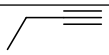
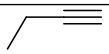
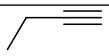
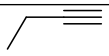
Table 1S: Predicted pharmacokinetic values[a]

S.No.	Comp. Code	R_1	R_2	MW	clog *P* [b]	log BB[c]	Caco-2 Permeability (nm/sec)	Violations of Lipinski's rule of 5	CNS activity
1	**10a**	H		559.75	5.859	-1.355	590	2	--
2	**10b**	H		587.80	6.684	-1.550	613	2	--
3	**10c**	Cl		594.19	6.187	-0.740	1263	2	-
4	**10d**	Cl		622.24	7.366	-1.281	890	2	--
5	**10e**	H		557.73	5.786	-1.508	445	2	--
6	**10f**	H		585.78	6.671	-1.308	999	2	--
7	**10g**	Cl		592.17	6.231	-1.280	477	2	--
8	**10h**	Cl		620.23	6.918	-1.020	1350	2	--

a Predicted values using program QikProp v. 2.5[34]. [b] Calculated octanol/water partition coefficient. [c] Brain/blood partition coefficient.

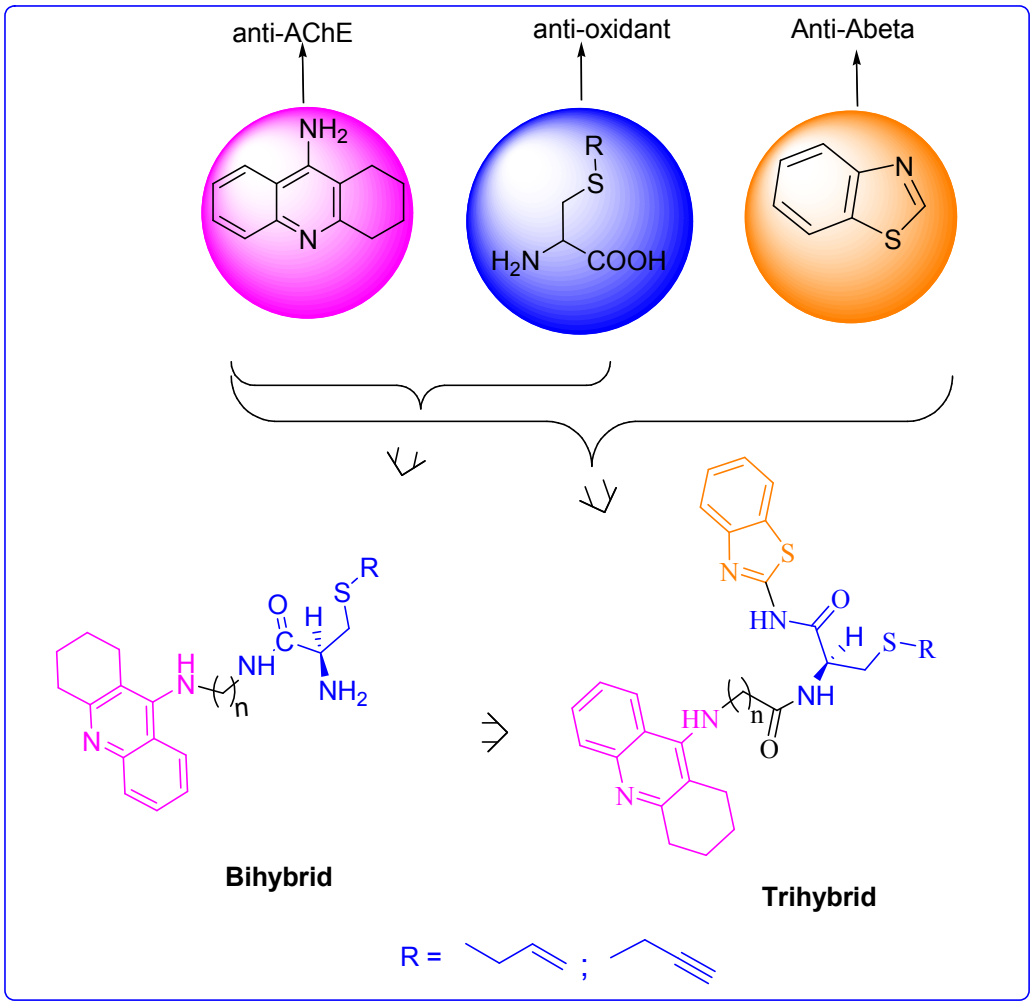
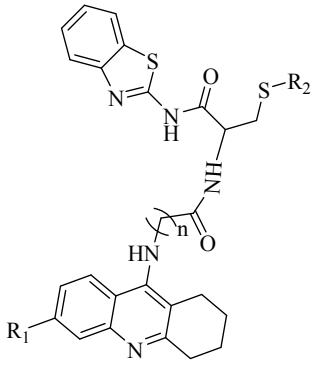


Figure 1: Design stratergy for the novel trihybrids TAC-SAC-BTA and TAC-SPRC-BAT compounds.



10

10	a	b	c	d	e	f	g	h
R_1	H	H	Cl	Cl	H	H	Cl	Cl
R_2								
n	3	5	3	5	3	5	3	5

Figure 2: Synthesized TAC-SAC-BTA (R_2 = allyl) and TAC- SPRC-BTA (R_2 = propargyl) compounds.

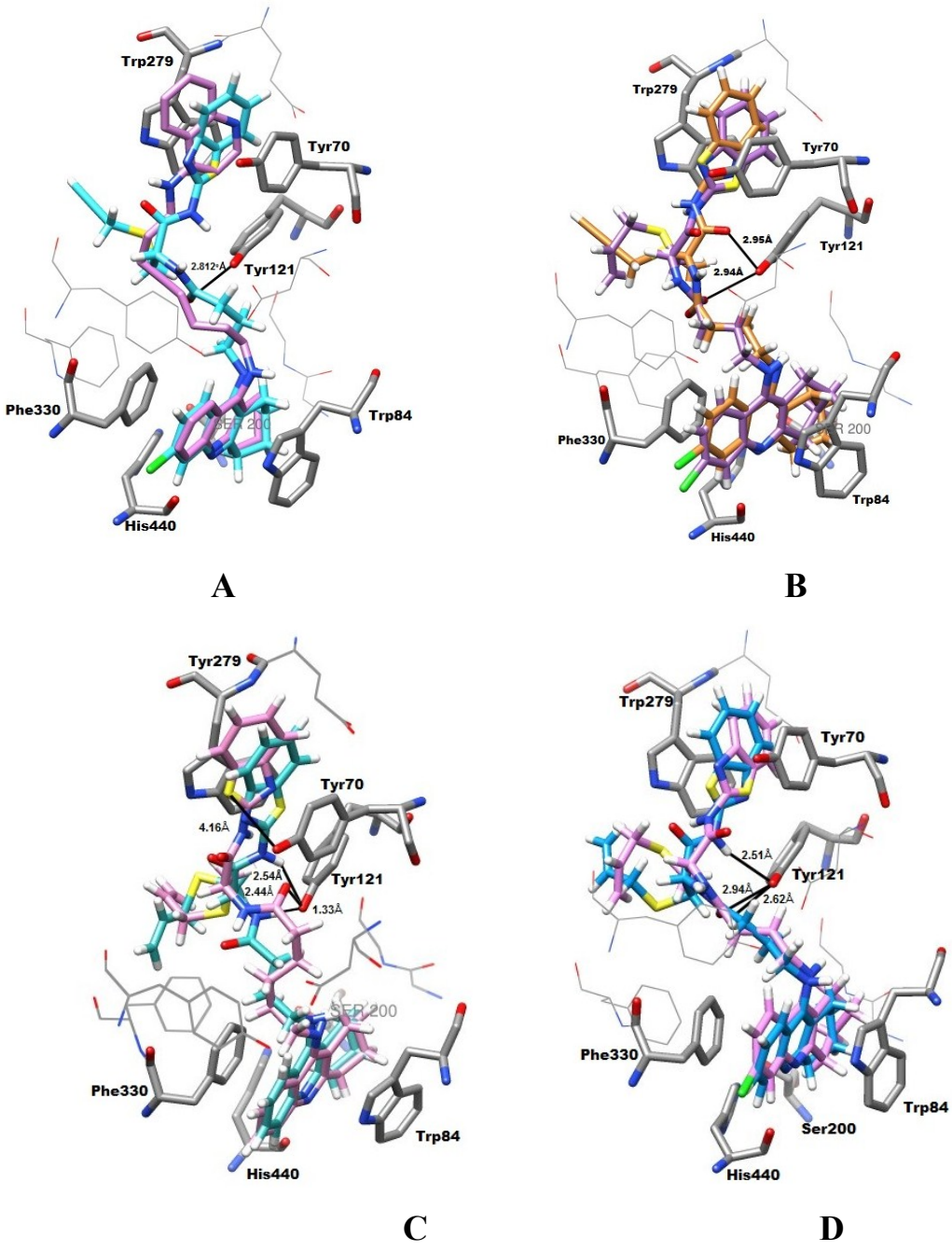


Figure 3: Docking results for the TAC-SAC-BTA and TAC-SPRC-BTA trihybrids with *Tc*AChE: (A) superimposition of the original ligand (PDB entry 1ODC) (pink) and **10g** (cyan); (B) superimposition of **10c** (purple) and **10g** (brown); (C) superimposition of **10b** (pink) and **10a** (cyan); (D) superimposition of **10c** (pink) and **10a** (blue).

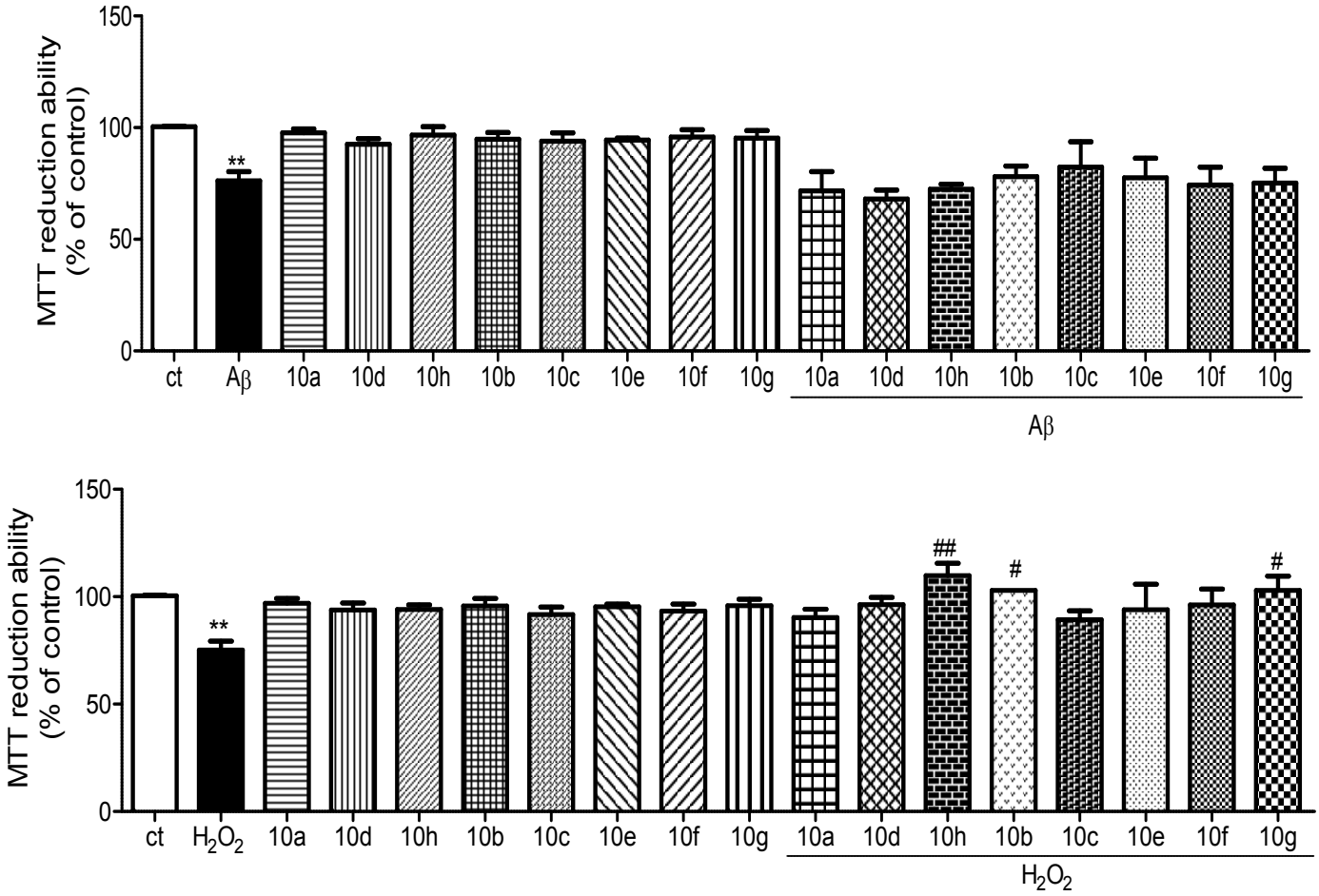


Figure 4 Effect of the described compounds on Aβ42 peptide or H_2O_2 toxicity in SH-SY5Y cells. SH-SY5Y cells were treated with Aβ42 (1 μM) or H_2O_2 (100 μM) for 24h, in the absence or the presence of the compounds. Evaluation of cell viability was performed by using MTT reduction test. Results are expressed as the percentage of SH-SY5Y untreated cells, with the mean ± S.E.M. derived from 3 different experiments. **$p < 0.01$, significantly different when compared with SH-SY5Y untreated cells; #$p < 0.05$; ##$p < 0.01$, significantly different when compared with H_2O_2 treated cells.