Supplementary files:

Exploring the binding pattern of Geraniol with acetylcholinesterase through in-silico docking, molecular dynamics simulation and in-vitro enzyme inhibition kinetics studies

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Figure S1. Interaction of target protein, AChE with non-hydrolysable structural analogs peripheral anionic site (PAS); (A) Superimpose image of non-hydrolysable structural analogs in PAS locations of AChE, (B & C) Interactions between PAS residues of AChE and non-hydrolysable structural analogs. (No binding of acetylcholine was observed at the peripheral anionic site (PAS)).

Figure S2. Interaction of target protein, AChE with non-hydrolysable structural analogs and acetylcholine at catalytic active site (CAS); (A) Superimpose image of non-hydrolysable structural analogs and acetylcholine in CAS locations of AChE, (B & C) Interactions between CAS residues of AChE and non-hydrolysable structural analogs, (D) Interactions between CAS residues of AChE and Acetylcholine.

Supplementary Table 1. Molecular docking parameters for the interaction of acetylcholinesterase (AChE) with some non-hydrolysable structural analogs at catalytic active site (CAS), and peripheral anionic site (PAS).

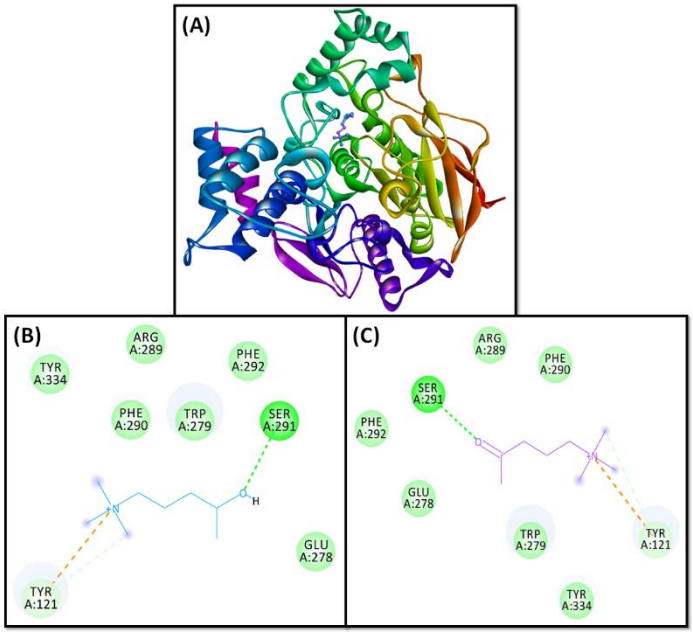

Figure S1. Interaction of target protein, AChE with non-hydrolysable structural analogs peripheral active site (PAS); (A) Superimpose image of non-hydrolysable structural analogs in PAS locations of AChE, (B & C) Interactions between PAS residues of AChE and non-hydrolysable structural analogs. (No binding of acetylcholine was observed at the peripheral catalytic site (PAS)).

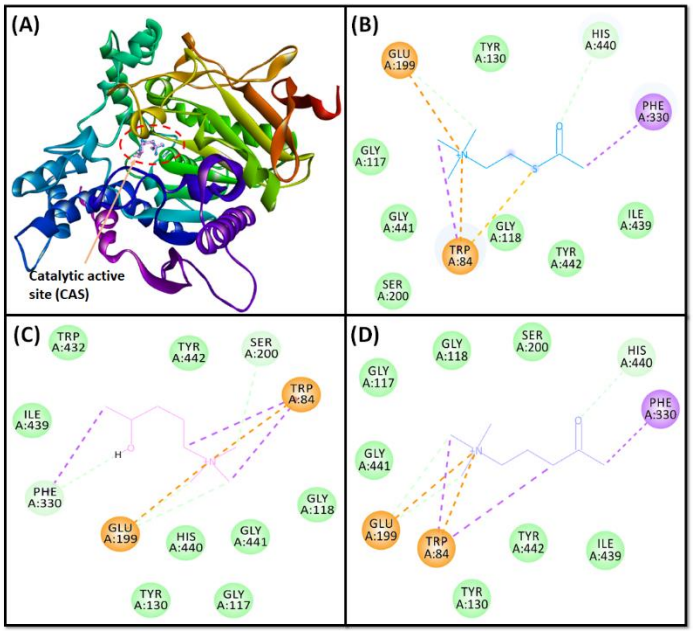

Figure S2. Interaction of target protein, AChE with non-hydrolysable structural analogs and acetylcholine at catalytic active site (CAS); (A) Superimpose image of non-hydrolysable structural analogs and acetylcholine in CAS locations of AChE, (B) Interactions between CAS residues of AChE and Acetylthiocholine. (C & D) Interactions between CAS residues of AChE and non-hydrolysable structural analogs.

Supplementary Table S1. Molecular docking parameters for the interaction of acetylcholinesterase (AChE) with some non-hydrolysable structural analogs at catalytic active site (CAS), and peripheral anionic site (PAS).

Donor-Acceptor pair	Distance (Å)	Category of Interaction	Type of Interaction	Docking energy, kcal mol^{-1}	Binding affinity, M^{-1}
Acetylthiocholine (CAS)*					
LIG:N - GLU199:OE1	3.881	Electrostatic	Attractive Charge	-4.5	1.99 x 10^3
HIS440:CD2 - LIG:O	3.66	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:C - GLU199:OE1	3.52	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:N - TRP84	4.27	Electrostatic	Pi-Cation		
LIG:C - TRP84	3.72	Hydrophobic	Pi-Sigma		
LIG:C - PHE330	3.61	Hydrophobic	Pi-Sigma		
LIG:S - TRP84	3.70	Other	Pi-Sulfur		
4,4-Dihydroxy-N,N,N-trimethylpentan-1-aminium (CAS)					
LIG:N - GLU199:OE1	4.08	Electrostatic	Attractive Charge	-5.0	4.65 x 10^3
LIG:C - GLU199:OE1	3.62	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:C - SER200:OG	3.60	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:C - GLU199:OE1	3.77	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:N - TRP84	4.87	Electrostatic	Pi-Cation		
LIG:N - TRP84	4.23	Electrostatic	Pi-Cation		
LIG:H - PHE330	3.05	Hydrogen Bond	Pi-Donor Hydrogen		
LIG:C - TRP84	3.95	Hydrophobic	Bond		
LIG:C - TRP84	3.84	Hydrophobic	Pi-Sigma		
LIG:C - PHE330	3.53	Hydrophobic	Pi-Sigma		

			Pi-Sigma		
N,N,N-trimethyl-4-oxopentan-1-aminium (CAS)					
LIG:N - GLU199:OE1	3.949	Electrostatic	Attractive Charge	-5.0	4.65 x 10^3
HIS440:CD2 - LIG:O	3.62	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:C - GLU199:OE1	3.55	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:C - GLU199:OE1	3.58	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:C - GLU199:OE2	3.78	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:N - TRP84	4.94	Electrostatic	Pi-Cation		
LIG:N - TRP84	4.23	Electrostatic	Pi-Cation		
LIG:C - TRP84	3.67	Hydrophobic	Pi-Sigma		
LIG:C - PHE330	3.59	Hydrophobic	Pi-Sigma		
LIG:C - TRP84	3.80	Hydrophobic	Pi-Sigma		
4,4-Dihydroxy-N,N,N-trimethylpentan-1-aminium (PAS)					
SER291:HN - LIG:O	2.16	Hydrogen Bond	Conventional H-Bond	-4.8	3.32 x 10^3
SER291:CB - LIG:O	3.49	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:C - TYR121:OH	3.56	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:N - TYR121	4.86	Electrostatic	Pi-Cation		
N,N,N-trimethyl-4-oxopentan-1-aminium (PAS)					
SER291:HN - LIG:O	2.14479	Hydrogen Bond	Conventional H-Bond	-4.8	3.92 x 10^3
SER291:CB - LIG:O	3.49151	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:C - TYR121:OH	3.59372	Hydrogen Bond	Carbon Hydrogen Bond		
LIG:N - TYR121	4.88618	Electrostatic	Pi-Cation		

*No binding of acetylcholine was observed at the peripheral anionic site (PAS).