass
G421-0271	CO/C1=C/C(=CC(=C1)OC)N/C3=N/C=C2CN(CCC2=N3)C/C4=C/C=CC([F])=C4	pass
G900-0252	O=C(NCC1([H])CCN(CC1)C/C2=C/C=CC([Cl])=C2)C4=CC=C3C=C/C=C(/O)C3=N4	pass
D305-0628	CC(=O)N1CCN(CC1)C/C3=N/C2=CC(=CC=C2N3CC)NC(=O)C4=C/C=C(/OC)C(=C4)OC	pass
F687-0560	COCC(=O)N/C1=C/C=C(/C=C1/C(=O)O)N2CCN(CC2)C/C3=C/C=C/C=C3/[F]	pass
D434-0535	CN(C)[S](=O)(=O)C1=CC=C(C=C1)C2=NC(C#N)=C(O2)N3CCN(CC3)C/C4=C/C=CC=C4	pass
G115-0283	C/C1=C/C=C/C=C1/CN2CCC([H])(CC2)CN[S](=O)(=O)C4=CC=C3NC(=O)CCCC3=C4	pass
G801-0274	CN2C1=CC=C(C=C1N(C)C2=O)[S](=O)(=O)NCC3([H])CCN(CC3)C/C4=C/C=C(/[F])C=C4	pass
F048-0694	O=C(N/C2=N/C=1CCN(CC=1[S]2)C/C3=C/C=CC=C3)C5=CC=C4OCCOC4=C5	pass
C599-1080	CO/C1=C/C=C(/C=C1/OC)C=4/N=C(/CN2CCN(CC2)C3=CC=C(C=C3)[N+](=O)[O-])ON=4	fail
C590-0150	CO/C1=C/C=C(C=C1)C=2C=C(NN=2)C(=O)N4CCN(C/C3=C/C=C(/[F])C=C3)CC4	pass
S211-1317	[H]C2(CCN(C/C1=C/C=CN1)CC2)OC/C3=N/C(=NO3)C4=CN=CC=N4	pass
S211-1044	COCCC=3/N=C(/COC2([H])CCN(C/C1=C/C=CO1)CC2)ON=3	pass
P867-0190	O/C1=C/C=C(/[Br])C=C1CN2CCN(CC2)C3=CC(=NN3)C4=CC=NC=C4	fail

Table S2. The predicted CLogP and Binding energy of all the 5 validated hits.

Chemdiv ID	ChEs inhibition IC_{50} (μM)		CLogP [a]	Binding energy (kcal/mol) [b]	
	AChE	BuChE		AChE	BuChE
C629-0196	1.28 ± 0.83	nd	4.21	47.78	-
G070-1566	2.10 ± 0.40	0.78 ± 0.14	3.29	46.33	49.98
G115-0283	6.61 ± 2.73	5.11 ± 4.21	3.72	49.19	44.11
G801-0274	2.05 ± 0.11	0.031 ± 0.006	3.00	54.51	53.96
F048-0694	3.78 ± 0.32	2.03 ± 0.35	3.77	46.07	40.82
donepezil	0.008 ± 0.001	nd	4.60	-	-

a CLogP is predicted by ChemDraw package 13.0.

b Binding energy is predicted by CDOCKER module in BioVIA Discovery Studio

package.