Structural and molecular features of acetylcholinesterase targeting small molecules: Leveraging in-silico tools to combat Alzheimer's disease

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Supplementary information

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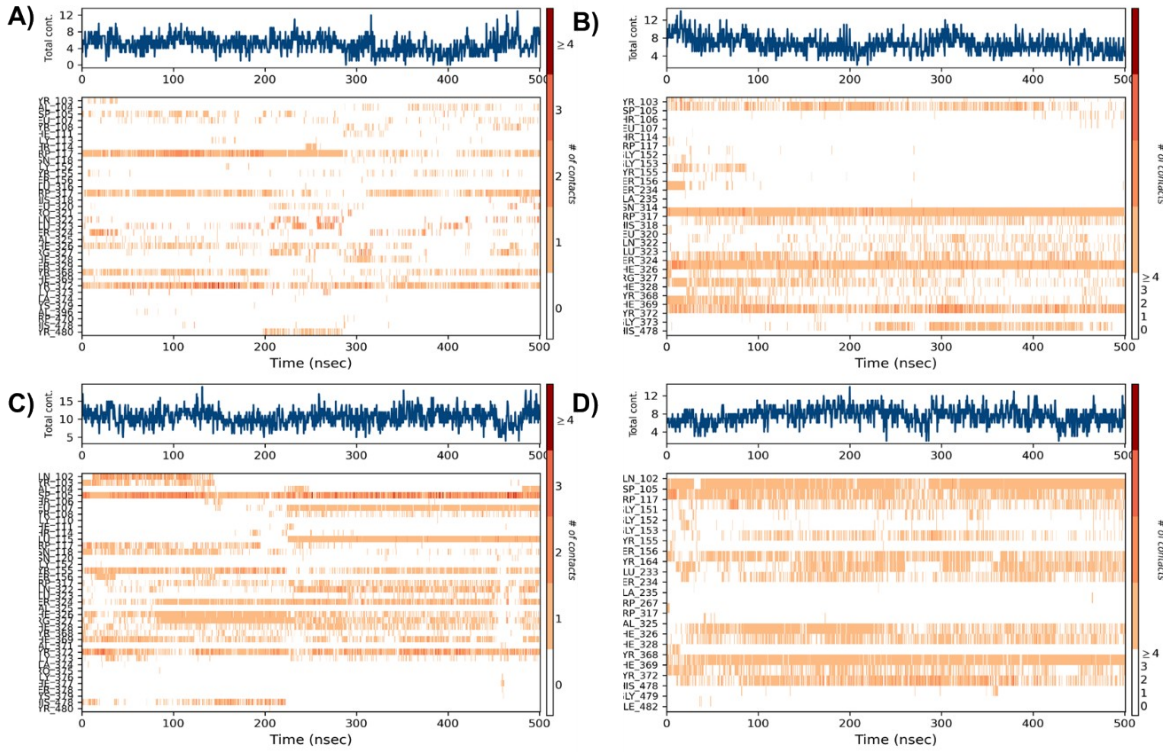
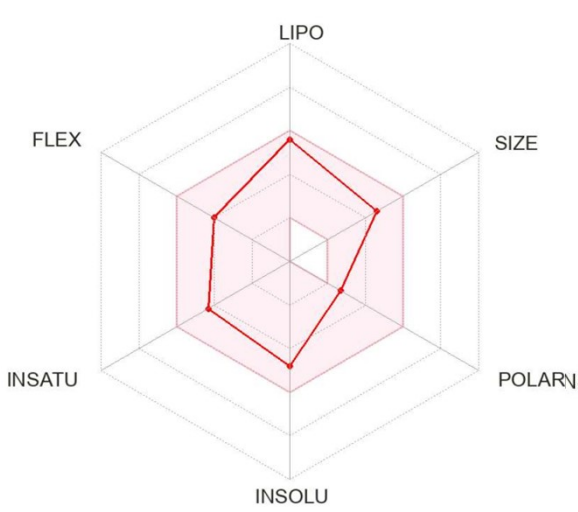


Figure SF1: Interactions and contacts formed between the compounds and hAChE complexes in a timeline format during the 500 ns MD simulation. The protein-ligand contacts of (A) donepezil, (B) 73058259, (C) 141100002, and (D) 44285707.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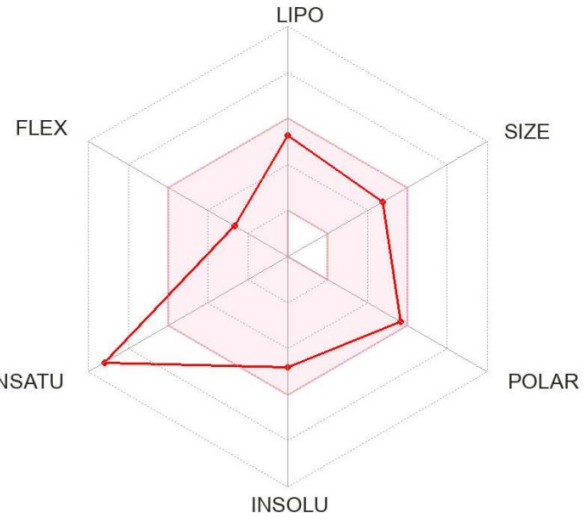
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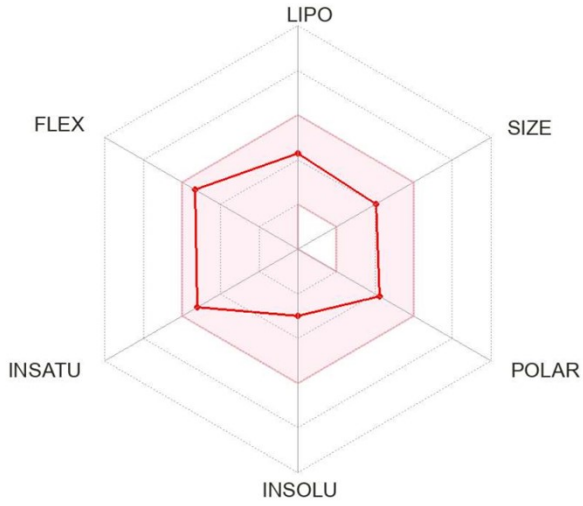
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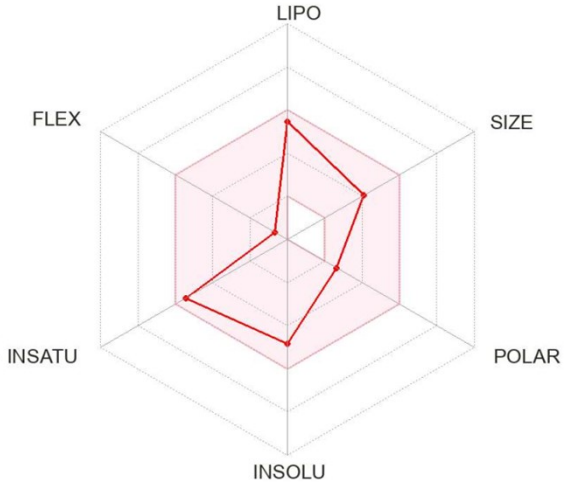
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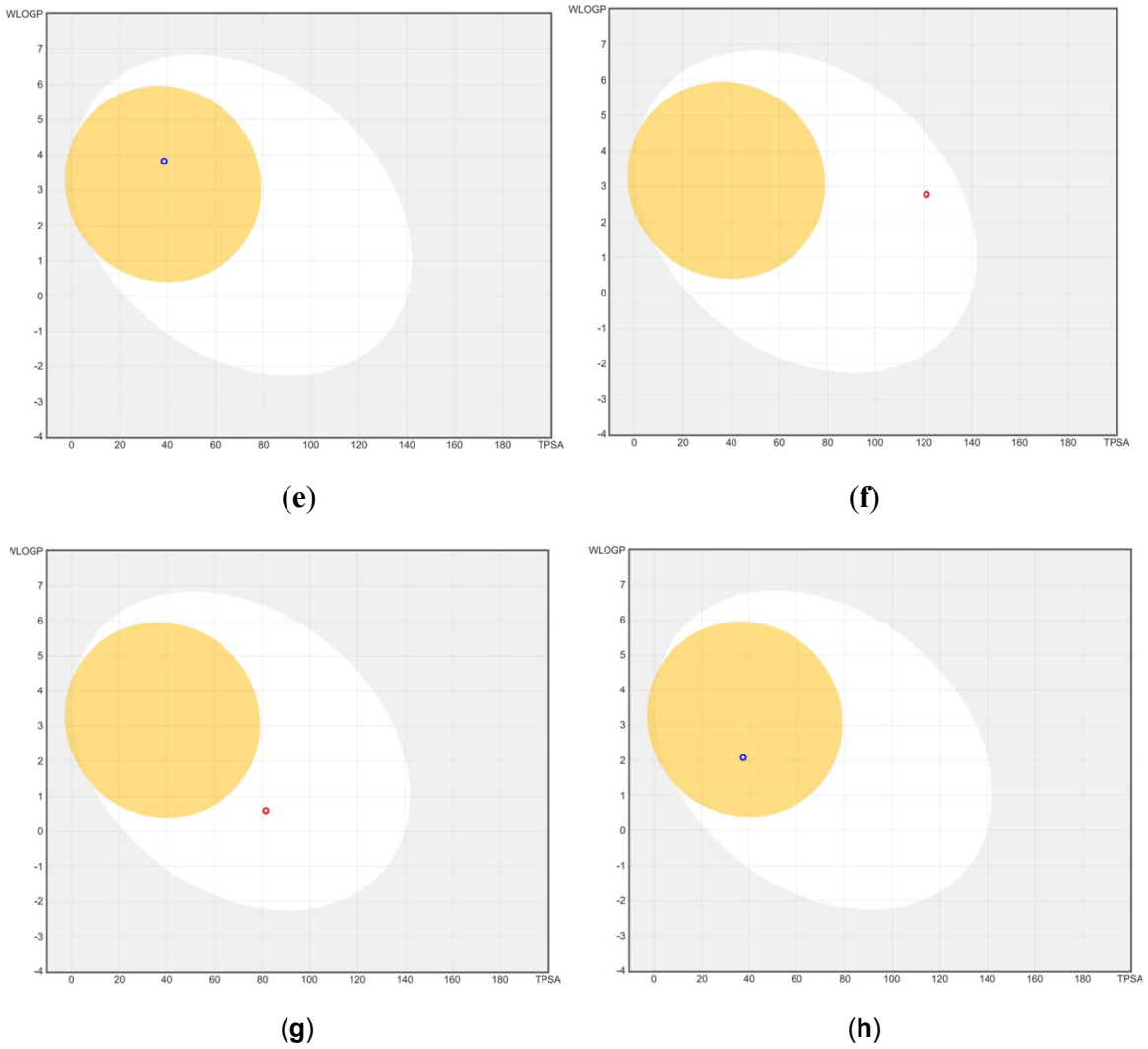

Figure SF2: Predicted radar plots and Brain Or IntestinaL EstimateD permeation (BOILED)-Egg diagram. Plots were obtained using the SwissADME web tool and the result of donepezil (a/e), 73058259 (b/f), 141100002 (c/g) and 44285707 (d/h) are shown. Typical values for a molecule to fall the pink area are as follows: lipophilicity = −0.7 to + 5.0; size: 150 g/mol < molecular weight < 500 g/mol; polarity: 20 $Å^2$ < topological polar surface area (TPSA) < 130 $Å^2$; insolubility: 0 < LogS < 6; and INSATU (insaturation): 0.25 < fraction of carbons in sp^3 hybridization < 1; and flexibility: 0 < number of rotatable bonds < 9.

Table ST1: SMILES strings of the reference and identified compounds.

Comp.	SMILES
Donepezil	O=C1C(CC2=CC(OC)=C(OC)C=C21)CC3CCN(CC3)CC4=CC=CC=C4
73058259	O=C1C2=C(C=C(COC(C3=CC=C(O)C=C3)=O)C=C2O)C(C4=CC=CC(O)=C41)=O
141100002	O=C(C(C)(C)O)C(C=C1)=CC=C1C([NH2+]CCC[NH3+])C2=CC=CC=C2
44285707	OC1=CC(C23CC(C(C([NH+](C)CC3)C2)=C4)=NC5=C4C=CC=C5)=CC=C1

Table ST2: The drug-likeness properties of the shortlisted compounds.

Compound	# Rotatable Bonds	CNS	Mol MW	Dipole	SASA	FOSA	FISA	PISA	Volume	HBD	HBA	PSA	RO5
Donepezil	6	1	379.49	3.54	714.44	415.7	46.23	252.47	1282.94	0	5.5	50.15	0
141100002	10	0	326.44	4.92	661.09	257.96	133.80	269.33	1159.48	4	5.25	81.60	0
44285707	1	1	330.43	2.83	602.22	194.04	71.18	336.99	1070.21	1	3.75	39.22	0
73058259	6	-2	390.35	3.18	663.28	34.29	271.39	357.60	1158.13	1	6.25	150.75	0

Table ST3: The ADMET properties of the selected compounds were assessed.

Title	QPpolrz	QPlog PC16	QPlog Poct	QPlog Pw	QPlog Po/w	QPlog S	CIQP logS	QPlog HERG	QPP Caco	QPlog BB	QPPM DCK	QPlog Kp	QPlog Khsa	%HOA
Donepezil	43.748	12.287	17.068	7.564	4.435	-4.68	-4.338	-6.711	900.253	0.118	488.543	-2.969	0.616	100
141100002	36.399	12.74	20.654	12.876	2.42	-2.351	-2.158	-7.386	33.18	-0.61	15.253	-6.202	0.105	68.337
44285707	39.252	11.258	16.498	8.883	3.80	-4.504	-4.365	-6.451	522.124	0.23	271.129	-3.611	0.765	100
73058259	39.757	13.641	18.787	11.891	2.47	-5.077	-5.849	-6.407	26.444	-2.56	9.752	-4.685	0.277	66.839