

Supplementary Table 1. Effect of the HT hybrids on acetylcholinesterase, butyryl-cholinesterase and BACE-1 activity.

	AChE			BuChE			BACE-1	
HT hybrid	Concentration (μM)	IC₅₀ (μM)		Concentration (μM)	IC₅₀ (μM)		Concentration (μM)	IC₅₀ (μM)
HT1	2.5 – 5.0	6.5 ± 0.8		5 – 10	20.3 ± 2.4		2.5 – 25	11.3 ± 1.2
HT1a	2.5 – 5.0	4.3 ± 0.7		1.5 – 10	4.2 ± 0.4		2.5 – 25	16.9 ± 0.1
HT2	2.5 – 5.0	3.8 ± 0.3		5 – 10	31.8 ± 5.7		2.5 – 25	128.0 ± 42.0
HT3	2.5 – 5.0	4.0 ± 0.4		5 – 10	7.2 ± 0.9		2.5 – 25	76.8 ± 3.0
HT3a	2.5 – 5.0	2.6 ± 0.2		2.5 – 5	4.3 ± 0.9		2.5 – 25	19.7 ± 0.7
HT4	2.5 – 5.0	4.9 ± 0.5		5 – 10	22.9 ± 7.1		2.5 – 25	52.2 ± 2.1
HT4a	2.5 – 5.0	2.9 ± 0.2		2.5 – 5	4.1 ± 0.5		2.5 – 25	115.0 ± 5.1
Donepezil	0.01 – 0.1	0.01 ± 0.005		2.5 – 5	1.3 ± 0.4		0.1 – 0.5	0.18 ± 0.04
Inhibitor I ^b	–	–		–	–		0.5 – 5.5	1.27 ± 0.44
Inhibitor IV ^b	–	–		–	–		0.1 – 0.5	0.12 ± 0.05

^a C: competitive; NC: non competitive; U: uncompetitive; M: mixed

^b Known inhibitor of BACE-1 activity

Values are expressed as mean ± SD calculated on three, and four different determinations for ChE, and BACE-1, respectively

Supplementary Table 2. Inhibition by HT hybrids on the A β fibril formation.

HT hybrid	Concentration (μM)	IC₅₀ (μM)
HT1	20 – 240	375.0 \pm 142.8
HT1a	20 – 240	106.4 \pm 11.1
HT2	20 – 240	417.6 \pm 41.1
HT3	20 – 500	n.d. ^a
HT3a	20 – 500	n.d. ^a
HT4	20 – 500	n.d. ^a
HT4a	20 –	n.d. ^a
Donepezil	20 – 240	183.8 \pm 14.7

^a Inhibition not detectable up to the maximum concentration used

Values are expressed as mean \pm SD calculated on three different determinations