

SUPPORTING INFORMATION

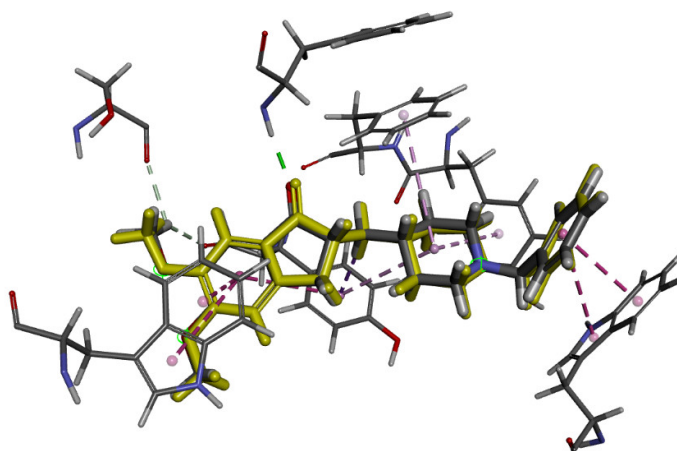
Discovery of novel tryptanthrin derivatives with benzenesulfonamide substituents as multi-target-directed ligands for the treatment of Alzheimer's disease

Contents

Heavy Atom RMSD to the conformation of co-ligand (CDOCKER).....	2-3
The effect of compound 4h on BV2, PC12 and SY5Y cells viability <i>in vitro</i> cytotoxicity study.....	4
The effect of compound 4h on ROS production in H ₂ O ₂ -induced PC12 and SY5Y.....	5
The effect of compound 4h on DPPH free radical scavenging.....	6
LD ₅₀ determination results of compound 4h on mice after intragastric administration for 7 days.....	7

Figure and Table of contents:

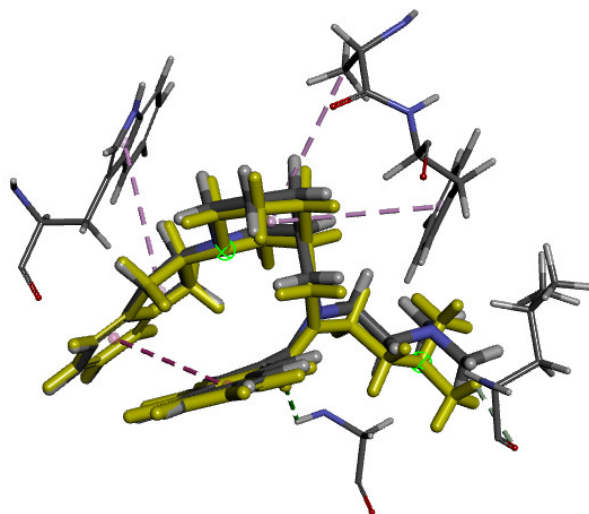
Figure S1 and Table S1. Heavy Atom RMSD to the conformation of co-ligand (CDOCKER).



AChE:

Comformation	^a RMSD (Å)	Comformation	^a RMSD (Å)
1	0. 226	7	1.827
2	1.287	8	2.045
3	1.493	9	2.416
4	1.545	10	3.215
5	1.594	co-ligand	0
6	1.775		

^a RMSD: root mean square deviation.



BuChE:

Conformation	^a RMSD (Å)	Conformation	^a RMSD (Å)
1	0. 539	7	4.299
2	0.733	8	5.670
3	1.693	9	5.781
4	2.947	10	7.182
5	3.489	co-ligand	0
6	4.013		

^a RMSD: root mean square deviation.

Table S2. The effect of compound **4h** on BV2, PC12 and SY5Y cells viability *in vitro* cytotoxicity study.

Cell viability (% of control) ^a	Control	30 μ M	50 μ M
BV2	100	101.23 \pm 1.82	97.44 \pm 1.36
PC12	100	99.62 \pm 0.94	99.21 \pm 1.57
SY5Y	100	97.84 \pm 1.24	91.33 \pm 1.48

^a Cell viability was determined using MTT assay protocol. Data are expressed as the mean \pm SEM of the three independent experiments.

Table S3. The effect of compound **4h** on ROS production in H₂O₂-induced PC12 and SY5Y.

	ROS in PC12 cells ^a (%)	ROS in SY5Y cells ^a (%)
Control	100	100
Trolox (100 μ M)	127.33 \pm 3.51	126.06 \pm 2.68
4h (1 μ M)	139.83 \pm 5.48	140.33 \pm 4.04
4h (7.5 μ M)	132.96 \pm 4.08	135.32 \pm 2.32
4h (15 μ M)	124.17 \pm 1.83	125.38 \pm 6.18
4h (30 μ M)	119.83 \pm 3.25	117.35 \pm 3.6
4h (50 μ M)	114.13 \pm 2.07	108.30 \pm 1.65
H ₂ O ₂ group	155.2 \pm 3.45	151.76 \pm 1.85

^a The percentage of intracellular ROS compared with the control (untreated control cells). The results were calculated from the average of three experiments (mean \pm SD).

Table S4. The effect of compound **4h** on DPPH free radical scavenging.

compd	Concentration of DPPH ^a (% , 10 μ M)	Concentration of DPPH ^a (% , 100 μ M)	Concentration of DPPH ^a (% , 1000 μ M)
4h	84.76 \pm 4.21	74.6 \pm 2.51	36.51 \pm 2.78
AA	77.43 \pm 2.76	58.10 \pm 3.42	24.2 \pm 1.85

^a The concentration of DPPH in the experimental group compared with the no drug or compound group. The results were calculated from the average of three experiments (mean \pm SD).

Table S5. LD₅₀ determination results of compound **4h** on mice after intragastric administration for 7 days.

Group	Dose (mg/kg)	Number of deaths	Mortality rate (%)
1	100	4	66.7
2	80	3	50
3	64	1	16.7
4	51.2	0	0
5	40.96	0	0