SUPPLEMENTARY TABLES

Supplementary Table 1. Enzyme binding sites identified in blind docking experiments with acetylcholinesterase (AChE; PDB: 4M0E) [90] and butyrylcholinesterase (BChE; PDB: 4TPK) [91] for senolytic and nootropic drugs 1-6 using Molecular Operating Environment 2022.02 (Chemical Computing Group ULC, Montreal, Quebec, Canada).

Compound	AChE blind docks					BChE blind docks				
	Site **I**	Site **II**	Site **III**	Site **IV**	Site **V**	Site **I**	Site **II**	Site **III**	Site **IV**	Site **V**
1	–[a]	12/15	3/15	–	–	–	6/15	9/15	–	–
2	–	6/15	6/15	–	3/15	–	–	12/15	–	3/15
3	12/15	3/15	–	–	–	3/15	–	9/15	3/15	–
4	6/15	9/15	–	–	–	9/15	–	6/15	–	–
5	3/15	9/15	3/15	–	–	–	–	15/15	–	–
6	6/15	3/15	–	6/15	–	6/15	–	6/15	–	3/15

[a]The number of docking poses for 1-6 at each indicated binding site (enzyme active site gorge (I), cholinesterase (ChE) pocket behind acyl loop (II), pocket behind ChE catalytic glutamate (III), pocket behind key ChE active site tryptophan (Back Door, IV), or other site (V)) are shown from triplicate blind docking experiments (3 x 5 poses).

Supplementary Table 2. *In silico* predicted inhibition constants (K_i values) for compounds 1-6 with acetylcholinesterase (AChE; PDB: 4M0E, 2.00 Å) [91] and butyrylcholinesterase (BChE; PDB: 4PTK, 2.70 Å) [92].

Compound	Predicted AChE K_i[a] (μM)	Predicted BChE K_i[a] (μM)
1	27.63*	0.35*
	126.20†	3.04†
2	16.17*	1.04†
	61.33†	5.09⁜
	110.20⁜	
3	5.32	16.49
	243.12*	32.46†
		55.33◊
4	5.14	16.66
	177.24*	24.76†
5	0.73	10.30†
	89.63*	
	361.53†	
6	11.92	16.14
	191.53*	42.96†
	299.72◊	48.38⁜

[a]Sites selected for directed docking were the enzyme active site (Site I, no symbol) or alternate sites (II-V) identified from blind docking experiments (II, *; III, †; IV, ◊; V, ⁜). Molecular docking experiments were completed using Molecular Operating Environment 2022.02 (Chemical Computing Group ULC, Montreal, Quebec, Canada).

Supplementary Table 3. *In silico* binding interactions of senolytics 1-5 and nootropic 6 with acetylcholinesterase (AChE, PDB: 4M0E) [91] and butyrylcholinesterse (BChE, PDB: 4TPK) [92] for top site-directed docking poses at cholinesterase (ChE) binding sites I-V.

Compound	Enzyme	Binding site (I-V)	Bonding residues[a]	Bond type[a]	Bond length[a] (Å)	Enzyme structure location[b]
1	AChE	**II**	N233	H-acceptor	3.08	Bottom wall of site gorge
			R296	H-acceptor	2.89	Acyl Loop
			R296	H-acceptor	3.21	Acyl Loop
		III	K332	H-acceptor	3.00	Site gorge wall
			R525	H-acceptor	3.19	Site gorge wall
			R525	π-H	4.03	Site gorge wall
	BChE	**II**	S235	H-acceptor	3.03	Acyl Loop
			S235	H-acceptor	3.04	Acyl Loop
			R242	H-acceptor	3.48	Acyl Loop
			V288	π-H	3.95	Acyl Loop, ABP
			F357	H-donor	3.16	Site gorge wall
			N397	H-acceptor	3.31	Site gorge wall
		III	D324	H-donor	2.92	Site gorge wall, beside Ɛ-helix
2	AChE	**II**	R296	H-acceptor	3.06	Acyl Loop
			R296	H-acceptor	3.21	Acyl Loop
		III	R521	H-acceptor	3.06	Site gorge wall
			R525	H-acceptor	3.50	Site gorge wall
		V	Q181	π-H	3.92	Site gorge wall
	BChE	**III**	K323	H-acceptor	3.05	Site gorge wall
			V377	π-H	4.69	Site gorge wall
			D391	H-donor	2.99	Site gorge wall
			R515	H-acceptor	3.11	Site gorge wall
		V	-	-	-	-
3	AChE	**I**	Y72	H-donor	2.88	Ω-loop, PAS
			W86	H-donor	3.09	Ω-loop, PCS
			W86	π-π	3.77	Ω-loop, PCS
			W86	π-π	3.79	Ω-loop, PCS
			E202	H-donor	2.76	Bottom wall of site gorge
		II	R247	H-acceptor	3.02	Site gorge wall
	BChE	**I**	W82	π-π	3.74	Ω-loop, PCS
			W82	π-π	3.80	Ω-loop, PCS
			W82	H-donor	2.92	Ω-loop, PCS
			E197	H-donor	2.78	Bottom wall of site gorge
		III	Y373	π-H	3.99	Site gorge wall
			E387	H-donor	2.74	Site gorge wall
			D391	H-donor	2.89	Site gorge wall
			R515	H-acceptor	3.47	Site gorge wall
		IV	H77	π-H	3.49	Ω-loop
			M81	H-donor	3.81	Ω-loop
4	AChE	**I**	W86	π-π	3.79	Ω-loop, PCS
			W86	π-π	3.86	Ω-loop, PCS
			E202	H-donor	2.78	Bottom wall of site gorge
		II	R296	π-cation	3.48	Acyl Loop
			R296	π-cation	3.94	Acyl Loop
	BChE	**I**	W82	π-π	3.79	Ω-loop, PCS
			W82	π-π	3.81	Ω-loop, PCS

			E197	H-donor	2.77	Bottom wall of site gorge
		III	Y373	π-H	3.99	Site gorge wall
			E387	H-donor	2.74	Site gorge wall
			D391	H-donor	2.89	Site gorge wall
			R515	H-acceptor	3.47	Site gorge wall
		I	Y341	H-π	4.23	Ɛ-helix, PAS
		II	N233	H-donor	3.66	Bottom wall of site gorge
5	AChE	**III**	S399	H-acceptor	2.96	Site gorge wall
			D400	H-donor	2.82	Site gorge wall
			W442	H-donor	2.86	Opposite S336 of Ɛ-helix
			R525	π-cation	3.75	Site gorge wall
	BChE	**III**	-	-	-	-
		I	Y341	H-π	3.82	Ɛ-helix, PAS
			H447	π-H	3.98	Catalytic Triad
	AChE	**II**	R247	H-acceptor	3.06	Site gorge wall
			R247	H-acceptor	3.08	Site gorge wall
		IV	R463	H-acceptor	3.36	Site gorge wall
6		**I**	W82	π-H	4.36	Ω-loop, PCS
			W82	π-H	4.43	Ω-loop, PCS
		III	R515	H-acceptor	3.33	Site gorge wall
	BChE		Q517	H-acceptor	3.14	Site gorge wall
			Q518	H-acceptor	3.07	Site gorge wall
		V	Q47	H-acceptor	3.13	Site gorge wall
			Q176	H-acceptor	3.32	Site gorge wall

[a]Bonding interactions, type, and lengths were calculated using built-in Molecular Operating Environment (MOE) 2022.02 features (Chemical Computing Group ULC, Montreal, Quebec, Canada).

[b]ChE active regions are also denoted, catalytic active site (CAS), peripheral anionic site (PAS), acyl binding pocket (ABP), π-cationic site (PCS), and oxyanion hole (OAH). Docks that did not show any binding interactions are denoted with dashes.