Supporting Information

Table 2. ATCI molecular docking interactions with AChE amino acid residues. Binding contacts of best docked pose of the ligand with key residues in the active site of the model were determined (PDB entry code 1ACJ).

Amino acid residue of AChE or water molecule with its binding atom	ATCI interacting atom[a]	Distance (Å)	Type of interaction
Trp84/NE1-H	O3	3.96	H-bond
His440/O	S1	3.25	Polar
wat634/O-H	N3	2.92	H-bond
Trp84/CD1	C5	4.04	Hydrophobic
Trp84/CE3	C6	4.09	Hydrophobic
Phe330/CD2	C10	4.08	Hydrophobic
Ile439/CG2	C10	3.84	Hydrophobic
Gly118/CA	C6	3.99	Hydrophobic
Phe330/CE2	C4	3.74	Hydrophobic
Phe330/CZ	C9	3.89	Hydrophobic

[a] Ligand numbering according to PyMol v. 0.99c

Table 3. **THA** molecular docking interactions with AChE amino acid residues. Binding contacts of best docked pose of the ligand with key residues in the active site of the model were determined (PDB entry code 1ACJ).

Amino acid residue of AChE or water molecule with its binding atom	THA interacting atom[a]	Distance (Å)	Type of interaction
His440/O[b]	N7	3.23	H-bond
wat643/O	N15	3.15	Bridged H-bond
wat636/O	N15	3.13	H-bond
wat634/O[b]	N15	3.12	Bridged H-bond
Trp432/CZ2[b]	C1	3.69	Hydrophobic
Phe330/CD1[b]	C1	3.31	Hydrophobic
Phe330/CE1[b]	C1	3.88	Hydrophobic
Trp432/CZ2	C1	3.69	Hydrophobic
Phe330/CG[b]	C1	3.82	Hydrophobic
Phe330/CG[b]	C2	3.71	Hydrophobic
Phe330/CD1[b]	C2	3.65	Hydrophobic
Tyr442/CE1	C2	3.79	Hydrophobic
Trp84/CE2[b]	C3	3.83	Hydrophobic
Trp84/CG[b]	C4	3.78	Hydrophobic
Trp84/ CD1[b]	C4	3.38	Hydrophobic
Phe330/CE1[b]	C4	3.72	Hydrophobic
Phe330/CZ[b]	C4	3.87	Hydrophobic
Trp84/CD1[b]	C5	3.50	Hydrophobic
Phe330/CD1[b]	C5	3.73	Hydrophobic
Phe330/CE1[b]	C5	3.35	Hydrophobic
Phe330/CD1[b]	C6	3.35	Hydrophobic
Phe330/CE1[b]	C6	3.45	Hydrophobic
Trp432/CZ2	C6	3.49	Hydrophobic
Trp84/CE2[b]	C8	3.84	Hydrophobic

Trp84/CG[b]	C9	3.80	Hydrophobic
Trp84/CD2[b]	C9	3.59	Hydrophobic
Trp84/CE3[b]	C9	3.88	Hydrophobic
Trp84/CB[b]	C10	3.84	Hydrophobic
Trp84/CG[b]	C10	3.39	Hydrophobic
Trp84/CD1[b]	C10	3.54	Hydrophobic
Trp84/CD2[b]	C10	3.69	Hydrophobic
His440/CD2[b]	C11	3.62	Hydrophobic
Gly441/CA	C11	3.63	Hydrophobic
Trp84/CZ3[b]	C12	3.81	Hydrophobic
Glu199/CD	C12	3.84	Hydrophobic
Trp84/CD2[b]	C14	3.97	Hydrophobic
Gly118/CA[b]	C13	3.81	Hydrophobic
Trp84/CE3[b]	C14	3.77	Hydrophobic

[a] Ligand numbering according to PyMol v. 0.99c

[b] Common amino acid residue with ATCI

Table 4. **GNT** molecular docking interactions with AChE amino acid residues. Binding contacts of best docked pose of the ligand with key residues in the active site of the model were determined (PDB entry code 1ACJ).

Amino acid residue of AChE or water molecule with its binding atom	GNT interacting atom[a]	Distance (Å)	Type of interaction
Ser200/OG	O17	2.97	H-bond
Glu199/OE1	O18	2.72	H-bond
wat820/O	O5	3.07	Bridged H-bond
wat712/O	N10	3.29	Bridged H-bond
wat820/O	O17	3.24	Bridged H-bond
wat820/O	O18	2.66	Bridged H-bond
Gly118/CA[b]	C1	3.69	Hydrophobic
Trp84/CE3[b]	C2	3.49	Hydrophobic
Trp84/CZ3[b]	C2	3.86	Hydrophobic
Gly118/CA[b]	C2	3.74	Hydrophobic
Trp84/CE3[b]	C3	3.70	Hydrophobic
Trp84/CZ3[b]	C3	3.55	Hydrophobic
Trp84/CZ3[b]	C4	3.72	Hydrophobic
Trp84/CH2[b]	C4	3.83	Hydrophobic
His440/CD2[b]	C4	3.84	Hydrophobic
Phe331/CE2	C6	3.60	Hydrophobic
Phe331/CZ	C6	3.51	Hydrophobic
Phe290/CE1	C7	3.69	Hydrophobic
Phe290/CZ	C7	3.56	Hydrophobic
Phe331/CE2	C7	3.45	Hydrophobic
Tyr121/CE2	C8	3.68	Hydrophobic
Tyr121/CZ	C8	3.85	Hydrophobic
Trp84/CG[b]	C11	3.76	Hydrophobic
Trp84/CD1[b]	C11	3.80	Hydrophobic

Phe288/CE1	C16	3.21	Hydrophobic
Phe288/CZ	C16	3.78	Hydrophobic
Phe290/CE2	C16	3.73	Hydrophobic
Phe290/CZ	C16	3.49	Hydrophobic
Phe331/CE2	C16	3.79	Hydrophobic
Phe331/CZ	C16	3.70	Hydrophobic

[a] Ligand numbering according to PyMol v. 0.99c

[b] Common amino acid residue with ATCI

Table 5. **CRT** molecular docking interactions with AChE amino acid residues. Binding contacts of best docked pose of the ligand with key residues in the active site of the model were determined (PDB entry code 1ACJ).

Amino acid residue of AChE or water molecule with its binding atom	**CRT interacting atom**[a]	**Distance (Å)**	**Type of interaction**
Tyr121/OH [b]	O20	3.60	H-bond
Wat634/OH [b c]	O13	4.01	H-bond
Asp285/N	019	2.86	H-bond
Phe330/CZ [b c]	C1	2.13	Hydrophobic
Phe330/CZ [b c]	C4	2.73	Hydrophobic
Tyr121/CZ [b]	C21	3.18	Hydrophobic
Phe330/CZ [b c]	C21	3.91	Hydrophobic
Phe330/CE2 [b c]	C7	3.24	Hydrophobic
Phe331/CE2 [b]	C5	4.05	Hydrophobic
Phe290/CE1[b]	C5	3.61	Hydrophobic
Asp285/CG	C5	1.36	Hydrophobic
Arg289/C	C24	3.93	Hydrophobic
Phe290/CZ [b]	C24	4.07	Hydrophobic
Phe290/CA[b]	C24	4.06	Hydrophobic
Ile287/CD1	C16	3.30	Hydrophobic
Ile287/CA	C17	3.55	Hydrophobic
Ile287/CA	C18	3.63	Hydrophobic
Ser286/C	C18	3.00	Hydrophobic
Ser286/C	C15	2.28	Hydrophobic
Ser286/CA	C10	3.03	Hydrophobic
Leu358/CD2	C23	3.80	Hydrophobic
Phe284/C	C12	3.64	Hydrophobic

Asp285/C	C12	1.77	Hydrophobic
Asp285/CA	C6	1.54	Hydrophobic
Leu358/CD2	C6	3.59	Hydrophobic
Asp285/CA	C6	1.88	Hydrophobic
Asp285/CA	C8	1.18	Hydrophobic
Asp285/CB	C8	1.85	Hydrophobic
Asp285/CG	C3	2.18	Hydrophobic

[a] *Ligand numbering according to PyMol v. 0.99c*

[b] *Common amino acid residue with THA and GNT*

[c] *Common amino acid residue with ATCI*

Table 6. **DMCRT** molecular docking interactions with AChE amino acid residues. Binding contacts of best docked pose of the ligand with key residues in the active site of the model were determined (PDB entry code 1ACJ).

Amino acid residue of AChE or water molecule with its binding atom	**DMCRT interacting atom** [a]	**Distance (Å)**	**Type of interaction**
Tyr121/OH[b]	O46	3.09	Bridged H-bond
Wat616/OH	O46	2.42	H-bond
Asp285/N	O42	3.46	H-bond
Phe284/N	O42	3.15	H-bond
Phe284/O	O42	3.77	H-bond
Pro283/O	O42	3.36	H-bond
Asp72/CG	C51	2.63	Hydrophobic
Asp72/CB	C51	3.20	Hydrophobic
Phe330/CE1[b c]	C44	2.72	Hydrophobic
Tyr334/CE2	C44	3.77	Hydrophobic
Tyr334/CD2	C44	3.67	Hydrophobic
Phe330/CZ [b c]	C1	2.61	Hydrophobic
Phe330/CE1 [b c]	C1	3.22	Hydrophobic
Phe330/CZ [b c]	C25	1.94	Hydrophobic
Phe330/CE2 [b c]	C25	2.91	Hydrophobic
Phe330/CD2 [b c]	C25	3.36	Hydrophobic
Trp279/CH2	C2	3.91	Hydrophobic
Trp279/CZ3	C2	4.09	Hydrophobic
Trp279/CZ3	C5	2.78	Hydrophobic
Trp279/CH2	C5	3.43	Hydrophobic
Trp279/CZ3	C5	2.78	Hydrophobic
Trp279/CH3	C9	3.18	Hydrophobic
Phe284/C	C22	3.77	Hydrophobic

Asp285/CA	C6	1.88	Hydrophobic
Asp285/CA	C8	1.18	Hydrophobic
Asp285/CB	C8	1.85	Hydrophobic
Asp285/CG	C3	2.18	Hydrophobic

[a] *Ligand numbering according to PyMol v. 0.99c*

[b] *Common amino acid residue with THA and GNT*

[c] *Common amino acid residue with ATCI*

Table 7. CRC molecular docking interactions with AChE amino acid residues. Binding contacts of best docked pose of the ligand with key residues in the active site of the model were determined (PDB entry code 1ACJ).

Amino acid residue of AChE or water molecule with its binding atom	**CRC interacting atom** [a]	**Distance (Å)**	**Type of interaction**
wat640/OH	O37	2.57	H-bond
Asn230/OH	O38	3.69	H-bond
His398/NE2	O41	3.93	H-bond
Pro232/OH	O46	2.87	H-bond
Asp285/OD2	O15	1.23	H-bond
Asp285/OD1	O14	3.06	H-bond
Ser235/O	O36	2.63	H-bond
Asn230/ND2	O45	3.28	H-bond
Trp524/O	O43	3.38	H-bond
wat650/OH	O28	3.36	H-bond
His398/ND1	O42	3.42	H-bond
Arg289/CD	C50	4.02	Hydrophobic
Pro361/CG	C53	3.29	Hydrophobic
Pro361/CG	C54	3.50	Hydrophobic
Pro361/CB	C55	2.45	Hydrophobic
Pro361/CA	C55	2.67	Hydrophobic
Pro361/CA	C66	3.31	Hydrophobic
Cys357/CE	C61	3.53	Hydrophobic
Asp285/CG	C8	3.11	Hydrophobic
Phe284/CB	C56	2.63	Hydrophobic
Phe284/CG	C55	3.13	Hydrophobic
Phe284/CG	C54	2.53	Hydrophobic
Pro361/CB	C54	2.49	Hydrophobic

Pro232/CA	C39	3.55	Hydrophobic
Asp285/CB	C8	3.86	Hydrophobic
Asp285/CG	C7	3.30	Hydrophobic
Phe284/CB	C57	3.62	Hydrophobic
Phe284/CB	C58	3.74	Hydrophobic

[a] *Ligand numbering according to PyMol v. 0.99c*

Table 8. **SFR** molecular docking interactions with AChE amino acid residues. Binding contacts of best docked pose of the ligand with key residues in the active site of the model were determined (PDB entry code 1ACJ).

Amino acid residue of AChE or water molecule with its binding atom	**SFR interacting atom**[a]	**Distance (Å)**	**Type of interaction**
Wat634/OH [b, d]	O19	3.92	H-bond
Trp84/CD1 [b, d]	C10	3.52	Hydrophobic
Trp84/CZ2 [b, d]	C10	3.68	Hydrophobic
Trp84/CH2 [b, c, d]	C1	3.59	Hydrophobic
Trp84/CE3 [b, c, d]	C3	3.04	Hydrophobic
Phe330/CE2 [b, d]	C14	3.00	Hydrophobic
His440/CD2 [b, c, d]	C14	3.46	Hydrophobic
Gly118/CA [b, c, d]	C21	3.50	Hydrophobic

[a] *Ligand numbering according to PyMol v. 0.99c*

[b] *Common amino acid residue with THA*

[c] *Common amino acid residue with GNT*

[d] *Common amino acid residue with ATCI*

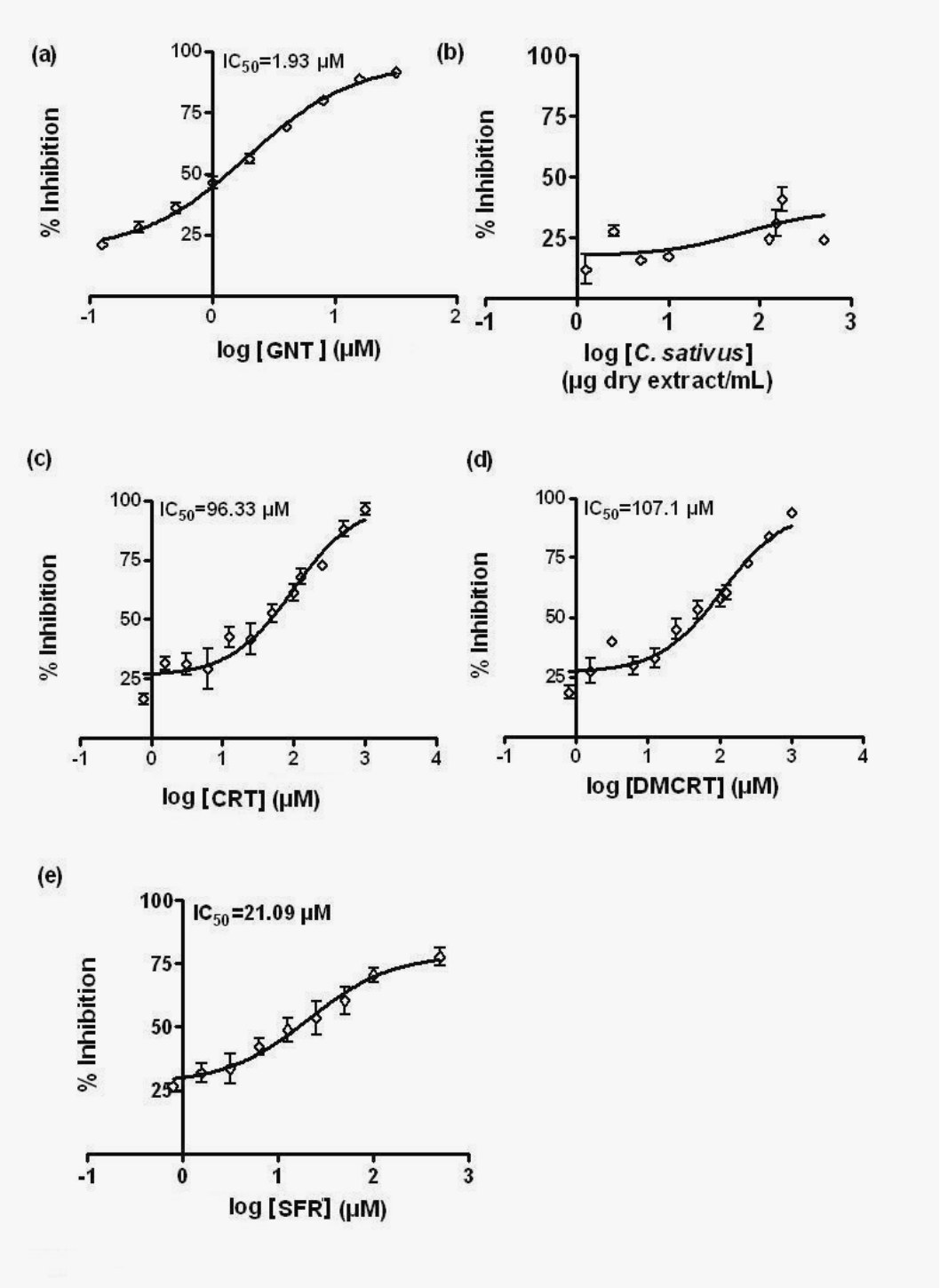

Fig. 3 *In vitro* ACHE (from electric eel) inhibitory activity of (a) GNT (final concentration of 1–32 µM), (b) saffron and (c-e) its constituents (final concentrations 5-200 µg/mL and 5–500 µM, respectively. The final concentration of ATCI used was 1.875 mM. IC_{50} values were calculated from log µM back to µM.