Supplementary Data

Tripeptides inhibit dual targets AChE and BACE-1: a computational study

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Supplementary Data

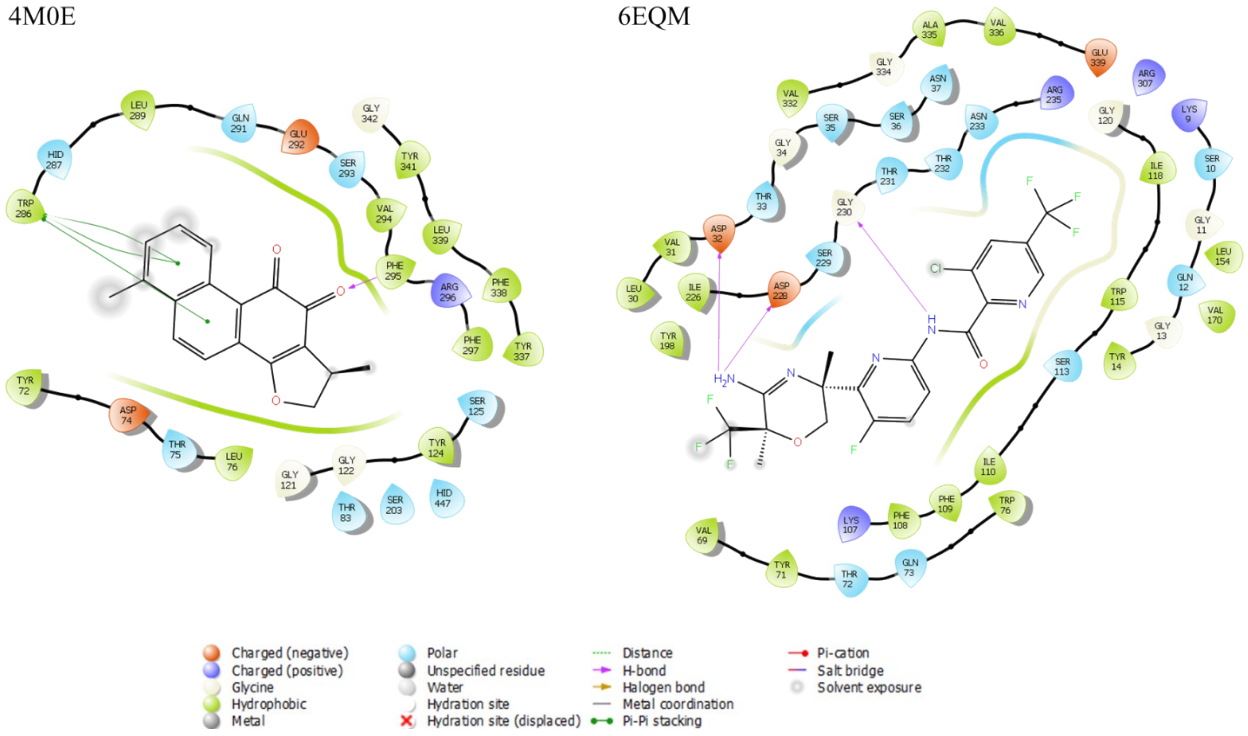
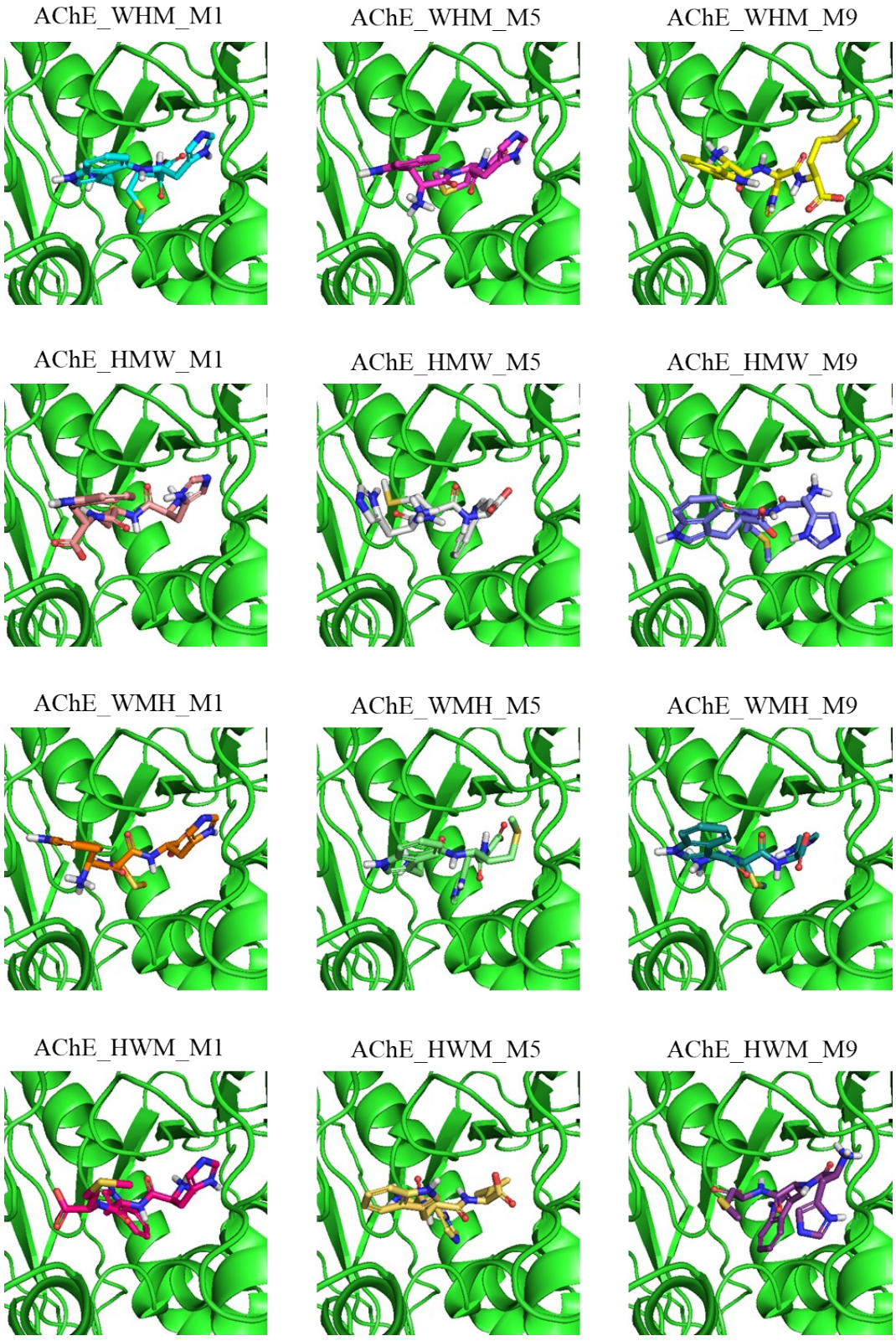


Figure S1. Residues in the active sites of AChE (PDB: 4M0E) and BACE-1 (PDB: 6EQM).

Supplementary Data

A



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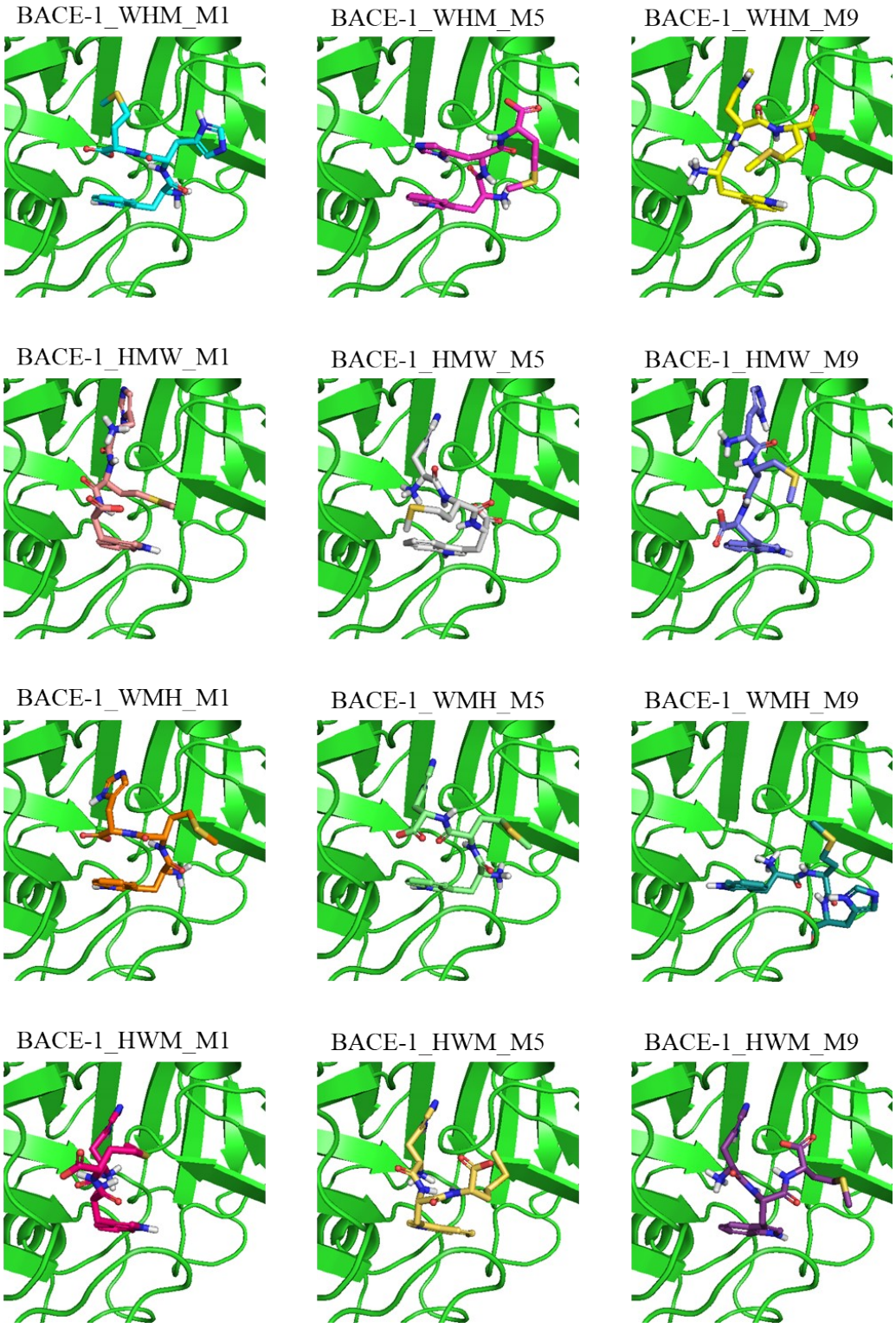

Figure S2. Representative binding poses (Model 1, Model 5, and Model 9) obtained from mVina docking of the four tripeptides with AChE (A) and BACE-1 (B)

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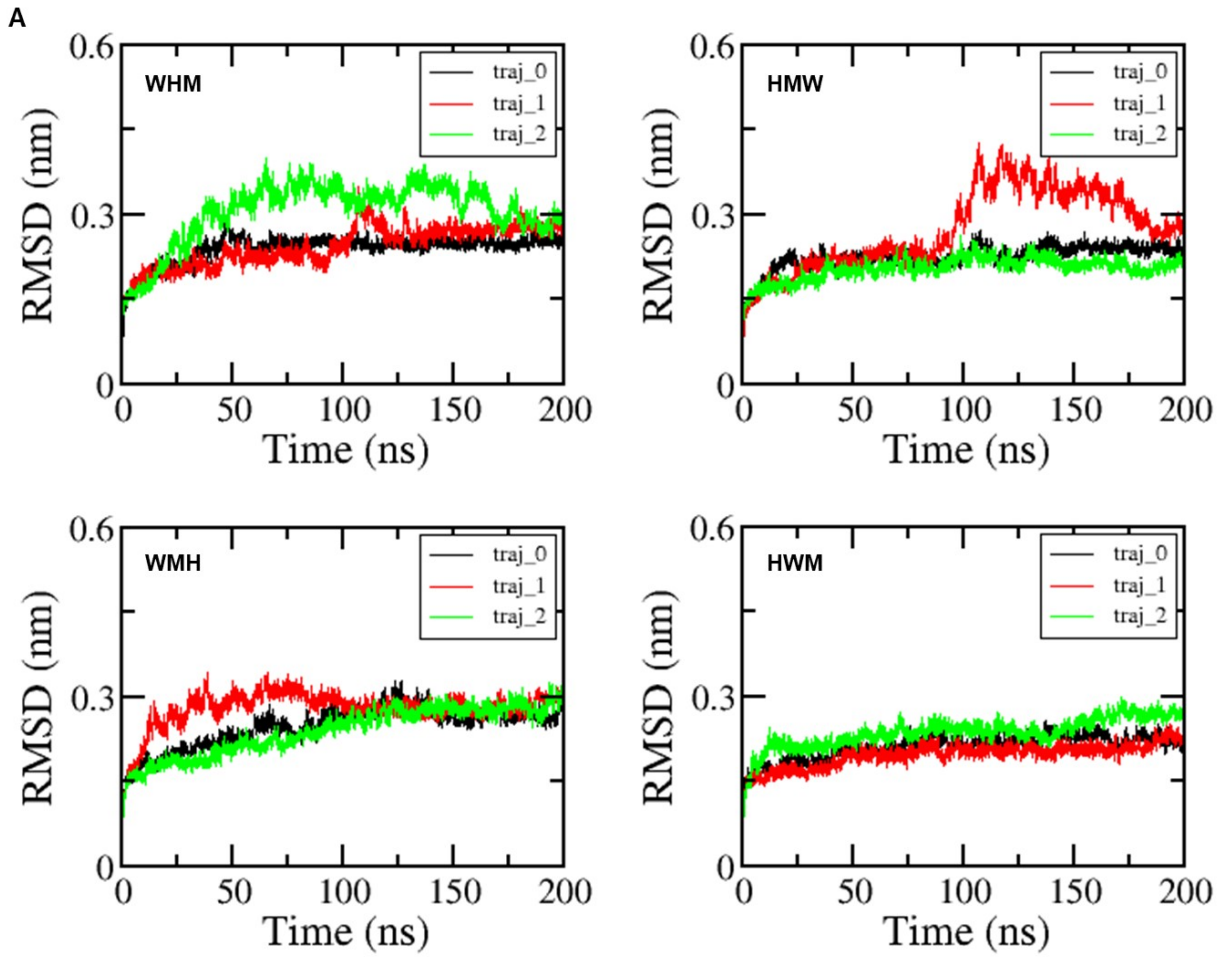

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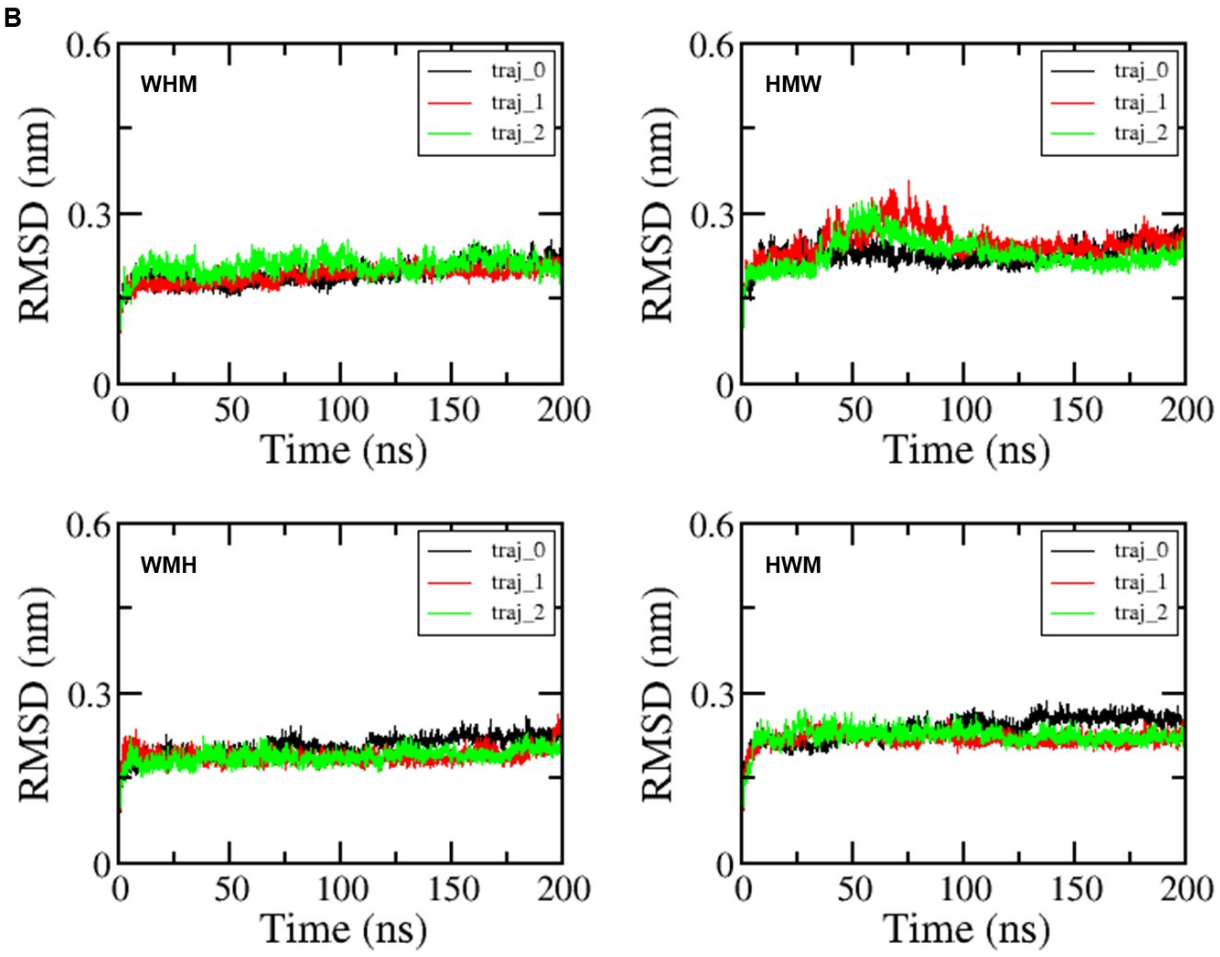

Figure S3. All-atom RMSD of simulated AChE/BACE-1 complexes over 3 independent 200 ns-MD simulations. (A) AChE complexes. (B) BACE-1 complexes

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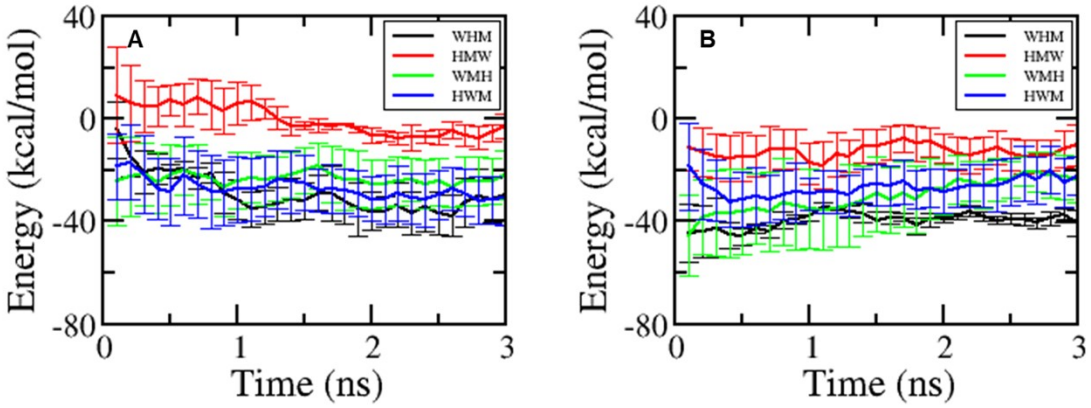

Figure S4. Time dependence of energies for complexes. The error bars show the standard error of mean. (A) Energy of AChE complexes. (B) Energy of BACE-1 complexes.

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Table S1. Docking scores obtained using mVina, ranked from the highest (MODEL 1) to the lowest (MODEL 9)

	AChE				BACE-1			
MODEL	WHM	HMW	WMH	HWM	WHM	HMW	WMH	HWM
1	-16.6	-16.3	-16.9	-16.9	-14.4	-15.1	-14.5	-15.2
2	-16.3	-16.2	-16.7	-16.6	-14.3	-15.0	-14.2	-14.9
3	-16.0	-16.1	-16.3	-16.5	-14.0	-14.9	-14.2	-14.7
4	-15.9	-16.0	-16.2	-16.2	-14.0	-14.9	-14.1	-14.7
5	-15.8	-15.7	-16.2	-16.0	-13.9	-14.9	-13.8	-14.6
6	-15.8	-15.7	-16.1	-15.8	-13.8	-14.8	-13.8	-14.6
7	-15.7	-15.3	-15.9	-15.7	-13.7	-14.8	-13.8	-14.5
8	-15.6	-15.2	-15.8	-15.5	-13.7	-14.8	-13.8	-14.5
9	-15.6	-15.0	-15.8	-15.3	-13.6	-14.8	-13.8	-14.4

Table S2. The coordinate of the minima corresponds to the most stable configuration.

No	**AChE complex**	**Projection on eigenvectors (nm)**	
		CV1	**CV2**
1	WHM	4.17679	-4.87185
2	HMW	10.24750	-3.35025
3	WMH	5.18017	1.34624
4a	HWM	1.61920	2.22383
4b		4.58528	-1.93793
No	**BACE-1 complex**	**Projection on eigenvectors (nm)**	
		CV1	**CV2**
5	WHM	1.50125	0.80849
6a	HMW	-1.09593	-3.85557
6b		-3.86125	2.22181
7a	WMH	3.43023	-0.47795
7b		-4.13640	-0.51194
8	HWM	-2.27997	2.19805

Table S3. ADMET profiles of the four tripeptides

Parameter	WHM	HMW	WMH	HWM	Note
AlogP98[a]	0.0056	0.0056	0.0056	0.0056	-0.4 < log P <5.6 (Ghose filter) [1]
LogBB	-1.458	-1.469	-1.456	-1.461	logBB < 0: poorly distribution in the brain [2]
BBB	0.0348129	0.0339737	0.0350283	0.034576	1>BBB: limited blood–brain barrier penetration [2]
HIA	54.860	54.860	54.860	54.861	30% ≤ HIA ≤ 80%: moderate absorption
PPB	48.843504	52.436912	48.740752	48.274259	50% ≤ PPB ≤ 90%: Moderate binding
Caco2 permeability	20.7489	20.9695	20.9777	20.7643	4 ~ 70: moderate
CYP_2D6_inhibition	Non	Non	Non	Non	Non: Acceptant
CYP_2D6_substrate	Non	Non	Non	Non	
Ames_test	mutagen	mutagen	mutagen	mutagen	
Carcino_Mouse	negative	negative	negative	negative	
hERG_inhibition	high_risk	high_risk	high_risk	high_risk	

[a]AlogP98, introduced in 1998, is a specialized version of AlogP, an advanced refinement of logP. Unlike logP, which provides a general measure of the partition coefficient, AlogP accounts for the individual contributions of each atom in a molecule, offering a more detailed and accurate representation of molecular properties.

References

[1] A.K. Ghose, V.N. Viswanadhan, J.J. Wendoloski, J. Comb. Chem. 1 (1999) 55.
[2] Ajay, G.W. Bemis, M.A. Murcko, J. Med. Chem. 42 (1999) 4942.